

**Integrating Cardiovascular Diseases, Hypertension, and Diabetes with HIV Services: A Systematic Review**

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## Abstract

Non-communicable diseases (NCDs), including cardiovascular diseases (CVD), hypertension and diabetes together with HIV infection are among the major public health concerns worldwide. Health services for HIV and NCDs require health systems that provide for people's chronic care needs, which present an opportunity to coordinate efforts and create synergies between programmes to benefit people living with HIV and/or AIDS and NCDs. This review included studies that reported service integration for HIV and/or AIDS with coronary heart diseases, chronic CVD, cerebrovascular diseases (stroke), hypertension or diabetes. We searched multiple databases from inception until October 2015. Articles were screened independently by two reviewers and assessed for risk of bias. 11,057 records were identified with 7,616 after duplicate removal. After screening titles and abstracts, 14 papers addressing 17 distinct interventions met the inclusion criteria. We categorized integration models by diseases (HIV with diabetes, HIV with hypertension and diabetes, HIV with CVD and finally HIV with hypertension and CVD and diabetes). Models also looked at integration from micro (patient focused integration) to macro (system level integrations). Most reported integration of hypertension and diabetes with HIV and AIDS services and described multidisciplinary collaboration, shared protocols, and incorporating screening activities into community campaigns. Integration took place exclusively at the meso-level, with no micro- or macro-level integrations described. Most were descriptive studies, with one cohort study reporting evaluative outcomes. Several innovative initiatives were identified and studies showed that CVD and HIV service integration is feasible. Integration should build on existing protocols and use the community as a locus for advocacy and health services, while promoting multidisciplinary teams, including greater involvement of pharmacists. There is a need for robust and well-designed studies at all levels - particularly macro-level studies, research looking at long-term outcomes of integration, and research in a more diverse range of countries.

**Key Words:** Integration, Cardiovascular Disease, Diabetes, Hypertension, HIV, Chronic Disease

## Introduction

Non-communicable diseases, including cardiovascular diseases (CVD), hypertension and diabetes together with HIV infection are among the leading contributors to the global burden of disease (GBD 2013 Mortality and Causes of Death Collaborators, 2014; WHO, 2013). The burden of CVD is greatest in low and middle-income countries, where treatment is largely unaffordable or unavailable (Rasha, McKee, Shannon, Chow, & Rangarajan, 2016; WHO, 2013; Yusuf, Wood, Ralston, & Reddy, 2015). It is estimated that over 700 million adults worldwide will be diagnosed with diabetes by 2025; increasingly and disproportionately in low and middle income countries, which lack affordable and available insulin and other essential medicines (NCD-RisC, 2016; WHO, 2016). HIV, despite decreases in overall new infections globally, remains a major threat among vulnerable groups worldwide and particularly in parts of Africa; nearly half of new HIV infections are people living in Nigeria, South Africa and Uganda, where HIV and AIDS is the number one cause of life-years lost (Collaborators, 2016; Piot, Abdool Karim, Hecht, & Legido-Quigley, 2015).

Consequently, many countries are now coping with the dual burden of HIV and NCDs (UNAIDS, 2011). People living with HIV are living longer and are at greater risk of developing non-communicable diseases (including coronary heart disease, cervical cancer, other cancers, mental illness, kidney and liver disease) for various reasons, including the direct consequence of HIV infection, shared risk factors and side effects of HAART regimes (UNAIDS, 2011)(UNAIDS, 2011)(UNAIDS, 2011).

Health systems, particularly in low-income countries, are often ill prepared to identify at risk patients and ensure life-long care (M Rabkin, Melaku, & Bruce, 2012). However, given that HIV and non-communicable diseases have common needs for chronic care, there is an opportunity to coordinate efforts and achieve synergies to benefit patients (Haregu, Setswe, Elliott, & Oldenburg, 2015).

Although such integration is intuitively appealing, relatively little is known about the integration models and factors that facilitate or hinder integration in different contexts.

To address this gap, we systematically reviewed the literature examining programs or services integrating diabetes, hypertension or CVDs with HIV and AIDS, reporting outcomes where available, exploring barriers and facilitators to integration, and making recommendations for future research and policy.

## Methods

This review was developed according to PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) and is part of a larger systematic review of service integration for HIV and other conditions. Where possible, we follow the PICOS structure for study characteristics, adapted where necessary for purely descriptive studies. Drawing on definitions proposed by Briggs (2006), Atun et al (2010) and Legido-Quigley et al (2013), the concept of integration is described in Box 1 (R. Atun, de Jongh, & Secci, 2010; WHO, 2008). We also drew on a dimensions of integration typology which defined service integration as that where different clinical services are integrated through teams or multidisciplinary professionals and a clinical integration as that where care is integrated into a single or coherent process within and/or across professionals (Curry & Ham, 2010).

[Box 1 – about here]

### **Inclusion criteria**

To be considered for inclusion the study should report a program that integrates HIV with CVDs and their risk factors (hypertension or type 2 diabetes mellitus) coronary heart disease, or cerebrovascular diseases (stroke). We included all studies that reported on the effects of different models of integrated HIV and AIDS and chronic disease services using quantitative, qualitative and mixed methods. The following types of studies were included:

- Studies that include a description or evaluation of a management or organizational change strategy made within an existing health system, aiming to increase integration between HIV and cardiovascular disease care at service delivery level.
- Studies reporting actual integration experiences.
- Studies reporting screening or treatment for HIV within a service targeting other chronic diseases or vice versa.
- Studies describing some element of treatment.
- Studies describing services provided in health facilities or in the community and with respect to any adult population.
- Reports describing patients' experiences or perspectives on integration of HIV with CVDs.
- We did not exclude reports based on study design; nor did we require them to include outcome measures.
- There were no date or language restrictions. Furthermore, no studies were excluded based on risk of bias, although this was assessed and is reported.

### **Search strategy**

We developed a search strategy with an information specialist to be consistent with methods used by other authors for systematic reviews of health services integration (Box 2). The following electronic databases were searched from inception until October 2015: Global Health, Medline and Embase. In addition, the following databases were searched using a simplified search strategy to ensure representation from low and middle income: Cochrane library, LILACs, Africa Wide, WHOLIS and abstracts from the International AIDS Society (IAS) Online Resource Library from 2006 to 2015, the HIV Implementers meetings from 2007 to 2012 and International conferences on NCDs.

[Box 2 – about here]

### **Search and Retrieval of Studies**

Two reviewers independently reviewed the retrieved article list to identify those relevant, based on title or title and abstract. Two reviewers independently assessed the retrieved articles to determine whether they met inclusion criteria. Any disagreements were resolved by discussion with a third reviewer.

### **Data Synthesis**

Two reviewers independently extracted data from included studies using standardized forms developed for extracting data on study characteristics and results for both quantitative and qualitative studies. Differences in data extraction or interpretation of studies were resolved by discussion and consensus. Data were extracted from both the findings and discussion sections of the studies. The data were compared and any disparities resolved. Due to the heterogeneity in study design, intervention types, participants and outcomes, we did not conduct a meta-analysis, but instead present a summary of the program descriptions and results and where available report outcomes.

### **Levels of Integration**

We defined levels and types of integration based on typologies of integrated care (Curry & Ham, 2010). This typology differentiated integration at the micro-level as that which focused on the patient, such as case management, whereas meso-level integration focused on groups or populations, such as screening, and macro-level involved integration of larger delivery systems. Within these levels, the typology distinguishes integration types; as such we classify a clinical integration as that where care is integrated into a single process through shared guidelines and protocols across professions and service integration as that where different clinical services are integrated within an organization and provided through multidisciplinary teams.

## **Risk of Bias Assessment**

Two reviewers independently assessed studies which present evaluative data for risk of bias using the Cochrane risk of bias tool for randomized studies, an adapted checklist for qualitative studies and a simple proforma for observational descriptive studies (Harden et al., 2001; Rees, Harden, Brunton, Oliver, & Oakley, 2001). This last proforma has three domains: selection bias, information bias (differential misclassification and non-differential misclassification) and confounding. Each domain was assessed as low, unclear or high. We classified studies that had a low risk of bias in all domains as having a low overall risk of bias. Studies that had a high or unclear risk of bias in one or more domains were classified as having an overall high or unclear risk of bias.

## **Results**

11,057 records were identified with 7,616 remaining after duplicate removal. These were screened by title and abstract for inclusion. Of the 340 assessed for eligibility, 153 studies were included in full-text screening. Of these, 138 were found to be ineligible, resulting in 14 articles eligible for inclusion. These 14 articles represent 17 studies, which met eligibility criteria for this review (Figure 1).

[Figure 1 – about here]

## **Models of integration**

We identified four models of integrated care defined by the conditions integrated; within these models integration services took place in various settings and through screening, referral and treatment activities, as well as through training and procedure development (Figure 2). The first model integrated HIV and AIDS services with diabetes (NCD-RisC, 2016; Tierney, Kimaiyo, & Mamlin, 2011; WHO, 2016). The second model integrated HIV and AIDS services with diabetes and hypertension (Chamie, Kwarisiima, Clark, Kabami, & Jain, 2012; Edwards, Bygrave, & Van Den Bergh, 2015; Kotwani,



Balzer, & Kwarisiima, 2014; Monroe, Rowe, Moore, & Chander, 2012; Noble, Reeves, Jackson, & Abrahams, 2012; Tiam, Oyebanji, & Nkonyana, 2012; UNAIDS, 2011). The third model integrated cardiovascular services with HIV and AIDS services (Gwarzo, Maji, & Isa-Dutse, 2012; Nyabera, Yonga, Mwangemi, & Bukachi, 2011; UNAIDS, 2011); and the final model described studies where HIV and AIDS services were integrated with diabetes, hypertension, CVD and other diseases (Inouye et al., 2011; Namata, Kawuma, & Nakigudde, 2014; Tierney et al., 2011).

[Figure 2 – about here]

### **Characteristics of Included Studies**

Fourteen articles representing 17 distinct studies integrating HIV and AIDS with diabetes, hypertension and/or CVD met inclusion criteria (Adeyemi, Vibhakar, & Max, 2009; Bury, Stroup, Stephens, & Baker, 2007; Chamie et al., 2012; Edwards et al., 2015; Gwarzo et al., 2012; Inouye et al., 2011; Kotwani et al., 2014; Monroe et al., 2012; Namata et al., 2014; Noble et al., 2012; Nyabera et al., 2011; M Rabkin et al., 2012; Tiam et al., 2012; Tierney et al., 2011; UNAIDS, 2011). Six were full papers (Adeyemi et al., 2009; Bury et al., 2007; Chamie et al., 2012; Edwards et al., 2015; Inouye et al., 2011; Kotwani et al., 2014), one was a report with four case studies (UNAIDS, 2011), and seven were abstracts (Gwarzo et al., 2012; Monroe et al., 2012; Namata et al., 2014; Noble et al., 2012; Nyabera et al., 2011; Tiam et al., 2012; Tierney et al., 2011). Eleven studies were from Sub-Saharan Africa (Ethiopia, Kenya, Lesotho, Nigeria, South Africa Uganda), (Chamie et al., 2012; Edwards et al., 2015; Gwarzo et al., 2012; Kotwani et al., 2014; Namata et al., 2014; Nyabera et al., 2011; Tiam et al., 2012; Tierney et al., 2011; UNAIDS, 2011), four from the United States (U.S.) (Adeyemi et al., 2009; Bury et al., 2007; Inouye et al., 2011; Monroe et al., 2012), one from the United Kingdom (U.K.) (Noble et al., 2012) and one from South-East Asia (Cambodia) (UNAIDS, 2011) (Figure 3). The majority of papers were published in 2011 and 2012 (Figure 4). Seven studies took place in community/mobile service points (Chamie et al., 2012; Inouye et al., 2011; Kotwani et al., 2014; Tiam et al., 2012; Tierney et al., 2011; UNAIDS, 2011); three in

primary health centers or general outpatient clinics (Adeyemi et al., 2009; Edwards et al., 2015; UNAIDS, 2011); five in HIV clinics (Bury et al., 2007; Monroe et al., 2012; Namata et al., 2014; Nyabera et al., 2011; UNAIDS, 2011); and two were located in secondary health facilities (Gwarzo et al., 2012; Noble et al., 2012) (Table 2). There was one cohort study (Bury et al., 2007). One cross-sectional study (Noble et al., 2012), two retrospective record reviews (Adeyemi et al., 2009; Edwards et al., 2015); one qualitative study (Monroe et al., 2012); and 12 program descriptions (Chamie et al., 2012; Gwarzo et al., 2012; Inouye et al., 2011; Kotwani et al., 2014; Namata et al., 2014; Nyabera et al., 2011; Tiam et al., 2012; Tierney et al., 2011; UNAIDS, 2011) (Table 3). Further, the integration types described were entirely at the meso-level; these include clinical and service integrations (Table 4). Integration taking place at the macro-level and micro-level were not reported.

[Figure 3 – about here]

[Figure 4 – about here]

[Table 1 – about here]

[Table 2 – about here]

[Table 3 – about here]

[Table 4 – about here]

### *Model 1: Integrating Diabetes Services with HIV and AIDS Services*

Three studies integrated diabetes services into HIV services (Adeyemi et al., 2009; Bury et al., 2007; UNAIDS, 2011). Two studies examined whether goals set by the American Diabetes Association (ADA) were being met in an HIV clinic in the U.S. These studies involved clinicians acting as primary care physicians who managed HIV and other conditions, including diabetes. One case study from Ethiopia reported on adapting materials from an existing diabetes clinic in an HIV outpatient setting. .

Two examples reported clinical outcomes, assessed as meeting ADA goals; Bury et al. reported on diabetes treatment provision to 40 patients in an HIV clinic run by internal medicine physicians in the U.S., finding that most of the 40 patients achieved almost undetectable viral load and CD4 cell counts of 460 to 480 cells/ $\mu$ L and yet, less than 50% of patients achieved therapeutic goals for HbA1c, cholesterol, triglycerides, and blood pressure, with no statistically significant difference between groups receiving counselling or not (Bury et al., 2007). However, Adeyemi et al. in a retrospective record review providing diabetes treatment to 216 HAART patients at a large urban HIV clinic in the U.S., found that 54% of patients met the goal for HbA1c, 72% had HbA1c <8%, representing adequate control, and 151 patients (70%) had record of a complete lipid profile (Adeyemi et al., 2009). These figures were reported to be comparable with those achieved in general medical clinics amongst people who are HIV negative. The authors made several suggestions to improve outcomes, including the presence of a clinical pharmacist providing patient education and recommending treatment to other health professionals, checklists for diabetic patients, patient education targeting nutrition, care and diabetes and care monitoring with concomitant medications (Adeyemi et al., 2009). The case study from Ethiopia described adaptation of materials from an HIV clinic for use in diabetes care at a diabetes outpatient clinic, as well as staff training, peer training to support treatment adherence and patient education, and the introduction of multidisciplinary team meetings. The program reported that quality of care to diabetes patients living with HIV improved with an increase in the percentage of people receiving services; blood pressure checks (baseline = 40%, follow up = 80%), weight checks (baseline = <10%, follow up = >80%), funduscopy (baseline = <10%, follow up = 50%), foot exam (baseline = <10%, follow up = >80%) and adherence assessments (baseline = <10%, follow up = >60%)(UNAIDS, 2011).

#### *Model 2: Integrating Hypertension and Diabetes Services with HIV and AIDS Services*

Eight studies integrated diabetes and hypertension services with HIV and AIDS services (Chamie et al., 2012; Edwards et al., 2015; Kotwani et al., 2014; Monroe et al., 2012; Noble et al., 2012; Tiam et al.,

2012; UNAIDS, 2011). One program description from Cambodia utilized a patient-centered case management approach (UNAIDS, 2011). Others from Kenya, Lesotho and Uganda reported on screening for HIV, hypertension and diabetes, both in mobile sites and community health campaigns (Chamie et al., 2012; Kotwani et al., 2014; Tiam et al., 2012). One study from the U.K. described an integration within a hospital hypertension clinic that offered lifestyle advice, CVD risk assessment and diabetes screening (Noble et al., 2012). A qualitative study, from the USA., explored patient perspectives on comorbidities such as diabetes and hypertension amongst HIV patients (Monroe et al., 2012).

Three studies reported clinical outcomes. A program in Cambodia piloted integrated HIV, hypertension and diabetes care in 2 clinics, reaching 9000 patients, using a patient-centered case management approach, flow charts, generic medicines and routine cohort monitoring (UNAIDS, 2011). The program reported high retention rates, increase in CD4 counts, decrease in median HbA1c and target blood pressure attainment amongst hypertensive patients (UNAIDS, 2011). A retrospective record review of 2,206 patients at an MSF clinic in Nairobi, Kenya, describes the introduction of an NCD program into a primary health care setting (Edwards et al., 2015). The study found improvements in blood pressure and comparable diabetes outcomes among those with and without HIV; target systolic blood pressure was reached by 40% of those patients living with HIV and 50% of those who were HIV negative; target diastolic blood pressure was reached by 58% of those living with HIV as compared to 64.6% amongst those who were HIV negative (Edwards et al., 2015). The study also found comparable outcomes in diabetes patients who are HIV negative and those living with HIV; follow up HbA1c <7% was reached by 37.5% of those living with HIV compared to 19.6% of HIV negative patients (Edwards et al., 2015). A study from an in-reach hypertension clinic in the U.K. provided 36 patients with lifestyle advice and cardiovascular risk assessment and screening for diabetes (Noble et al., 2012). It reported reductions in blood pressure for most patients, with 63% achieving their target; it also found an average decrease in 10-year cardiovascular risk of 39% (Noble et al., 2012).

Other studies reported an increase in screening uptake but mixed results for subsequent referral, especially in mobile or community campaigns. A mobile service point screening initiative run by a multidisciplinary team of doctors, nurses, community workers, nutritionists, AIDS officers and pharmacists in Lesotho reached 8396 adults for HIV testing (Tiam et al., 2012). Among those testing HIV positive, 36.6% were enrolled into further HIV care; 4,434 adults underwent hypertension screening of whom 24.2% had elevated blood pressure and received treatment; 3,045 blood sugar tests were conducted, finding 3.1% participants to have elevated blood sugar and referring them on (Tiam et al., 2012). Multi-day campaigns offering diagnostic, preventive, treatment and referral services for HIV, malaria, tuberculosis, hypertension and diabetes held in Uganda have reported positive results, reaching 6,300 residents or upwards of 74% of adults in the community (Chamie et al., 2012). Chamie et al report that among newly detected HIV cases, 39% were referred and linked to care, but within a subgroup with CD4 <100, 83% linked to care and started ART within 10 days; 43% of newly diagnosed hypertensives were linked to care and 61% of newly diagnosed diabetics (Chamie et al., 2012). A different campaign from Uganda reported on a 5 day program for testing and referral to hypertension treatment (Kotwani et al., 2014). The study reported promising results for linkage to subsequent care, finding that amongst 2,252 people screened, 214 had hypertension and received care, 83% of these within 6 months; however, the remainder forwent follow up for various reasons including cost of transport and feeling better (Kotwani et al., 2014).

One study explored patient perspectives with focus groups involving 35 patients at an HIV clinic in Baltimore, USA. (Monroe et al., 2012). The study discussed barriers to treatment of comorbidities, reporting that patients viewed their comorbidities as a greater threat than HIV and expressed frustration at lack of control over them (Monroe et al., 2012). Patients also described the perceived ineffectiveness of medication for comorbidities and lack of clinical consequences following missed doses, as well as the importance of social support in adherence to medication for comorbidities and follow up care.

### *Model 3: Integrating CVD Services with HIV and AIDS Services*

Three studies integrated basic cardiovascular risk factor evaluation (high BMI, age and sex) with HIV and AIDS services. One cross sectional pilot study from Nigeria assessed the feasibility of routine screening for CVD risk factors in an HIV clinic (Adeyemi et al., 2009). A study from Kenya explored CVD care integration into HIV treatment sites through training, equipment provision and referral pathway establishment (Nyabera et al., 2011). Another study from Kenya briefly described in a UNAIDS report, sought to explore HIV and CVD service integration and reported on screening outcomes for hypertension amongst people living with HIV persons (UNAIDS, 2011).

The abstract from Nigeria piloted integrating CVD screening into HIV services in a clinic with 12,177 patients of whom 1,033 were randomly selected for screening. The study found that nearly 20% of those screened were identified with one or more CVD risk factor and sent for laboratory evaluation, concluding that CVD screening integration was feasible and necessary (Gwarzo et al., 2012). From a process perspective, Nyabera et al. described a program to train healthcare providers, provide equipment necessary for screening and to establish referral pathways in five HIV care and treatment sites in Kenya serving 5,786 patients (Nyabera et al., 2011). The study found that CVD service operationalization in an HIV setting was feasible, with staff reporting high acceptance and skills uptake; however, the study notes that despite successful care pathways and implementation, 1/3 of available CVD equipment was not in serviceable condition (Nyabera et al., 2011). A case study from Kenya described screening for hypertension amongst HIV infected persons and reported that persons living with HIV had significantly higher rates of hypertension than those who were HIV negative, pointing to the need for screening amongst persons living with HIV and AIDS (UNAIDS, 2011).

### *Model 4: Integrating Diabetes, Hypertension and CVD Services with HIV and AIDS Services*

Three studies integrated diabetes, hypertension, CVD and other services into HIV and AIDS service delivery. One study sought to develop NCD specific data collection tools, standard operating procedures and clinician training on management of HIV-NCD comorbidity (Namata et al., 2014). One

abstract described a screening and referral program (Tierney et al., 2011). Another described a culturally sensitive social cognitive theory framework to guide self-management interventions for HIV, diabetes and COPD (Inouye et al., 2011).

A study from the Mildmay Health System in Uganda, serving 10,285 clients described an integrated NCD program that employed new means to collect and record data (Namata et al., 2014). Using existing HIV structures it was possible to improve the diagnosis, tracking and management of NCDs within routine HIV care; of 10,285 active clients, 1,058 have been diagnosed as hypertensive, 8% of whom have diabetes (Namata et al., 2014). Tierney et al. reported on a community health worker led referral initiative in Kenya for community screening in 50 rural and urban health centers that has reached 454,598 persons, of whom 96% were screened for HIV, and is now expanding to provide hypertension and diabetes screening and expanding referral clinics to provide care for heart and lung disease, diabetes and other NCDs (Tierney et al., 2011). The study reports linkage with clinic-based care as challenging with only 17% of those referred visiting affiliated clinics; except amongst pregnant women where almost 90% have kept visits. A study by Inouye et al. described a culturally sensitive social cognitive theory framework to guide self-management interventions for HIV, diabetes and COPD to Asian and Pacific Island populations in Hawaii, USA. and reports developing a culturally appropriate strategy for HIV and NCD integrated care and stresses the importance of an interdisciplinary approach and collaboration in these initiatives (Inouye et al., 2011).

### **Outcomes Reported**

Studies reported both clinical and descriptive outcomes (Table 4). Clinical outcomes included improvements in measures relating to NCDs and HIV and AIDS such as blood pressure, hemoglobin A1c (HbA1c), cholesterol levels and CD4 count. Descriptive outcomes included reports of process improvements, staff acceptance or patient satisfaction with services.

### **Risk of Bias Assessment**

We screened all studies and found only one study eligible for risk of bias assessment as it presented evaluative data (Bury et al., 2007). This cohort study was at moderate risk of selection bias due to small sample size and high performance bias due to non-blinding; other measures including detection bias, reporting bias and attrition bias were low or not applicable resulting in an overall moderate risk of bias.

### **Measures of Effectiveness of Integration**

One study reported on measures of effectiveness of integration (Bury et al., 2007). The study included patients with HIV in an integrated care setting and sought to evaluate whether seeing a clinical pharmacist improved diabetes outcomes. There was no statistically significant difference between groups in attainment of ADA goals.

## **Discussion**

The four models described seek to integrate HIV and AIDS services with diabetes, hypertension and/or CVD services through various interventions and campaigns. The first model integrates diabetes services into HIV and AIDS services through diabetes service provision at HIV clinics as well as through adaptation of HIV protocols for use in identifying and treating diabetes in a low-income HIV treatment setting. The second model goes a step further and integrated care for hypertension, as well as diabetes and HIV and AIDS services. Most studies identified were under this model. There were relatively fewer studies under the third model of CVD and HIV integrations, or the fourth model, which integrated HIV and AIDS services with diabetes, hypertension and CVD.

A common finding with all models was the use of existing HIV protocols and systems to both create NCD protocols and facilitate integration of NCD care into HIV clinics. Primarily in low-income countries with a high burden of HIV, these established HIV systems provide a platform for collaboration, staff



training and acceptance in introducing diabetes, hypertension and CVD care. Further, in these countries, community campaigns, health fairs and mobile service points offered scope for delivering screening and referral services for HIV and multiple NCDs; however, there ensues a challenge in ensuring referral and follow up. In high-income countries (e.g. the USA), cohort data suggest that integrating diabetes with HIV services is feasible, with dedicated clinical pharmacists playing an important role.

These models have advantages and disadvantages (Table 5). In integrations that provide screening only, there is the potential to increase case detection and provide a platform for patient education on CVD risk factors and prevention (Tierney et al., 2011). However, screening activities require appropriate training, equipment, linkage to care and a supportive referral system (Namata et al., 2014). Integrations that incorporate treatment may be better able to address patients' multiple needs and can leverage on existing services, yet these integrations may introduce competing demands on primary care providers or exclude other NCD's (Nyabera et al., 2011). These integrations require well trained staff, appropriate human resources for operationalization and culturally appropriate standard operating procedures and protocols to meet integrated care needs (Inouye et al., 2011). Further, there is a need for leadership at the service delivery level to catalyze change and drive integration of CVD, and other NCD's, with HIV service provision(UNAIDS, 2011).

[Table 5 – about here]

### **Study Strengths and Limitations**

One of the strengths of our review was the inclusion of studies from a varied range of databases and conference archives, which served to increase the number of papers from low- and middle-income countries. The review also included studies published in languages other than English. A limitation of our review is that the majority of papers were descriptive, which although providing insightful knowledge on strategies and approaches, we were unable to infer the effectiveness of described programs. As a result, this review is highly descriptive.

## **Implications for Research**

Our review finds that the majority of research on integrating CVD, hypertension and diabetes with HIV and AIDS has focused on incorporating care for these conditions into existing HIV care. Studies mainly describe programs or interventions carried out on a small scale and in conjunction with other clinic activities or community campaigns. There is a need for evidence on the effectiveness of these integrations (including issues that facilitate or hinder integration), and for research into integrations occurring at the micro and macro-level.

There is also a need for research looking at long-term outcomes and the impact of integration on HIV and AIDS and CVD, hypertension and diabetes. The longest follow up was 6 months. Further, there is a need for economic analysis, which featured in none of the studies.

There is a growing intersection of persons with HIV and NCDs in low- and middle-income countries and as such there is a need for further study to evaluate the types of integrated services that are most effective in these countries (Yusuf et al., 2015). Thirteen of 19 studies were from sub-Saharan Africa, only one case report was from Asia and there were no studies from Latin America, highlighting the need for further research in these regions.

The integrated approaches to NCD and HIV/AIDS care resonate with the recommendation that the NCD movement can leverage on existing HIV and AIDS activities (Jonathan et al., 2016; M Rabkin & El-Sadr, 2011). This includes using the community as a locus of action for activism, advocacy, accountability and service delivery; the importance of partnerships to facilitate multidisciplinary collaborations; as well as the need for evidence, data and research to evaluate advances in practice and treatment. Overall there is limited robust, long term and systematic evidence as to the cost and clinical effectiveness of HIV and CVD integration. As such there is a need to explore potential limitations of integrated models with well-designed studies that include long term results and evaluations. Further, as no papers described the use of incentives, there is need to explore if and what type would be appropriate and effective in facilitating greater integration of CVD and HIV services.

## Conclusions

Several innovative initiatives have been described for integrating CVD, hypertension and diabetes services with HIV and AIDS services. Many involve multidisciplinary collaboration, and integrating NCD care into existing HIV and AIDS services through shared and repurposed protocols, as well as incorporating screening activities into wider community campaigns. Further evidence on the merits of the different models of integration is needed using appropriate outcome measures. The need for robust research speaks to the greater general need for more initiatives that bring people living with HIV into mainstream NCD services.

The evidence from our review shows that integration studies on HIV and CVD services are occurring largely in low income countries in Sub Saharan Africa and through channels that rely mainly on existing infrastructure used for HIV and AIDS care. The studies describe collaboration, staff education, and building on the existing standard operating procedures, work flows and other processes put in place to address the high burden of HIV and AIDS in these communities. Further development of these approaches could help to further disseminate integrated approaches to HIV and NCD care. Community, mobile and HIV campaigns have also shown to be able to screen and detect risks of or other NCDs in people living with or at risk of NCDs; however, these programs require strong linkage to follow up care that is currently underdeveloped.

As the burden of NCDs increases and persons with HIV live longer, policy makers and planners will need to plan for the increasing number of people with both these conditions and evaluate the best strategies to provide care for them.

(Word Count: 4211)

[Table 6 – about here]

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## Appendices

### Box 1: Definition of Integration

Managerial or operational changes to health systems to bring together inputs, delivery, management and organization of particular service functions as a means of improving coverage, access, quality, acceptability and (cost)-effectiveness. This may include:

- Service integrations that combine 'different packages of services'
- Integration of service delivery points
- Integration at different levels of service delivery
- Process modifications
- Introduction of technologies aimed at aiding integration
- Integration of management decisions

**Box 2: Search Strategy used for Medline, Embase and Global Health via Ovid (adapted to only include CVD, Hypertension and Diabetes terms)**

Database: Embase <1980 to October 2015>, Global Health <1910 to October 2015>, Ovid MEDLINE(R) <1946 to October Week 4 2015>

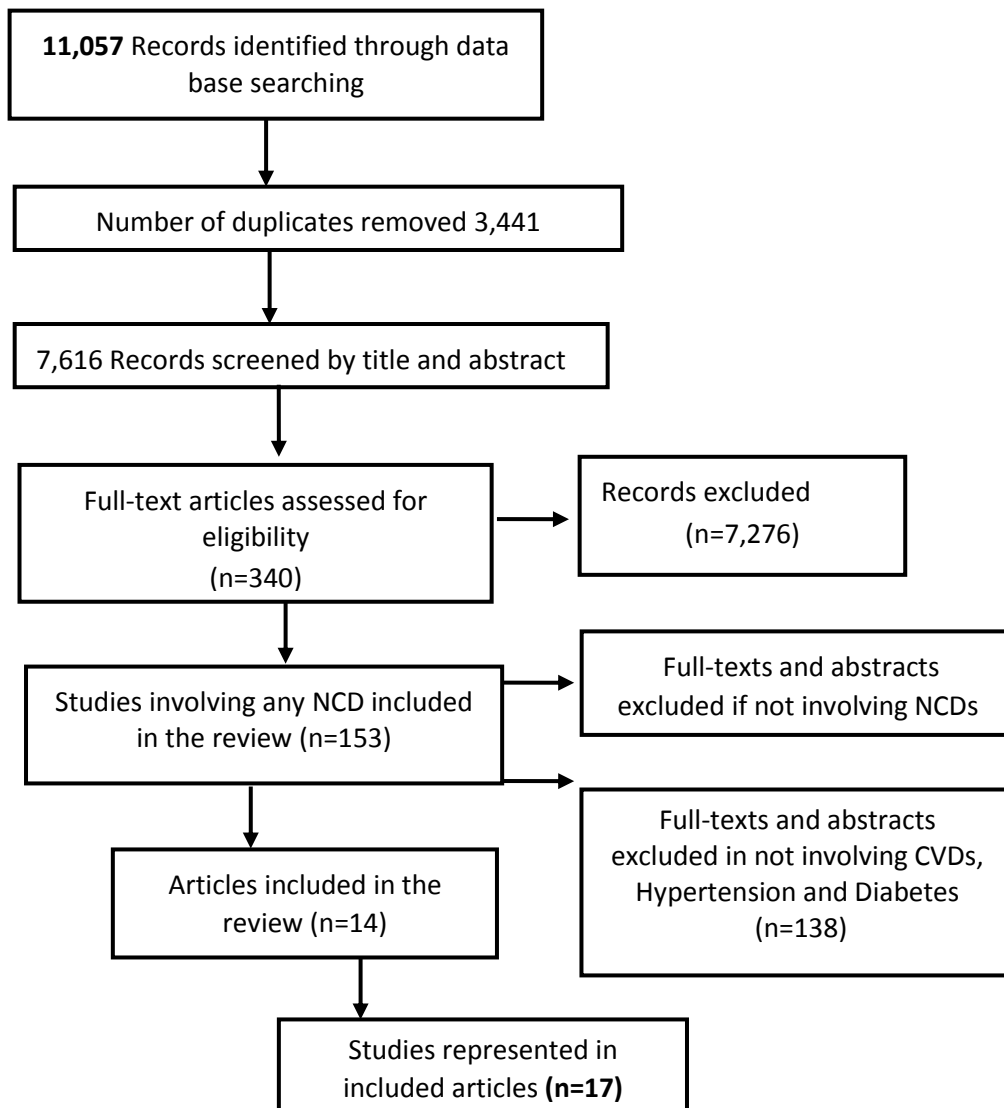
1. ((vertical or horizontal or integrat\* or coordinat\* or co-ordinat\* or link\*) and (program\* or care or service\*)).mp. or delivery of health care, integrated/ or primary healthcare/

2. exp HIV infections/ or HIV.mp. or Human immunodeficiency virus.mp. or "HIV/aids".mp.

3. (All introduced in a separate line) chronic disease/ or long-term care/ or ((chronic\* or persistent or long\* term or ongoing or degenerative) adj3 (disease\* or disab\* or ill\* or condition\* or health condition\* or medical condition\*)).tw. or long\* term care.tw. or (non-communicable disease\* or NCD).tw. or exp diabetes mellitus/ or (diabetes or diabetic).tw. or exp hypertension/ or (hypertension or high blood pressure).tw. or exp cerebrovascular disorders/ or (cerebrovascular disease\* or cerebrovascular disorder\* or brain ischaemia or cerebral infarction or carotid artery disease\* or stroke).tw. or exp dementia/ or (dementia or alzheimer\*).tw. or exp epilepsy/ or epilep\*.tw. or exp myocardial ischemia/ or (myocardial isch\* or ischaemic heart disease or ischemic heart disease or angina or coronary disease\* or coronary heart disease\* or coronary artery disease\* or myocardial infarction).tw. or exp heart failure/ or heart failure.tw. or exp obesity/ or (obesity or obese).tw.

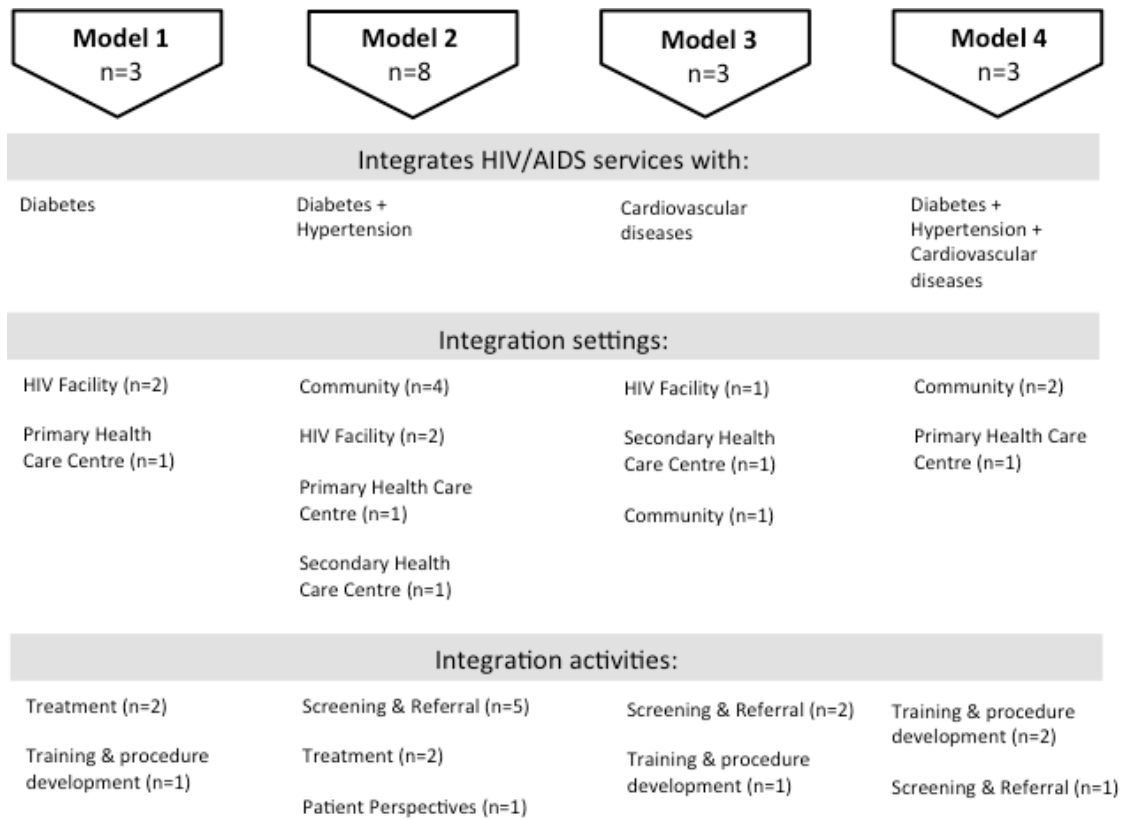
4. 1 and 2 and 3

**Figure 1: Study flow diagram**

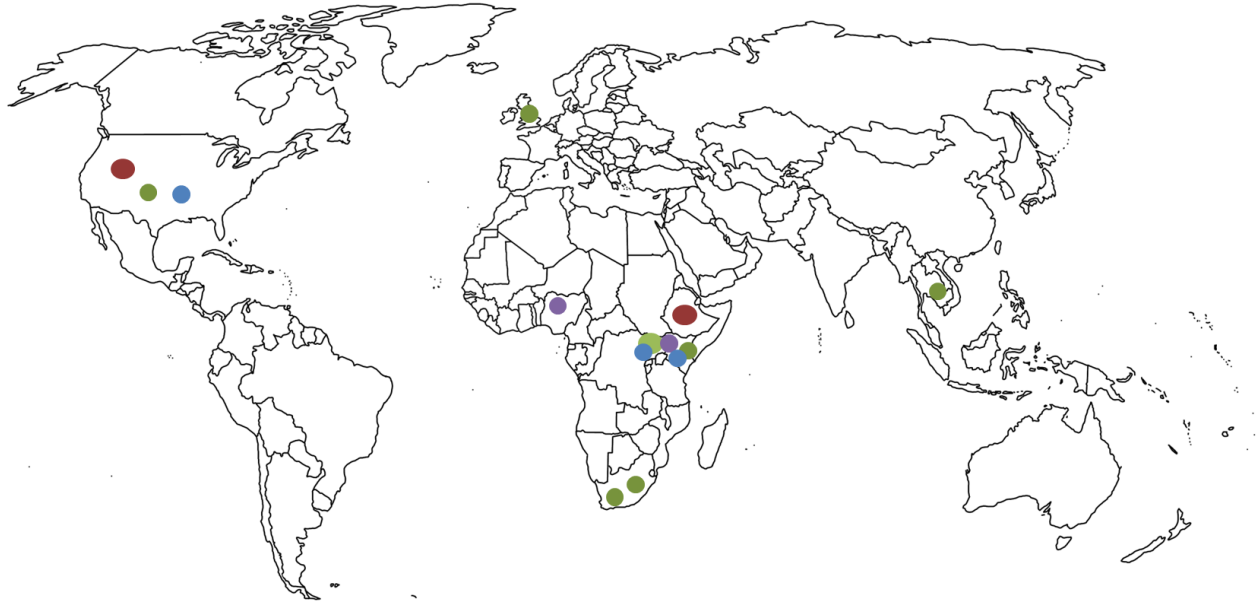




**Figure 2: Overview of Models**

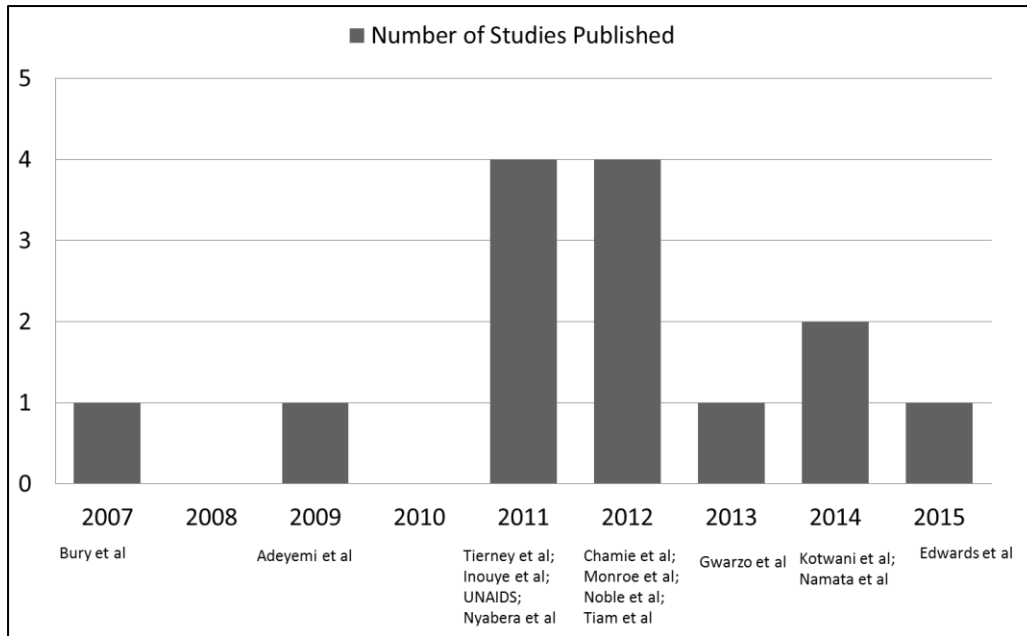


**Figure 3: Map of Integrations by Model**



Type	Country	No.
● HIV + DM	USA	2
	Ethiopia	1
● HIV + HPT + DM	Cambodia	1
	South Africa	1
	Uganda	2
	Lesotho	1
	Kenya	1
	UK	1
	USA	1
● HIV + CVD	Kenya	2
	Nigeria	1
● HIV + HPT + CVD + DM	Uganda	1
	Kenya	1
	USA	1

**Figure 4: Summary of Year of Publication for Reviewed Papers**



**Table 1: Summary of Study Setting by Integration Model**

<b>Integration Model</b>	<b>Setting</b>	<b>n=</b>	<b>Author</b>
HIV and AIDS + Diabetes	HIV Facility	2	Bury et al 2007(32); UNAIDS 2011(9);
	Primary Health Care Centre	1	Adeyemi et al 2009(33)
HIV and AIDS + HT + Diabetes	Community/Mobile location	4	Chamie et al 2012(22); Tiam et al 2012(27); Kotwani et al 2014(24); UNAIDS 2011(9)
	HIV Facility	2	UNAIDS 2011(9); Monroe et al 2012(25);
	Primary Health Care Centre	1	Edwards et al 2015(23);
	Secondary Health Care Centre	1	Noble et al 2012(26)
HIV and AIDS + CVD	HIV Facility	1	Nyabera et al 2011(29);
	Secondary Health Care Centre	1	Gwarzo et al 2012(28);
	Community	1	UNAIDS 2011(9)
HIV and AIDS + HT + CVD + Diabetes	Community	2	Inouye et al 2011(30); Tierney et al 2011(21);
	Primary Health Centers	1	Namata et al 2014(31)

**Table 2: Summary of Study Designs by Integration Model**

<b>Integration Model</b>	<b>Study Design</b>	<b>n=</b>	<b>Author</b>
HIV and AIDS + Diabetes	Cohort Study	1	Bury et al 2007(32);
	Retrospective Record Review	1	Adeyemi et al 2009(33)
	Program Description	1	UNAIDS 2011(9)
HIV and AIDS + HT + Diabetes	Program Description	5	Chamie et al 2012(22); Tiam et al 2012(22); Kotwani et al 2014; UNAIDS 2011(9)
	Retrospective Record Review	1	Edwards et al 2015(30)
	Cross Sectional Study	1	Noble et al 2012(26)
	Qualitative Study	1	Monroe et al 2012(25)
HIV and AIDS + CVD	Program Description	3	Nyabera et al 2011(29); Gwarzo et al 2012(28); UNAIDS 2011(9)
HIV and AIDS + HT + CVD + Diabetes	Program Description	3	Inouye et al 2011(30); Tierney et al 2011(21); Namata et al 2014(31)

**Table 3: Summary of Integration Types by Model**

<b>Integration Model</b>	<b>Integration Type</b>	<b>n=</b>	<b>Author</b>
HIV and AIDS + DM	Meso – Service Integration	3	Bury et al 2007(32); Adeyemi et al 2009(33); UNAIDS 2011(9)
HIV and AIDS + HT + Diabetes	Meso – Service Integration	7	Chamie et al 2012(22); Tiam et al 2012(22); Kotwani et al 2014(22); Edwards et al 2015(30); Noble et al 2012(26); Monroe et al 2012(25)
	N/A	1	UNAIDS 2011(9)
HIV and AIDS + CVD	Meso - Clinical Integration	1	Gwarzo et al 2012(28)
	Meso - Service Integration	1	Nyabera et al 2011(29)
	N/A	1	UNAIDS 2011(9)
HIV and AIDS + HT + CVD + Diabetes	Meso - Service Integration	2	Namata et al 2014(31); Tierney et al 2011(21)
	Meso - Clinical integration	1	Inouye et al 2011(30)

**Table 4: Reported outcomes by the model of integration**

<b>Model of integration</b>	<b>Outcome indicator reported</b>	<b>Reported in n =</b>
<b>Diabetes services integrated into HIV and AIDS services</b>	Glomerular filtration rate	1
	HbA1c	2
	Blood Pressure	2
	Cholesterol level	2
	Low density lipoprotein cholesterol level	2
	Triglyceride level	2
	High density lipoprotein level	2
	Body Mass Index	2
	Descriptive outcomes (satisfaction/acceptance/processes)	2
<b>Hypertension and Diabetes integrated into HIV and AIDS Services</b>	HbA1c	1
	Fasting glucose	1
	Cholesterol	1
	Qualitative outcomes	1
	Provision of medication	1
	Decrease in 10 year cardiovascular risk	1
	CD4 count	2
	Blood Pressure	4
	Linkage to care	4
	Descriptive outcomes (satisfaction/acceptance/processes)	4
<b>CVD Services integrated into HIV and AIDS services</b>	Referral to laboratory	1
	Descriptive outcomes (satisfaction/acceptance/processes)	2
<b>Diabetes, Hypertension and CVD services integrated into HIV and AIDS services</b>	Descriptive outcomes (satisfaction/acceptance/processes)	3

**Table 5: Summary of advantages, disadvantages and factors impacting integration of CVD services with**

**HIV/AIDS**

<b>Advantages</b>	<b>Disadvantages</b>	<b>Factors</b>
<i>Screening only:</i>		
<ul style="list-style-type: none"> <li>- Case detection</li> <li>- Platform for patient education</li> </ul>	<ul style="list-style-type: none"> <li>- Requires adequate linkage to care</li> </ul>	<ul style="list-style-type: none"> <li>- Need for adequate referral system and linkage to care</li> <li>- Need for adequate equipment to carry out screening</li> </ul>
<i>Screening and treatment:</i>		
<ul style="list-style-type: none"> <li>- Case detection and monitoring</li> <li>- Addresses patients' multiple needs</li> <li>- Can leverage on existing HIV services</li> <li>- Platform for patient education</li> <li>- Improvements in blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>- Competing demands on primary care providers</li> <li>- May miss other NCDs</li> </ul>	<ul style="list-style-type: none"> <li>- High quality training of clinical staff, appropriate human resources for mobile and community initiatives</li> <li>- Creation of culturally appropriate standard operating procedures and protocols to meet the needs of integrated care</li> <li>- Leadership at service delivery level to drive and implement change</li> </ul>



**Table 6: Summary of findings of studies examining integration of HIV with Diabetes, Hypertension and CVD**

Type of Integration	Study	Setting and Sample Size	Study Design	Integration Activities	Results	Risk of Bias
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HIV + Diabetes	Adeyemi, 2009	USA-Chicago Primary care in a large, urban HIV clinic. n=216	Retrospective Record Review	Provide diabetes treatment to HAART patients; Comprehensive primary care delivered by the same staff.	<ul style="list-style-type: none"> <li>- HIV infected DM patients achieved ADA goals at rates similar to uninfected patients.</li> <li>- 54% of patients met the ADA goal for HbA1c (&gt;7%); rate of achievement for ADA lipid level goals was &gt;50% except for triglyceride levels (elevated triglyceride levels is a common complication of HAART).</li> </ul>	N/A
HIV + Diabetes	Bury et al, 2007	USA-Oklahoma HIV clinic run by internal medicine physicians n=40	Cohort Study	Provide Diabetes treatment to patients on HAART.	<ul style="list-style-type: none"> <li>- Less than 50% of patients were achieving goals of therapy for hemoglobin <u>HbA1c</u>), cholesterol, triglycerides, and blood pressure.</li> <li>- 5% were documented as receiving aspirin therapy.</li> <li>- The medication adherence counseling was not a significant factor in the results.</li> </ul>	Moderate Risk of Bias
HIV + Diabetes	UNAIDS 2011 – case study in report	Ethiopia	Program description	Adapting materials from the HIV clinic for DM care use in outpatient clinic; staff training; peer training for adherence support and education; multidisciplinary team meetings.	<ul style="list-style-type: none"> <li>- Quality of care provided to people with DM improved notably - including percentage of people receiving DM services (measuring BP, weight, examining eyes, feet and assessing adherence).</li> </ul>	N/A
HIV + HT + Diabetes	Chamie et al 2012	Uganda – rural communities n=4343	Program description	5-day campaign offering diagnostic, preventive, treatment and referral services for HIV, malaria, TB, HT and diabetes.	<ul style="list-style-type: none"> <li>- Feasible: campaign reached 74% of adults in the community.</li> <li>- Identified a high burden of undiagnosed disease.</li> <li>- Detected HIV cases at high CD4 counts.</li> </ul>	N/A
HIV + HT + Diabetes	UNAIDS 2011 – case study in report	Cambodia n=9000	Program description	Pilot of 2 clinics for HIV, diabetes and hypertension; patient-centered case management approach, flow charts, generic drugs and routine cohort monitoring.	<ul style="list-style-type: none"> <li>- Retention rates = 70 - 90%.</li> <li>- Median CD4 count rose from 53 to 316 per mm<sup>3</sup> at 24 months.</li> <li>- Median HbA1c of people with DM fell from 11.5% to 8.6%.</li> <li>- 68% of people treated for HT reached target BP within six months.</li> <li>- No difficulties noted in terms of stigma.</li> </ul>	N/A

HIV + HT + Diabetes	UNAIDS 2011 – case study in report	South Africa	Program description	South Africa plans to test 15 million people for HIV, elevated BP and blood sugar level.	- N/A	N/A
HIV + HT + Diabetes	Noble 2012 (Abstract)	UK – in-reach HT clinic n=36	Cross Sectional Survey	HIV patients were given appropriate lifestyle advice, underwent full cardiovascular risk assessment and screening for diabetes.	<ul style="list-style-type: none"> <li>- 44% patients referred for echocardiogram, 43% of these showed an abnormality.</li> <li>- Anti-hypertensive medications were introduced or changed in 85% of patients.</li> <li>- BP reduction seen in most patients attending the clinic with 63% achieving their target BP.</li> <li>- The average decrease seen in the 10-year cardiovascular risk was 39% with a range of 8% to 74%.</li> <li>- All patients rated clinic as good or great on all aspects and were happy with the care they were receiving.</li> </ul>	N/A
HIV + HT + Diabetes	Kotwani 2014	Rural Uganda n=2252	Intervention description	5-day program for testing and referral for hypertension treatment.	<ul style="list-style-type: none"> <li>- 2252 adults were screened for hypertension and 214 hypertensive adults received a linkage intervention for further management. Of these, 178 (83%) linked to care within 6 months (median = 22 days).</li> <li>- Barriers for patients who did not see care included expensive transport (59%) and feeling well (59%).</li> </ul>	N/A
HIV + HT + Diabetes	Monroe 2012 (Abstract)	USA. – Baltimore HIV Clinic n=35	Qualitative (6 focus groups)	No integrated activities/ intervention. Barriers and facilitators elicited may give insight on what is important for an integrated intervention.	<ul style="list-style-type: none"> <li>- Perceptions of HIV vs. other conditions: comorbid conditions viewed as a greater threat than HIV; expressed frustration at not being able to control comorbidities.</li> <li>- Attitudes towards medication: perceived ineffectiveness of medications for comorbidities and lack of clinical consequences of missed doses.</li> <li>- Acceptance of HIV and integration of multiple diagnoses into daily life: importance of social support in medication adherence and use of various reminder systems.</li> </ul>	N/A

HIV + HT + Diabetes	Edwards 2015	Kibera, Nairobi, Kenya – MSF clinic n=2206	Descriptive study: Retrospective Record Review	NCD chronic disease health care package offered at clinic - compared those PLHIV and those without who presented with hypertension and/or DM and were enrolled in the NCD package.	<ul style="list-style-type: none"> <li>- For those with hypertension - improvements in blood pressure regardless of HIV status - target SBP reached by 40% PLHIV and 50% for HIV negative, target DBP reached by 58% PLHIV and 64.6% HIV negative.</li> <li>- Comparable outcomes for DM patients - follow up HbA1c &lt;7% reached by 37.5% for PLHIV and 19.6% for HIV-negative patients.</li> </ul>	N/A
HIV + HT + Diabetes	Tiam 2012 (Abstract)	Rural Lesotho – mobile service delivery points	Program description	Integrated health services provided at mobile service delivery points in rural settings staffed by multi-disciplinary teams of doctors, nurses, community workers, nutritionists, AIDS officers and pharmacists.	<ul style="list-style-type: none"> <li>- 8,396 adults were tested for HIV (67.3% female; 32.6% male). 588 (7%) tested HIV-positive (6.7% female; 7.1% male).</li> <li>- 4,454 adults (24.7% male; 75.3% female) were screened for hypertension, and of those screened, 24.2% had elevated BP and linked to care centers. 3,045 adults had blood sugar tests (27.0% males; 73.0% females); 3.1% had elevated blood sugar and linked to care.</li> </ul>	N/A
HIV +CVD	UNAIDS 2011 - case study in report	Kenya	Descriptive	Screening for HT amongst HIV infected persons.	<ul style="list-style-type: none"> <li>- When people were screened for both HIV infection and NCD, HIV positive people had significantly higher rates of hypertension than those who were HIV negative.</li> </ul>	N/A
HIV + CVD	Nyabera 2011 (Abstract)	Kenya – 5 HIV care and treatment sites n=5786	Descriptive report	Training of healthcare providers, provision of equipment for basic evaluation of cardiovascular risk factors and common CVDs, establishment of referral pathways for specialist treatment.	<ul style="list-style-type: none"> <li>- Counselling and clinician consultation services easily integrated and high staff skills uptake acceptance.</li> <li>- Care pathways adequately implemented in all sites but 1/3 of CVD equipment not in serviceable condition.</li> <li>- Overall, integration of CVD screening and management into routine HIV care is feasible.</li> </ul>	N/A

HIV+ CVD	Gwarzo et al, 2012 (Abstract)	Nigeria- secondary health facility n=1033	Descriptive study	Targeted CVD screening for PLHA and referral to an on-site cardiac clinic.	<ul style="list-style-type: none"> <li>- 205 (19.8%) of 1033 screened had one or more CVD risk factors; 42% of whom had a CVD risk of &lt; 20%, and 2.4% a CVD risk of ≥20%.</li> <li>- The most common risk factors identified were age (25.7%), male sex (25.9%), high BMI (21.8%), and hypertension (15.2%).</li> </ul>	N/A
HIV + DM + HT + CVD	Namata 2014	Uganda – Mildmay health system n=10285 clients	Program description	Development of: NCD specific data collection tools; SOPs for NCD diagnosis and management; Medical records/ files for HIV positive clients with HT or other NCDs have been tagged and clinicians sensitized on management of HIV-NCD co-morbidity.	<ul style="list-style-type: none"> <li>- The existing HIV care and treatment infrastructure provides a viable platform for screening and managing NCD especially for a population aging with HIV.</li> <li>- Improvement in diagnosis, tracking and management of NCDs, particularly Hypertension, diabetes, cardiovascular disease and mental health as part of routine HIV care.</li> </ul>	N/A
HIV + DM + HT + Others	Tierney et al 2011 (Abstract)	Kenya – 50 rural and urban health centers	Program description	Community health workers refer patients with HIV and other diseases to clinics through home counselling and testing	<ul style="list-style-type: none"> <li>- Screening has been successful and will roll out HT and DM screening but referral to clinic for treatment/monitoring has been challenging; success amongst pregnant women.</li> <li>- HCT counsellors outreach = 454,598 persons; 98% agreed to HCT interview; HIV and TB screening = 96%; clinic visits = 17% kept visits; clinic visits amongst pregnant women = &gt;90% kept visits.</li> </ul>	N/A
HIV + DM + COPD	Inouye 2011	USA - Hawai'i Primary Health Care settings & community site	Intervention description	Culturally sensitive social cognitive theory framework to guide self-management interventions to Asian and Pacific Island populations.	<ul style="list-style-type: none"> <li>- Framework for using social cognitive theory to support self-management interventions; paper reports the experience of developing an interdisciplinary research center focused on self-management of chronic conditions</li> <li>- Highlights the interdisciplinary approach and collaboration needed for integrated initiatives.</li> </ul>	N/A

## **Figure and Table Captions List**

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