INTEGRATION OF HEALTH SYSTEM RESPONSES TO HIV/AIDS AND NONCOMMUNICABLE DISEASES IN DEVELOPING COUNTRIES

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PROJECT SUMMARY

Introduction: HIV/AIDS and Noncommunicable diseases (NCDs) are major diseases of public health significance worldwide, especially in developing countries, and increasing research has reported important relationships between them. Recently, there is emerging evidence suggesting strategically important similarities between health system responses to these conditions and thus the need to consider more integrated approaches in the future. Such integrated approaches can maximize synergy and improve efficiency of response. However, the evidence base to inform this approach is limited. Therefore, there is an urgent need to conduct more research in relation to such an integrated approach in the context of health systems of low and middle income countries.

Aims and objectives: The aims of this PhD research were to *analyse* the interrelationships (Convergence, Linkage, Co-occurrence and Parallels) between HIV/AIDS and NCDs; and to *develop* a model and a guiding tool to inform implementation of a more appropriate responses by health systems to HIV/AIDS and NCDs in the context of developing countries.

Methods: The overall PhD research was a - Health policy and system research that employed a pragmatic mixed method and modelling techniques based on the constructivist approach. In this research, different methods were applied at different stages. To analyse connections between HIV/AIDS and NCDs, four methods were used: Correlational and cluster analysis (for convergence), framework development using thematic research synthesis (for linkage), systematic and critical reviews (for co-occurrence), and qualitative content analyses (for parallels). For the development of action model, multi-level (integrative, configurative and interpretive) evidence syntheses methods were applied. The integration tool was formulated based on the action model from best available evidence and was conceptually validated through further literature review and expert consultations.

Results: With rapidly increasing NCD magnitude and stabilizing HIV epidemic, many low-and middle income countries are facing an overlapping double burden of HIV/AIDS and NCDs. The overlap, however, is different in the Sub-Saharan African and Asian Context. After identifying two forms, two types and six pathways of epidemiological linkages between HIV/AIDS and NCDs, a Public Health framework illustrating these linkages was developed. The magnitude of NCD comorbidities in HIV infection was high for cardiovascular abnormalities and pre-cancerous lesions with the dynamics being highly reverted by the scale-up of anti-retroviral treatment coverage. The responses to HIV/AIDS and NCDs, both at Global and National levels, are similar in models and approaches. However, they are different in content. In this PhD research, an action model and a guiding tool for integration are also developed. Finally, evidence about the rationale, policies and models relevant to HIV-NCD integration is consolidated systematically.

Conclusions: The strength of inter-relationships between HIV/AIDS and NCDs and the similarities between the responses to these conditions require improved and integrated responses as appropriate to specific local contexts. In addition to generating evidence relevant to HIV-NCD integration, this PhD research has yielded three important research outputs – a public Health Framework for linkage, a model of integration, and a guiding tool for integration. Further research is needed to refine these outputs and to test their applicability in specific contexts.

GENERAL DECLARATION

Declaration for thesis based or partially based on conjointly published or unpublished work

General Declaration

In accordance with Monash University Doctorate Regulation 17.2 Doctor of Philosophy and Research Master's regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes nine original papers published in peer reviewed journals and two unpublished publications. The core theme of the thesis is: ***Integration of Health system responses to HIV/AIDS and NCDs***. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the School of Public Health and Preventive Medicine under the supervision of ***Professor Brian Oldenburg***.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of [chapters 1-8] my contribution to the work involved the following:

Thesis chapter	**Publication title**	**Publication status***	**Nature and extent of candidate's contribution**
1	Integration of HIV and Noncommunicable Diseases in Health Care Delivery in Low- and Middle-Income Countries	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
2	Epidemiological Patterns of HIV/AIDS and Diabetes in Developing Countries: A Cluster Analysis	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
3	Developing a Public Health Framework for the Epidemiological Linkages between HIV/AIDS and NCDs: *A Thematic Research Synthesis*	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
4	Perspectives, Constructs and Methods in the measurement of Multimorbidity and Comorbidity: A Critical Review	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
5	The incidence of cardiovascular disease, cancer and type 2 diabetes comorbidities in HIV infection: A systematic review	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
6	Epidemiology of Comorbidity of HIV/AIDS and Non-communicable Diseases in Developing Countries: A	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of

	systematic review		the manuscript
7	Global responses to HIV/AIDS and NCDs: Analysis of similarities and differences	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
8	National responses to HIV/AIDS and NCDs: Analysis of parallels and differences	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
9	Developing an Action Model for Integration of Health System Response to HIV/AIDS and Noncommunicable Diseases (NCDs) in Developing Countries	Published	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript
10	Rationale, Policies and Models of HIV-NCD integration in developing countries	Submitted	Conceptualization of manuscript, data analysis and interpretation and write up of draft and final versions of the manuscript

[* For example, 'published'/ 'in press'/ 'accepted'/ 'returned for revision']

I have / **have not** (circle that which applies) renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Signed: 

Date: Jun 30, 2014

Note: I also declare that I have published both as *Tilahun Nigatu* and *Tilahun Nigatu Haregu*.

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I am very thankful to my wife, *Mrs Mulu Abraha*, who provided continuous technical help and moral encouragement for the successful accomplishment of this PhD research; and for her exceptional devotion and commitment in shouldering family responsibility during the period of my PhD study in Australia.

Last but not least, I extend my special acknowledgement to Monash University for providing a scholarship for PhD study and for availing all the necessities required during the whole period of my PhD study.

ABBREVIATIONS

ADC: AIDS Defining Cancers

AIDS: Acquired Immune Deficiency Syndrome

ART: Anti-retroviral Treatment

BSS: Behavioural Surveillance Survey

CBO: Community-based Organization

CCM: Country Coordinating Mechanism

CD4: Cluster of Differentiation 4

CIN: Cervical Intraepithelial Neoplasia

CRD: Chronic Respiratory Disease

CSW: Commercial Sex Worker

CVD: Cardiovascular diseases

DALY: Disability Adjusted Life Years

DEPM: Department of Epidemiology and Preventive Medicine

DHS: Demographic and Health Survey

DM: Diabetes Mellitus

DOH: Department of Health

EXP: Exponent

FBO: Faith-based Organization

FHI: Family Health International

FREQ: Frequency

GHO: Global Health Observatory

GHSU: Global Health and Society Unit

HAART: Highly Active Anti-retroviral Treatment

HAPCO: HIV/AIDS Prevention and Control Office

HDL: High Density Lipoprotein

HEI: HIV Exposed Infant

HIV: Human Immunodeficiency virus

HSS: Health System Strengthening

ICDM: Integrated Chronic Disease Management

IDF: International Diabetes Federation

IDU: Intravenous Drug use(r)

M&E: Monitoring and Evaluation

MAC: Malaysian AIDS Council

MARPS: Most at Risk Populations

MOH: Ministry of Health

MPH: Masters of Public Health

MSM: Men Having Sex with Men

NADC: Non-AIDS Defining Cancers

NCDs: Noncommunicable Diseases

NCM: National Coordination Mechanism

NCPI: National Commitment and Policy Index

NGO: Non-governmental Organization

NSACP: National STD and AIDS Control Program

NSP: National strategic plan

PEPFAR: President's Emergency Plan for AIDS Relief

PhD: Doctor of Philosophy

PHDP: Positive Health Dignity and Prevention

PLHIV: People Living With HIV

PMTCT: Prevention of Mother-to-child Transmission

PYLD: Prevalent Years Lived With Disability

PYLL: Potential Years of Life Lost

SANAC: South African National AIDS Council

SCC: Squamous Cell Carcinoma

SIL: Squamous Intraepithelial Lesion

SIM: Strategic Information Management

SPHM: School of Public Health and Preventive Medicine

SPM: Strategic Plan Management

SRH: Sexual and Reproductive Health

STI: Sexually Transmitted Infections

TB: Tuberculosis

UN: United Nations

UNAIDS: Joint United Nations Program on HIV/AIDS

UNDP: United Nations Development Program

VIA: Visual Inspection with Acetic acid

WHO: World Health Organization

ARTICLES RELEVANT TO PHD

(All are peer-reviewed and open-access articles)

Nigatu T. Integration of HIV and Noncommunicable Diseases in Health Care Delivery in Low- and Middle-Income Countries. *Prev Chronic Dis* 2012; 9:110331. DOI: http://dx.doi.org/10.5888/pcd9.110331

Haregu TN, Elliott J, Setswe G, Oldenburg B. Epidemiological Patterns of HIV/AIDS and Diabetes in Developing Countries: A Cluster Analysis. *International Journal of TROPICAL DISEASE & Health* 2013; 3(1):1-12.

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Haregu TN, Oldenburg B, Elliott J, Setswe G.: Rationale, Policies, and Models of HIV-NCD integration in developing countries: *A qualitative synthesis* (submitted).

OTHER PUBLICATIONS

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Haregu TN, Oldenburg B, Setswe G, Elliott J. Magnitude of Diabetes Comorbidity among People Living with HIV: A Systematic Review. *International Journal of Diabetes Research* 2012; 1(5):81-6

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Nigatu T, Oldenburg B, Abraha M, editors. Addressing Noncommunicable diseases in developing countries: Setting the evidence base. 13th World Congress on Public Health; 2013: Medimond s.r.l.

Temesgen TM, Umer JY, Buda DS, **Haregu TN**. Contribution of traditional birth attendants to the formal health system in Ethiopia: the case of Afar region. *Pan Afr Med J*. 2012; 13(15).

CONFERENCE PRESENTATIONS

Haregu TN, Oldenburg B, Elliott J, Setswe G. Global Responses to HIV/AIDS and Noncommunicable Diseases: Analysis of Similarities and Differences. AMREP World Health Day, April 2013, Melbourne Australia.

Nigatu T, Oldenburg B, Abraha M. Addressing Noncommunicable diseases in developing countries: Evidences for health systems. XIIIth World Congress on Public Health 2012, Addis Ababa, Ethiopia: Abstract no. 265

STRUCTURE OF THE THESIS

This PhD thesis consists of 9 chapters. Six of the nine chapters (2, 3, 4, 5, 6, and 7) are based on published papers. The thesis addresses two main constructs: *Interrelationships* between HIV/AIDS and NCDs, and *integration* of responses to HIV/AIDS and NCDs in the context of developing countries. With a purpose of setting the context, **Chapter 1** provides a background/context of the HIV/AIDS and NCD epidemiology, conceptualizations of key constructs, rationale for the study, research aims and objectives and an overview of overall methodology.

Analysis of interrelationships between HIV/AIDS and NCDs was analysed at four levels. **Chapter 2** presents the interrelationships at population level, epidemiological *convergence,* using correlational and cluster analysis. **Chapter 3** summarizes interrelationships at disease level, epidemiological *linkages*, through the development of a public health framework for linkages. **Chapter 4** addresses interrelationships at patient level, described as *co-occurrence*, through assessment of magnitude of comorbidity and multimorbidity. **Chapter 5 and 6** explore the *parallels* between responses to HIV and NCDs at global and national levels, respectively.

Using the evidence from analysis of interrelationships between HIV/AIDS and NCDs and additional literature review, a systematic *action model* for integration of health system responses to HIV/AIDS and NCDs was developed. This model was then operationalized in to *a guiding tool* – a step-by-step instrument - that illustrates steps for system level horizontal integration of responses to HIV/AIDS and NCDs. The action model and the guiding tool are presented in **Chapter 7**.

In **chapter 8**, a consolidation of research-based, policy-related, and practice-oriented evidence about the integration of HIV/AIDS and NCD responses is presented. An integrated discussion of the summary of the research outputs, implications of the findings, and the limitations of the overall research study is reported in **chapter 9**. Throughout the thesis, sections of published papers are not renumbered to create consistent styles.

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Chapter 1

Introduction

CHAPTER 1 OVERVIEW

HIV/AIDS and Noncommunicable disease are the major current public health threats, especially in low-and middle income countries. Though the epidemiological, nutritional and demographic transitions in those settings have resulted in double-burden of diseases, the relative contribution of the two public health problems to the overall disease burden varies considerably across countries. Prior to analysing the major themes of this PhD research, it is essential to set the scene by outlining the aims and objectives of the research and why this is important. In this regard, this chapter serves three major purposes. First, it Summarizes the the public health importance of HIV/AIDS and NCDs globally, particularly within the context of developing countries. Second, it conceptualizes and defines the major constructs that are essential for the subsequent chapters. These constructs are conceptualized from the perspective of HIV/AIDS and NCDs and based on the contexts of health systems of developing countries. Third, this chapter establishes the rationale and foundations for the overall PhD research. This chapter includes an article that establishes the need for integration of HIV/AIDS and NCD services in low and middle income countries. The specific aims, objectives, and methodology of this doctoral research are also outlined in this chapter.

Citation: Nigatu T. Integration of HIV and Noncommunicable Diseases in Health Care Delivery in Low- and Middle-Income Countries. *Prev Chronic Dis* 2012; 9:110331. DOI: http://dx.doi.org/10.5888/pcd9.110331

HIV/AIDS AND NCDs

HIV/AIDS and NCDs are major global public health issues in developing countries. After three decades in to the HIV epidemic, there are more than 33 million People living with HIV/AIDS (PLHIV). Two-thirds of these PLHIV live in sub-Saharan Africa. HIV/AIDS caused about 1.8 million deaths in 2010. Similarly, about two-third of HIV-related deaths were in sub-Saharan Africa. In the same year, about 2.1 million new HIV infections have occurred. About 90% of these new HIV infections were in sub-Saharan Africa. The global incidence of HIV has declined by about 19% between 2001 and 2009. However, there exists dramatic variability in the change of incidence rate across different countries (1). About 7.2 million PLHIV are currently receiving anti-retroviral treatments. Only by US President's Emergency plan for AIDS Relief (PEPFAR), more than $7.2 billion been invested in the fight against the HIV pandemic as of 2012. As a result of all the mitigation efforts, the HIV epidemic has stabilized and is now considered as a chronic disease condition (2).

On the other hand, Noncommunicable Diseases (NCDs) are the major current causes of mortality worldwide. About 36 million of the 57 million total deaths (62%) in 2008 were due to NCDs. NCDs cause three out of five deaths at global level. Of all NCD related deaths, 25% were under the age of 60 years and 80% were in low-and-middle income countries. About 30% of NCD deaths in low-and-middle income countries occur below the age of 60 years. Global annual NCD deaths are expected to reach 52 million in 2030 if appropriate actions are not going to be taken. Four common NCDs, Cardiovascular diseases, Cancers, Chronic respiratory diseases, and Diabetes,

account for about 80% of the total NCD deaths. Of these deaths, Cardiovascular diseases, Cancers, Chronic respiratory diseases and Diabetes accounted for 57%, 25%, 14% and 4% respectively. These four common NCDs share four common risk factors: Unhealthy diet, Insufficient physical activity, Tobacco use and Harmful use of alcohol (3).

Beyond being a major epidemic on their own, HIV/AIDS and NCDs have share many common features in terms of epidemiology, disease etiology, progression, and management. From aetiological perspective, both HIV/AIDS and NCDs have behavioural components in their risk factors. HIV/AIDS is associated with high-risk sexual behaviour. Commercial sex workers, men having sex with men and intravenous drug users are generally classified as high risk groups for HIV (4). Similarly, the common NCDs-Cardiovascular disease, cancers, diabetes and chronic respiratory disease- are associated with four major behavioural and lifestyle risk factors-Unhealthy diet, insufficient physical activity, tobacco use, and harmful use of alcohol (5).

Slow progression is a common feature in the pathogenesis of both HIV/AIDS and common NCDs. HIV has an average of ten years of clinically asymptomatic stage between primary HIV infection and the development of AIDS (19). Studies have indicated that the risk of many NCDs is set during development of an individual. Nutritional imbalance and exposure to environmental chemicals during development can increase NCD risk later in life, indicating the need for life-course

approach (6). Most NCDs are associated with persistent exposure to the risk factors. Many NCDs also have 'pre-diagnosis' stages that may last for years (7-9).

Recent evidence suggests that there are essential inter-relationships, between HIV/AIDS and the common NCDs. These inter-relationships occur at different levels. The inter-relationships could affect the risk of disease development, severity of progression, the management of the diseases and prognosis of the outcome. As HIV has evolved to become a chronic condition following the rapid scale up of anti-retroviral treatment coverage, the differences between HIV/AIDS and chronic NCDs is narrowing down. Thus, in the current antiretroviral treatment (ART) era, PLHIV on treatment tend to live longer and their corresponding risk of having NCDs is increasing (10).

Moreover, there is emerging evidence that suggest some functional similarities between the responses to HIV/AIDS and NCDs. As both HIV/AIDS and NCDs have a behavioural dimension in their risk of development, prevention efforts of both disease conditions are targeted at behavioural and/or lifestyle modification. Similarly, care and treatment interventions of both HIV/AIDS and NCDs involve long-term follow up targeted at improving quality of life through close monitoring of treatment adherence and health status. These similarities raised the issue of "why should we re-invent the wheel?" for the prevention and control of NCDs (11).

SYNDEMICITY OF HIV/AIDS AND NCDS

Beyond the fact that HIV/AIDS and NCDs are the major diseases of public health importance worldwide, they have *an epidemiological convergence*, an overlapping pattern of HIV/AIDS and NCD epidemics, in low-and-middle income countries where health systems are weak and resources to strengthen these health systems are scarce.

In those settings, the NCD epidemic is rapidly increasing while the HIV epidemic is still significant. Due to this convergence effect, many developing countries are facing "double-burden" of communicable and Noncommunicable diseases (12). Though it will be imperative to consider a *syndemicity* of HIV/AIDS and NCDs in developing countries, a macro-level study that establishes the joint epidemiological patterns of HIV/AIDS and NCDs hasn't yet been conducted.

LINKAGES BETWEEN HIV/AIDS AND NCDS

In low-and-middle income countries communicable diseases still cause a significant burden of morbidity and mortality. Communicable diseases account for 63% of deaths in Sub-Saharan Africa. Although their relative burden has decreased, communicable, newborn, nutritional and maternal causes remained to be the major causes of morbidity and mortality in Sub-Saharan Africa. On the other hand, the magnitude of common NCDs is constantly increasing in these settings as these parts of the world are undergoing rapid Demographic, Epidemiological, and Nutritional

transitions (13). While NCDs are the leading causes of death globally, communicable diseases remained to be the dominant causes of death in sub-Saharan Africa (14).

It is well acknowledged that infectious agents may predispose to Noncommunicable diseases. For example some viral infections are associated with the risk of developing cancers. Kaposi's sarcoma is caused by infection with the virus called *Kaposi's sarcoma herpesvirus*, also known as *Human Herpesvirus 8* (HH8). Cervical cancer is strongly associated with *Human Papilloma Virus* (HPV) infection. The most common risk factor of liver cancer is chronic infection with Hepatitis B virus (HBV) or Hepatitis C virus (HCV). Moreover, the two most common communicable diseases in Africa, HIV/AIDS and Tuberculosis, can also trigger the development of many NCDs by creating a favourable ground for other viral infections.

Conversely, NCDs can also predispose people to communicable diseases. For instance, the presence of Diabetes can predispose an individual to Tuberculosis (15). Studies have also shown that treatment of Communicable diseases, such as HIV, may be associated with the risk of developing metabolic abnormalities which are typical features of NCDs (16). Hence, there are complex linkages between Communicable diseases, like HIV/AIDS, and NCDs.

Linkage between diseases, any form of associative relationship between diseases at any stage of their development, can be viewed from two different perspectives. The first one is the view that the presence of one disease is associated with either

increased or decreased risk of developing the other disease. This could happen as a result of shared risk factors, or when the presence of the first disease affects the causal pathway of the second one in one way or another; or when the individual is highly susceptible to both diseases (17). The second view of linkage is when the first disease affects the progression and/or the prognosis of the second disease. This is usually due to the additive or synergistic effect of the two or more diseases on the individual (18).

HIV/AIDS is associated with the risk of developing several other diseases, including NCDs, due to the effects of the infection itself or the effects of the treatment of the infection. There are also other infections that are independently associated with HIV/AIDS and NCDs. The presence of some NCDs is also expected to affect the progression and prognosis of HIV infection (19). It is clear that the relationship between HIV/AIDS and NCDs is very complex to comprehend without stipulating the different aspects and forms of the relationship in to a simpler framework. Such a framework can be a basis for the study of the issues related to both HIV and NCDs and design interventions that target both HIV and NCDs.

HIV-NCD COMORBIDITIES

There is no standard definition of comorbidity. *Comorbidity* usually refers to the co-occurrence of two or more diseases or disorders in an individual (multimorbidity). It may also refer to the diseases or disorders that co-exist with an *index* disease. Defining comorbidity in a certain context requires clear understanding of the nature

of the co-occurring health conditions, the relative importance of these conditions, the chronology of their occurrence, and the domains of interest (20).

A number of different factors, ranging from genetic and biologic characteristics of an individual to the political and policy context which exert influence on health of people, play a role in the co-occurrence of diseases (17). Two diseases can co-occur by chance, selection bias or due to genuine etiological association. Genuine etiological association between diseases can occur in four ways: *Direct causation* (the presence of one disease or its management is directly responsible for the occurrence of the other), *associated risk factors* (the risk factors of one disease are associated with the risk factors of the other), *heterogeneity* (uncorrelated risk factors each capable of causing both diseases), and *independence* (the presence of diagnostic features of each disease is actually due to a third distinct disease) (21).

Comorbidity is usually associated with rapid disease progression, worse prognosis, complex disease management and high health care costs. Multiple diagnostic facilities, multidisciplinary health team, and multiple treatment regimens are needed for the management of comorbidities. Integrated health promotion and disease prevention approaches are also needed to prevent the occurrence of comorbidities. As the causes of comorbidities are different, it follows that the best approach for dealing with comorbidity depends on why a given pair of disorders tends to co-occur (18).

Comorbidities between HIV/AIDS and NCDs are important as the double-burden due to the two disease conditions in low-and-middle income countries is currently increasing. Evidence about the magnitude of comorbidity between HIV/AIDS and common NCDs is, therefore, needed to illustrate the extent of overlap between the two diseases and thereby designing strategies that address both disease conditions in an integrated manner.

RESPONSE PARALLELS

Previously, it was thought that there is a solid borderline between infectious disease, like HIV/AIDS, and NCDs. As HIV has now turned out to be a chronic condition, as many of the common NCDs are also chronic conditions, the interventions in the prevention and control of HIV/AIDS and NCDs share important similarities, the *response parallels*. Prevention efforts of both conditions are targeted at modifying risk behaviours. Treatment and care measures are targeted at improving quality of life through promotion long-term treatment adherence, regular monitoring of biomarkers, and sustained social support using the chronic care model (22).

Despite all these similarities between HIV/AIDS and NCDs in terms of chronic disease management models, the extent to which these similarities are reflected in the global and national level responses are not well explored. Analysis of the strategic level similarities between the response for HIV and NCDs will be helpful in identifying areas of overlap and thereby facilitate the coordination and integration of responses.

THE CONCEPT OF INTEGRATION

Integration is a multidimensional concept and can be interpreted in several different ways. Within the context of health systems integration means the organization of structures/functions to deliver a better quality service (23). The working definition of integrated services provided by the World Health Organization (2008) is "The management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system (24)." This definition implies that integration is a function of both management and delivery of health services, and its purpose is to ensure continuity of services that are needed to address client needs. Worth noting is that the central driving element in integrated healthcare is addressing client needs in a smart manner (25).

There are other similar terms which are usually confused with *integration* including *collaboration*, *linkage*, and *referral*. *Collaboration* refers to a mutually beneficial and well-defined relationship aimed at achieving common goals. Collaboration is to work jointly with others to achieve a common goal. *Linkage* is a formal process to ensure that the client has received the services to which he/she was referred and that the client's needs have been addressed. *Referral* on the other hand refers to a process by which immediate client needs for prevention, care, and supportive services are assessed and prioritized and clients are provided with assistance in identifying and accessing services. Referral can be both intra-facility and inter-

facility or community-facility and facility-community depending on the need of the client to be referred (26).

Integrated healthcare may mean different things for different peoples in the health system. From the perspective of *Healthcare service users* the key characteristics of an integrated healthcare include shorter waiting and service provision time, adequate presence of the needed services, limited number of steps and smooth flow through the steps, friendly provider-client interaction, and simple and easily understandable procedures in the process of service provision. For a healthcare provider it may mean meeting the technical standards and for a manager it may mean joining units in to same functions to reduce budget needs. For a policy maker, integration may mean putting things in to one policy framework (27).

HIV/AIDS AND INTEGRATION

Integration within HIV/AIDS program, *internal* integration, can be *horizontal* or *vertical*. Integration among prevention, care and treatment programs at a specific level of a health system can be considered as horizontal while integration of prevention programs across different levels of a health system can be viewed as vertical integration. These forms of integration are within the scope of the control of the HIV/AIDS responses (28).

On the other hand, integration of HIV/AIDS programs in to other programs, mainstreaming or sectoral integration, has remained to be the major modality of multi-sectoral response to the HIV/AIDS epidemic in most high HIV prevalent countries. Such responses are coordinated by one multi-sectoral response coordinating body and guided by one action framework. This type of integration also has one monitoring and evaluation framework in most cases (29).

Similarly, integrating other programs in to existing HIV/AIDS programs, for the benefit of PLHIV, has been one of the modalities of improving health and quality of life of PLHIV. Integration of Hepatitis C services, family planning services, in to HIV/AIDS programs are key examples of this form of integration (30, 31). Integration between HIV and other programs at the same level, inter-program integration, was in most cases based on the connectedness between HIV/AIDS and the other programs that are going to be integrated with HIV/AIDS. Key examples of this form of integration are integration of HIV/AIDS programs with reproductive

health programs, sexually transmitted infection programs and Tuberculosis programs (32-34).

As a result of the several parallels between HIV/AIDS and NCDs, integration of the responses could maximize synergy and improve efficiency. Though it seems appealing to integrate HIV/AIDS and NCDs programs in the health system context of developing countries, there are no models that can guide the integration process. This study will therefore develop a model that can help in designing, implementing and evaluating the integration of HIV/AIDS and NCDs programs in developing countries.

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ESSAY

Integration of HIV and Noncommunicable Diseases in Health Care Delivery in Low- and Middle-Income Countries

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HIV infection, a communicable disease, and noncommunicable diseases (NCDs) are among the major health concerns worldwide. An estimated 33 million people live with HIV, two-thirds of them in sub-Saharan Africa, where three-fourths of all AIDS-related deaths occur (1). Illness and death from NCDs exceed these numbers. In 2008, the last year for which figures are available, 36 million deaths were attributed to NCDs (2). In that same year, approximately 12.7 million people worldwide were living with cancer (2), and in 2011 approximately 366 million people worldwide were living with diabetes (3). The NCD burden is greatest in low- and middle-income countries, which account for an estimated 80% of all NCD-related deaths; about one-third of these deaths occur before age 60 years (4).

Until recently, diseases were considered either communicable (infectious) or chronic. As a result of advances in treatment, HIV infection now challenges that model so that the definition of chronic disease is not as simple or clear-cut as it once was. The World Health Organization describes chronic disease as a disease of long duration and slow progression (5). HIV and NCDs, a medical condition or diseases that are noninfectious, are now the major chronic diseases of public health concern, especially in low- and middle-income countries. Integrated approaches to address HIV infection and NCDs as well as other chronic diseases in these countries need to be developed.

Different chronic diseases have different clinical interrelationships. For example, people with HIV infection are at increased risk of other chronic infectious diseases such as tuberculosis and NCDs such as cancer, diabetes, and cardiovascular diseases (6). Antiretroviral treatments of HIV infection increase the risk of hyperlipidemia and diabetes. People living with HIV infection have 3 sources of risk of contracting NCDs: first, from HIV infection itself; second, from antiretroviral treatments; and third, from the risk associated with increasing age (7).

Chronic diseases share similarities in their risk factors, progression, and management. Unsafe sexual behavior is the major risk factor for HIV infection, and lifestyle factors such as unhealthy diet, insufficient physical activity, tobacco use, and alcohol abuse are the major risk factors for NCDs. Strategies for preventing HIV infection and NCDs are directed at modifying these behaviors and lifestyles. Effects of both HIV infection and NCDs develop progressively over time. As with management of NCDs, management of HIV infection focuses on positive health behaviors. The essential elements of prevention and management of HIV infection and NCDs — community and family support, patient involvement, and continuous follow up — are similar despite differences in the origin, pathogenesis, and clinical features of the diseases.

HIV/AIDS programs may be the largest chronic care programs implemented in most low- and middle-income countries. HIV programs involve the same elements of management of NCDs: promotion of healthy behaviors, long-term adherence to recommended treatment, regular monitoring of treatment outcomes, and active involvement of the client and family in care and treatment. Given the similarities in the prevention and management of HIV infection and NCDs, the models, tools, and approaches developed in the implementation of HIV programs could be adapted to address NCDs.

Many disease management programs are vertical; that is, they are implemented and directed in whole or to a large extent by a specialized health-delivery service and specialized health workers (8). These vertical programs have been effective in reducing the incidence of HIV infection in most low- and middle-income countries. We may need similar vertical programs to reduce the incidence of NCDs. However, it is not only the vertical nature of HIV programs that has

reduced incidence in low- and middle-income countries but also the coordinated efforts among the different stakeholders — associations of people living with HIV infection, partners of people with HIV infection, nongovernment organizations, and the communities in which people with HIV live — and funding support. This approach is similar to that employed in developed countries where NCD management is more integrated and decentralized, that is, centered in the lower levels of health care rather than centrally managed.

Low- and middle-income countries need to have strong and dynamic health systems that can respond effectively to changes in the epidemiologic pattern of diseases. These countries cannot afford to address diseases turn by turn. Chronic disease requires design of an all-inclusive model of management that is health-centered rather than disease-centered. The future direction of health care systems in developing countries should be health management rather than management of a single disease.

Integrated health systems that focus on the health needs of communities can offer several advantages in low- and middle-income countries. Integrated approaches provide people with holistic options centered on health needs of people and communities and thereby enhance community self-reliance. For example, the integration of HIV/AIDS, diabetes, and hypertension management in Cambodia has demonstrated high acceptance and good outcomes (9). Implementation of more integrated programs also helps to develop system effectiveness and cost-effectiveness, particularly in health systems with limited human resources.

Several arguments have been made for vertical health care programs. A vertical approach is believed to yield more rapid results in weak health systems (10). However, vertical programs aggravate weak health systems by diverting resources from more comprehensive approaches. Another argument for vertical approaches is related to accountability, that is, fear that integrated programs may not produce distinct deliverables and may not promote a transparent environment for accountability. However, integrated programs can be designed for transparency and accountability. It may be wise to take into account the opportunity costs of vertically designed health programs, which are more expensive than comprehensive vertically integrated programs.

In spite of its apparent advantages, integration is not a panacea. Context matters a lot. One of the risks of integrating a high-profile vertical program with a weak health system is that integration may weaken the program. Although in most situations the advantages of integrated approaches seem to outweigh the risks, integration will not mitigate the problems of limited resources and weak infrastructures. Different health system contexts should be considered on a case-by-case basis to determine whether smart and appealing integrated approaches can also have smart outcomes.

In some countries, HIV/AIDS interventions and services are already integrated with other health services and interventions, such as reproductive health, sexually transmitted infection, family planning, maternal health, nutrition, and other programs. The HIV-family planning integration in Kenya and Ethiopia is an example (10). In considering integration of HIV and NCD management, several critical questions must be considered. What would the effect on these programs be if HIV and NCD services are integrated? How do these existing programs affect the HIV–NCD integration? Should we fit NCDs into already existing integrated HIV programs?

An integrated approach to management of HIV and NCDs is appropriate not only for low- and middle-income countries but also may be appropriate for all countries. Although context-specific factors affecting integrated approaches vary from place to place and must be considered, the overall costs and outcomes of integrated HIV–NCD management should be thoroughly investigated before considering adoption of integrated approaches. More evidence on the feasibility and cost-effectiveness of different models of integration is also needed before pursuing integrated management of HIV and NCD in low- and middle-income countries.

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SUMMARY OF RATIONALE OF THE STUDY

The presence of convergence, linkages, and parallels between HIV/AIDS and NCDs and their responses warrants integrated responses in order to maximize synergy and improve efficiency. Acknowledging this fact, the political declaration of the high level meeting of the United Nations General assembly on the prevention and control of NCDs has adopted a resolution that states:

> Note with concern the possible *linkages* between non-communicable diseases and some communicable diseases, such as HIV/AIDS, and call to *integrate*, as appropriate, responses for HIV/AIDS and non-communicable diseases and, in this regard, for attention to be given to people living with HIV/AIDS, especially in countries with a high prevalence of HIV/AIDS and in accordance with national priorities (35).

From this declaration, it is evidence that there is a political acknowledgement of the linkages between HIV and NCDs. There is also a clear call for integration of responses. Despite this political acknowledgement of the linkages between HIV/AIDS and NCDs, and thereby the need for integrated responses, there exist paucity of evidence with regard to the frameworks of linkages, magnitude of comorbidities, extent of parallels and models of integration. Therefore, there is an urgent need to address these evidence gaps, especially in the context of developing countries. This research has been planned to contribute to closing this evidence gap.

RESEARCH AIM AND OBJECTIVES

Aim 1

To analyse the inter-relationships between HIV/AIDS and NCDs

Objectives

1. To analyse the epidemiological *convergence* between HIV/AIDS and NCDs;
2. To develop a Public Health framework for the possible epidemiological *linkages* between HIV/AIDS and common NCDs;
3. To assess the *co-occurrence* of HIV/AIDS and NCDs; and
4. To examine the *similarities and differences* between responses to HIV/AIDS and NCDs

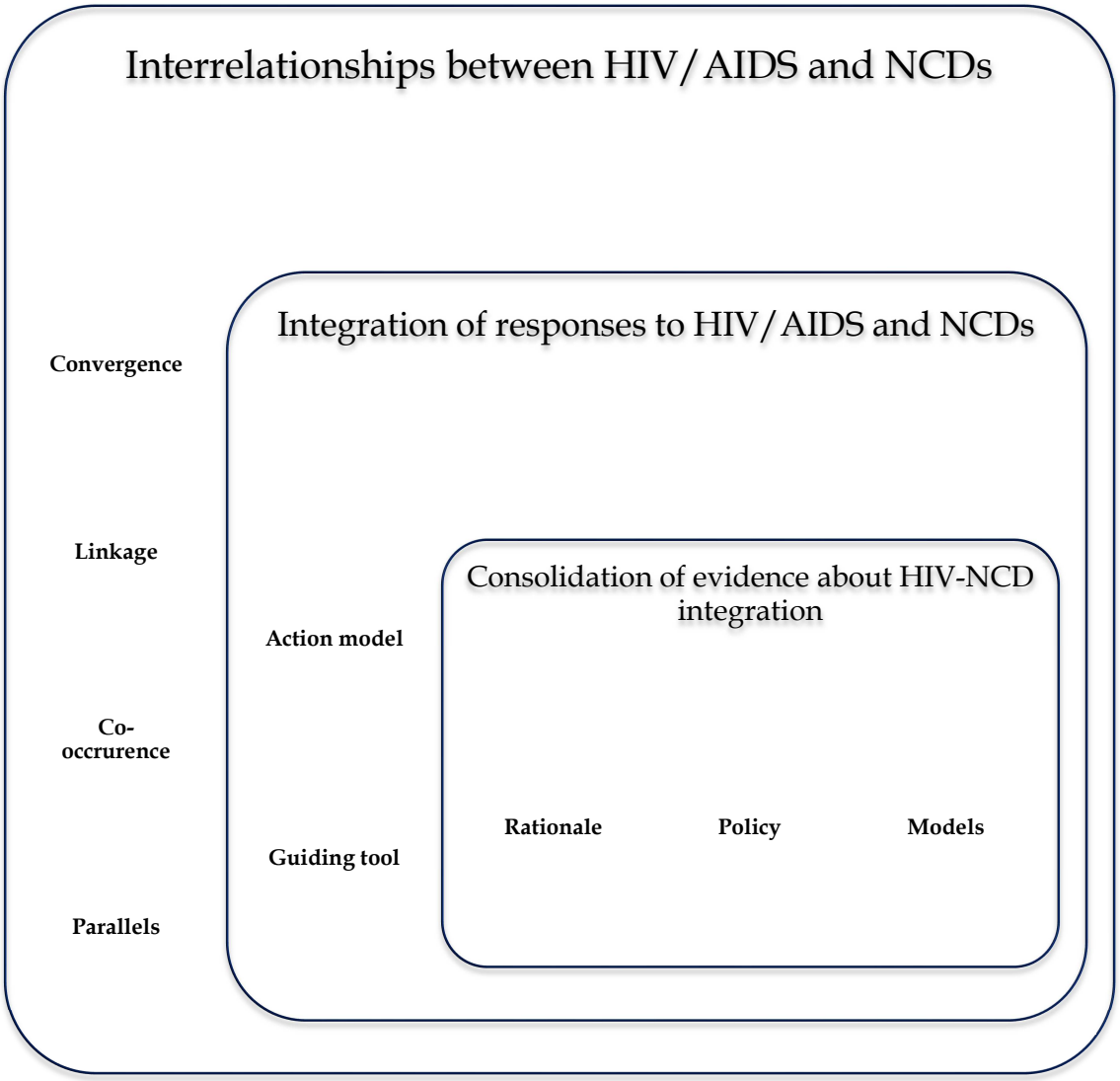
Aim 2

To develop an action model that can assist the integration of health system responses to HIV/AIDS and NCDs in developing countries

Objectives

1. To design an action model for the integration of health system responses to HIV/AIDS and NCDs
2. To develop a guiding tool for the integration of health system responses to HIV/AIDS and NCDs
3. To summarize the rationale, policies and existing models of HIV-NCD integration in developing countries

Fig 1: The framework of the overall PhD research



OVERVIEW OF METHODOLOGY

The overall PhD research is focuses on the context of macro-level Health systems, national and global levels, of developing countries. It used mixed-method research and model development as its overarching study designs. This PhD research is comprised of seven studies. The first four studies **generate** evidence about the inter-relationships between HIV/AIDS and NCDs at population, disease, individual, and health system response levels. The next two studies **apply** the evidence about inter-relationships in to the development of action model and guiding tool. The final paper consolidates evidence on rationale, policies and models of HIV-NCD integration based on the contexts of developing countries.

Analysis of the similarities and differences between health system responses to HIV/AIDS and NCDs is the central element of this PhD research. The similarities and differences between global and national responses (in four case countries) was analysed using qualitative content analysis of information collected from policy and programmatic documents and key informant interviews.

Using evidence of the inter-relationships between HIV/AIDS and NCDs at population, disease and individual levels; and knowledge of the similarities and differences between the responses to HIV/AIDS and NCDs, a model of integration is developed. Pragmatic approach and the constructivist paradigm were used in the development of the integration model. Different methods were applied at different stages of this PhD research. The methods used at different stages of this PhD research are presented in the following table.

Table 1: Methods used at different stages of the PhD research

Title	Summary of methods
Epidemiological patterns of HIV/AIDS and NCDs	Ecological study using correlational and cluster analysis
Epidemiological Linkage between HIV/AIDS and NCDs	Thematic research synthesis (aggregative and integrative) and framework development (configurative synthesis)
Epidemiology of comorbidities between HIV/AIDS and NCDs	Critical and systematic reviews: One critical review and two systematic reviews of magnitude of common NCDs in HIV+ people
Parallels/similarities and differences between responses to HIV/AIDS and NCDs	Qualitative content analysis of global and national responses to HIV/AIDS and NCDs to explore similarities and differences.
Developing action model for integration of responses	Inductive approach to modelling with multi-and-trans disciplinary review of evidence
Preparation of a guiding tool for integration	Operationalization of the action model, conceptual validation and expert consultations
Rationale, policies and models of HIV-NCD integration	Qualitative interpretive synthesis of policies, feasibility studies and pilot HIV-NCD integration projects.

Details of the methods are presented inside the articles included in the subsequent chapters.

Chapter 2

Epidemiological convergence of HIV/AIDS and NCDs

CHAPTER 2 OVERVIEW

Having established the rationale and objectives of the overall PhD research, chapter 2 presents a study on the first level of interrelationships between HIV/AIDS and NCDs: Epidemiological convergence, a population level inter-relationship, of HIV/AIDS and NCDs in developing countries. With the aim of exploring epidemiological convergence of HIV/ADS and NCDs at macro-level, this chapter presents an ecological study of epidemiological patterns of HIV/AIDS and Diabetes (considered to be a prototype NCD) in 68 developing countries in Sub-Saharan Africa, Southern Asia and South-Eastern Asia region. National level HIV prevalence and Diabetes prevalence data at four time points between 2000 and 2010 were used in this analysis. Using correlational analysis of logit transformed data, the study examines whether countries with higher HIV prevalence also have higher prevalence of Diabetes. It also examines the relationship between trends of HIV and Diabetes prevalence across time and geographic regions. More importantly, the study identified groups of countries with similar joint patterns of HIV/AIDS and Diabetes using cluster analysis techniques. The findings are expected to inform macro-level policies and approaches in the prevention and control of HIV/AIDS and NCD epidemics.

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PUBLICATION DECLARATION
Declaration for Thesis Chapter 2

Declaration by candidate

In the case of Chapter 2, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
TNH designed the study, wrote the protocol, performed the statistical analysis, and wrote the first draft of the manuscript.	75%

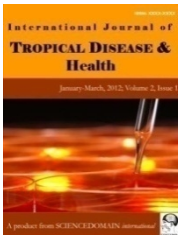
The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Brian Oldenburg	Supervised the study and reviewed the manuscript	N/A
Julian Elliott	Supervised the study and reviewed the manuscript	N/A
Geoffrey Setswe	Supervised the study and reviewed the manuscript	N/A

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.



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Epidemiological Patterns of HIV/AIDS and Diabetes in Developing Countries: A Cluster Analysis

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Authors' contributions

This work was carried out in collaboration between all authors. Author TNH designed the study, wrote the protocol, performed the statistical analysis, and wrote the first draft of the manuscript. Authors BO, JE and GS supervised the study and reviewed the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Introduction: HIV/AIDS and Noncommunicable diseases are the major public health threats of developing countries. Analysis of joint epidemiological patterns of these diseases will help in designing and implementing appropriate interventions to mitigate their impacts.
Objectives: The overall aim of this study was to analyze Epidemiological patterns of HIV/AIDS and Diabetes in developing countries.
Methods: Country level HIV/AIDS and Diabetes prevalence data at four time points, between 2000 and 2010, for 68 countries in Sub-Saharan Africa, Southern and South Eastern Asia were transformed and analyzed. Joint geographic and temporal trends were described using numerical and graphic summaries. The level of Covariation between HIV and Diabetes prevalence was measured by Pearson correlation. K-means cluster analysis was conducted after the appropriate number of clusters was determined using scree plot technique. Analysis of variance was used to identify factors that differentiate

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the clusters.
Results: Diabetes had higher mean prevalence with increasing trend while HIV/AIDS had higher disability-weight adjusted mean prevalence with a decreasing trend during the study period. The findings suggest that HIV/AIDS and Diabetes were negatively correlated throughout the study period ($r > 0.3$, $P < .05$ in all four time points). Hence, countries with higher prevalence of Diabetes tend to have lower prevalence of HIV/AIDS and vice versa. Four clusters of countries with size 29, 12, 12 and 14 countries were identified. These clusters were found to have significant variation with respect to their mean HIV and Diabetes prevalences as well as time trends in their mean prevalences.
Conclusions: Diabetes and HIV are heading in reverse directions during the study period in the study regions. The identified clusters were found to describe these patterns of variation across geography and time. The clusters may be useful in considering a set of coordinated country level interventions.

Keywords: Epidemiological patterns; HIV/AIDS; diabetes; cluster analysis.

1. INTRODUCTION

Due to the emergence of Noncommunicable diseases (NCDs) in the developing world, the prevalence of Diabetes has been continuously increasing in developing countries during the last decade. Developing countries currently bear the largest share of magnitude and burden of diabetes mellitus. The current increase in the magnitude of diabetes is attributed to both population growth and actual increase in the incidence of diabetes. Most of diabetes related deaths also occur in developing countries as health systems in these settings are weak and most cases are left undiagnosed or diagnosed at near-miss stage. Currently, Southern and South Eastern Asia regions have highest diabetes prevalence. Sub-Saharan Africa is expected to have to have the highest increase in its diabetes magnitude in the upcoming years [1-6].

Developing countries, especially those in sub-Saharan Africa and Southern and South Eastern Asia, have also been severely affected by the HIV pandemic. Due to the intensified and multi-sectoral response, the HIV prevalence in these regions is currently stabilizing. HIV Deaths and new HIV infections has dramatically decreased in these regions. However, a few countries are still having an increasing number of new HIV infections [7-10].

Recent evidences suggest that there are important relationships between HIV and Diabetes. These relationships are mainly expressed in three forms: Epidemiological overlap, clinical interaction and Health system parallels. The epidemiological overlap indicates that there is a co-occurrence of HIV and Diabetes, double-burden, in developing countries while the clinical interaction addresses the effect of HIV in the risk, management and complications of Diabetes. The parallels in the Health system responses to HIV and Diabetes warrant possible integration of the responses [11-16].

Although Sub-Saharan Africa, South and South Eastern Asia regions are presumed to have Epidemiological overlap of Diabetes and HIV/AIDS, little is known about the joint patterns of HIV and Diabetes in these geographical regions. The joint time and geographical trends, and the relationship in these trends are not well clearly understood. Whether countries with high prevalence or changes in prevalence of diabetes also have the same or opposite patterns in HIV are not well established. Thus, countries which have similar patterns in the joint epidemiological pattern of HIV and Diabetes need to be identified for coordinated responses.

In light of these, the overall aim of this study was to analyze the Epidemiological patterns of HIV and Diabetes in developing countries. The specific objectives were to describe the trends, to determine the level of co-variation, to identify operational clusters of countries and to describe the factors of that differentiate the identified clusters.

2. MATERIALS AND METHODS

2.1 Study Design

This study on the Epidemiological patterns of HIV and Diabetes in developing countries was a time-series cross-sectional study, with cross-sectional dominance on country level prevalence of HIV and Diabetes. Besides the comparison across time and geography for each, HIV and Diabetes prevalence data were also compared at four major time points during the study period.

2.2 Study Period

The analysis period considered for this study was the period from 2000 to 2010. Four time points were considered in this study period. These were 2000, 2003, 2007 and 2010. These points were selected based on the availability of complete HIV and Diabetes prevalence data for the selected countries. This analysis was conducted from Jan to Mar 2012.

2.3 Sample and Sampling

Three regions (based on the UN classification) were purposively selected for this study. The regions were Southern Asia, South Eastern Asia and Sub-Saharan Africa. The purpose of the selection was based on magnitude of HIV and Diabetes. Morbidity and Mortality statistics of HIV and Diabetes in these regions showed that the regions already have high burden of HIV and currently are bearing rapid emergence of diabetes. This study took in to account all countries in the selected regions as units of analysis during the study period. A total of 68 countries with a total population of nearly 3 billion were included in the analysis.

2.4 Data Sources

Country level HIV and Diabetes prevalence data were retrieved from relevant secondary sources including World Health Organization (WHO), Joint United Nations Program on HIV/AIDS (UNAIDS), and International Diabetes Federation (IDF) documents. Other relevant background variables were also collected along with the prevalence data. The background and prevalence data were matched for each country. To ensure completeness of the prevalence data, relevant country level data sources were explored.

2.5 Study Variables

The main study variables used in this study were the prevalence of HIV among the 15-49 years of age group population, and the prevalence of diabetes in the 20-79 years of age population in 2000, 2003, 2007 and 2010 for those selected countries. The rest of the variables were background characteristics of the countries like development category, income group, population size, and Human Development Index (HDI).

2.6 Data Quality Issues

Country level data for those indicators were obtained for the majority of the countries from UNAIDS and IDF data tables and reports of the specific years. For some countries, their Diabetes prevalence (for the year) 2000 was calculated from their estimated number of diabetes cases reported by WHO. For a few countries having only the upper limit of the HIV prevalence, that upper limit was considered in this study. For one country with HIV prevalence reported in intervals only, the mid-point of that interval was taken.

2.7 Data Transformation

As HIV and Diabetes prevalence data were proportions bounded between 0 and 1, they didn't fit with or couldn't be approximated by the normal distribution. Besides, the majority of the data were close to zero making arcsine transformation less appropriate. Therefore, the logit transformation [Y=log(X/(1-X)] was applied to the data before any statistical analysis. Descriptive measures were back-transformed to original data form, i.e. the anti-logit (X= Exp (Y)/ (1+EXP(Y)).

2.8 Data Analysis

2.8.1 Description of trends

Prevalence data were first described using both numerical and graphical summaries of geographical and time trends. After logit transformation, confidence intervals were used to test the statistical significance of the difference between paired values of prevalence figures across groups of countries. HIV and Diabetes prevalence data were also compared across time and geographic regions. The mean prevalence of HIV and Diabetes were adjusted by their respective disability weights to take in to account the severity of the diseases during the comparison.

2.8.2 Assessment of covariation

In order to assess the level of co-variation between the prevalence of HIV and Diabetes across countries at the study time points, Pearson product moment correlation coefficient was used. This was applied on pairs of HIV and Diabetes data at the four time points of analysis. The trend of the Covariation across time was observed. The correlation was also determined at regional and income group levels. The correlation between ratios of Diabetes prevalence to HIV prevalence among the different years was analyzed to see if there were consistencies in the ratio across time. The serial correlation in HIV and Diabetes prevalence was also analyzed. P values less that .05 were considered to indicate statistical significance of the correlation.

2.8.3 Cluster analysis

K-means cluster analysis was used to explore patterns of the prevalence of HIV and Diabetes among the study countries. This method was chosen due to small number of time points involved in the study, a cross-sectional dominance data. The number of clusters was determined by scree plot and its explained variance in the transposed dataset. Iterate and classify method with convergence criterion of zero was used in the cluster analysis. The

resulting clusters were described in terms of their geographical location, development category and income groups.

Analysis of variance was used to determine which variables differentiate between the clusters identified in the cluster analysis. Actual tests of the differences in the mean prevalence of diabetes and HIV at those points of time among the clusters were conducted by multiple comparison (post-hoc) tests. Variables that significantly vary across clusters were considered to be predictors of those specific clusters.

3. RESULTS AND DISCUSSION

3.1 Description of Joint Trends

Persistently high Diabetes prevalence during the study period was observed in Singapore, Seychelles, Mauritius, Brunei, and Reunion. Persistently high HIV prevalence was observed in Swaziland, Botswana, Zimbabwe, Lesotho, Zambia, and South Africa. On the other hand, persistently lower Diabetes prevalence was observed in Eastern Africa region while constantly lowest HIV prevalence was observed in Southern Asia region. As to the overall change in prevalence between 2000 and 2010, Sri Lanka and Reunion had the highest increase in diabetes while Zimbabwe and Namibia had the highest decrease in HIV prevalence.

The overall time trend of HIV and Diabetes prevalence indicated that the HIV prevalence was getting stabilized in the study regions while diabetes prevalence was continuously increasing during the study period. The increase in the mean prevalence of diabetes looks to follow exponential pattern while the decrease in the mean HIV prevalence fits better with the logarithmic pattern. The difference between the mean prevalence of Diabetes and HIV was also getting higher across time. This difference had increased by more than two-fold during the study period. The trends in the mean prevalence of diabetes and HIV in the study area is shown in Fig. 1.

The mean prevalence of HIV and Diabetes across time, separately calculated for the Africa and Asia study regions showed that the Asia region had a wide disparity between prevalence of HIV and Diabetes while the Africa region had narrow disparity between HIV and Diabetes prevalence. The prevalence lines of both HIV and Diabetes for the Africa region lies between the prevalence lines of diabetes and HIV for the Asia region. Besides, there were reversals at two points between the mean prevalence of HIV and Diabetes in the African region.

Adjusting the mean prevalence of HIV and Diabetes by the average disability weights of the two diseases, which were 0.135 and 0.015 for HIV and Diabetes respectively [17], had reversed the trends in the mean prevalence of HIV and Diabetes. This suggested that burden of HIV was still much higher than that of Diabetes even though the prevalence figures informs the opposite in terms of proportions of people with the disease (Fig. 2).

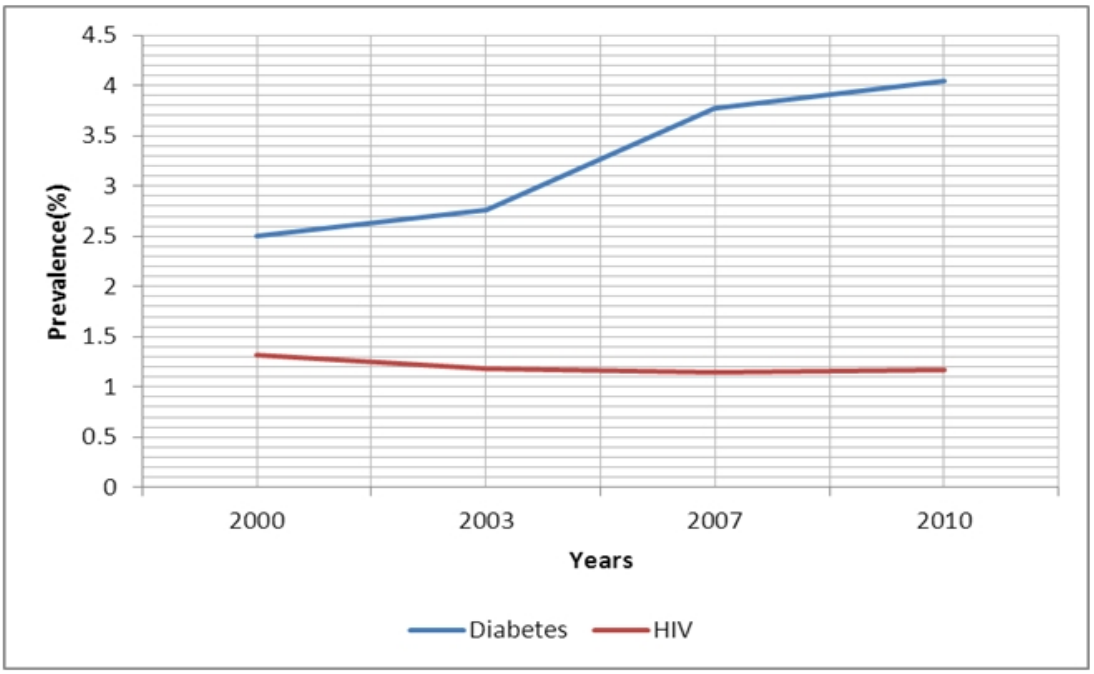

Fig. 1. Trends in the mean prevalence of HIV and Diabetes in the study region (2000-2010)

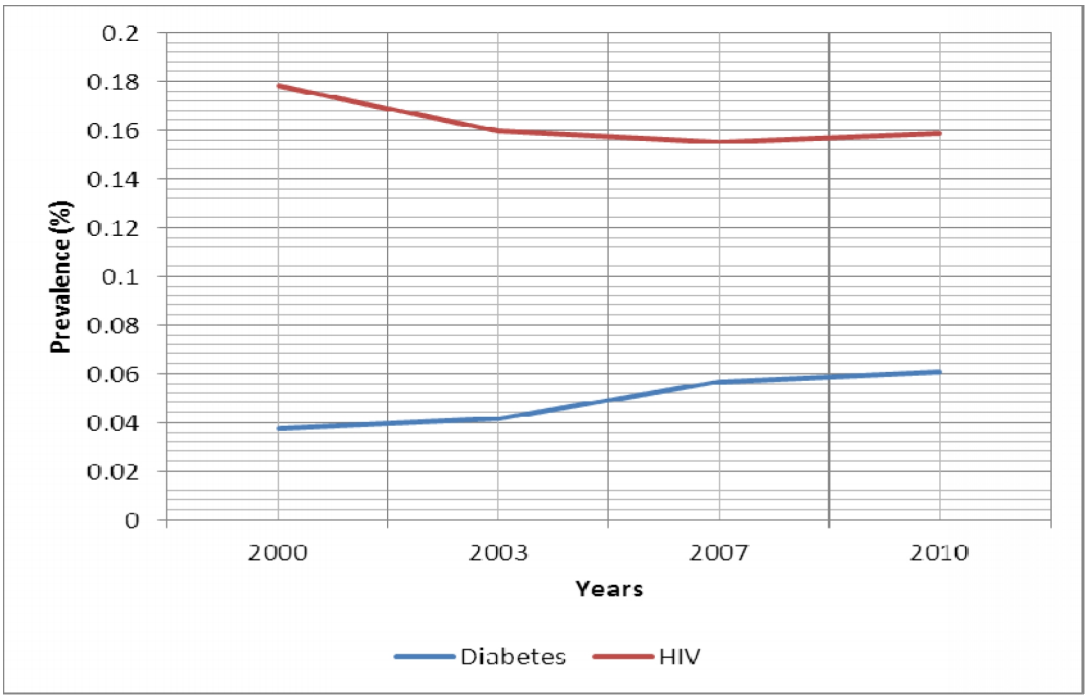

Fig. 2. Disability weight adjusted mean prevalence of HIV and Diabetes (2000-2010)

Disaggregated analysis of adjusted prevalence of HIV and Diabetes for the Africa and Asia regions indicated that the African HIV burden is more than 3-fold of the Asian Diabetes burden which has been demonstrating a rapid increase in the recent years. The Asian HIV and the African Diabetes burden were relatively lower. However, these prevalence figures were showing an increasing pattern in the more recent years.

3.2 Association between HIV and Diabetes Prevalence

The serial correlations between subsequent time points for diabetes prevalence had shown an increasing pattern suggesting persistence in countries' diabetes prevalence. The average serial correlation for Diabetes was 0.624 (0.498 for Asia and 0.655 for Africa). The serial correlations for HIV prevalence had stabilized at higher level and showed minimal increment across time. The average serial correlation for HIV prevalence was 0.955 (0.843 for Asia and 0.953 for Africa).

On the other hand, the serial correlations among the ratios of Diabetes prevalence to HIV prevalence at all the four time points was very high (each more than +0.90 and P=0.000) indicating that the ratio of diabetes to HIV prevalence in countries is persistent across time, i.e. countries which had high ratio in 2000 are still having high ratio in 2010 and vice versa.

The findings of this study suggested that HIV and Diabetes were negatively correlated throughout the study period indicating that countries with higher prevalence of diabetes tend to have lower prevalence of HIV and vice versa. However, the level of correlation is relatively lower though it attained statistical significance at all-time points. The correlation between HIV and Diabetes prevalence had shown a decrement between 2000 (r=-0.434, P <.001) and 2003 (r=-0.281, P=0.02). After this decrement, it was showing a constant increase in 2007 (r=-0.346, P=.004) and 2010 (r=-0.440, P < .001) indicating that the disparity between the prevalence of HIV and Diabetes the study countries was getting higher and higher.

Disaggregated analysis of the correlation between the prevalence of HIV and Diabetes for the Africa and Asia regions indicated no statistically significant correlation except for the Africa region in the year 2000 when the correlation was -0.382 (P=.008). Examination of the correlation between changes in HIV and Diabetes prevalence between 2000 and 2010 indicated that there was no statistically significant correlation between the changes in Diabetes prevalence and the changes in HIV prevalence across countries (r=-0.102, P=.43).

Comparison of the correlation between the prevalence of HIV and Diabetes between low income and non-low income (middle plus higher income) countries indicated that the level of correlation in the low income countries was higher than the overall correlation and the correlation for non-low income countries at all of the time points. The correlation for the years 2000, 2003, 2007 and 2010 were -0.0402,-0.530,-0.472 and -0.475 respectively all with P < .001. The correlation between prevalence of HIV and Diabetes in non-low income countries was statistically significant for the years 2000 (r=-0.361, P <.001) and 2010 (r=-0.424, P < .001) only. In 2003 and 2007, the correlation between HIV and Diabetes prevalence for the non-low income countries was negative but hasn't attained any statistical significance.

3.3 Cluster Analysis

The scree plot on the transposed data using the principal component analysis extraction method indicated that the eigenvalues start to level off at about four components. Hence, the number of clusters was determined to be four. The K-means cluster analysis has thus resulted clusters with cluster sizes of 29, 12, 12 and 14. The cluster analysis was based on the logit transformed prevalence of HIV and Diabetes at the four time points considered in this study. The following are the clusters identified.

Cluster I: This cluster is composed of 3 countries from South Eastern Asia, 5 countries from Eastern Africa, 6 countries from middle Africa, and 15 countries from western Africa. Based on their income groups, this cluster consisted of 18 lower income, 10 middle income and 1 high income countries.

Cluster II: This cluster encompasses 3 countries from South Eastern Asia, 3 Island countries from Africa 3 and 6 countries from Southern Asia. Four of these countries are in the low income group while the rest 6 are in the middle-income group.

Cluster III: This cluster had 3 countries from Southern Asia, 4 countries from Eastern Africa, and 5 countries from South Eastern Asia. In this cluster 2 countries are high income and 2 countries are low income while the rest were middle income groups.

Cluster IV: All the members of this cluster are entirely African countries. Two countries from middle Africa, 5 countries from Southern Africa, and 7 countries from Eastern Africa were the members of this cluster. Half of the countries in this cluster are in low income groups while the rest half are in the middle income groups.

Comparison of the Human Development Index (HDI) for the year 2011 among the clusters indicate a statistically significant difference between cluster I and II which had mean HDI of 0.42 and 0.56 respectively.

Table 1. List of countries by clusters of HIV/AIDS and diabetes prevalence

Clusters	Prevalence categories	List of countries
I	HIV/AIDS: Medium Diabetes: Low	Angola, Chad, Congo, Democratic Republic of Congo, Equatorial Guinea and Gabon, Benin, Burkina Faso, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo, Cambodia, Myanmar, Thailand
II	HIV/AIDS: Very low Diabetes: Medium	Cape Verde, Comoros, Madagascar, Indonesia, Lao PDR and Philippines, Bangladesh, Bhutan, Maldives, Sri Lanka, Afghanistan, Iran
III	HIV/AIDS: Low Diabetes: High	Reunion, Seychelles, Somalia, Sudan, India, Mauritius and Nepal, Brunei Darussalam, Malaysia, Singapore, Timor-Leste, Vietnam
IV	HIV/AIDS: High Diabetes: Low	Cameroon and Central African Republic, Botswana, Lesotho, Namibia, South Africa and Swaziland, Kenya, Malawi, Mozambique, Uganda, Tanzania, Zambia, Zimbabwe

3.4 Patterns of HIV and Diabetes in the Clusters

Analysis of variance indicated that the clusters vary significantly with respect to all HIV and Diabetes prevalence variables. By categorizing the trend in the mean HIV and Diabetes prevalence of the clusters in to high, medium, low and very low, the pattern of HIV and diabetes prevalence in the clusters can be characterized as follows.

Cluster I: The mean prevalence of Diabetes in this cluster had increased from 1.54% to 3.30% between 2000 and 2010. In the same cluster, the mean prevalence of HIV has decreased from 3.19% to 1.76% between 2000 and 2010. In this cluster, there was reversal of mean HIV and Diabetes prevalence between 2000 and 2003.

Cluster II: The HIV prevalence was constantly low in this cluster but with smaller increases across time, about 0.2% in 10 years. Though still at lower level the mean prevalence of Diabetes in this cluster had increased from 2.75% to 5.01% between 2000 and 2010.

Cluster III: The mean Diabetes prevalence for this cluster was above 5% in at all the points of the study period. The general trend in the mean prevalence for this cluster was also increasing. The HIV prevalence in this cluster, though still low, was higher than that of cluster II. The mean HIV prevalence for this cluster had an increasing trend. It had increased from 0.21% to 0.29% during the 10 years study period.

Cluster IV: The mean HIV prevalence in this cluster was still above 10% though it had shown a declining trend between 2000 and 2010. The mean Diabetes prevalence in this cluster had shown an increasing trend from 1.64% to 3.22% between 2000 and 2010.

Mean diabetes prevalence significantly varied between clusters I and III at all-time points. It also significantly varied between cluster III and IV at all points. The difference in mean diabetes prevalence between cluster II and III was also significant for the years 2000 and 2003. All the cluster combinations at all the four years had differences mean HIV prevalence that varies significantly.

On the other hand, mean diabetes prevalence hasn't shown a statistically significant variation between clusters I and II, I and IV and II and IV at all-time points. Besides, the mean difference in diabetes prevalence between cluster III and IV hasn't attained statistical significance for the years 2007 and 2010.

4. DISCUSSION

The prevalence figures indicate that diabetes in the study area had higher magnitude as compared to HIV. The number of people with diabetes is also much higher than that of people living with HIV in the region. However, the burden of HIV, based on the disability weights, was much higher than that of Diabetes at all the time points. This paradox indicates that HIV is putting much burden even though diabetes is affecting more people. But this viewpoint changes when the Sub-Saharan Africa and the Asia study regions are seen separately. The Sub-Saharan Africa had higher magnitude and burden of HIV while Southern and South Eastern Asia had higher magnitude and burden of Diabetes [18,19].

Looking in to the trends of prevalence across time, the prevalence of diabetes was increasing at a rapid rate while the prevalence of HIV was getting stabilized. This implies that

the incidence of diabetes was much higher than that of HIV in these study regions. Clearly, the prevalence of HIV in Sub-Saharan Africa was greater than that of Diabetes, while the prevalence of Diabetes in Southern and South Eastern Asia was greater than that of HIV. But in both regions the incidence of Diabetes was much greater than that of HIV.

The high level of serial correlation in HIV and Diabetes prevalences imply that the relative prevalence of HIV and Diabetes in the study countries had a persistence nature. This means countries tend to 'retain' their relative prevalence during the study period. This was also verified by the serial correlations in the ratio of diabetes to HIV prevalence across time. Both HIV and Diabetes prevalence tend to change in a similar manner among countries.

This study has indicated that correlation between HIV and Diabetes prevalence at all points was negative. This crudely suggests that countries with high HIV prevalence have relatively lower Diabetes prevalence and vice versa. This was partially explained by the high prevalence of HIV in Sub-Saharan Africa and a correspondingly low prevalence of diabetes in the same region, and low prevalence of HIV in the Asian study region which had high diabetes prevalence.

The clusters identified in this study have several importances for public health policy and practice. It informs whether HIV, Diabetes or both should be major priorities among countries in the clusters. The classification also informs what models of integrating HIV and Diabetes services could be applicable for countries in the different clusters. Above and beyond, the cluster analysis has suggested international level focus countries for HIV, Diabetes and both HIV and Diabetes.

There were a few limitations associated with this study. Firstly, the data used in this study were prevalence estimates and all the weaknesses of these data can affect the interpretations of the findings. Secondly, the K-means clustering method was applied as the dataset was very short time-series data. The autocorrelation among the variables may to some extent affect the quality of the cluster analysis. Finally, the study addresses only three major regions of developing countries and thus the findings may not apply to other regions of the world.

5. CONCLUSION

Overall, this study has indicated that the joint epidemiologic patterns of prevalence of HIV and Diabetes tend to be heading in opposite directions suggesting that the incidences of the two diseases are also advancing in opposite direction. This pattern, however, varies from region to region.

CONSENT

Country level HIV/AIDS and Diabetes prevalence data were retrieved from information within the public domain. All the data sources used were cited and acknowledged as per the guidelines provided along with the information. No other form of consent was required as this study didn't involve human subjects at any stage.

ETHICAL APPROVAL

All authors hereby declare that this study is conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All the processes involved in this study were carried out as per local and international Ethical requirements.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Chapter 3

Epidemiological linkage between HIV/AIDS and NCDs

CHAPTER 3 OVERVIEW

Having described the epidemiological convergence of HIV/AIDS and NCDs at population level, Chapter 3 presents an article about a second level of interrelationships between HIV/AIDS and NCDs: Epidemiological linkages between HIV/AIDS and NCDs. Linkage in this study is defined as any form of disease-level associative relationship between HIV/AIDS and the four common NCDs (Cardiovascular diseases, Cancer, Type 2 Diabetes, and Chronic Respiratory diseases). Linkages related to risk of development of diseases and severities of progression of disease are considered. Direct and indirect pathways of linkage are also described. The study used thematic research synthesis (aggregative and integrative) to identify the different forms and types of linkage; and a configurative synthesis to develop a public health framework that summarizes the important epidemiological linkages between HIV/AIDS and the common NCDs. Evidence about these linkages is expected to be useful in the design of intervention packages that target HIV/AIDS and NCDs, especially in resource-limited settings. The public health framework will also be an important tool for public health research, policy and practice.

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Publication Declaration

Declaration for Thesis Chapter 3

Declaration by candidate

In the case of Chapter 3, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Tilahun Nigatu Haregu conceptualized and refined the concept of the study, designed the study, conducted data extraction, analysis and writing.	70%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Brian Oldenburg	Critically revised the manuscript	N/A
Julian Elliott	Contributed to refinement of the framework	N/A
Geoffrey Setswe	Critically reviewed the manuscript	N/A

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**Jun 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

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Developing a Public Health Framework for the Epidemiological Linkages between HIV/AIDS and NCDs: *A Thematic Research Synthesis*

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Abstract The Political Declaration of High-level Meeting of the General Assembly on the Prevention and Control of NCDs has noted possible linkages between HIV/AIDS and NCDs. The aim of this study was to develop a public health framework for those linkages between HIV/AIDS and the common NCDs. The overall method used in this study was a thematic research synthesis. Descriptive, integrative and configurative syntheses of evidence on linkages between HIV/AIDS and NCDs were conducted. The searching process was iterative; appraisal was stepwise; and extraction was verbatim. All retrieved information was described, analysed and then configured in to a concept map using major pathways of relationships between HIV/AIDS and NCDs. The concept map was developed in to the public health framework through progressive review and revisions. Two major forms and pathways of linkages between HIV/AIDS and NCDs were identified. There are five nodes that mediate the indirect HIV-NCD linkage: common underlying factors, life style factors, antiretroviral treatment, common complications, and other mediating disease conditions. These linkages along with mediating factors are organized in to a public health framework. In conclusion, the main pathways and forms of relationship between HIV/AIDS and NCDs were described; and a public health framework for the epidemiological interrelationships between HIV/AIDS and NCDs was developed.

Keywords Epidemiological Linkage, Public Health Framework, HIV/AIDS , NCDs

1. Introduction

After three decades in to the HIV epidemic, there are more than 33 million People living with HIV (PLHIV), two third of which are in sub-Saharan Africa. HIV/AIDS was a cause for about 1.8 million deaths in 2010. In the same year, 2.1 million new HIV infections have occurred. About 90% of these new HIV infections were in sub-Saharan Africa. Globally, the incidence of HIV has decreased by about 19% between 2001 and 2009. However, there is still dramatic variability in the change in incidence rate in specific settings[1]. About 7.2 million PLHIV are currently receiving antiretroviral treatment (ART). A lot has also been invested in the fight against this pandemic[2].

On the other hand, Noncommunicable diseases (NCDs) are the major killers worldwide. About 36 million of the 57 million total global deaths in 2008 were due to NCDs. NCDs cause three of the five deaths globally. The four common NCDs, Cardiovascular diseases (CVD), cancers, chronic respiratory diseases (CRD), and Diabetes, account for about 80% of the total NCD deaths. The majority, 80%, of the total NCD deaths occur in low-and-middle income countries. About 30% of NCD deaths are among people below 60 years of age[3]. The total NCD deaths are expected to reach 52 million if appropriate actions are not going to be taken. The four common NCDs share four common risk factors: unhealthy diet, insufficient physical activity, tobacco use and harmful use of alcohol.

The possible linkages between HIV/AIDS and NCDs are recognized at a higher level political declaration of the United Nations General Assembly on NCDs. The General assembly has acknowledged important linkages, associative relations, between the two disease conditions. These important linkages between HIV and NCDs are recommended for consideration, as appropriate, in the integration of health system responses to HIV/AIDS and NCDs[4]. The translation of these linkages in to the concept of integration of interventions needs public health models that illustrate broader perspectives of their relationships.

The interrelationship between HIV/AIDS and NCDs is complex and multidimensional. It also has various impacts

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on the development, progression and outcomes of both disease conditions. Nevertheless, there is minimal research documenting the impact and burden of common comorbidities of HIV/AIDS and NCDs. There are several studies that have examined the effect of antiretroviral treatments on the risk of developing NCDs. A few studies have also assessed the association between HIV infection itself and NCDs. Many other studies have reported factors that affect the risk for developing NCDs among PLHIV/AIDS who are receiving antiretroviral treatment[5-8].

While there has been some clinical comorbidity studies focusing on the relationship between HIV/AIDS and NCDs, there is no public health model for the complexities of HIV/AIDS and NCDs. In this regard, a public health framework can be an essential tool for research and programmatic activities involving HIV and NCDs. It guides the conceptualization of public health research, as well as the development of public health interventions for HIV/AIDS and NCDs by illustrating key themes and their interrelationships. It also depicts other possible factors that should be considered during the design and management of research and intervention programs. Thus, a public health framework for the linkages between HIV/AIDS and NCDs can be a foundation for the integration and interpretation of relevant information in the relationship between HIV/AIDS and NCDs[9-11]. In light of these, the aim of this study was to develop a public health framework for the epidemiological linkages between HIV/AIDS and the four common NCDs.

2. Methods

2.1. Search Strategy

This study was a thematic synthesis of studies that describe the linkages between HIV/AIDS and NCDs. Any associative relationship between HIV/AIDS and NCDs was considered as a *linkage*. The search process was iterative. An initial search from simple electronic databases (Embase and Medline) was conducted to identify initial set of studies using the key words of HIV and at least one NCD term. Four studies were purposively selected for initial review.

After identification of initial themes from this review, a theme-based purposive searching of literature was conducted with the intention of maximizing heterogeneity of concepts. We aimed for purposive rather than exhaustive search as the purpose of the study was interpretive explanation and not prediction. Accordingly, more preference was given to recently published and review articles. We continued the iterative searching process till the point of 'conceptual saturation,' i.e. till no further new concept emerged.

2.2. Appraisal

We took the view that quality of the studies should be assessed before inclusion in to the review process. Accordingly, each article was assessed for its relevance to the major themes of the synthesis; reporting clarity of rationale, aims, methods, and findings; appropriateness of the methods used to assess the linkages between HIV/AIDS and NCDs; and added value of the study to the synthesis. These criteria were applied in a stepwise manner. Forty-eight studies that add new concepts or substantiate existing concepts were included in the synthesis.

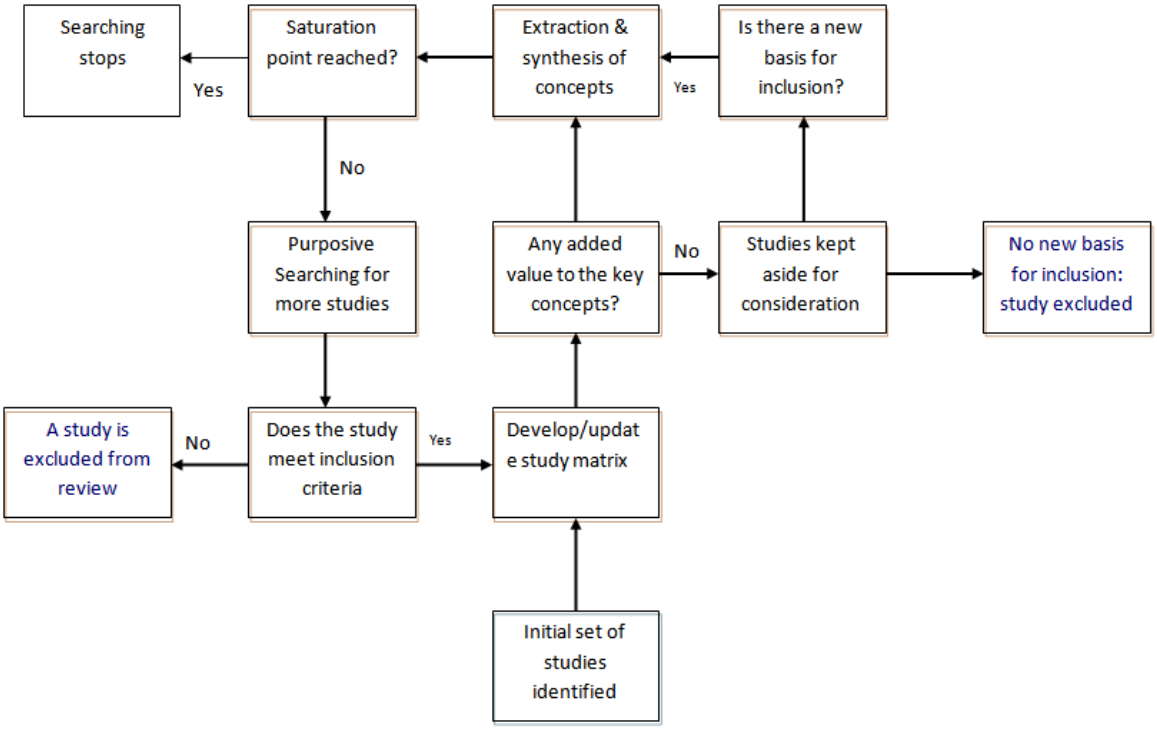


Figure 1. Flow chart of the searching, appraisal and extraction process

2.3. Data Extraction

Information was extracted from the retrieved articles using a matrix that contains variables on the identifying information of the articles and the 'key concepts' documented by the article. These include the authors, title of the study, year of publication, study design, the type of NCD involved, study population, and 'key concepts' addressed by the article with regard to the linkage between HIV/AIDS and NCDs. Authors' own words were used in the extraction of key concepts-verbatim extraction. When extracting the key concepts, we have carefully reviewed *abstract, result and conclusion* sections of the studies. We extracted key concepts and imported then in to *open code version 3.4* qualitative data analysis software program for coding and sorting (**Figure 1**).

2.4. Synthesis of Information

While this study is a thematic (qualitative) research synthesis in its overall design, it has used three key evidence synthesis approaches - descriptive, integrative, and configurative – to examine the interrelationships and to develop a public health framework that explains these interrelationships between HIV/AIDS and NCDs. We haven't considered these approaches to be sequential or experientially distinct.

A descriptive synthesis was conducted to aggregate relevant evidence that addressed similar descriptive themes of linkages between HIV/AIDS and NCDs. Key concepts were coded using broader categories, themes and subthemes. Information relevant to the interrelationship between HIV/AIDS and NCDs was sorted and summarized under different categories.

An integrative synthesis of the information summarized during the descriptive synthesis was the second form of synthesis in this study. The aggregated information was integrated in to major analytical themes and subthemes. These themes and subthemes were used to represent categories of information that address analytical concepts in the relationship between HIV/AIDS and NCDs. These themes were then formulated in to forms and types of relationships.

Configurative synthesis (Framework development) was the third form of synthesis in this study. The themes and subthemes were configured in to a concept map, a diagram showing the relationships among concepts, which was used as a draft framework for displaying the relationships among the themes. Revision of the concept map was conducted through reflexive analysis of the evidence aggregated in the descriptive synthesis. This iterative and progressive approach has resulted in several versions of the draft public health framework. The final version of the framework was prepared after a series of reviews and revisions of the draft framework. The themes were considered as pathways of relationships among key variables in the framework.

2.5. Presentation of Findings

In the presentation of the findings, we have described the characteristics of the included studies that address concepts of linkage. We have also presented the analytical themes in the form of pathways of linkage and nodes that mediate the indirect pathways by citing the related studies. The public health framework that organizes all the information about HIV-NCD linkage is also included in the findings.

3. Findings

3.1. Study Characteristics

The studies included in this synthesis were published between 1990 and 2012. However, the majority of the studies[33/48] were published after 2005. Of the included studies, 10 mainly address direct linkage between HIV/AIDS and NCDs. The rest 38 mainly address indirect relationships between HIV and NCDs. With regard to the common NCDs they mainly address, 27 studies address at least one of the four common NCDs as a primary consideration. By their design, about half of the studies were review articles. The rest were cohort, experimental and cross-sectional studies (**Table 1**).

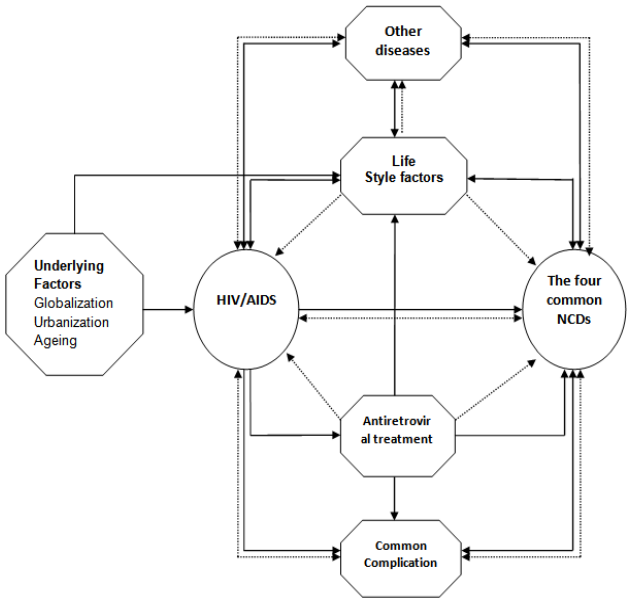
Table 1. Characteristics of the studies included in the thematic synthesis

Study characteristics	Categories	Number of studies
Publication year	1990-1995	2
	1996-2000	5
	2001-2005	8
	2006-2012	33
Primary design	Review articles	28
	Experimental studies	5
	Cohort studies	8
	Cross-sectional studies	7
NCD primarily addressed	Cardiovascular disease	4
	Cancer	7
	Chronic respiratory disease	7
	Diabetes	9
Primary theme	Direct HIV-NCD linkage	10
	Underlying/background factors	3
	Lifestyle factors	7
	Antiretroviral treatment	14
	Common complications	5
	Other disease conditions	9

3.2. Linkages between HIV/AIDS and NCDs

Two major forms of relationships between HIV and NCDs emerged from the synthesis process. These were the *determinant linkage*, where the presence of one affects the

probability of having the other, and the *severity linkage*, where the presence of one makes the progression and outcome of the other more or less worse. We have also identified two pathways of linkage between HIV/AIDS and NCDs: Direct and indirect (**Figure 2**).



Note: Solid lines show determinant; broken lines show severity

Figure 2. Public Health framework for the possible linkages between HIV/AIDS and NCDs

3.2.1. Direct Linkage between HIV/AIDS and NCDs

HIV itself increases the risk of developing some NCDs. Studies have suggested that HIV-positive individuals have higher risk of developing common NCDs as compared to HIV-negative individuals[12]. People infected with HIV have higher rates of cancers, cardiovascular diseases and diabetes. A weakened immune system caused by HIV infection is among the contributing factors for the development of cancer in PLHIV[13]. HIV infection is also associated with low levels of HDL that increases the risk of cardiovascular diseases[14].

Even though some studies have suggested that HIV infection itself was not associated with increased risk of diabetes, others substantiate the evidence that insulin resistance may have an HIV disease associated component as well[15, 16]. Due to its autoimmune effect, untreated HIV could also be associated with higher risk of developing diabetes.

Type II diabetes could be a complication of untreated HIV infection; and effective viral suppression can reverse the disorder[17]. Other studies also support the association between HIV related lipodystrophy and insulin resistance. Treatment of HIV related lipodystrophy with metformin may ameliorate insulin resistance[18]. This evidence suggested that diabetes could be a direct complication of HIV infection itself.

PLHIV have increased risk of CRD[19]. HIV infection itself is an independent risk factor for CRD[20]. Although some of the increased risk of CRD among PLHIV can be attributed to smoking and drug abuse, the risk of CRD among this population group has remained high even after controlling the effect of these factors[21]. The increasing age among PLHIV due to treatment could also contribute to increased risk of CRD.

3.2.2. Indirect Relationship between HIV/AIDS and NCDs

The indirect relationship between HIV/AIDS and NCDs is mediated by five nodes: common underlying/background factors, life style factors, antiretroviral treatment, common complications, and other mediating disease conditions.

Common underlying/background factors

Major underlying socio-economic, cultural, political and environmental determinants of chronic diseases, such as globalization, urbanization and ageing are common to both HIV and NCDs. Globalization and urbanization are the major driving factors for HIV/AIDS epidemic in low-and-middle income countries. Rapid changes in lifestyle due to the effects of the same factors are the major reasons for the emergence of NCDs in these countries[22, 23].

Due to the effect of these common underlying and background factors, HIV and NCDs are having an *epidemiological convergence* (Syndemicity) in low-and-middle income countries. As a result, urban areas in low-and-middle income countries have the highest share of both HIV and NCD burden. Hence, a macro-level relationship between HIV/AIDS and NCDs could be better explained by these common underlying and background factors.

Along with the traditional life style related risk factors of NCDs that emanate from the underlying socio-economic and cultural factors, ageing of PLHIV as a result of the intended effect of HIV treatment is also among the factors that increase the predisposition of PLHIV to a higher risk of NCDs like Diabetes[24]. On the other hand, recent evidence shows that NCDs in the general population tend to occur at earlier age than normally expected. Early onset NCDs that occur before 60 years of age is presumably higher in low and middle income countries where the prevalence of HIV has been high for decades.

Lifestyle factors

HIV/AIDS and HIV treatment are associated with changes in life style factors such as dietary habits and physical exercise that influence the risk of developing NCDs among PLHIV[25]. Concerns revolving around the belief that physical exercise could result in decrease effectiveness of the immune system and low CD4 cell count, despite the existence of strong evidences against such belief, are still common in low-and-middle income countries and could possibly affect the physical activity pattern of a person living with HIV[26].

Two common body changes associated with HIV/AIDS are lipodystrophy and wasting syndrome. These changes are manifested by loss of fat in the face, arms, legs and buttocks and gain of fat in the abdomen, back of the neck and breasts. More than the usual but carefully planned exercise is needed to prevent the effects of these body changes. The absence of

the required level of physical exercise may increase the risk of high cholesterol, triglycerides and blood glucose levels[27]. These metabolic disorders are the major causes of cardiovascular diseases and diabetes.

PLHIV may require modifications in their dietary habits in order to protect themselves from the dangers of HIV and HIV treatment. While the intake of high quality diet may help slow the progressive HIV infection and prolong life, the intake of high calorie diet could increase blood cholesterol and blood sugar levels as a result of the metabolic changes that occur along with lipodystrophy such as insulin resistance and dyslipidaemia. Therefore, both the amount and kind of food are equally important in dietary modifications associated with HIV/AIDS[28].

Malnutrition, in areas where HIV prevalence is high and food insecurity is endemic, has multiple effects on the immune system such as decrease in CD4 cell count, suppression of delayed hypersensitivity and production of abnormal β-cells, a condition leading to the development of diabetes. The immune suppression effect of malnutrition is similar to that of the HIV infection itself[29-31].

The effect of antiretroviral treatment on the risk of developing NCDs

Quite a lot of research confirmed that some antiretroviral drugs increase the risk of cardiovascular diseases and Diabetes[6, 32, 33]. Low HDL cholesterol levels may be caused by ART-associated lipodystrophy[34]. Different possible mechanisms of insulin resistance and diabetes in HIV infection has been pointed out[7, 34]. However, the actual mechanisms by which antiretroviral drugs increase the risk of developing these diseases are not clearly established though several possible pathways have been postulated[34].

The risk of antiretroviral drugs related cardiovascular diseases and diabetes depends on the type of the drugs used, the duration of treatment, and other patient related factors. In this regard, the use of protease inhibitors and longer duration of exposure to antiretroviral treatment have strong association with higher risk of these diseases. There is also a hypothesis that the recovery of the human immune system immediately after initiation of antiretroviral treatment may predispose a person to autoimmune disease in the form of type 1 diabetes[27, 35].

On the other hand, antiretroviral treatment is associated with decreased risk of cancer in PLHIV. The incidence of both AIDS-related cancers and non-AIDS-related cancers was found to be lower among those PLHIV who have started ART[36, 37, 38]. This might be due to the effect of the treatment in suppressing HIV replication and thereby reconstituting the immune system. There is also suggestive evidence that some ARV drugs may have antitumor effect[39].

Studies addressing the relationship between antiretroviral treatment and CRD indicate that airway obstruction may be one of the latest complications linked to ART. Explanations include direct drug effect, restoration of the immune system and development of autoimmunity[40, 41].

Common complications

Besides the proposition that NCDs can be a direct complication of untreated HIV infection and antiretroviral treatment, HIV/AIDS and NCDs share some important common complications. Among these are metabolic, neurologic, cardiovascular, and renal complications[42]. For instance, albuminuria, which is a key marker of kidney disease, can be a complication of both HIV and Diabetes. Evidence has shown that the prevalence of albuminuria among people with both HIV and diabetes was twofold greater than those with either disease alone[43]. This was attributed to the additive effect of the impacts of the two diseases. Kidney diseases are also associated with some cardiovascular diseases. Treatment with combined ART in PLHIV can also induce several metabolic complications like lipodystrophy, and dyslipidaemia. The same complications can also result from poorly managed diabetes. While cardiovascular diseases can be a complication of diabetes, they also share common metabolic complication with diabetes.

There are also some neurological complications which are common to HIV, antiretroviral treatment and NCDs. Neurologic complications are also associated with cardiovascular diseases[44]. Neurological complications such as stroke, nerve damage and cognitive impairment can also be complications of poorly managed Diabetes too[45]. CRD can increase the risk of pulmonary infections and cardiovascular diseases, both of which are also complications of HIV infection[56].

Cancers also have some cardiovascular and metabolic complications that are also complications of the HIV infections and antiretroviral treatment. The relationship between HIV and NCDs through common complications is very complex. But several studies have generated evidence that affirm the relationship between HIV, ART and NCDs via common complications.

Other disease conditions

As both HIV/AIDS and NCDs are related to several other disease conditions, which may complicate or be a complication of them, the relationship between HIV/AIDS and NCDs can be mediated by several other disease conditions.

Cancer-related viruses such as Human herpsvirus 8 (HHV-8), Human Papilloma virus (HPV), Epsteinbarr virus (EBV), hepatitis B virus (HBV) and Hepatitis C virus (HCV) are more common among PLHIV. As HIV affects the body's ability to fight these infections, cancers related to these viruses are higher among PLHIV[47, 48]. HCV is also related with Diabetes. HCV infection prevalence may reach 40% among HIV positive people in some settings. HCV infection has many risk factors in common with HIV. The HCV load is usually higher in HIV co-infected people than people with HCV alone. As HCV affects the liver, it increases the risk of developing diabetes among PLHIV[49]. This makes HCV infection to be one of the mediating factors in the relationship between HIV/AIDS and NCDs.

Tuberculosis (TB) is associated with HIV, Diabetes and CRD. As a result of the HIV-associated weakening of the immune system, HIV-positive people have higher rates of Tuberculosis, as compared to HIV-negative individuals[50].

People with Diabetes also have an increased risk of Tuberculosis[51]. Studies have indicated that Diabetes and TB epidemics are now converging. The prognosis among patients with both diseases is poor. Some studies went further and considered the possibility that tuberculosis may cause Diabetes[52]. TB is also associated with CRD. CRD patients have a higher risk of developing active TB compared to the general population[53]. Hence TB is related with both HIV and CRD and acts as a linking factor between the two diseases.

Another important issue is the relationship between vitamin D Deficiency and Diabetes in HIV infection[54]. The presence of vitamin D deficiency is associated with poor health outcomes in PLHIV. Some ARV drugs, like Nevirapin, also lower the concentration of vitamin D in the body. Vitamin D deficiency is also associated with cardiovascular disease[55]. Though there is limited evidence on the underlying mechanisms, vitamin D deficiency could be one of the mediating factors in the epidemiological linkage between HIV/AIDS and NCDs.

4. Discussion

This synthesis has outlined the major forms and pathways of epidemiological linkages between HIV and NCDs. The linkages are related to stages of development, progression, management and outcomes of HIV/AIDS and NCDs. These links provide a basis for integrated prevention and management of HIV and NCDs. Understanding these interrelationships between HIV and NCD also helps the management of complications of the two disease conditions. It will also facilitate integration of HIV and NCD programs[56].

The public health framework developed in this study is expected to be an important input to public health researches that address the intersection of HIV/AIDS and NCDs. It will help locate where a research theme lies within the broader framework of the relationship between HIV/AIDS and NCDs.

This public health framework integrates the various interrelationships between HIV/AIDS and NCDs in the course of development, progression and outcome. This knowledge is important for coordinated approaches in the provision of HIV/AIDS and NCDs prevention, treatment and care services.

From the perspective of program design, implementation and evaluation, the public health framework developed in this study could be a useful guide at all stages. In the problem analysis phase of HIV/AIDS and/or NCD program development, this public health framework can inform program development experts about important aspects that should be considered in the program package.

Understanding the relationship between HIV and NCDs also fosters the integration of services and consideration of HIV-NCD comorbidity during program implementation. During program evaluation, the public health framework could help in formulating appropriate evaluation questions and developing applicable evaluation tools. It will also help in interpreting and attributing evaluation findings from HIV and NCD programs.

In this period of high political commitment devoted to the prevention and control of both NCDs and HIV/AIDS, this public health framework is expected to be a basis for more comprehensive chronic disease prevention and control approaches in future policy decisions.

However, this study had some limitations. There was some conflicting evidence encountered in the analysis of the relationship between HIV/AIDS and NCDs. Those relationships with contradicting evidence were considered to be possible and are included in the framework. Information from single case studies is considered to be suggestive rather than conclusive. Second, this public health framework was developed based on epidemiological associations between HIV and the four common NCDs. Thus, it may not reflect cause-and-effect relationships.

In conclusion, this study has pointed out possible linkages between HIV/AIDS and NCDs. The public health framework illustrates these important interrelationships. Though such a framework may not fit all conditions, it is expected to serve as a generic framework for visualizing major issues in the relationship between HIV/AIDS and NCDs. The framework should be adapted to specific contexts before application for research and intervention programs.

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Chapter 4

Co-occurrence of HIV/AIDS and NCDs

CHAPTER 4 OVERVIEW

*Having explored the epidemiological convergence and epidemiological linkages between HIV/AIDS and NCDs, chapter 4 focuses on the **third** form of inter-relationship between HIV/AIDS and NCDs: Co-occurrence of HIV/AIDS and NCDs at individual level. The two major underpinning concepts in this chapter are comorbidity and multimorbidity. Using systematic review of the literature, this section presents evidence on the magnitude of co-occurrence of HIV/AIDS and the common NCDs. The chapter contains two articles. The first article summarizes the incidence of common NCD comorbidities in HIV infection. Evidence from this study, though sourced mainly from developed countries, provides insights in to the level of risk of NCDs in PLHIV, important information for prevention strategies. The second article reviews the evidence-base of the prevalence of NCD comorbidities among PLHIV specifically from developing countries in Africa and Asia. In overall, the evidence from this chapter is expected to inform the planning and management of comorbidities and multimorbidity of HIV/AIDS and NCDs.*

Citations

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Publication Declaration

Declaration for Thesis Chapter 4

Declaration by candidate

In the case of Chapter 4, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Co-conceptualized and refined the concept, designed the studies, conducted data extraction and analysis and write up of the manuscript	75%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Brian Oldenburg	Conceptualized the paper, reviewed the manuscript	N/A
Julian Elliott	Critically reviewed the manuscripts	N/A
Geoffrey Setswe	Critically reviewed the manuscripts	N/A

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

ORIGINAL RESEARCH

The incidence of cardiovascular disease, cancer and type 2 diabetes comorbidities in HIV infection: A systematic review

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Abstract

Introduction: Epidemiological linkages between HIV/AIDS and common Noncommunicable diseases are established. However, the incidence of these diseases among people living with HIV is not well examined.

Objectives: To describe the incidence of cardiovascular diseases, cancers, and type 2 diabetes among people living with HIV.

Methods: We have conducted a systematic review of incidence studies. Studies reporting on the incidence of cardiovascular diseases, cancers and type 2 diabetes among People living with HIV were retrieved from Embase and Medline databases. We used explicit eligibility and quality appraisal criteria to screen and select studies. We extracted study characteristics, outcome values and key conclusions. Findings were reported using tables and narrative summaries.

Results: A total of 30 studies were included in this systematic review. The incidence of cardiovascular diseases, cancers, and type 2 Diabetes comorbidities among people living with HIV was found to range from 1.19 to 11.3, 6.63 to 43.77, and 4.42 to 36.26 per 1000 person years, respectively. HIV infection was associated with increased risk of cardiovascular diseases and cancers. Specific types of antiretroviral drugs and longer duration of antiretroviral treatment were among the determinants of cardiovascular diseases and type 2 Diabetes in HIV infection. While the introduction of antiretroviral treatment was followed by a rapid decline in the incidence of AIDS-defining cancers, its effect on the incidence of non-AIDS defining cancers looks minimal.

Conclusion: The current evidence suggests that policies and interventions targeting people living with HIV should prioritize the prevention of the risk of common Noncommunicable diseases together with the rapid scale up of HIV treatment.

Key words

HIV-NCD comorbidity, Magnitude, Incidence

1 Introduction

The epidemiological transition towards double-burden of diseases is expected to result in higher rates of comorbidity [1]. It is generally well understood that some infectious diseases are associated with increased risk of Non-communicable diseases (NCDs). On the other hand, NCDs predispose people to opportunistic infectious diseases [2]. Furthermore, some infectious diseases affect the risk of contracting other infectious diseases resulting in greater co-infection rates [3]. This also applies for NCDs. Hence, the relationships between and within disease categories are so complex but are worth considering. These complexities manifest as comorbidity.

There is no single agreed up on definition of comorbidity. Comorbidity may refer to diseases or disorders that exist together with an index disease; or it may refer to the co-occurrence of two or more diseases in an individual. Measurement of comorbidity has currently received more attention in medical research. Different data sources that are available to measure comorbidity include medical records, patient self-report, clinical judgment and administrative databases. Comorbidity can assume four major roles in statistical analysis: a confounder, an effect modifier, an exposure and an outcome. Most comorbidity studies involve the development and application of comorbidity indices to understand the effect of comorbidities on defined health outcomes [4-6].

NCD comorbidity in HIV infection, the occurrence of an NCD in an individual with HIV, currently requires more attention along with the rapid emergence of NCDs as a major disease of public health importance in high HIV prevalent areas. Low-and-middle income countries which already have high magnitude of HIV are expected to share high burden of NCD comorbidity due to the associated increase in the incidence of NCDs [7].

Though more is known about the clinical relationship between HIV and NCDs and the factors associated with their relationship, little is known about the epidemiology of their comorbidity. With the emergence of double mortality burden in low-and-middle income countries, better understanding of the epidemiology of HIV-NCD comorbidity is essential [8]. Data on the incidence and prevalence of common NCDs among people with HIV are available from different studies in different parts of the world. There are also several studies that have reported the effect of antiretroviral treatment on the risk of developing NCDs among people living with HIV (PLHIV). However, to the knowledge of the investigators, there is no research effort that summarizes the incidence of comorbidities of common NCDs in HIV infection.

Therefore, the aim of this study was to review and summarize the incidence of comorbidities of the cardiovascular diseases, cancers, and Diabetes and to describe the determinants of incidence of these comorbidities among people living with HIV.

2 Methods

2.1 Search strategy and selection

Studies reporting the incidence of cardiovascular disease, cancer and type 2 diabetes comorbidities among people living with HIV/AIDS were retrieved from Embase and Medline electronic databases. The key words used contain HIV/AIDS, one NCD term and incidence. The search was then filtered for cohort studies and registry matches only. References of review articles [9-12] were also assessed to identify additional studies. The titles and abstracts of the resulting studies were reviewed for eligibility. The eligibility criteria used were: 1) Studies that report incidence of cardiovascular diseases (CVD), cancers or diabetes; 2) Studies mainly conducted on people living with HIV; and 3) published between 2000 and 2012. Studies that meet all these eligibility criteria were considered for review.

2.2 Appraisal of the studies

We assessed all the eligible studies for the following appraisal criteria: 1) clearly defined cohort study design or registry match; 2) Sufficient sample size (more than 500 PLHIV); 3) Adequate follow up period (at least one year); 4) assessment at index visit and appropriate outcome ascertainment stated; and 5) explicitly stated comparison group including self (time- series) comparison. These criteria were rated on a dichotomous scale (1=Yes and 0=No). Studies that met all these criteria were included in the final review. In those cases where more than one study reported from the same cohort met the appraisal criteria, the most recent study was included.

2.3 Data extraction

We extracted relevant study and outcome characteristics using a standardized checklist. This checklist was pre-tested on 5 studies before application. Necessary amendments were made based on the results of the pre-test. The information extracted include name of first author, year of publication, study design, study population characteristics, follow up period, sample size for PLHIV, country of the study, number of new cases, total person-years of follow, incidence rates, associated risk factors, measures of association and major conclusion of the study. All these variables were double entered independently to ensure consistency of the extraction.

2.4 Synthesis techniques

Incidences of comorbidities were examined among studies within each NCD and among the three common NCDs. The findings were discussed based on the characteristics of the studies and the relative magnitude of the NCDs. Meta-analytic combination of findings was precluded by high level of heterogeneity among the studies. Even though confidence intervals of the incidence rates were recalculated from the available information, these were used for descriptive purpose only. For three studies person-years of follow up was estimated from average duration of follow up. Key findings of the studies that compared the incidence of the comorbidities of the three NCDs between 1) PLHIV (not on ART) versus HIV uninfected; 2) PLHIV (on ART) versus HIV uninfected; 3) PLHIV on ART versus PLHIV not on ART; and 4) PLHIV treatment groups (by type of drug and by duration of treatment) were also highlighted. Findings were reported using PRISMA guideline [13].

3 Results

3.1 Study characteristics

The search strategy had resulted in a total of 533 studies. Ninety eight studies met the initial eligibility criteria. Full texts of these 98 studies were retrieved and reviewed. A total of 30 studies had met the quality appraisal criteria and were included in the final review (see Table 1).

Table 1. Number of studies addressing incidence of NCD comorbidities in HIV

S#	Type of NCD	Screened	Eligible	Included
1	Cardiovascular disease	274	22	10
2	Cancers	176	50	14
3	Type 2 diabetes	83	26	6
	Total	**533**	**98**	**30**

The majority of the included studies were conducted in USA. All the included studies were conducted in the developed world, i.e. USA, Europe and Australia. Most of the studies that hadreported incidence of cancer was registry match studies while most of the studies that had reported incidences of CVD and Diabetes were prospective cohort studies. Most of the

studies that had reported incidence of cancer were published between 2000 and 2005 while most of the studies that had reported the incidence of CVD and Diabetes were published after 2005.

3.2 Cardiovascular diseases (n=10)

A total of 186,867 people living with HIV were followed for about 705,772 person-years. During this follow up period a total of 1,654 new cases of cardiovascular disease were identified. From the included studies the incidence of CVD among PLHIV ranges from 1.19 to 11.13 per 1000 person-years of follow up (see Table 2).

Table 2. Cohort studies reporting the incidence of CVD among HIV infected people

Author	Year	Follow up period	PLHIV	New CVD cases	Person years	Incidence# (HIV+)	Country
Lang S [14]	2010	2000-2006	74958	360	298156	1.24	France
Triant VA[15]	2007	1996-2004	3851	189	16983	11.13	US
Klein [16]	2007	2000-2006	6702	95	25200	2.40	US
Holmberg [17]	2002	1993-2002	5672	21	17712*	1.19	US
Mary-Krause [18]	2003	1996-1999	34956	60	88029	4.90	France
Iloeje [19]	2005	1996-2003	7542	127	23765*	5.34	US
SMART [20]	2008	2004-2007	2752	112	26047*	4.30	UK, Den, AU.
Brothers [21]	2009	1997-2004	14174	43	11921	3.61	US
Worm S [22]	2010	1999-2007	33308	580	178835	3.24	US, EU, AU
Obel N [23]	2010	1995-2005	2952	67	19124	3.50	Denmark

#Per 1000 person years of follow up; *Estimated from average duration of follow up and incidence rates; US=United States; UK=United Kingdom; EU=Europe; AU=Australia

Studies included in this review indicated that HIV-positive people have increased risk of cardiovascular disease as compared to HIV-negative people. The risk of myocardial infarction among people living with HIV was about 1.5 times that of HIV negative people [14]. In comparison to other cardiovascular diseases, the relative risk of acute myocardial infarction was higher at about 1.75 times that of HIV-negative people [15]. The risk of coronary heart disease was also about 1.78 times more among PLHIV in late HAART [16].

Studies had also indicated that the risk of CVD among PLHIV taking Antiretroviral treatment (ART) depends on the specific type of the Antiretroviral drug used. Holmberg et al had found that the hazard ratio of myocardial infarction among PLHIV who were taking Protease inhibitors was about 6.5 (95% CI: 0·9-47·8) times as compared to its hazard ratio among those who were not taking protease inhibitors [17]. Compared to treatment naïve PLHIV, PLHIV taking Protease inhibitors had about 2.56 (1.03, 6.34) times more risk of myocardial infarction [18]. Although statistically significant, the findings from a study by Iloeje et al indicated modest level of risk of CVD associated with Protease inhibitor use, a Hazard ration of 1.71 (1.08, 2.74) as compared to Non-Protease inhibitor users [19]. PLHIV taking abacavir containing ART were about 2 times at a higher risk of CVD as compared to those taking other regimens that do not containing this drug [20]. However, the study by Brothers et al reported no supportive evidence of increased risk of CVD among Abacavir users [21].

Other studies from the D: A: D cohort indicated that both Abacavir and Didanosine use were associated with about 2 times increased risk of Myocardial infarction as compared to other antiretroviral drugs [24]. From the same cohort, it was reported that the duration of exposure to ART was also a factor for increased risk of CVD. A study from D: A: D showed that ART was independently associated with a 26% relative increase in the rate of Myocardial Infarction per year of exposure during the first four to six years of its use [25].

3.3 Cancers (n=14)

Fourteen studies that had reported the incidence of cancers among PLHIV were reviewed. Most of the studies used registry match as their major method of identifying HIV cases with cancer. The others were prospective cohort studies. The incidence rate of cancer ranged from 6.63 to 43.77 per 1000 person years of follow up. Overall, 84,374 cancers were reported in 3,422,910 person years of follow up. The majority (81.4%) of these were AIDS defining cancers (ADC). The rest 18.6% were non-AIDS defining cancers (NADC). High variations of among incidence rates were observed (see Table 3).

Table 3. Incidence rates of cancer (all types) per 1000 person years of follow up

Author (Ref)	Year	Follow up	PLHIV	Person years	Incidence (ADC)	Incidence (NADC)	Incidence (All)	Country
Frisch [26]	2001	1980-1996	302834	1438462	21.45	3.07	24.52	US
Glurich [27]	2002	1985-1999	13067	77114	5.72	2.54	8.26	Australia
Allardice [28]	2003	1981-1996	2754	15913	8.67	1.51	10.18	Scotland
Dal Maso [29]	2003	1985-1998	12104	60421	16.42	2.81	19.23	Italy
Clifford [30]*	2005	1985-2002	7304	28836	17.06	4.58	21.64	Switzerland
Newnham [31]	2005	1985-2001	33190	189758	8.33	2.33	10.66	UK
Engels [32]	2006	1980-2002	317428	477368	39.68	3.41	43.09	US
Mbulaiteye [33]	2003	1990-1996	82217	107728	40.44	3.33	43.77	US
Guiquet [34]*	2009	1998-2006	52278	255353	4.21	2.42	6.63	France
Patel [35]*	2008	1992-2003	54780	157819	4.49	18.01	22.49	US
Seaberg [36]*	2010	1984-2004	2940	32383	23.28	2.87	26.16	US
Glaceran [37]	2007	1981-1999	1659	7050	24.26	2.98	27.24	Spain
Bedimo [38]*	2004	1989-2002	2882	7452	23.89	6.58	30.46	US
Gallagher [39]	2001	1981-1994	122993	567254	14.13	8.25	22.39	US

*prospective cohort studies

The overall relative risk of NADC cancer was 2.7 (95% CI: 2.7-2.8) in Frisch et al study. But the incidence of NADC didn't appear to be influenced by advanced imunosupression associated with HIV disease progression [26]. People with HIV who are only mildly immune deficient may not be at increased risk of NADC [27]. A study by Allardice et al, conducted before ART become widely available, had reported Standardized incidence ratio (SIR) of 10.8 (95% CI: 9.2-12.6) for all cancers. The SIR for NADC in this study was 1.8 (95% CI: 1.1-2.6) [28]. Another study conducted in Italy had reported SIR of 2.3 (95% CI: 2.0-2.7) for NADC. Anal cancer, lung cancer and brain tumours were among those NADCs with the highest SIR [29].

A study that examined the influence of behavioral risk factors and ART on the risk of cancer using data from the Swiss HIV cohort study didn't find any cancers of lip, mouth, pharynx and lung among non-smokers. This study had also suggested that ART may not prevent the risk of NADC [30]. A study conducted in Southeast England reported SIR of 2.8(95% CI: 2.6-3.1) for NADC. In this study men were at a higher risk of cancer [31]. A study that had investigated the effect of ART on cancer trend in US indicated that ART was associated with a dramatic decline in Kaposis Sarcoma and Non-Hodgkin Lymphoma. The risk of cervical cancer didn't change with ART. Decline in risk of lung cancer but an increase in risk of Hodgkin lymphoma was observed. No overall change in risk of NADC was associated with ART [32].

A study that examined the relationship between cancer risk and AIDS-related immunosupression (as measured by CD4 count at AIDS onset) had illustrated that the risks of Kaposis Sarcoma and Non-Hodgkin Lymphoma were positively associated with CD4 count. However, the risks of cervical cancer and NADCs were not related to CD4 counts, suggesting

that increased risks of NADCs may be a result of lifestyle factors [33]. A prospective cohort study from France had also indicated that ART might be more beneficial the reducing the risk of cancer if it can restore or maintains CD4 count above 500 cells per micro litre, thereby indicating the need for an earlier diagnosis of HIV infection and an earlier treatment initiation [34].

A study on the incidence of cancer among HIV infected people as compared to the general population in the US reported that the incidence of many NADCs was higher among HIV infected persons [35]. In the multicentre AIDS cohort study among men, the incidence of Kaposis Sarcoma and Non-Hodgkin lymphoma has decreased while the incidence of anal cancer has increased in the HAART era as compared to the pre-HAART era [36]. Increased risks of Hodgkin's lymphoma, liver cancer, lung cancer, and in situ cervical cancer among AIDS patients were also reported by a study conducted in Spain [37]. A longer duration of survival during the HAART era was proposed to be one of the explanations for increased risk of NADC among PLHIV [38].

Elevated risks of Hodgkin's disease; cancer of rectal area, respiratory tract, brain and central nervous system were found in a study of AIDS patients in New York State. Increasing trends of increase relative risks from the pre-AIDS to the post-AIDS period were observed for cancers of the rectal and anal area, respiratory tract, skin, and connective tissues among men and invasive cervical cancer in women [39].

3.4 Diabetes (n=6)

Six prospective cohort studies that measured the incidence of diabetes among people living with HIV were included in this review. Three of these studies recruited PLHIV receiving treatment, treatment naive PLHIV and HIV-negative people in the follow up. One study recruited PLHIV receiving treatment and treatment naive PLHIV only. The rest three studies had focused on PLHIV taking ART only.

Over a total of 175,202 person-years of follow up 1,178 of the 44,484 HIV positive persons developed type 2 diabetes. The incidence of diabetes ranged from 4.42 cases per 1000 person years in Swiss HIV cohort study to 36.26 cases per 1000 person years in the multicenter AIDS cohort study. A study from the D: A: D cohort which had the highest number of study participants and person years of follow up had reported an incidence of 5.72 per 1000 person years (see Table 4).

Table 4. Incidence of Diabetes among PLHIV in the seven prospective cohort studies

Author	Year	Follow up period	Number of HIV+	New DM cases	Person years	Incidenceb# (HIV+)	Incidenceb* (ART users)
Capeau [40]	2012	2000-2009	1,046	111	7,846	14.18	14.18
De Witt [41]	2008	1999-2006	33,398	744	130,151	5.72	5.72
Justman [42]	2003	1994-1999	1,435	56	3,673	15.25	17.33
Brown [43]	2005	1999-2003	568	28	772.1	36.26	47.17
Ledergerber [44]	2007	2000-2006	6,513	123	27,798	4.42	4.99
Tein [45]	2007	2000-2006	1,524	116	4,962	23.37	27.36

#Studies conducted on ART users only

*Incidence per 1000 person-years of follow up

Older age and adiposity were linked with higher risk of diabetes among PLHIV who had started on combination antiretroviral treatment at French clinical sites [40]. The use of two thymidine analogs (Stavudine and Zidovudine) was significantly associated with diabetes after the adjustment of potential confounders in a study reported from D: A: D cohort. In the same study, the incidence of diabetes was found to increase with cumulative exposure to combination antiretroviral treatment after adjustment for potential risk factors of diabetes [41].

Protease inhibitors use was found to be associated with a three-fold increase in the risk incident diabetes. Age and body mass index were also important predictors of risk of diabetes among PLHIV [42]. In the Muticenter AIDS cohort study, the relative risk of diabetes among HIV infected men taking HAART was more than four times that of HIV sero-negative men after adjustment for age and body mass index [43].

In a study reported from the Swiss HIV cohort, traditional risk factors, and current treatment with protease inhibitor- and nucleoside-reverse transcriptase- containing regimens were associated with risk of type 2 diabetes mellitus [44].

In the women's interagency HIV cohort study, there was 1.4 fold increased incidence of diabetes in HIV infected women as compared to HIV negative women, but the difference was not statistically significant. This study had also reported a relative hazard of 2.64 [95% CI: 1.11-6.32] for the risk of diabetes among PLHIV who were exposed to Nucleoside reverse transcriptase for more than three years suggesting that longer exposure to Nucleoside reverse transcriptase inhibitors may increase risk of diabetes [45].

4 Discussion

The incidence of CVD as reported by the studies included in this review was between 2.24 and 5.34 per 1000 person years except for one study which reported an incidence of 11.3 per 1000 person years and two studies which have reported incidence rates below 1.5 per 1000 person years. The higher incidence in Traint VA et al study could be due to the recruitment of older patients from a higher risk background population in tertiary hospitals [15]. The incidence of CVD was relatively low in the two studies due to the low level of incidence of the problem in the background population [14, 17].

The findings support the notion that HIV infection is generally associated with increased risk of cardiovascular disease. They are also in favor of the importance of antiretroviral treatment in decreasing the risk of cardiovascular diseases. However, the use of specific antiretroviral drugs is found to be associated with a higher risk of cardiovascular disease as compared to the use of other antiretroviral drugs.

The incidence of cancers was highly variable among the studies. The SIR of ADCs was very high while that of NADC was modest. Antiretroviral treatment was associated with a rapid decline in the incidence of ADCs. However, the effect of ART on the incidence of NADCs seems low. In some cases an increasing trend of NADC was observed among PLHIV receiving ART (36). Several body parts were found to be affected by NADCs. Longer survival and the role of traditional risk factors were also found to be more important.

The two largest studies reported the incidence of type 2 Diabetes among PLHIV to be 5.72 and 4.42 per 1000 person years [41, 44]. The other studies have reported incidence rates of greater than 14 per 1000 person years. The risk of diabetes associated with antiretroviral use also varied by the type of the drugs considered. Protease inhibitors are associated with about 3 times increased risk of diabetes as compared to other types of drugs. Nucleoside reverse transcriptase inhibitors such as Stavudine, Didanosine, Zidovudine and Indinavir are also associated with increased risk of diabetes.

5 Limitations

We have encountered higher level of heterogeneity among the characteristics and outcomes of the included studies during the review. This had effect on the overall interpretation of the findings of the study. Besides, the number of studies that met the inclusion criteria for type 2 diabetes was low. The review had also looked in to cardiovascular and cancers in general terms and specific types of cardiovascular diseases and cancers are not well addressed by this review. Moreover, all the included studies were from the developed world and could not reflect the magnitude and determinants of major NCDs in high HIV prevalent areas of the developing world like Sub-Saharan Africa.

6 Conclusions

The current evidence suggests that cardiovascular diseases, cancers and type 2 Diabetes are important comorbidities of HIV infection. Policies and interventions targeting people living with HIV should prioritize the prevention of the risk of common Noncommunicable diseases along with the rapid scale up of HIV treatment. Integrated provision of HIV and NCD services for PLHIV could maximize synergy and improve efficiency.

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Epidemiology of Comorbidity of HIV/AIDS and Non-communicable Diseases in Developing Countries: *A systematic review*

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Abstract

Background: Access to treatment for HIV/AIDS has turned the disease into a chronic disorder. The disease joins the ranks of the emerging epidemics of non-communicable diseases. The increasing age of people living with HIV/AIDS raises an important concern of the coexistence of HIV with non-communicable diseases. The aim of this study was to identify, review and summarize studies reporting the magnitude and determinants of co-morbidity of HIV/AIDS and non-communicable diseases in developing countries.

Methods: A systematic review of studies from Medline and Embase (2000-2012) reporting the magnitude and determinants of non-communicable diseases in people living with HIV was conducted. The review focused specifically on the common non-communicable diseases of global priority: cardiovascular diseases, cancers, diabetes and chronic respiratory diseases.

Results: A total of 37 studies from 20 countries involving more than 30,000 HIV infected people met the inclusion criteria. More than one-third of people living with HIV who attended health facilities had cardiovascular abnormalities. In the Antiretroviral treatment era, the magnitude of both AIDS defining and non-AIDS defining cancers was low. But precancerous lesions had a higher prevalence. The prevalence of metabolic syndrome ranged from 13% to 28%. The prevalence of diabetes was below 5% in most studies. No study reporting chronic respiratory disease met the inclusion criteria. The major determinants of these comorbidities were related to HIV infection itself.

Conclusion: The cardiovascular disease profile of HIV infected people is different from the usual cardiovascular disease profile. Precancerous lesions are more common. The results do not support increased prevalence of diabetes and metabolic syndrome in HIV infected people. Early and regular screening remains to be the key prevention and control strategy. The findings warrant coordination of HIV/AIDS and non-communicable disease interventions in developing countries.

Keywords: HIV/AIDS, non-communicable diseases, comorbidity, developing countries

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Epidemiology of Comorbidity of HIV/AIDS and Non-communicable Diseases in Developing Countries: *A systematic review*

HIV/AIDS is associated with several diseases. Non-communicable diseases (NCDs) are among health conditions that coexist with HIV/AIDS (Hirschhorn, Kaaya, Garrity, Chopyak, & Fawzi, 2012). With the emergence of the NCD epidemic in developing countries, which already have persistently higher levels of HIV/AIDS epidemic for the last three decades, a *syndemic* situation is expected at population level (Koehlmoos, Anwar, & Cravioto, 2011). Increased access to anti-retroviral treatment has turned HIVin to a chronic disorder. HIV positive people live longer. The increasing age comes with an increase risk of NCD comorbidity from the traditional risk factors. Importantly, HIV positive status is associated with increased likelihood of NCDs (Nigatu, 2012). Complex inter-linkages between HIV/AIDS and NCDs contribute to higher levels of NCDs among people living with HIV (PLHIV) (Rabkin & Nishtar, 2011).

The risk of NCD comorbidity among PLHIV is expected to rise in developing countries. Presence of another disease would affect the prognosis and the quality of life of the PLHIV, and the cost of care (Armstrong & Charland, 2004). Weak health systems in those countries may also face greater challenges in addressing the overwhelming patient needs. NCDs are the major causes of death in PLHIV. Without taking in to account of the NCDs, externally funded HIV/AIDS programs in those countries would only end up in preventing death from HIV, but not death of the patients (Emanuel, 2012).

Considering these facts, NCD comorbidities in PLHIV have a critical public health and clinical importance (Narayan, Ali, del Rio, Koplan, & Curran, 2011). Understanding the epidemiology of the coexistence of HIV/AIDS and NCDs in developing countries is thus a priority for policy and practice (Levitt, Steyn, Dave, & Bradshaw, 2011). The problem is that the evidence base to inform decisions is weak and highly fragmented. Most of the existing studies report specific diseases on a small number of study subjects from different settings in developing countries. A broader view of the extent of NCD comorbidities in HIV infection conducted across diseases, countries and years is lacking. The evidence from large-scale cohort studies conducted in developed countries is not context-free and is less applicable to the context of health systems of developing countries.

In light of this, the envisaged review is designed to identify, review and summarize studies describing epidemiology of comorbidities due to common NCD among PLHIV in developing countries. It summarizes the magnitude and determinants of comorbidities of common NCDs in HIV infection with specific focus on the four most common NCDs: cardiovascular diseases, cancers, diabetes and chronic respiratory diseases (Maher, Harries, Zachariah, & Enarson, 2009). It also discusses the implications of these comorbidities on the possible integration/coordination of HIV and NCD interventions in developing countries.

METHODS

Search Strategy

A systematic search of the Medline database (via Ovid) was conducted to identify eligible studies published between January 2000 and July 2012, inclusive, with the assistance of a senior librarian. The searches were conducted with Medical Subject Headings (MeSH) where relevant. The main search terms included "HIV or AIDS", "Cardiovascular diseases", "Cancers", "type 2 diabetes" and "chronic obstructive pulmonary disease." These search terms were 'exploded' to consider other synonyms and subcategories of these diseases. Different combinations of these were coupled with the epidemiologic indicators of disease such as "prevalence" and "incidence." The search outputs were limited to English

language articles only. In addition, we searched the Embase database to locate other relevant publications. Reference lists of identified systematic reviews were also reviewed to identify additional publications.

Inclusion/Exclusion criteria

Two investigators (TN and VN) independently reviewed the titles and abstracts of the identified studies to check if they fulfil the eligibility criteria. Differences were resolved through consensus. The inclusion criteria used include the following: (a) The study should primarily address magnitude of at least one of the four common NCD(s); (b) the study subjects should mainly be People living with HIV or AIDS; (c) the study should be entirely conducted in African and Asian countries; and (d) the design of the study should be observational studies (cross-sectional, cohort, case-control). Studies reporting the magnitude of HIV in people having NCDs were excluded. Review articles and studies reporting on infections related to NCDs were also excluded.

Methodological Appraisal

For the assessment of methodological quality, we adapted the quality assessment tool for systematic review of observational studies (Wong, Cheung, & Hart, 2008). The appraisal criteria include the representativeness of the sampling method, the size of the study population, the ascertainment method of NCD outcome, reporting of non-response or loss to follow up, and control of potential confounding factors. The adapted tool was reviewed by all the investigators. Two investigators (TN and VN) appraised the quality of the studies using this tool. The quality assessment results are summarized item by item.

Extraction of Information

Data from the eligible studies were extracted using a pre-tested data abstraction tool. The information extracted includes the study characteristics (first author, title, country, year of publication), study population characteristics (age and sex composition, treatment status), study methods (study design, study period, sample size, outcome measurement, and statistical analysis), outcomes (number and percent of NCD cases, risk factors), and main conclusion of the studies. All these variables were populated into a matrix. The populated matrix was reviewed by a second person for accuracy of the extraction.

Synthesis of Information

Characteristics of the included studies were presented by diagrammatic and narrative summaries. Magnitude of the NCD comorbidities and their variations based on different patient characteristics were described for each NCD and then analysed using the *comparative perspective* approach. Three major axes of comparison include time (years), geography, and study population characteristics. The magnitude of the comorbidities of the different NCDs was also compared relative to each other. The determinants of the magnitude of NCD comorbidities were presented using *thematic* summaries. Finally, the implications of the findings on health systems were discussed.

RESULTS

Study Characteristics

A summary of the results of the search outlining the number of potentially relevant studies initially identified and the number of studies included in the review is shown in Figure 1. A total of 37 studies (representing 31,344 PLHIV) from 20 countries met the inclusion criteria. Most of the included studies were published between 2005 and 2012. Twenty-five of the 37 studies were reported from African countries. The rest 12 studies were from Asian countries. The majority of the studies (25 studies) reported malignant comorbidities. Five and seven studies reported on cardiac abnormalities and metabolic conditions (including type 2 diabetes), respectively. No study that has reported on chronic respiratory diseases met the inclusion criteria.

All but five studies used a non-experimental cross-sectional design. Nine studies used HIV negative comparison groups. Regarding the treatment status of the HIV positive population, 24 studies have reported the treatment status of the study participants. For four studies, all the study participants were receiving antiretroviral treatment. Three studies have involved antiretroviral treatment naive PLHIV only. In two studies, the study subjects were entirely children living with HIV.

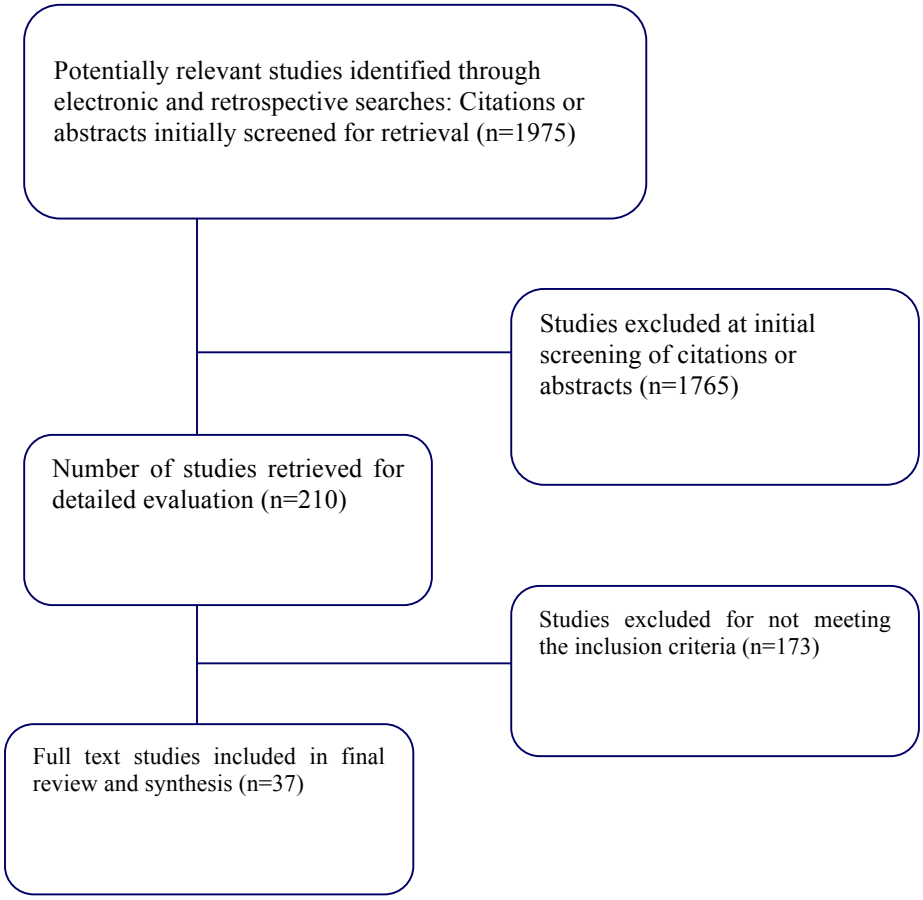

Figure 1.
Summary of the search and selection results.

Methodological Quality of the Studies

In almost all of the studies, study subjects were selected *consecutively* from HIV clinics where they sought care. All of the studies used clinical samples. The enrolment of the participants was conducted over a period that varied from five months to five years across the studies. Except in eight studies, the sample size was less than 500 individuals. In all studies the ascertainment of NCD outcome was either by laboratory diagnosis or review of clinical records. No study has used self-report as a method of outcome ascertainment. Almost all the studies have reported non-response or loss to follow-up from the study. In all cases, these were at minimum. Regarding the control of confounding variables during analysis, 13 studies accounted for potential confounding factors. The rest of the studies were mainly descriptive with or without internal comparisons using P values.

Magnitude of NCD Comorbidities

Cardiovascular diseases/abnormalities

More than one-third of PLHIV attending health facilities and/or receiving antiretroviral treatment (ART) had some form of cardiovascular disorders in most studies. The cardiovascular disorders in PLHIV are mostly muscle and nerve disorders rather than vascular disorders. A summary of the prevalence of cardiovascular abnormalities is presented in Table 1. About three-fourths of children with HIV, 84% of whom had AIDS, were reported to have cardiovascular dysfunction as ascertained by echocardiography in Nigeria (Okoromah, Ojo, & Ogunkunle, 2012). Prevalence of QTC prolongation was 45% among AIDS patients as compared to 28% in HIV-positive cases (Sani & Okeahialam, 2005). Other cardiovascular abnormalities were also at high level. The only lower level reported is the prevalence of dilated cardiomyopathy in Rwanda (Twagirumukiza et al., 2007). However, this study has enrolled patients during their initial assessment for ART. Besides, this study has also excluded patients with known cardiovascular disease.

Table 1

Prevalence of cardiovascular abnormalities in people living with HIV

First author, Year	Country code	PLHIV	Type of abnormalities	Patient characteristics	Prevalence
(Okoromah et al., 2012)	NG	83	Cardiovascular dysfunction	Children 18mo-12 years	75.9%
Aggarwal, Sharma, Bhardwaj, and Raina (2009)	IN	52	Myocardial dysfunction	Adults (ART naive)	42.3%
(Compostella, Compostella, & D'Elia, 2008)	MZ	30	CV Autonomic neuropathy	Adults (50% ≥stage 3)	30.0%
(Twagirumukiza et al., 2007)	RW	416	Dilated cardiomyopathy	Adults (all ART naive)	17.7%
Sani and Okeahialam (2005)	NG	178	QTc interval prolongation	Adults (56% AIDS+)	37.4%

Cancers/Malignancies

The prevalence of both AIDS defining and non-AIDS defining cancers among PLHIV receiving ART was low (<5%) except in a few studies. Pre-cancerous lesions, especially cervical Squamous Intraepithelial Lesion (SIL) and Anal SIL, had a high prevalence. About 10-15% of newly diagnosed women and more than 20% of those on ART have cervical cytological abnormalities, low grade SIL and above.

Of the 25 studies that reported malignant comorbidities, 18 reported cervical lesions and the rest 7 reported other forms of malignancies. The prevalence of cervical SIL was higher than 10% in all the studies except in one study reported from Pune, India (Joshi et al., 2005), which reported a prevalence of 6.3%. As this study had recruited HIV positive clients from voluntary counselling and testing clinic, low values were expected. The highest prevalence of SIL is 76% reported from Zambia among women using HIV care services (Parham et al., 2006). The same study reported a 20% prevalence of squamous cell carcinoma (SCC) of the cervix. In a cohort of 246 HIV infected and 381 HIV negative women followed for an average of 2.2 years in Senegal, the overall risk of developing High grade SIL was 11% (Hawes et al., 2006). In a study of colposopic-histopathologically confirmed cervical intraepithelial neoplasia (CIN), 27.7% of the patients had ≥ CIN1 lesions and 16.5% had advanced neoplastic lesions (≥CIN2) (Sahasrabuddhe et al., 2010). HIV infected women have at least two times increased risk of cervical SIL as compared to HIV negative women (Chirenje et al., 2002). Detailed prevalence figures for different types of cervical abnormalities are shown in Table 2.

Table 2
Prevalence of Cervical Squamous intraepithelial lesions (SIL) among PLHIV

First author, Year	PLHIV	ASCUS	LSIL	HSIL	≥LSIL	Country
(Obure et al., 2009)	103	-	19.4%	11.6%	32.2%	Tanzania
(Agaba, Thacher, Ekwempu, & Idoko, 2009)	369	39.3%	15.2%	13.8%	29.0%	Nigeria
(Hluangdansakul, Phinchantra, & Bowonwatanuwong, 2006)	231	2.6%	2.2%	8.3%	12.5%	Thailand
(Joshi et al., 2005)	287	-	-	-	6.3%	India
(Mogtomo et al., 2009)	70	-	24.3%	31.4%	55.7%	Cameroon
(Mangclaviraj et al., 2008)	385	-	12.2%	4.7%	16.4%	Thailand
(Peedicayil et al., 2009)	75	-	1.0%	13.0%	14.3%	India
(Sirivongrangson et al., 2007)	210	5.7%	8.1%	4.3%	20.5%	Thailand
(Firnhaber et al., 2010)	1010	8.3%	23.5%	18.0%	41.5%	S. Africa
(Moodley et al., 2009)	109	11.0%	37.0%	10%	44.5%	S. Africa
(Swende, Ngwan, & Swende, 2012)	253	39.9%	6.3%	11.5%	17.8%	Nigeria
(Dim, Ezegwui, Ikeme, Nwagha, & Onyedum, 2011)	150	1.3%	8.0%	3.3%	11.3%	Nigeria
(Anorlu et al., 2007)	227	0.9%	3.0%	7.9%	10.9%	Nigeria
(McKenzie et al., 2011)	267	11.0%	26.0%	8.0%	34.0%	Kenya
(Chirenje et al., 2002)	207	12.6%	9.7%	3.4%	13.1%	Zimbabwe
(Parham et al., 2006)	150	17.3%	23.3%	32.6%	76.0%	Zambia

Note. ASCUS=Atypical cells of undetermined significance; LSIL=Low grade Squamous intraepithelial lesion; HSIL=High grade Squamous intraepithelial lesion.

Of the seven studies that reported other forms of cancers, two assessed all types of cancers, both AIDS defining and non-AIDS defining cancers (Kiertiburanakul, Likhitpongwit, Ratanasiri, & Sungkanuparph, 2007; Mbulaiteye et al., 2006). The overall prevalence of cancer from these studies was relatively low. From the rest of the studies that reported specific forms of cancers, a 7.8% prevalence of conjunctival SCC and a 17.8% of anal SIL were identified among patients referred to eye unit and men who have sex with men, respectively (Chisi, Kollmann, & Karimurio, 2006; Li et al., 2009). A study conducted among PLHIV who were on ART demonstrated a low prevalence of Kaposi's sarcoma (Iregbu & Elegba, 2006). In contrast a study conducted among PLHIV with advanced disease reported a 27% prevalence of head and neck neoplasms (Butt, Chindia, Rana, & Machigo, 2008). Table 3 summarizes these results.

Table 3
Prevalence of other forms of malignancies in HIV infection

First author, Year	Type of malignancy	PLHIV	Magnitude	Remarks
(Iregbu & Elegba, 2006)	Kaposi's sarcoma	1591	0.8%	Patients on ART
(Chisi et al., 2006)	Conjunctival SCC	409	7.8%	Patients in eye unit
(Pancharoen et al., 2005)	Malignancies in children	8034	0.3%	Incidence in children
(Kiertiburanakul et al., 2007)	Malignancies (all types)	1416	42 cancers	Prevalent cancers
(Butt et al., 2008)	Head and neck neoplasms	200	27.0%	Most in stage 3&4
(Mbulaiteye et al., 2006)	Cancers (all types)	12073	181 cancers	Prevalent cancers
(Li et al., 2009)	Anal SIL	118	17.8%	MSM subjects

Diabetes and Other Metabolic Conditions

The prevalence of diabetes among PLHIV receiving ART is less than 5% in most of the included studies. Of the seven studies that have reported metabolic abnormalities, six have reported prevalence of diabetes mellitus (DM) and five have reported prevalence of metabolic syndrome (MS). A summary is presented in Table 4. The prevalence of diabetes is generally below 5% except in one study from Benin where it is 8% (Zannou et al., 2009). However, the average age of the study subjects was 30-40 years. As most of the included studies are cross-sectional, it was not possible to observe the effects of type of drug and duration of treatment.

Based on IDF criteria, the prevalence of metabolic syndrome among PLHIV ranges from 13%-28%. It is at or above 20% in most of the studies except one, which reported 13% prevalence of metabolic syndrome. This study was conducted on patients starting Non-Nucleoside reverse transcriptase and reported new onset of diabetes and metabolic syndrome. Up to 13% prevalence of insulin resistance (Awotedu, Ekpebegh, Longo-Mbenza, & Iputo, 2010) and 35% prevalence of hypercholesterolemia are reported (Zannou et al., 2009). However, a 63.1% overall prevalence of dyslipidaemia was also reported from a study conducted in Kenya (Manuthu, Joshi, Lule, & Karari, 2008).

Table 4
Prevalence of DM and MS (based on IDF criteria) among PLHIV

First author, Year	PLHIV	Patient characteristics	DM	MS	Country
(Wu et al., 2012)	877	Adults (all on ART)	3.5%	26.2%	Taiwan
(Julius et al., 2011)	304	Adults 18-45 (on HAART)	1.3%	28.3%	S.Africa
(Gupta, Biswas, & Sharma, 2011)	68	Adults (6 months on ART)	2.1%	19.1%	India
(Manuthu et al., 2008)	295	Adults (on HAART)	1.5%	-	Kenya
(Puttawong, Prasithsirikul, & Vadcharavivad, 2004)	278	Adults (77% taking ART)	4.6%	-	Thailand
(Awotedu et al., 2010)	86	Adults (on ART)	-	22.7%	S.Africa
(Zannou et al., 2009)	88	Adults (initiating cART)	7.6%	12.7%	Benin

Determinants of NCD Comorbidities

The determinants of NCD comorbidities in HIV/AIDS varied based on the specific NCD considered. In general, increased *age* and increased *immune* suppression or advanced AIDS disease (marked by low CD4 count and/or high viral load) were associated with higher risks of most of the common NCDs. The presence of co-existing *viral infections* and *social deprivation* were also reported to be among the determinants. Longer duration of exposure to antiretroviral treatments, especially to protease inhibitors,

also increases the risk of some cardio-metabolic disorders. However, use of antiretroviral treatments in general was associated with decreased risk of malignancies.

Gender and higher levels of traditional NCD risk factors among PLHIV were also among the associated risk factors. Longer duration with HIV infection, longer survival and presence of some opportunistic infections like tuberculosis were also reported to increase the risk of NCDs among people living with HIV. While increased risk of AIDS defining cancers and cardiac abnormalities are clearly associated with HIV, there is no sufficient supporting evidence about the association between HIV and increased metabolic syndrome. A summary of the determinants is shown in the following figure.

Sociodemographic	HIV-related	Others
Age	CD4 count	Body mass index
Gender	Viral load	Smoking
Income	Co-infections	Social deprivation
	Drug type	Nutritional deficiencies
	Treatment duration	
	Condom use	

Figure 2. ***Determinants of NCD comorbidities in HIV/AIDS***

DISCUSSION

Summary of the Evidence

The magnitude of cardiovascular abnormalities in people living with HIV is consistently high though. Over one-third of the study subjects in the included studies have some form of cardiac abnormality. Most of the cardiac abnormalities reported were muscle and nerve disorders rather than vascular disorders which is a key characteristic of cardiovascular diseases that are often considered under NCDs. Most of the studies reporting cardiac abnormalities that were included in this review recruited ART naive, PLHIV at advanced HIV disease on ART or children and may not provide a relatively higher estimates. However, the population groups are also important in the context of developing countries where access to ART is not universal. Though some studies attempted to attribute higher risks of cardiac abnormalities to the effect of ART, this evidence was very inadequate. Therefore, the results do show the significance of cardiac abnormalities among PLHIV in developing countries.

In most of the studies, the prevalence of cervical SIL was very high though the prevalence of SCC is not reported by most of the studies. This high prevalence of SIL is associated with Human papilloma virus (HPV) infection. As HIV disproportionately affects women, the high prevalence of this precancerous lesion has a great public health importance, especially in sub-Saharan Africa. The prevalence of anal SIL among Men having Sex with Men (MSM) is also another concern as per the findings reported from Asian countries. Other forms of cancer have relatively lower prevalence. The effect of ART in the risk of developing malignancies is also reported to be significant. It seems that the prevalence of cancers is low but the prevalence of precancerous lesions is high in the ART era.

On the other hand, this review has shown low prevalence of diabetes among PLHIV. Most of the studies included in this review reported diabetes prevalence of less than 5%. This could possibly be due to younger mean age (30-40 years) of the study subjects included in those studies. The prevalence of metabolic syndrome and other metabolic abnormalities like dyslipidaemia were high. About 13%-28% of

PLHIV assessed in these studies have metabolic syndrome. This prevalence of metabolic is not higher than that of the general population. However, the international diabetes federation (IDF) criteria, which use central obesity as its central element, may underestimate the prevalence of metabolic syndrome in PLHIV who often have lower body mass index.

Implications of the Evidence

The high level of cardiac abnormalities indicates the need for early screening of PLHIV for cardiovascular abnormalities. This may include routine Echocardiography. Similarly, the high magnitude of precancerous cervical lesions warrants early and regular cervical and anal cancer screening, detection and managements. HPV vaccination and condom promotion along with reduction of number of sexual partners may also have importance for these population groups. Screening and optimal management of malignancies in general is needed. Frequent biochemical monitoring for metabolic abnormalities is also essential to prevent further progression and complications. Above all, easy access and adequate adherence to antiretroviral medications is critical to address the underlying cause of the development of these comorbidities. Addressing traditional NCD risk factors is also important in PLHIV.

From health systems perspective, the magnitude of the non-communicable disease comorbidities in HIV infection warrants the integration of screening programs for cardiovascular diseases, metabolic conditions and malignancies in to HIV care and treatment programs. Other prevention and control strategies of common NCDs should also be integrated to HIV prevention, care and treatment programs to address the eminent needs of PLHIV. These integrated approaches to service delivery need integrated policies and systems.

Limitations

There are some important limitations. Firstly, the studies included in this review are cross-sectional with small samples sizes, consecutive sampling techniques, and mostly without appropriate comparison groups. They may not provide wider picture over a longer period. Secondly, the studies have enrolled "enriched" samples from clinical settings. Findings from such samples usually provide higher estimates of magnitude of comorbidities. Thirdly, different countries have different HIV profiles. The variations in the findings across countries may be due to these differences in country profiles. Fourthly, most of the studies have narrow analytic horizon and stratified analysis was not well conducted and the effect of ART on the magnitude of NCD comorbidities could not be ascertained. Finally, there were some limitations related the quality of diagnostic procedures and medical records.

CONCLUSION

In the ART era, the 'pre-disease' conditions are more common among PLHIV. Immune suppression as marked by CD4 count and viral load is the major determinant for the occurrence of NCD comorbidities. Given the lower average but increasing age of PLHIV, the findings warrant integration of HIV/AIDS and NCDs. Integrated services need integrated policies/systems.

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Chapter 5

Parallels between Global responses to HIV/AIDS and NCDs

CHAPTER 5 OVERVIEW

Having investigated the inter-relationships between HIV/AIDS and NCDs at population, disease and individual levels, this chapter examines another most important level of inter-relationship between HIV/AIDS and NCDs: The parallels, shared attributes, between the Health system responses to HIV/AIDS and NCDs. In addition to parallels/similarities, it also illustrates essential differences between the responses. Health System response in this chapter comprises macro-level policy response, programmatic response, institutional arrangement and strategic information. The chapter contains one published article which is mainly based on qualitative content analysis global HIV/AIDS and NCD responses evidence base. The article assesses the similarities and differences between Global level responses to HIV/AIDS and NCDs. The identified parallels/similarities suggest potential areas of integration while the differences indicate essential areas of differentiation in the coordinated health system response to HIV/AIDS and NCDs at global levels.

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Publication Declaration

Monash University

Declaration for Thesis Chapter 5

Declaration by candidate

In the case of Chapter 5, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Wrote the proposal, collected the data, analysed the data, wrote the manuscript, revised the manuscript	75%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Julian Elliott	Supervised & reviewed the study	
Geoffrey Setswe	Supervised & reviewed the study	
Brian Oldenburg *	Supervised & reviewed the study	

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

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Global Responses to HIV/AIDS and Noncommunicable Diseases: Analysis of Similarities and Differences

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Authors' contributions

This work was carried out in collaboration between all authors. Author TNH designed the study, performed the review and analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors BO, JE and GS supervised the design, data extraction and analysis. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Recent evidence suggests that HIV/AIDS and Noncommunicable diseases (NCDs) share essential commonalities in their risk factors, progression and management. However, the interrelatedness between the global responses to HIV/AIDS and NCDs hasn't been systematically analyzed.
Objective: To examine the similarities and differences between global responses to HIV/AIDS and NCDs.
Methods: Using preliminary review of literature, we identified four major themes of the global response: Strategies, Systems, Intervention and Monitoring and Evaluation. Detailed review of purposively selected documents was then conducted under these four themes. Similarities and differences between the global response to HIV/AIDS and NCDs were then examined for each major theme using qualitative content analysis and interpretive synthesis. The findings were presented using narrative summaries, tables and boxes.
Findings: HIV/AIDS and NCD strategies are similar in their general approach. However,

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HIV strategies are geared towards improving effectiveness and efficiency of programs while NCD ones focus on increasing access to and coverage of services and enhancing the priority accorded to NCDs. The organizational systems involved in the global response to both HIV/AIDS and NCDs involve multi-sectoral, multi-stakeholder and multi-level approaches that require global coordination mechanisms. The presence of many diseases in the NCD group means more complex coordination of the NCD response. HIV/AIDS and NCD interventions use similar models and approaches despite their differences in the technical content of the interventions and the demographic characteristics of the target population groups. The indicators and the target populations for monitoring and evaluation of HIV/AIDS and NCD programs differ in their timeframe, level of specificity, and relative magnitude. Besides, the current NCD targets are voluntary. However, the Monitoring and Evaluation frameworks share important similarities in the methods used to generate and manage information.

Conclusion: The similarities between the global responses to HIV and NCDs indicate that there are many processes that could be coordinated and/or integrated to improve synergy and efficiency. The differences, on the other hand, warrant the need for maintaining the integrity of the responses to each disease condition.

Keywords: HIV/AIDS; Noncommunicable diseases; global response.

1. INTRODUCTION

Many disease conditions share different characteristics. Besides their epidemiological convergence in developing countries, HIV/AIDS and the common Noncommunicable diseases (NCDs) share important similarities that are related to their etiology, pathogenesis, and management. Knowledge of interconnectedness among these diseases is important for the design and implementation of integrated prevention and control programs.

From etiological perspective, HIV/AIDS is mostly associated with high-risk sexual behavior. Commercial Sex Workers (CSW), Men having Sex with Men (MSM) and Intravenous Drug Users (IDUs) are generally classified as high risk groups for HIV [1]. Correspondingly, the common NCDs (Cardiovascular disease, cancers, diabetes and chronic respiratory disease) are associated with four major behavioral and lifestyle risk factors (Unhealthy diet, insufficient physical activity, tobacco use, and harmful use of alcohol) [2]. This signifies the importance of 'behavioral' domain in the etiology of both HIV/AIDS and NCDs.

Slow development and progression are common to the pathogenesis of HIV/AIDS and common NCDs. HIV/AIDS has an average of ten years of clinically asymptomatic stage between primary HIV infection and the development of AIDS [3]. Studies indicate that the risk of many NCDs is set during development of an individual. Nutritional imbalance and exposure to environmental chemicals during development can increase NCD risk later in life [4]. Most NCDs are associated with long-term and persistent exposure to their risk factors. Many NCDs also have 'pre-disease' stages that may last for a number of years [5].

Previously, there was a big divide between infectious disease, like HIV/AIDS, and NCDs. As HIV/AIDS has now turned out to be a chronic condition, similar to many of the common NCDs, the prevention and control strategies of HIV/AIDS and NCDs have several similarities. Prevention approaches of both HIV/AIDS and NCDs are targeted at modifying risk behaviors. Treatment and care interventions are directed at improving quality of life

through promotion of long-term adherence to treatment, regular monitoring of biomarkers, and sustainable social support [6].

At Global level, the responses to both HIV/AIDS and NCDs involve a multi-sectoral approach and whole-of-government efforts in order to mitigate the multi-faceted risk factors and multidimensional impacts of these problems [7,8]. The implementation of such complex approaches needs well-coordinated policies, strategies and systems. Above all, the global response needs to be informed by global level evidence on the epidemiology of the diseases and local effectiveness of responses.

Despite the existence of several similarities between HIV/AIDS and NCDs in acquisition, progression and response; the extent to which those similarities are actually reflected in the response to these pandemics is not well investigated. Analysis of commonalities between the response functions to HIV/AIDS and NCDs will be useful in identifying potential areas of overlap and thereby facilitate the coordination and integration of the responses. Therefore, this study was designed to examine global level similarities and differences between the response to HIV/AIDS and common NCDs.

2. METHODS

We conducted a structured review and analysis of global level policies, strategies, reports, and organizational profiles relevant to the global response to HIV/AIDS and NCDs. We used four pre-defined thematic areas: Strategies, systems, interventions and Monitoring and Evaluation. These themes were selected based on their relevance to the global response. Global responses are often characterized by a written action framework (strategies), a list of participating organizations and their relationships (systems), a set of action/program areas (interventions), and a clearly designed Monitoring and Evaluation of the response (M and E). After review of the main documents selected for detailed review (Table 1), information relevant to global level response to HIV/AIDS and NCDs was extracted under the four themes. The extracted information for each theme was then summarized separately for HIV/AIDS and NCDs. Additional information was sought from additional sources as necessary.

Table 1. List of major documents that selected for detailed review

HIV/AIDS	NCDs
UNAIDS strategy (2011-2015)	NCD global action plan (2008-2013)
WHO HIV strategy (2011-2015)	Global strategy on diet, physical activity & health
Declaration of commitment, 2001	Global strategy to reduce harmful use of alcohol
“Three ones” Key principles	Framework convention on tobacco control
HIV Political declaration, 2006	Political declaration on NCDs, 2011
UNAIDS: The first 10 years	Draft Global NCD action plan (2013-2020)
Global strategy framework on HIV/AIDS	Global NCD monitoring framework
Global AIDS response progress report, 2012	Global status report on NCDs, 2010
AIDS and Global Health	A framework for M&E of GSDPAH
Political declaration on HIV and AIDS 2011	WHO cluster strategy on NCDs and Mental Health

In this report, we first described the progress of global response to HIV/AIDS and NCDs during the last few decades in an attempt to establish the historical context for the global response. By analyzing each thematic area separately, we then examined the similarities and differences between the attributes of the global response to HIV/AIDS and NCDs. The review of the documents was basically a qualitative content analysis and interpretive synthesis. We presented the analysis results for each thematic area using narrative summaries and tables as appropriate. Detailed descriptions at sub-theme level were also used when found relevant. Where appropriate the implications of the findings of the analysis are highlighted.

Box 1. Operational definitions of the four research themes

Strategies:
Global HIV/AIDS and NCD prevention and control strategies as indicated in strategic documents including global strategies, strategic plans, strategic frameworks, and policies.

Systems:
The global level institutional arrangements and coordination mechanisms which are involved in the design, implementation, coordination, and financing of the global response to HIV/AIDS and NCDs.

Interventions:
The action/program areas put forward to tackle the causes and consequences of the diseases. These include prevention, treatment, care and structural interventions.

M and E:
The core elements of a health information system that are of great relevance to global response to HIV/AIDS and NCDs. These include M&E frameworks, indicators, targets and data collection methods.

3. RESULTS AND DISCUSSION

3.1 Historical Context of the Global Responses to HIV/AIDS and NCDs

Currently, both HIV/AIDS and NCDs are major global health challenges that demand global response [9,10]. HIV/AIDS is a single disease condition that can be managed with a defined set of interventions. NCDs represent group of diseases which are generally defined by 'what they are not' (i.e. Noncommunicable). The global responses to HIV/AIDS and NCDs have undergone several historical processes. These processes of global response occurred during the last three decades for HIV/AIDS but mainly during the last decade for NCDs [11,12]. The major progresses of in the development of global response to HIV/AIDS and NCDs are presented in Table 2.

Table 2. Major elements of the global response to HIV/AIDS and NCDs

End points	HIV/AIDS	NCDs
Recognition as a public health problem	WHO's first official acknowledgement of the HIV was in 1983. WHO Control Programme was set up in 1986. Global program on AIDS set up in 1987	Health consequences of smoking were recognized by WHO since 1970. NCDs have been the leading causes of morbidity and mortality since 1990 in all burden of disease reports.
WHA resolutions related to HIV/AIDS and NCDs	Global strategy for the prevention and control of AIDS adopted in 1987. Avoidance of discrimination in 1988. Role of NGOs in 1989. Women, children and AIDS in 1990. Updated global strategy in 1992. Comprehensive resolution on HIV/AIDS in 2000. Global fund and WHO medicine strategy adopted in 2001.	Global Strategy for the Prevention and Control of NCDs developed in 2000. FCTC adopted in 2003. Resolution WHA60.23 on Prevention and control of NCDs: implementation of the global strategy adopted in 2007. Resolution WHA61.4 on Strategies to reduce the harmful use of alcohol and Action Plan for the Global Strategy for the Prevention and Control of NCDs adopted in 2008
Formulation of a global strategies for Prevention and control	Global strategy framework (2001). Uniting for universal access: towards zero new HIV infections, zero discrimination and zero AIDS-related deaths (2011).	WHO Framework Convention on Tobacco Control (2003); Global Strategy on Diet, Physical Activity and Health (2004, 2008). Global NCD action plan (2013-Draft).
UN level meeting and declarations	Millennium development goals (2000), Declaration of commitment (2001); Political Declaration on HIV/AIDS (2006, 2011).	Political declaration on the prevention and control of NCDs adopted by UN general assembly (2011).
Current Global targets	Getting to Zero: Zero new HIV infections. Zero deaths from AIDS-related illness. Zero discrimination	25% reduction in premature mortality from Noncommunicable diseases by 2025
Global coordination mechanisms	Joint United Nations Program on HIV–AIDS (UNAIDS) since 1996.	WHO playing a leading role in the global response; NCD alliance plays advocacy role.
Major resourcing	Global Fund to Fight AIDS, Tuberculosis, and Malaria (2001). US government announced PEPFAR (2003)	No major global level funding mechanism/commitment is identified in during the period of this review

3.2 HIV/AIDS and NCD Response Strategies

3.2.1 Strategies targeted at reducing incidence through prevention

3.2.1.1 HIV/AIDS prevention strategies

The current global HIV prevention strategy is about revolutionizing HIV prevention in order to reach at a level of zero new infections [13]. The primary goals are to reduce sexual transmission of HIV by half; to eliminate vertical transmission of HIV; and eliminate new infections among drug users [14]. The strategies to achieve these goals are framed under three major areas: Improving political palatability, renewing prevention approaches and empowering people. In order to generate *political commitment* that address how and why people gets infected, HIV prevention strategies aim to create positive incentives for leaders so that they can do the right things in responding to HIV by better recognizing the critical efforts.

Renewing prevention approaches is related to directing resources to epidemic hot spots through implementation of the right interventions. Prevention strategies emphasize priority prevention programs and include bold prevention targets based on “know your epidemic, know your response” [15]. To *mobilize communities* in order that they effectively demand transformative social and legal change, HIV prevention efforts intend to create shared social commitment to health, overcome stigma and discrimination and support people in changing their behavior. HIV prevention strategies also aim to maximize the empowerment and facilitation of young people as change agents through peer-led approaches and through Positive health, dignity and prevention [16].

3.2.1.2 Noncommunicable disease prevention strategies

NCD prevention strategies attempt to counteract the risk of NCDs from the four common risk factors [17]. As the ultimate decision of adoption healthy behavior depends on an *individual choice,* the NCD prevention strategies are geared towards influencing individual decisions. The major NCD prevention strategies can be categorized in to three broad classes [12,18]. The first is about *framing Public policies* that influence the standards for food composition and marketing; the planning of cities that are appropriate for physical activities; the regulation of contents of tobacco products, tobacco product disclosures and marketing of tobacco products; and the availability, composition and marketing of alcohol [19].

The second is *creating enabling environment* by reducing modifiable risk factors and facilitating health promoting environments for individuals who are expected to make healthy choices. This includes increasing availability of healthy food choices and improving the labeling of food composition; improving physical environments to be appropriate of walking, cycling and other relevant physical activities; creating smoke free environments and provision of support for economically viable alternative activities; enhancing community capacity to encourage and coordinate the reduction of harmful use of alcohol.

The third one is *building individuals’ capacity* by providing adequate information related to health diet, adequate level of physical activity, harmful effects tobacco and alcohol use. Clear public messages about physical activity, information on healthy diet, and risks of tobacco and alcohol use should be communicated with individuals [20-23].

3.2.1.3 Similarities and differences between HIV and NCD prevention strategies

The prevention strategies for both HIV/AIDS and NCDs address overlapping arenas: Policies, environments and individuals. In the policy arena, HIV prevention strategies are targeted towards *generating political commitment* to prevention throughout society by improving its political palatability while NCD prevention strategies mainly focus on *formulation of policies* that encourage healthy food choices and adequate physical activity; and reduce the demand for and supply of tobacco and alcohol. Thus, the focus of current policy related HIV strategies is mainly on policy implementers (leaders) while that of NCDs is on the policies.

In the environmental arena, HIV prevention strategies tend to *focus prevention efforts* where they will deliver the greatest returns to investment; incorporating new technologies (vaccine and drugs) and approaches as they are developed. On the other hand, the approach of NCD prevention strategies is towards creating an enabling environment by improving availability and accessibility of healthy foods, environments suitable for physical activity, smoke free environments, and enhancing community capacity against harmful use of alcohol. It looks that the HIV prevention strategies are more concerned about effectiveness and efficiency while NCD strategies are centered on increasing coverage and access.

In the individual domain, HIV prevention strategies aim at *empowering people* to overcome stigma and discrimination and their risk of HIV infection through comprehensive sexuality education and the engagement of networks of people living with HIV and other key populations. In the same domain, NCD prevention strategies give priority to *building individuals' capacity* to make healthy choices by strengthening the informational basis for healthy foods, physical activity, and harmful effects of tobacco and alcohol use among individuals. Empowerment and capacity building are in the same continuum engagement.

3.2.2 Strategies for optimizing treatment care and support

3.2.2.1 HIV/AIDS treatment, care and support strategies

Achieving universal access to treatment for all eligible individuals is the main goal of the HIV strategy. Achievement of this goal is expected to reduce AIDS-related deaths and new HIV infections [24]. As a result of coordinated efforts, people infected and affected by HIV are expected to have improved access to essential care and support services and national protection strategies. One focus area of HIV/AIDS treatment, care and support strategies is *renovating approaches* [13]. The development of simpler, more affordable and effective treatment regimens and tools are among the global strategies for HIV treatment. The adoption of innovative service delivery models that reduce costs and empower communities to demand and deliver better and more equitable treatment, care and support services is another strategy to renovate treatment approaches. Maximizing links with other health and community services is also expected [25].

Another area of focus of HIV/AIDS treatment, care and support strategies is the strengthening of national and community *systems* to deliver decentralized and integrated services. As the majority of care and support is provided by families and communities, strengthening community systems is the main focus. The scale up of community-health provider relations is therefore essential. Moreover, *leveraging broader outcomes* is a key element of HIV/AIDS treatment and care strategies [26]. This involves working with partners to scale up access to tailored care and support. Both international and national level

partnerships need to be strengthened to generate HIV-sensitive social protection policy to accelerate the establishment of effective and transformative programs. Optimizing program links between HIV and other key health areas is also crucial for leveraging broader health outcomes. Such links are also important to ensure that HIV responses benefit from investments in other related health program areas [26].

3.2.2.2 NCD treatment, care and support strategies

The global response to NCDs aims to strengthen and re-orient health systems to address NCD prevention and control through people-centered primary care and universal coverage. Cognizant of this objective, NCD strategies related to treatment, care and support fall under three thematic areas: Reorientation, strengthening and integration. Health systems, especially in developing countries, needs to be re-oriented in order that they put NCDs at the forefront of their priorities. Strengthening the capacity of those health systems to deliver adequate treatment, care and support for people with NCDs is also one of the main priorities. Strengthened health systems are expected to provide comprehensive and integrated services to those in need of such services [27].

3.2.2.3 Similarities and differences in treatment, care and support strategies

HIV/AIDS treatment, care and support strategies call for *renovating systems* for treatment, care and support. Similarly, NCD strategies are directed towards *reorienting systems* to ensure that NCDs are considered as key priorities of the healthcare system. Strategies in this category for both disease conditions give due emphasis for *strengthening systems*. Another major overlapping area in these strategies is the need for integrated response. *Leveraging* broader outcomes by optimizing links between HIV and other health areas is among the HIV strategies, while *integrating* cost-effective NCD interventions in to healthcare systems is among the major strategies of NCDs.

3.2.3 Strategies for addressing vulnerability and structural barriers

3.2.3.1 HIV/AIDS strategies for addressing vulnerability and structural barriers

Current HIV strategies have put human rights, equity and gender equality at the center of the HIV response. Addressing these issues requires a major shift in coverage, content and resourcing of HIV programming [28]. HIV programs introduce measures to eliminate all forms of discrimination and to ensure the full enjoyment of all human rights and fundamental freedoms by people living with HIV/AIDS and other vulnerable groups. They also empower women to have control over and decide freely and responsibly on matters related to their sexuality to increase their ability to protect themselves from HIV infection. Advancing human rights and gender equality in HIV response is a means of ending the HIV-related stigma, discrimination, gender inequality and violence against women and girls[29]. This means putting laws, policies and programs in place to create legal environments that protect people from infection and support access to justice.

HIV/AIDS strategies under this category include there major priority issues. The first one is w*orking with right holders*. HIV programs work with and through people living with HIV, people at higher risk of HIV, civil societies, women and girls. They also actively engage men in addressing negative male behavior and changing harmful gender norms. The second priority issue is *advancing country capacity.* Countries' capacity to create protective social and legal environments, to reduce stigma and discrimination, to realize equitable access to

services, to address the needs and rights of women and girls in the context of HIV, and to include gender issues in the design, delivery and monitoring of health services need to be strengthened. The third priority issue is *addressing vulnerability.* Empowering women is essential to reduce their vulnerability to HIV. HIV responses also need to address factors that make individuals particularly vulnerable to HIV infection. Children orphaned and affected by HIV/AIDS need special assistance. Conflicts and disasters contribute to the spread of HIV/AIDS [30]. All these are well considered in the HIV strategies.

3.2.3.2 NCD strategies for addressing vulnerability and structural barriers

Prevention and control of NCDs is directly related with universal right of people to enjoy the maximum health they can attain. However, women in developing countries bear disproportionate burden of NCDs as they tend to be less physically active than men, more likely to be obese and take up smoking from household fuels at alarming rates. NCD responses, therefore, need to promote gender-based programs that address the critical differences in the risks of morbidity and mortality from non-communicable diseases for women and men.

At global and national levels, NCD responses need to strengthen advocacy efforts in order to raise the priority accorded to prevention and control of NCDs in the UN development agenda. Prevention of NCDs is a pre-condition for and an outcome of sustainable human development. It is interdependent with social, economic and environmental dimensions of development. Therefore, a coherent cross-sectoral response is needed to reduce the NCD burden and enhance the social and economic development, particularly in low- and middle-income countries. Critical to the NCD response is strengthening capacity, leadership, governance and accountability to accelerate countries' response to NCDs. Strengthening national policies and systems in order to effectively plan and execute appropriate NCD programs remains to be among the key strategies in the global response to NCDs.

3.2.3.3 Similarities and differences between Strategies addressing vulnerability and structural barriers

Both HIV/AIDS and NCD strategies address gender-related issues but they seem to be at different levels of gender mainstreaming. HIV strategies advocate for higher levels of women empowerment whereas NCD strategies focus on promotion of gender-based programs to address disproportionate burden of NCD morbidity and mortality. This difference may be due to the variations in the level of previous responses to the diseases. In addressing structural barriers, HIV/AIDS strategies call for advancing countries' capacity to improve protective and legal environments whereas NCD strategies call for accelerating countries' response with actions on policies, systems and leadership. In right related issues, HIV/AIDS strategies endorsed the approach of working with right holders including PLHIV, MARPs, women, civil societies, and engaging men in gender issues. In this aspect, NCD strategies adopted the integration of NCDs with development strategies to promote coherent cross-sectoral response.

3.2.4 Strategies for leadership and coordination of response

3.2.4.1 HIV/AIDS strategies for leadership and coordination

HIV/AIDS, as a global public health problem, needed strong global, regional and national level leadership and coordination of efforts. UNAIDS has been playing major roles in global

leadership on policy and coordination of HIV/AIDS prevention and control through strong collaborations and partnerships with UN agencies, public sectors, civil societies and private sectors. Regional, sub-regional, and inter-regional coordination, cooperation, approaches and strategies have also been designed and implemented to mitigate the impacts of the HIV/AIDS epidemic. Local and national organizations have been enabled to expand their regional partnerships, coalitions and networks [31].

At national level, the HIV/AIDS response adopted the multisectoral and multi-stakeholder approaches in the development and implementation of national strategies. These approaches were needed because of the multifaceted nature of both the impacts and the interventions of HIV/AIDS. The multisectoral approaches facilitated the financing plans for combating HIV/AIDS, the protection of human rights, the wider participation of people living with and affected by HIV, and the effective contribution of international cooperation. It also enhanced the mainstreaming of HIV/AIDS response efforts in to development strategies of the countries. The mainstreaming has further improved accountability through shared ownership. During the course of implementation, HIV/AIDS response was positioned to adapt with the changing world. Strategic directions and leadership roles were also renewed accordingly by building up on progresses in order to address the dynamics of diverse and evolving HIV epidemics [32].

The “Three ones” principle, which emphasizes on the need for one coordination mechanism, one action framework and one monitoring and evaluation framework, has been one of the key steps in the harmonization and alignment HIV/AIDS interventions and actors at national level. Accordingly, in most countries where HIV/AIDS is a major public health problem, there exist a multisectoral response coordinating authority, strategic plan and monitoring and evaluation framework. The multisectoral response coordinating authority provides leadership for the national response in partnership with governmental sectors, non-governmental organizations, civil societies, international organizations and the private sector. At all levels, people living with HIV and at higher risk of HIV, are at the center of the efforts to lead and own the overall response [7].

3.2.4.2 NCD strategies for leadership and coordination

NCDs have a complex set of risk factors that make vicious cycle with poverty. NCD prevention and control approaches promote a whole-of-government and whole-of-society approach for multisectoral action and partnerships. As the primary specialized agency for health, the World Health organization (WHO) plays leadership and coordination role in promoting and monitoring global action against NCDs. The NCD alliance along with its national partners mainly plays an advocacy role to raise the priority accorded to NCDs [10].

International cooperation, including collaborative partnerships, is considered to be among the major strategies in addressing NCDs [33]. Given the diverse nature of risk factors of NCDs, the involvement of both health and non-health sectors is essential. The participation of patient associations and other civil societies is also crucial. Though there is no single model suggested for the leadership of NCD response at country level, a multisectoral approach is imminent. The experience from HIV/AIDS indicates that multisectoral approaches need strong coordinating authority, agreed up on action framework and Monitoring and evaluation frameworks. Given the linkage of NCDs with several other health related issues, integrated approaches will also be needed [34].

3.2.4.3 Similarities and differences between leadership and coordination strategies

Both HIV/AIDS and NCDs are major challenges to development with multi-faceted impacts. Their response requires whole-of-government and whole-of-society efforts with multisectoral and multi-stakeholder approaches. Strong and adaptive coordination mechanisms at all levels as well as international cooperation and collaboration are needed. Active role of people affected by the diseases and those at higher risk of the diseases is also important in the leadership and coordination of the responses. Ensuring synergies, linkages and integration with other programs is a feature of leadership and coordination strategies of both HIV/AIDS and NCDs [35].

3.3 HIV/AIDS and NCD Response Systems

Due to the multi-dimensional nature and impacts of HIV/AIDS and NCDs, several organizations and institutions are involved in the global response [10, 36]. Therefore, there is a need for complex coordination mechanisms within and among these organizations. The analysis of the similarities and differences between these institutional arrangements and coordination mechanisms needs to disentangle such complexities [37].

3.3.1 HIV/AIDS institutional structures and coordination system

Global HIV/AIDS response is coordinated by UNAIDS. This joint and co-sponsored United Nations Program of HIV/AIDS represents an internationally coordinated response of the United Nations system organizations to the HIV/AIDS pandemic. The main objectives of the program are to provide leadership, promote global consensus on policy and approaches, strengthen capacity, promote political and social mobilization and advocate for greater political commitment. To achieve these objectives, UNAIDS collaborate with National governments, inter-governmental organizations, Non-governmental organizations, United Nations system organizations and people living with HIV. The governance structure of the program includes program coordination board which has the representation of governments, co-sponsoring organizations, Non-governmental organizations and civil societies including associations of PLHIV. The standing committee of the program coordination board is the committee of co-sponsoring organizations. The UNAIDS secretariat is comprised of the Executive director, and technical and administrative staff [38].

UNAIDS and its Cosponsoring organizations work together to provide technical assistance to countries to facilitate the implementation of national HIV/AIDS plans. In order to ensure that countries receive the best possible technical assistance in respective areas, and to avoid any possible duplication of efforts, a *division of labor* between the Cosponsor organizations guides the technical support offered to countries [39]. Based on the comparative advantages of each of the UNAIDS organizations, the division of labor enables UNAIDS to deliver a unified and consolidated UNAIDS-sourced technical support plan throughout the program.

Other global mechanisms include the Global Fund, which is essentially a *financial model* dedicated to attracting and disbursing additional financial resources to countries. The central element of the Global Fund partnership strategy is country coordinating mechanism (CCM), country-level partnership composed of all stakeholders in a country's response, which develop grant proposals based on priority needs and oversees its implementation. A principal recipient, designated by CCM, receives the fund and implements the program and/or sub-grant the money. Under the governance of a board, the Global fund secretariat

manages the grant portfolio. A trustee manages the Global Fund money. At country level firms are contracted to monitor the implementation of a grant [40].

Another major part of Global response to HIV/AIDS is the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). PEPFAR is the largest commitment by any nation to combat a single disease internationally. Under the leadership of the U.S. Global AIDS Coordinator, the implementing agencies use inter-agency coordination mechanisms to work together. Coordination with countries is based on partnership frameworks [41]. Other major global mechanisms that mainly play advocacy role in the global response to HIV/AIDS include the Global Network of PLHIV, International alliance of civil society organizations, and International society of HIV/AIDS professionals.

3.3.2 NCD institutional structures and coordination system

The highest level of global response to NCDs is that of the United Nations system. Many UN agencies involve in the global response to NCDs. In the global response to NCDs, the World Health Organization (WHO), as a primary specialized agency for health, plays a leading role in the prevention and control of NCDs [10, 41, 42]. Guided by its strategy for Health, Nutrition and Population results, the World Bank has also outlined a number of approaches and roles in the global response to NCDs [43, 44]. UNICEF began to tackle NCDs in children and adolescents. The World Trade Organization (WTO) can also influence trade agreements related to food, alcohol and tobacco. Other UN agencies like UFP and ILO also have important roles. Multi-stakeholder forums, like Global agenda council on NCDs of the World Economic forum, are also relevant to the response coordinating mechanisms.

The NCD alliance, which is founded by four international NGO federations representing the four common NCDs–cardiovascular disease, diabetes, cancer, and chronic respiratory disease- is an essential mechanism for global advocacy. The four international NGO federations in NCD alliance are the International Diabetes Federation (IDF), Union for International Cancer Control (UICC), World Heart Federation (WHF) and International Union against Tuberculosis and lung disease (The union). These four federations have member organizations in many countries [45].

There are also global level foundations acting as independent, non-profit organizations to support the response to NCDs. World Diabetes foundation, world heart foundation, and world lung foundations are examples. These organizations provide technical assistance and implement NCD programs in different countries. In addition, there are also different forms of networks that are organized to facilitate the implementation of NCD prevention and control strategies and plans. Global NCD network, a voluntary collaborative arrangement organized to help implement the NCD action plan, is an example. In this network are United Nations agencies, intergovernmental organizations, academia, research centers, non-governmental organizations, and the business community. Putting in place effective collaboration focused on achieving results in low- and middle-income countries was a priority agenda of this network.

Framework convention alliance works on development, ratification and implementation of FCTC. Other alliances such as Global alliance against chronic respiratory disease (GARD) and Global alliance for chronic disease (GACD) addresses specific diseases or specific element of the NCD response. They also serve as a consortium of several other organizations. International organizations whose primary goal is to advance global health in general, such as Global Health Council, also have important stakes in the global response to

NCDs. Moreover, many other global initiatives, institutes, societies, associations, bilateral development agencies, and partnerships could contribute to the global response to NCDs in terms of advocacy, research, technical assistance or program implementation. As NCDs represent a group of diseases, rather than a single disease, different forms arrangements of professional, patient, civil society exist at global level.

Many of the global level mechanisms have regional level arrangements that take care of the NCD response in their respective geographic regions. Regional mechanism like Pan-American Health Organization Partners Forum to Fight Chronic Disease and regional offices of the different international and global organizations, alliances, and platforms also provide important opportunity for coordination of NCD responses at regional level. African Tobacco alliance and center for Tobacco control in Africa are also examples of other regional organizations.

3.3.3 Similarities and differences between HIV/AIDS and NCD systems

Both HIV/AIDS and NCDs are shared global health challenges that have global determinants. The response to these global challenges needs whole-of-society efforts and an enormous amount of resources that can only be addressed through better coordination of several organizations and mechanisms at global level. With the large proliferation of global stakeholders and emergence of several global initiatives, a global coordination mechanism became the center of the response to HIV/AIDS and NCDs. A key characteristic of the global response to both HIV/AIDS and NCDs is the need for a global multi-sectoral response *coordinating mechanism*.

The presence of global alliances for advocacy that involve people living with disease, health professionals are civil society organizations is another similarity between global responses to HIV/AIDS and NCDs. This indicates that a global level coordination of advocacy go in line with country level coordination of responses. Global level foundations and institutions that implement programs in different countries also have coordination mechanisms within and among themselves. Intra-and inter-institutional coordination are thus the key characteristics that are common to both HIV/AIDS and NCD responses. Global financial mechanisms exist for HIV/AIDS, TB and Malaria. However, such mechanisms for NCDs are currently lacking. In this regard, the global NCD threat demands global level financial commitment and financial mechanisms.

While the involvement of many stakeholders is a characteristic of the responses to both HIV/AIDS and NCDs, the number of stakeholders and the complexity of the coordination are higher in the NCD response. This is due to the fact that NCDs represent many diseases and there are many 'disease-specific' stakeholders that work together with organizations that address NCDs as an entity.

3.4 HIV/AIDS and NCD Interventions

As both HIV/AIDS and NCDs are considered to be *chronic conditions*, the relationships between their interventions can be investigated using different models of chronic disease interventions. Chronic disease interventions can be classified based on three dimensions: Level, approach and technical area. The inter-connected needs of people with chronic diseases mean that the boundaries between different categories of interventions can be difficult to draw, especially in developing countries. This is mainly because many interventions are often implemented by the same organizations or providers. Applying a

triangulated approach, the similarities and differences between HIV/AIDS and NCD interventions are discussed using the dimensions and sub-dimensions of chronic disease intervention frameworks.

3.4.1 Similarities and differences by levels of interventions

At individual (Micro) level, both HIV/AIDS and NCD interventions require *active participation* of the individual concerned. In many instances, self-management is also part of the intervention. To effectively engage people, there is a need to empower and prepare them to manage their own health and healthcare. Patients also participate in patient associations and societies to advocate right and equity related issues in to the policy making processes. While attaining and maintaining healthy behavior using different behavioral change models is the main goal of prevention interventions, early start-up and long-term adherence to treatment with regular monitoring of biomarkers are the main focuses of care and treatment interventions. Worth noting is that the *technical content* of interventions, what is actually delivered to eligible individuals, and the socio-demographic characteristics of the target populations are very different [46,47].

At Healthcare organization (Meso) level, HIV/AIDS and NCD interventions create a culture, organization, and mechanisms that promote safe and high quality care. Through different approaches of *health systems strengthening*, health facilities promote continuity and coordination of services. They also organize and equip *multidisciplinary healthcare teams* as the services for both HIV and NCDs demand multiple expertise. Moreover, healthcare organizations support self-management and prevention of chronic conditions. Use of information systems that generate practice-based evidence for evidence-based practice is also among the main pillars of health-facility level interventions.

Community (Meso) level HIV/AIDS and NCD interventions involve enabling community systems to effectively contribute to the health of communities. Most prevention interventions are implemented to raise awareness and reduce stigma. Extending care and support services to community and family level require mobilization and coordination of community resources to meet the need of patients. Through leadership and support, community-based organizations can provide complementary services.

Policy (Macro) level HIV/AIDS and NCD interventions aim to create *conducive policy environment* for the overall response to the diseases. These interventions involve formulation, promotion, implementation and evaluation of policies and strategies along with the integration of policies within and among different policies of sectors and stakeholders. Policy level interventions also involve the development and implementation of legislative frameworks that can reduce the burden of diseases and protect the rights of people with chronic diseases. Policy level interventions need to ensure the availability of consistent financing and human resources. Another key policy level intervention for chronic disease is strengthening partnerships and cooperation within and among all stakeholders in order to leverage resources and maximize synergy among different stakeholders.

3.4.2 Similarities and differences by approach of intervention

Both HIV/AIDS and NCDs are related with individual behavior. While HIV is related with high risk sexual behavior, NCDs are related to consistent unhealthy diets, physical inactivity, alcohol use and tobacco use. Accordingly, *behavioral/social* interventions constitute a major part of both HIV/AIDS and NCD interventions. These interventions are meant to reduce the

risk of the diseases by enabling individuals to modify their behavior. Behavioral interventions of both HIV/AIDS and NCDs use a broad range of communication techniques that are tailored to the target population and the risk factor involved.

Biomedical/biological interventions use medical and public health approaches to block the development of HIV/NCDs and reduce susceptibility [48]. For HIV/AIDS biomedical interventions can be designed for individuals who have higher risk of HIV and people living with HIV. These interventions reduce the risk of getting infected (pre-infection interventions) and the risk of transmitting the virus to another individual (post-infection interventions). The pre-ART period is a critical point where essential lifestyle changes are needed. On the other hand, the common NCDs have "pre-disease" conditions that can be managed by both lifestyle changes and medical interventions. Effective interventions can reverse or maintain these "pre-disease" conditions. The "pre-disease" conditions in both HIV and NCDs require the prevention and treatment of other associated conditions. Therefore, screening plays an essential role in both HIV and NCDs in identification of risk of disease at earlier time.

Once a chronic disease, HIV/NCD, is diagnosed in an individual, *clinical/therapeutic* interventions along with other complementary interventions will be the mainstay of the management. The aim of the clinical interventions is to control the disease and prevent and/or treat any other adjacent complications. The level of control of the disease is monitored by key biomarkers. CD4 count is the main biomarker for HIV. Blood glucose level, blood pressure, Lung function indices, ECG and tomography tests are the indicators of progress in NCD treatment. Long-term adherence to treatment as well as sustainable lifestyle changes are needed in clinical interventions of both HIV/AIDS and NCDs. The overall aim of the clinical interventions in most cases is not to cure the disease but to control it within acceptable limits and avoid any complications that could result from further progression of the disease or from its management [49].

Structural interventions for HIV/AIDS and NCDs include programs that change legal environments (often with community pressure or input) to make practicing safer behavior easier. They can also target the immediate social context of behaviors by changing the physical or normative environments within which they occur. Structural interventions also include programs to reduce or abolish inequalities, inequities and oppressions which create vulnerability to chronic diseases. Structural interventions often address issues that seem to be unrelated to the diseases. Factors affecting risk and vulnerability have to be considered when developing and evaluating prevention policies. Although the *social contexts* to be considered are different, structural interventions for both HIV/AIDS and NCDs lay the foundation for the prevention and control of these epidemics [50].

3.4.3 Similarities and differences by technical area of interventions

HIV interventions are usually classified in to four technical areas [51]. *Prevention* interventions, the main pillar of the response to both HIV/AIDS and NCDs, fall under five broad categories. These are interventions that affect knowledge, attitudes and beliefs and influence psychological and social risk correlates; harm reduction interventions that lower the risk of behavior, but do not eliminate the behavior; biological/biomedical interventions that strive to reduce development and progression of disease; interventions that mitigate the barriers to prevention and social and biological outcomes; and hybrid interventions, which bundle discrete intervention approaches, and which are in common use and are well standardized. However, the message content, the delivery mode, the target population,

setting, theory and planned outcomes of HIV/AIDS and NCD prevention interventions vary widely based on the specific contexts [52,53].

Treatment interventions of both HIV/AIDS and NCDs, with an overall goal of improving quality of life, have four major aims: controlling the disease; ensuring adherence to standard treatment and prevent any possible 'resistance' to drugs; preventing and/or treating associated diseases that may include co-infections, co-morbidities, opportunistic infections etc.; and preventing and/or appropriately managing possible complications of the treatment. The treatment approaches, models and tools of HIV and NCDs are largely similar though the technical content of the treatments vary [54].

Care and support interventions include psychological, clinical, social, economic, human rights, legal, family and community focused interventions [55]. Besides having larger overlap with treatment and prevention interventions, the provision of care and support interventions need collaborative effort of healthcare providers, patients, and community and family members to complete the continuum of care. In addition to individuals with the disease, the care and support interventions also address the needs of other peoples affected by the disease including immediate family members, children etc. Except for some disease-specific issues, NCD and HIV/AIDS care and support interventions are largely similar.

The creation of *enabling environment* for the prevention and control of HIV/AIDS and NCDs is another technical area. In broad terms, creating enabling environment describes the formulation and adoption of policies and systems that allow, favor and strengthen actions against HIV/AIDS and NCDs. Creating an enabling environment will have four dimensions: The *actors* who create the enabling environment, the *processes* through which enabling environment is created, the *context* under which enabling environment is created, and the *attributes* of the created enabling environment [56].

There is a significant overlap between creating enabling environment for HIV/AIDS and NCDs prevention and control interventions. *Multiple actors* will be involved in creation of enabling environment. Highly interactive *processes* are needed to create the enabling environment. Creation of the enabling environment happens in the same health system *contexts*. However, the attributes of the policies of HIV/AIDS and NCDs is major area of difference. The battle with HIV has lasted for more than three decades while that of NCDs is at earlier stage. Hence, the focus areas of new HIV policies will be to sustain and advance HIV mitigation efforts that are already in place while that of NCD policies will be to establish, strengthen and promote policies and strategies.

Overall, HIV/AIDS and NCD interventions share several similarities in terms of the attributes of the processes involved in the design and implementation of the interventions. The major areas of similarities are the interventions approaches, models, theories and tools involved in the planning and implementation of the interventions. On the other hand, the key areas of difference are the technical contents of the interventions, the target populations, the settings, and the expected outcomes. It will therefore be appropriate to consider some level of integration between HIV/AIDS and NCD interventions to the least to share important lessons from the HIV/AIDS interventions and to ensure coherence of the interventions.

3.5 HIV/AIDS and NCD Monitoring and Evaluation

Multisectoral responses to HIV/AIDS and NCDs need multisectoral monitoring and evaluation systems. The responses to both HIV/AIDS and NCDs require agreed upon monitoring and evaluation system. A single, unified and coherent Monitoring and Evaluation system for each of these disease conditions minimizes duplication of efforts and generates useful evidence for policy and practice. Because the interventions in both HIV/AIDS and NCDs programs involve diverse technical areas, *multidisciplinary* expertise is also needed for effective monitoring and evaluation of the responses.

Based on their epidemiological profiles and health system arrangements, different countries have different Monitoring and Evaluation needs. Tailoring HIV/AIDS and NCD programs and their Monitoring and Evaluation approaches to the epidemic context is needed. Moreover, the Monitoring and Evaluation of both HIV/AIDS and NCDs require multi-level structures and functions [57].

3.5.1 Goals and targets

For global HIV/AIDS response, there are seven major targets set under three broader themes that envision zero new infections, zero AIDS-related deaths and zero discrimination [13]. Similarly, there are nine voluntary NCD targets organized under three themes: Mortality and Morbidity, Risk factors and National systems response [58]. Three of the seven HIV/AIDS targets and four of the nine NCD targets are directly related with prevention. There are four underlying themes linking these targets: Reduction of risk factors or *prevention* of the occurrence of a disease; reducing the magnitude of *morbidity and mortality* from these diseases; improvement of access to *healthcare services* for those eligible clients affected by the diseases; and strengthening the *national response systems*. Thematic relationships between the targets for HIV/AIDS and NCDs are shown in Table 3.

Table 3. Thematic relationship between HIV/AIDS and NCD targets

Theme	HIV/AIDS targets	NCDs targets
Prevention	Reduce sexual transmission of HIV by 50% by 2015	30% reduction in prevalence of current tobacco use in persons aged 15+ years
	Reduce transmission of HIV among people who inject drugs by 50% by 2015	10% relative reduction of insufficient physical activity
	Eliminate mother-to-child transmission of HIV by 2015	At least 10% relative reduction in the harmful use of alcohol, as appropriate within the national context
		30% relative reduction in mean population intake of salt [/sodium intake]
Morbidity and Mortality	Substantially reduce AIDS-related maternal deaths	25 % relative reduction in overall mortality from cardiovascular diseases, cancer, diabetes or chronic respiratory diseases
	Reduce tuberculosis deaths in people living with HIV by 50% by 2015	25% relative reduction in the prevalence of raised blood pressure or contain the prevalence of raised blood pressure according to national circumstances
		Halt the rise in diabetes and obesity
Healthcare services	Have 15 million people living with HIV on antiretroviral treatment by 2015	At least 50% eligible people receive drug therapy and counselling (including glycaemic control) to prevent heart attacks and strokes
National	Reach a significant level of annual global	80% availability of affordable basic

response systems	expenditure (US$22-24 billion) in low- and middle-income countries Critical Enablers and Synergies with Development Sectors	technologies and essential medicines, including generics, required to treat major NCDs in both public and private facilities

All HIV targets are generally higher (in terms of percentage) than that of NCDs. Besides, the NCD targets are voluntary. The timeframe for expected achievement of most HIV targets is 2015 while for that of most NCD targets is 2025. Another key difference is that the HIV targets have more specific target population groups. The differences could be due to the differences in funding commitments, level of previous responses, baseline levels and global epidemiology of the diseases.

3.5.2 Indicators and methods of measurement

At global level there are 30 core HIV/AIDS indicators under the seven target areas [59]. Correspondingly, there are 25 NCD indicators under the nine target areas [58]. The majority of the indicators in both HIV/AIDS and NCDs are prevention indicators and thus demanding community-based data collection systems. In line with the targets, the indicators of both disease conditions fall under four major themes.

3.5.2.1 Behavioral/Lifestyle indicators

Indicators of *sexual transmission* of HIV address three population groups: young people aged 15-24 years, sex workers and Men having sex with Men (MSM). These indicators measure universal knowledge on HIV transmission, reach of prevention programs, rate of high risk sexual behaviors, and rate of condom use. The methods of measurement for these indicators are periodic surveys and surveillances of different kind.

HIV indicators that measure the reduction in *parenteral transmission* of HIV among people who inject drugs aim at measuring use of sterile injecting equipment, and use of condom among this population group. The number of syringes distributed is also considered to be relevant. Apart from the indicator on the number of syringes which needs program data as its method of measurement, the rest of the indicators in this group use surveys and surveillances as their method of measurement.

The behavioral/lifestyle indicators for NCDs address the prevalence of tobacco use, insufficient physical activity, harmful use of alcohol and unhealthy dietary habits. The target populations for these indicators are adolescents and/or adults. Surveys and surveillance will be the main methods of measurement for these indicators. While the target population groups for HIV/AIDS and NCD prevention indicators looks different, the methods of measurement are quite similar. It is also possible to notice that the majority of target population for HIV/AIDS prevention indicators is a sub-set of the target population for NCD prevention indicators [58,59].

3.5.2.2 Morbidity and mortality indicators

HIV/AIDS morbidity indicators measure the prevalence of HIV among youth 15-24 years of age, sex workers, MSM, people who inject drug, and HIV exposed infants (HEI). HIV/AIDS mortality indicators focus on reduction of AIDS-related maternal deaths and TB deaths among PLHIV. Surveys, surveillance and modeling are the main methods of measurement for morbidity and mortality indicators of HIV/AIDS. On the other hand, NCD morbidity

indicators measure prevalences of raised blood pressure, raised blood glucose, raised total cholesterol, overweight and obesity, and alcohol related morbidity among adolescents and/or adults. The NCD mortality indicators measure overall mortality from the four common NCDs among people 30-70 years of age, cancer incidence, and alcohol related mortality among adults and/or adolescents. Similar to the HIV indicators, survey and surveillance will be the key methods of measurement of these indicators [58,59].

3.5.2.3 Healthcare service indicators

Healthcare service indicators of HIV measure uptake of HIV test among youth 15-24 years of age, sex workers, MSM, people who inject drug, and HEI. They also measure coverage of and/or adherence to HIV treatment among those PLHIV who are eligible for treatment and HIV-positive pregnant mothers. Coverage of co-management of TB/HIV co-infection is also among these indicators. Facility-based ART registers and cohort analysis reports are the main methods of measurement of these indicators [60]. Healthcare service indicators of NCD measure availability of HPV vaccination, coverage HBV vaccination among infants, access to palliative care services among cancer patients, coverage of cervical cancer screening among women 30-49 years of age and coverage of counseling and therapy for heart attacks and strokes among eligible 40 years and more with cardiovascular risk factors [58]. The methods of measurement of these indicators will mainly be facility-based registers, surveys and surveillance.

3.5.2.4 National systems response

The main national systems response indicators for HIV/AIDS measure domestic and international AIDS spending using national AIDS spending assessment and indicators of critical enablers and synergies with development sectors including national commitment and policy instrument, intimate partner violence among women, orphans school attendance, external economic support to the poorest households affected by HIV and AIDS [61]. Surveys are the main methods of measurement for these indicators. National systems response indicators for NCDs measure the adoption of national policies related to food composition and marketing, and availability and affordability of NCD medicines in both public and private facilities. National commitment and policy index (NCPI) and National AIDS spending assessment (NASA) are two monitoring methods for the policy related indicators [62].

3.5.3 Surveys and surveillance

HIV/AIDS indicators database brings information from several surveys and surveillances. The common surveys that contribute to HIV/AIDS indicators include Demographic and Health Survey (DHS), Multiple Indicator Cluster Survey (MICS), Reproductive Health Surveys (RHS), Sexual Behavior Surveys (SBS), Behavioral Surveillance Survey (BSS), and Health Facility Surveys (HFS) [63].

There are also different types of HIV surveillance. The most commonly known are Behavioral surveillance (General population-based behavioral surveys, Sub-population-based behavioral surveys), Biological surveillance (Sentinel sero-surveillance, Cross-sectional sero-surveys in sub-populations at risk, General population-based HIV serosurveys), Second generation surveillance, HIV and AIDS case surveillance, and HIV Drug resistance surveillance [64,65].

Similarly, global and national level information systems for NCDs involve different forms survey and surveillance [66]. The prominent of one is the STEPS surveillance system which includes the STEPwise approach to risk factor surveillance and STEP wise approach to Stroke surveillance [67]. Two other common surveys are the Global Tobacco survey, which includes Global Adult Tobacco Survey (GATS) and Global Youth Tobacco Survey (GYTS), and Global survey on alcohol and health. Depending on the context of the countries there are also disease-specific survey and surveillances for NCDs [68,69]. As the priority accorded to NCDs increases, more and more survey and surveillance types are expected to evolve. From the analysis of monitoring and evaluation of HIV/AIDS and NCD responses, it is possible to learn that the target populations vary but the methods used are very similar. Comparison of HIV and NCD surveillance frameworks is shown in Table 4.

Table 4. Comparison of HIV and NCD surveillance frameworks

Major elements	HIV/AIDS	NCDs
Mortality	Involves deaths due to HIV disease. Compiled from mortality records and mortality surveys.	Involves 30-70 years group. Compiled from mortality records and mortality surveys.
Morbidity	Sero-prevalence of HIV and prevalence of AIDS are the main focus. Involve clinical and lab tests.	Cancer incidence, by type of cancer, per 100,000 population is the currently the only indicator in the global framework.
Risk factors	High risk behavior is the focus. Repeated behavioral surveys among youth and specific population groups.	Risk factors and pre-disease states are the main focus. Repeated behavioral surveys among adolescents and adults
Health service provision	Health facility records and cohort analysis are used to generate evidence on service utilization. Retention rates and CD4 counts are used as indicators of quality of service. Surveys are also relevant.	Follow up records will be useful in monitoring service utilization. Level of control of disease and prevalence of complications can also be retrieved from health facility records. Surveys also indicate community level utilization rates.

4. CONCLUSION

Globally, for HIV/AIDS, the focus moved from high risk approach to a more generalized approach and now back to high risk approach as most countries have localized epidemic in specific population groups. This is not true for NCDs, at least as of yet as we are still in the phase of a population approach. The attributes of the responses of HIV/AIDS and NCDs emanated from this basic epidemiology of the epidemics and the historical contexts of the response itself. HIV/AIDS and NCD strategies share several similarities in their approach.
They also overlap in systems strengthening components. The systems involved in the global response to HIV/AIDS and NCDs involve multi-sectoral, multi-stakeholder and multi-level approaches that require complex coordination mechanisms. HIV/AIDS and NCD interventions use similar models despite the major differences in the technical content of the interventions. Health system strengthening interventions of HIV and NCDs also converge to enhance the capacities of the same health system. The indicators and the target populations for monitoring and evaluation of HIV/AIDS and NCD programs differ to a larger extent.

However, the Monitoring and Evaluation approaches to be used share important similarities. Monitoring and Evaluation interventions of HIV/AIDS and NCDs that are directed towards strengthening health information systems do overlap.

Box 2. Summary of similarities and differences of HIV and NCD responses

Themes	Similarities	Differences
Strategies	The strategies address similar themes; both focus on health system strengthening and the need for integrated response.	HIV strategies geared towards effectiveness and efficiency of HIV programs while NCD strategies focus on increasing access to and coverage of services and the priority accorded to NCDs.
Systems	Multi-sectoral involvement, complex coordination mechanism, well established coordinating bodies	Interests of the organizations involved differ; many diseases in NCD category means more complex coordination
Intervention	Approaches, models, tools, techniques	Technical content of interventions, demographic profiles of target populations.
Monitoring & Evaluation	Need for unified M &E framework, similar data collection methods	Indicators, target populations, timeframe

In general, there are several important areas of response to HIV/AIDS and NCDs that can be coordinated and integrated. In general, the technical contents of the response to HIV/AIDS and NCDs differ. But the approaches, techniques, models and tools used share several communalities. These imply that the integrity of the responses to HIV/AIDS and NCDs need to be maintained while coordination and/or integration can be considered for approaches, models and tools used in the response. Such approaches will maximize synergy and improve efficiency of responses to both health problems.

CONSENT

Not applicable.

ETHICAL APPROVAL

None required.

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COMPETING INTERESTS

The authors declare that no competing interests exist.

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Chapter 6

Parallels between National responses to HIV/AIDS and NCDs

CHAPTER 6 OVERVIEW

Having explored the global level parallels between HIV/AIDS and NCDs responses, this chapter examines the second important level of parallels between HIV/AIDS and NCDs responses: The parallels, shared attributes, between the Health system responses to HIV/AIDS and NCDs at national/country level. Besides the parallels/similarities at national level, it also illustrates essential differences between the national level responses to HIV/AIDS and NCDs. National parallel is a national level interrelationship between HIV and NCDs responses. Parallels are shared attributes of the responses. The major research question was "What are the similarities and differences between national level responses to HIV/AIDS and NCDs?" Similar to the previous chapter, Health System response in this chapter comprises macro-level policy response, programmatic response, institutional arrangement and strategic information at country level. The chapter contains one published article which is mainly based on qualitative content analysis HIV/AIDS and NCD responses at national level. The article analyses national level parallels and differences between the national level responses to HIV/AIDS and NCDs in using a multiple comparative case study of four countries: South Africa, Malaysia, Sri Lanka and Ethiopia. The identified parallels/similarities indicate potential areas of integration while the differences indicate essential areas of differentiation in the coordinated health system response to HIV/AIDS and NCDs at national levels.

Citations

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Publication Declaration

Monash University

Declaration for Thesis Chapter 6

Declaration by candidate

In the case of Chapter 6, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Wrote the proposal, collected the data, analysed the data, wrote the manuscript, revised the manuscript	75%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Julian Elliott	Supervised & reviewed the study	NA
Geoffrey Setswe	Supervised & reviewed the study	NA
Brian Oldenburg *	Supervised & reviewed the study	NA

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

Reviews and Meta-Analysis

National responses to HIV/AIDS and non-communicable diseases in developing countries: analysis of strategic parallels and differences

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Significance for public health

This study explores the parallels and differences between national responses to HIV/AIDS and non-communicable diseases (NCDs). The identified parallels can be the basis for integrated response to HIV/AIDS and NCDs. In contrast, the important differences are essential for maintaining the integrity of the responses to HIV/AIDS and NCDs in the process of integration.

Abstract

HIV/AIDS and non-communicable diseases (NCDs) epidemics may have many important similarities in their aetiology, pathogenesis and management. Evidence about the similarities and differences between the national responses HIV/AIDS and NCDs is essential for an integrated response. The objective of this study was to examine the parallels and differences between national responses to HIV/AIDS and NCDs in selected developing countries.

This study applied a strategic level comparative case study approach as its study design. The main construct was national response to HIV/AIDS and NCDs. The 4 overarching themes were policy response, institutional mechanism, programmatic response and strategic information. Four countries were purposively selected as cases. Data were collected and triangulated from a multiple sources. The focus of analysis included identifying items for comparison, characteristics to be compared, degrees of similarity, and strategic importance of similarities. Analysis of data was qualitative content analysis with within-case, between-case, and across-case comparisons.

While the nature of the disease and the contents of national HIV/AIDS and NCD policies are different, the policy processes involved are largely similar. Functional characteristics of programmatic response to HIV/AIDS and NCDs are similar. But the internal constituents are different. Though both HIV and NCDs require both a multi-sectorial response and a national coordination mechanism, the model and the complexity of the coordination are different. Strategic information frameworks for HIV/AIDS and NCDs use similar models. However, the indicators, targets and priorities are different. In conclusion, the national responses between HIV/AIDS and NCDs are largely similar in approaches and functions but different in content.

Introduction

On top of the already existing burden of communicable diseases, maternal and child health problems and injuries/accidents, the epidemic of non-communicable diseases (NCDs) is a new additional public health threat to most developing countries.[1] Since the beginning of HIV epidemic, about 70 million people have been infected by the virus and 35 million people have died due to the virus. At the end of 2011, about 34 million people were living with HIV. An estimated 0.8% of adults aged 15-49 years are living with the virus. About 1.7 million people died of AIDS-related illnesses worldwide in 2011. Sub-Saharan Africa accounts 69% of people living with HIV worldwide. About 1 in 20 adults in Sub-Saharan Africa (4.9%) are living with the virus.[2] NCDs kill more than 36 million people every year. About 80% of NCD related deaths (29 million) occur in low-and-middle income countries. More than 9 million NCD related deaths occur before 60 years of age. The majority (90%) of premature NCD deaths occur in low and middle income countries. Four common NCDs (cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes) account for 80% of all NCD related deaths. These four common NCDs share four major risk factors: tobacco use, physical inactivity, harmful use of alcohol and unhealthy diet.[3] Development, industrialization, urbanization, investment, and aging are the major drivers of the NCD epidemic in those countries.[4]

In addition to their epidemiological overlap in developing countries, HIV/AIDS and NCDs share many additional commonalities that are related to their causation (aetiology), progression (pathogenesis), and response (prevention and control). Evidence about these inter-relationships is essential for the planning and implementation of coordinated and/or integrated programs.[5] From the viewpoint of risk factors, HIV/AIDS is mostly related to most-at-risk and vulnerable populations and are at higher risk of being infected or affected by HIV [most-at-risk and vulnerable populations includes commercial sex workers (CSW), men having sex with men (MSM), intravenous drug users (IDUs) and bridge population (Migrant workers and long distance truck drivers)]. Examples include unprotected sex with a partner whose HIV status is unknown, multiple sexual partnerships involving unprotected sex, and injecting drug use with contaminated needles and syringes.[6] Key populations for HIV vary based on context. The most common key populations include people living with HIV, their partners and families, people who sell or buy sex, men who have sex with men, people who use drugs, orphans and other vulnerable children, certain categories of migrants and displaced people and prisoners.[7] The common NCDs (cardiovascular disease, cancers, diabetes and chronic respiratory disease) are associated with four common behavioural and lifestyle risk factors (unhealthy diet, insufficient physical activity, tobacco use, and harmful use of alcohol).[8] The similarities and differences between the global responses to HIV/AIDS and NCDs have already been explored.[9] Largely influenced by the global level responses, national level responses to HIV/AIDS and NCDs apply a multi-sectorial approach and whole-of-government efforts in order to mitigate the multi-faceted risk factors and impacts of the problems.[10,11] The implementation of such approaches needs well-coordinated

policies/strategies and systems. As intervention against either HIV/AIDS or NCDs will affect the other, intervening jointly against HIV/AIDS and NCDs, rather than competing for limited funds, is an essential policy approach that requires innovative models and approaches.[12]

Although the similarities between HIV/AIDS and NCDs in risk factors, progression and management are known, the similarities and differences between national level responses to them are not well investigated.[9] Though the specific behavioural entities involved are different, this signifies the importance of behavioural dimension in the risk factors of both HIV/AIDS and NCDs.[13] Evidence from the analysis of the parallels and differences between the national response to HIV/AIDS and NCDs is useful in pinpointing potential areas of integration and differentiation. Therefore, this study was designed to examine the strategic level parallels and differences between national responses for HIV/AIDS and NCDs in selected developing countries and emerging economies.

Scope of the study

The major construct of this study was the national (strategic) level response to HIV/AIDS and NCDs. Adapted from the World Health organization's Health system framework; the overarching themes were policy response, programmatic response, institutional mechanism, and strategic information.[14] These themes were assumed to be inter-locked constituents of the main construct. Information related to the magnitude, determinants, trends, and distribution of the problems was used for the purpose of context setting.

Figure 1 shows the conceptual framework of this study. Coordination is the key element of multi-sectoral response to HIV/AIDS and NCDs as all major response functions require strong national level coordination. As indicated in the framework, country level responses are shaped by both global responses including MDGs and local contexts like local epidemiology of the diseases.

Study design

This study was a comparative case study. A case study approach was used as the main focus was on *how* countries are responding to the epidemics. Besides, there was a need to uncover contextual factors.

Selection of cases and study setting

The selection of countries was purposive (maximum variation) based on in the combined cluster analysis of epidemiological trends of prevalence of HIV/AIDS and Diabetes from a study that identified four clusters of countries.[15] One country from each cluster was selected based on ease of access to data sources. The selected countries are South Africa (17.3% HIV and 6.5% diabetes prevalence), Malaysia (0.4% HIV and 11.7% diabetes prevalence), Sri Lanka (0.1% HIV and 7.8% diabetes prevalence), and Ethiopia (1.4% HIV and 3.4% diabetes prevalence).[16,17] Malaysia and South Africa are upper middle income countries. Sri Lanka is a lower middle income country. Ethiopia is a least developed country.

Data collection

Multiple data sources were used in this study. These included policy documents, performance reports, databases, surveys reports and peer-reviewed literature. The primary policy documents reviewed were the most recent Health, HIV/AIDS, and NCD policies/strategies which were available in the public domain. Most recent annual health sector and HIV/AIDS were among the reports reviewed. This study also draws on publicly available NCD related data collected in 2010 from the Ministries of Health of countries as part of the WHO sponsored global key-informant surveys.[18] The data contains variables related to the capacity of countries to respond to HIV/AIDS and NCDs in five areas: public health infrastructure; the status of policies, strategies, action plans and programmes; health information systems, surveillance and surveys; the capacity of health care systems for early detection, treatment and care; and health promotion, partnerships and collaboration. Information from global and national level survey reports and other peer-reviewed literature relevant to health systems response to HIV/AIDS and NCDs with special reference to the case countries was also used.

Data collection tools

Using the four overarching themes, a data abstraction template was developed. Theme-based matrices were independently populated for each of the countries and the disease conditions. All the NCD data from Global Health observatory (2010) collected from the four case countries was extracted and included in this study.

The themes and sub-themes of the study are: i) *problem description*: magnitude of the problem, risk factors for the problem, historical overview of the response; ii) *policy response*: policy making bodies, policy frameworks, policy interventions; iii) *programmatic response*: prevention, treatment, care and support, cross-cutting areas (capacity building, health system strengthening etc.); iv) *institutional mechanism*: institutional structures (actors – state and non-state, and partners), national coordination mechanism; v) *strategic information*:

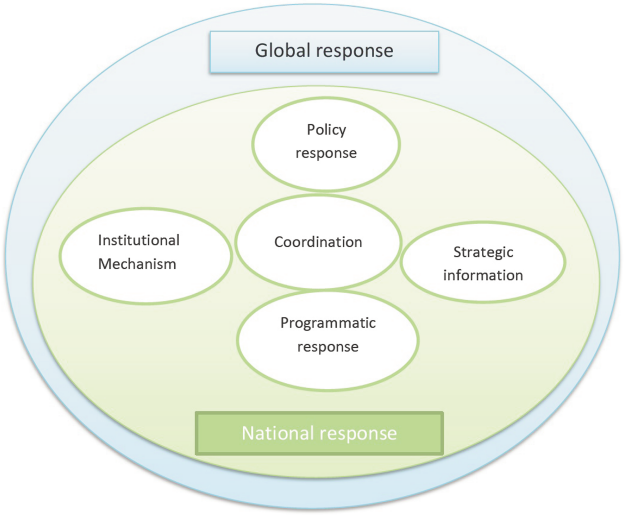

Figure 1. Conceptual Framework of the study: broken lines show the fact that national responses are shaped by global responses; the circles show the major elements of national response.

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monitoring and evaluation systems, surveillance systems, monitoring and evaluation interventions.

The sub-themes were used as categories in the coding process.

Data analysis and management

The overall analysis was a qualitative content analysis approach. Comparative analysis of strategic parallels within a country (within-case), comparison of strategic parallels of a disease between different cases (between-disease), and comparison of strategic parallels across all the cases and the two disease conditions (cross-case) were used. In this process, items to be compared were the core components of the response. The focus of analysis included identifying items for comparison, characteristics to be compared, degrees of similarity, and strategic importance of similarities. Findings were summarized using integrative synthesis.[19]

Problem description

Magnitude of HIV/AIDS and non-communicable diseases

HIV/AIDS is a generalized epidemic in South Africa and Ethiopia but a concentrated epidemic in Malaysia and Sri Lanka. NCDs cause more deaths than HIV/AIDS in all the case countries except South Africa. Table 1 illustrates, NCDs accounts about one-third of total annual deaths in South Africa and Ethiopia but about two-third of total annual deaths in Malaysia and Sri Lanka.[20,21] However, it would be important to consider age at death in the comparison of HIV and NCD related deaths. HIV related deaths generally occur at a lower age than that of NCDs. Thus, HIV related deaths are associated with higher DALYs.

Risk factors for the problem

Heterosexual intercourse is the main driver of HIV epidemics in all case countries. Intravenous Drug Users (IDU) and Men having Sex with Men (MSM) are more important in Sri Lanka and Malaysia. The burden of HIV/AIDS is higher among Females in South Africa and Ethiopia; but in Males in Malaysia and Sri Lanka. NCDs risk factors and risk groups have mixed picture in the case countries: South Africa and Malaysia have high rates for tobacco smoking, physical inactivity, and obesity as compared to Sri Lanka and Ethiopia. Magnitude of raised blood pressure and raised blood glucose are more or less similar across the case countries (Table 2).[20]

Historical overview of the response

The history of national response to HIV/AIDS started in the late 1980s or early 1990s (Table 3). National level policy/strategy/plan was formulated and national coordinating mechanism (NCM) was established during those years. National HIV/AIDS responses in the case countries have gone through at least three strategic periods.[22]

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Table 1. HIV/AIDS and non-communicable diseases profiles of the case countries, 2011.

Country	HIV prev. %	AIDS prev. %	PLHIV	HIV deaths	NCD deaths	NCD deaths %
South Africa	17.3	15.9	5,600,000	270,000	190,600	29
Sri Lanka	<0.	<0.1	4200	<500	117,900	65
Malaysia	0.4	0.4	81,000	5900	89,500	67
Ethiopia	1.4	3.6	790,000	54,000	338,300	34

NCD, non-communicable diseases.

Table 2. Prevalence of common non-communicable diseases risk factors in the case countries (2011).

Country	Daily tobacco smoking (%)	Physical inactivity (%)	Raised blood pressure (%)	Raised blood glucose (%)	Obesity (%)
South Africa	14	51.1	42.0	10.6	31.3
Sri Lanka	10.6	26.0	39.2	8.8	5.1
Malaysia	21.5	60.5	34.7	10.5	14
Ethiopia	2.4	17.9	35.2	NA	1.1

NA, Data not available.

Table 3. Milestones in the history of national response to HIV/AIDS and non-communicable diseases.

	South Africa	Sri Lanka	Malaysia	Ethiopia
First HIV/AIDS case reported	1982	1986	1986	1984
First HIV/AIDS NCM	1992	1986	1985	1985
First HIV/AIDS national plan	1994	1996	1988	1985
First Integrated NCD plan	2013	2009	2010	2010

NCM, national coordinating mechanism; NCD, non-communicable diseases.

Integrated national response to NCDs started during the past five years. However, disease-specific NCD responses were in place for years, although they received very little attention. Though NCDs were included in the sector-wide strategies and were being addressed by the sector-wide structures for years, integrated national responses to NCDs are either at the first strategic period.[23]

Policy response

Policy responses to HIV/AIDS and NCDs in this study include the incorporation of HIV/AIDS and NCDs in to sector-wide policies, the development of separate HIV/AIDS and NCD policies, and the rollout of policy/regulatory interventions that are important to curb the tide of the epidemics. All these require complex processes with a wide range of consultations and deliberations. Moreover, they are highly influenced by global policies.

Policy processes

Analysis of the policy-related processes involved in the national response to HIV/AIDS in the case countries has revealed four major processes. The first one is political leadership which involves the highest political bodies of a country (Cabinet/members/Ministers/President etc.). The second process is policy making process that involves drafting (and approving) policies and overseeing its implementation. The third process is policy advisory role that addresses policy and technical issues and plays advisory role on policies and technical issues. The final process is program governance which is usually provided by National (HIV/AIDS) secretariat/working group/taskforce (members).[24-27] With regard to NCDs, all four case countries have a responsible body in the Ministry of Health responsible for NCDs. NCD specific policy processes and governance structures vary widely across countries. South Africa has started establishing a National Health Commision to be chaired by the presidency and involving all relevant government sectors and others. In addition, it has established an advisory committee on the prevention and control of cancer in January 2013. South Africa also has inter-ministerial committee on prevention of substance abuse. The department of health currently has lead role in presenting a bill on control of the marketing of alochol. Sri Lanka has National Health Council for promoting collaboration, and National NCD steering committee for monitoring policy implementation. Malaysia proposed Cabinet Committee for Health Promoting Environment chaired by Deputy Prime Minister and involves the major ministries. In Ethiopia, a National Technical working group drafted the strategic framework for the prevention and control of NCDs. A national level NCD consortium is also established.[28-32]

Policy frameworks

Both HIV/AIDS and NCDs are included in the health sector policies in all the case countries. The 10 point NHS of south Africa, the 4th HSDP of Ethiopia, the 10 year Health Master plan of Sri Lanka, and the 10th Country Health Plan of Malaysia all have included both NCDs and HIV.[33-36] Besides, all the case countries have stand-alone policy/strategy frameworks for both HIV/AIDS and NCDs: at least the 3rd for HIV and the 1st for NCDs. Based on the data from Global Health Observatory (GHO), though the mix varies, all the countries have NCD related policies/strategies. Case countries also have HIV policies specific to some *population* groups, and specific *technical* areas. South Africa and Sri Lanka have operational policy documents on the four major NCDs and the four common NCD risk factors. At the time of this study, we haven't found specific operational policy document on diabetes and aclohol from Malaysia. At the time of this study, Ethiopia hasn't yet launched an operational policy/strategy/action plan on the four major NCDs and four common NCD risk factors.

There are concerns in the alignment of HIV/AIDS and NCD specific policies/strategies with the sector-wide policies/strategies. The alignment of NCD specific policies with disease/risk factor specific policies is also another area of concern in the integrated response to NCDs. Different types of Tobacco Acts are available in the case countries. At the time of this study, all the case countries except Ethiopia have ratified the WHO Framework Convention on Tobacco control (FCTC). Food Acts and Nutrition policies/strategis also exist in the case countries. Stand-alone policy frameworks for promotion of physical activity in the case countries were not identified in this study. South Africa has recently developed a policy addressing cervical cancer. The most recent policy frameworks for HIV/AIDS and NCDs are listed in Table 4.

Policy/regulatory interventions

HIV/AIDS policy/regulatory interventions focus on right, equity and justice related to HIV programming and People living with HIV. On the other hand, policy/regulatory interventions of NCDs focus on the use of policies to reduce exposure to the risk factors (regulatory measures) such as tobacco smoking, alcohol use and consumption of high calorie foods. Gender-based violence and discrimination got more attention in HIV/AIDS response as they are more related to HIV. Mandatory NCD screening for employees is being implemented in Malaysia. Malaysia has developed a guideline to control marketing of food and alcoholic beverages to children. Our review of documents shows that reporting cancer has been made compulsory by regulation in South Africa. Regulations to reduce salt content in specified foods are gazetted in South Africa. Regulations on trans-fatty acids have already been in practice since 2011 in South Africa. Our literature search hasn't found such regulations in in Sri Lanka and Ethiopia.

Table 4. List of most recent HIV/AIDS and non-communicable diseases policy frameworks.

Country	HIV/AIDS	NCD
South Africa	National strategic plan on HIV, STIs and TB: 2012-2016.[24]	South African NCD action plan 2013-2016.[32]
Sri Lanka	National HIV/AIDS strategic plan: 2013-2017.[27]	The National Policy & Strategic framework for Prevention & Control of chronic NCDs, 2009.[28]
Malaysia	National Strategy Plan on HIV and AIDS: 2011-2015.[26]	National Strategic plan for NCDs: 2010-2014.[29]
Ethiopia	Strategic plan for intensifying Multi-sectoral HIV and AIDS response in Ethiopia: 2010/11-2014/15.[25]	Prevention and Control of Chronic NCDs: Strategic Framework: Nov 2010.[30]

NCD, non-communicable diseases.

Programmatic response

Evidence from the case countries indicated that integrated NCD programs are not well instituted. Most of the existing NCD interventions are either sector-wide or disease/risk factor specific interventions. In the sector-wide interventions adequate priorities are not accorded to NCDs. As funding and donor interest in NCDs is generally low, disease/risk factor specific interventions are small and fragmented. In contrast, HIV/AIDS responses have attracted more resources and several sector-wide and HIV/AIDS specific programs have been implemented. However, most of the funding for HIV/AIDS was from external sources. Using these resources, several intervention protocols and guidelines have been developed and rolled out for the implementation of HIV/AIDS programs.[37-40]

Prevention of HIV/AIDS and non-communicable diseases

Both HIV/AIDS and NCD prevention strategies in the selected countries has been on behavioral/life style, structural, biomedical/biological, and policy/regulatory *dimensions*. Apart from Ethiopia, the other case countries have implemented fiscal interventions to influence behavior change and have earmarked taxes from fiscal interventions to influence behavior change used to fund health promotion programmes or a health promotion foundation. Individual, community-based, and institution-based *approaches* are used in the prevention approaches of both HIV/AIDS and NCDs. Most of the *stakeholders* (actors) in both HIV/AIDS and NCDs are those outside the healthcare system and includes several government sectors, NGOs, CBOs, FBOs etc. For instance, both HIV/AIDS and NCDs are integral to the school health program in South Africa. Influencing individual decision (to practice safe sexual behavior in case of HIV and to eat healthy foods, to stop smoking, to reduce alcohol or to improve physical activity; or to get screened/tested) is the *ultimate goal* of most of the prevention programs.

Malaysia has expanded communication for behavioral impact program for dengue to also include NCDs. It has also appointed a Malaysia Health Ambassadors to encourage Malaysians adopt healthy lifestyles. The country has also introduced an NCD risk factor intervention program – NCD prevention a Malaysia Program – in communities, workplace and schools. Media players are also actively engaged in NCD prevention interventions. Ministry of Health agreed to implement a new healthy eating guideline in schools

However, there are also essential differences in the prevention of HIV/AIDS and NCDs. Most of these differences emanate from the disease characteristics and epidemiology of HIV/AIDS and NCDs. Firstly, the main *target* populations for HIV/AIDS prevention are youth (15-24 years) and key populations (most at risk populations).[41] But the main target population considered in most NCD prevention are adults (>30 years of age). Secondly, the purpose of HIV/AIDS prevention programs is to reduce transmission and vulnerability while that of NCDs is to reduce the risk of developing NCDs. Thirdly, the content (package) of the prevention programs is different. The contents of HIV/AIDS prevention programs are geard towards reducing the risk of transmission of the virus through sexual, parenteral and/or vertical routes while that of NCDs are geard towards reducing the common NCD risk factors and adopting healthy lifestyles. Lastly, the socio-cultural *contexts* surrounding HIV/AIDS prevention and NCD prevention are different. HIV/AIDS risk factors, mainly high risk sexual behaviors, are generally considered to be more sensitive than that of NCD risk factors.

South Africa, which managed to screen 13 million people for HIV, has acknowledged that HIV testing offers an excellent opportunity for NCD screening and thus has instructed that health testing must become comprhensive so that NCDs are tested at the same time as HIV and TB. This country has also made a decision to provide Human Papiloma Virus (HPV) vaccine to pre-pubescent girls. In Ethiopia, a screening project for Gestational Diabetes was implemented together with the PMTCT program in healthcare facilities. As women on HIV/AIDS treatment may have higher risk of gestational diabetes, this project was considered to be exemplary. Healthy Lifestyle Centers (HLCs) in Sri Lanka are other examples of integrated prevention approaches.

Treatment of HIV/AIDS and non-communicable diseases

As the history of implementation of national treatment programs of HIV/AIDS and NCDs are very different, the main priorities of HIV/AIDS and NCD treatment strategies are also different. The main priorities of HIV/AIDS treatment programs are ensuring universal coverage to treatment for all eligible PLHIV and improving the quality of treatment programs. In contrast, the priorities of NCD treatment strategies are to increase availability of drugs and improve accessibility of treatment services. However, as both HIV/AIDS and NCDs are chronic diseases, the delivery of HIV/AIDS and NCD treatment services have the following charactorstics in common. Both require strong health *systems* and skilled multi-disciplinary health *teams*. Both need *long-term* monitoring and follow up. Both HIV/AIDS and NCD treatment also require *adjacent prevention* interventions, positive health, dignity and prevention (PHDP) for HIV/AIDS and improved health behavior/life style/ for NCDs. Based on data from Global Health Observatory guidelines for the management of diabetes and hypertension were available and implemented in all the case countries except Ethiopia. Most of the NCD tests were not available at primary health care level in Ethiopia. In the other three countries, at least half of the basic NCD tests were available at primary healthcare level. Regarding the general availability of NCD related medicines in the public health sector, Ethiopia has less than one fourth of the drugs considered for assessed while the other three countries have more than fourth-fifth of the drugs included in the list for the assessment. Assessment of the general availability of NCD related procedures (renal photocoagulation, renal replacement therapy, radiotherapy and chemotherapy); Ethiopia didn't have any of these. Malaysia has all the four, South Africa had all except renal replacement therapy, and Sri Lanka had all except renal photocoagulation. A symptom-based NCD diagnostic tool (known as primary care 101) is being developed in South Africa where NCDs are included in primary care package.

National Cancer Institute is a premier tertiary level hospital for diagnoses and treats cancer cases in Sri Lanka. Access to cancer treatment is limited. In rural areas, traditional healers have greater roles. In South Africa, only tertiary (specialised) hospitals and some private medical centres have cancer treatment facilities. In Ethiopia, where cancer is considered as a death sentence, there is only one cancer treatment centre for the whole population. In Sri Lanka and Malaysia, there are a few more cancer treatment centres.

Care and support for HIV/AIDS and non-communicable diseases

We have looked in to four major areas of care and support strategies for HIV/AIDS and NCDs: Continuity of care, control of disease progression, prevention of complications and integration of care services. *Continuum of care* for both HIV/AIDS and NCDs involves the patient, peers, family members, community systems and healthcare systems. Patient participation is important in both cases. In order to *control disease* progression, care and support programs of both HIV/AIDS and NCDs work for retaining patients in care with adequate treatment adherence. Both HIV/AIDS and NCDs are associated with a range of *complications* including co-infections and comorbidities. Accordingly, prevention of these complications is among the major priorities of care and support programs for HIV/AIDS and NCDs. Effective and efficient

provision of care and support services also require *integration* of services along the continuum and across the components.

HIV/AIDS Care and support programs often include care for orphan and vulnerable children and economic strengthening activities that are intended to reduce vulnerability. They also consider stigma and discrimination as a major area of focus. NCD care and support programs often include healthy ageing as its focus area. Self-care is considered to be more important in NCD care and support strategies. In both HIV/AIDS and NCD care, improving the quality of life patients through better adherence to recommended treatment and retention in care is considered to be a key strategy. Promoting positive living and decreasing risk of infectivity are relevant elements of HIV/AIDS care and support programs. Apart from generic strategies for NCD related care, countries also have disease specific care guidelines for specific NCDs (*e.g.* diabetes care guideline in South Africa).

Cross-cutting technical areas

The main crosscutting programmatic responses stated in both NCD and HIV policy documents are capacity building, Health System Strengthening (HSS), mainstreaming, partnerships and empowerment. HSS and reform is one of the three NCD strategies in South Africa. An important initiative of this is the development of integrated chronic disease (both communicable and Noncommunicable) management model in three districts. We considered that the capacity building and HSS interventions should focus on both disease-specific (HIV/AIDS and NCD) structures (for technical and analytical capacity) and sector-wide structures (for program planning, implementation, monitoring and evaluation capacity).

The capacity building *and HSS* interventions, however, seem to provide more weight to on HIV/AIDS and NCD specific structures and functions rather than sector-wide structures and functions. As mainstreaming of interventions is mainly to government sectors, most of the government sectors may end up in having both HIV/AIDS and NCD related activities. Both HIV/AIDS and NCD responses involve broader partnership frameworks though the types of individual partners vary. *Empowerment* of community is another important area of focus of national responses to HIV/AIDS and NCDs in the case countries.

Institutional mechanisms

Institutional structures for HIV and non-communicable diseases response

Institutional structures involved in the national response to HIV/AIDS and NCDs are of two categories: actors (state and non-state), and partners. For HIV, these can be further classified in to sector-wide structures, and HIV-specific structures. For NCDs the list includes sector-wide structures, NCD-specific structures (integrated), disease-specific structures (individual NCD) and risk factor specific structures (individual risk factors). Currently, the state actors for HIV/AIDS are the majority of government ministries/departments/bureaus/agencies. Despite the principle that NCD response is a whole of government and whole of society effort, most of state actors for NCDs are agencies whose roles are directly related to the common NCD risk factors: unhealthy diet, physical inactivity, tobacco use, and alcohol use. With regard to the non-state actors, the national responses to HIV/AIDS involve several UN agencies, Non-govermental organizations and civil society organizations. Most of these structures are currently engaged in either technical/finacial support and/or implementation of HIV/AIDS programs. On the other hand, non-state actors involved in the national response to NCDs are mostly disease and risk factor specifc civil society organization and networks/coalitions/consortiums who are involved in advocacy, training, service delivery and research.

In the national responses to HIV/AIDS in the selected countries, there is a strong partnership with international donors and technical partners. Some of these (*e.g.* global fund) requires a separate coordination mechanism. In HIV response, partnership is *in action* but duplication/overlap is a problem. In NCD response, partnership is in a form of working relation*s* and is a future strategy. Resources for HIV response are mostly from external sources. Resources for future NCD response are currently lacking and are expected from external sources too.

The Ethiopian National NCD consortium is a platform established by civil society organizations working on NCDs. It provides an excellent opportunity to promote a coordinated national response to NCDs. The consortium is working closely with both governmental and non-governmental organizations.

National coordination mechanisms

As the response to both HIV/AIDS and NCDs is multi-sectoral and multi-stakeholder in nature, a national coordination mechanism is needed. The location of the National coordination mechanisms (NCM) and its relation with sector-wide structures vary across countries. The current NCM for NCDs in all the case countries are under Ministry (Department) of health although new NCMs have been proposed. In Malaysia and Sri Lanka and NCM for HIV/AIDS are also under Ministry of Health. In South Africa and Ethiopia, the NCM for HIV/AIDS response is accountable to a higher government body than the Ministry (Department) of Health. The role of the NCMs is more of Planning, coordination and implementation, and M&E rather than a technical advisory one. A partnership forum for HIV in South Africa and Ethiopia has other partners as members of the advisory body. Establishment of NCD coordination *networks* seems the future direction of NCD actors.

The NCMs for national response to HIV/AIDS in the case countries are South African National AIDS Council (SANAC) in South Africa, National STD and AIDS Control Program (NSACP) in Sri Lanka, AIDS/STI sector of the Disease Control Division in Malaysia, and HIV/AIDS prevention and control offices (HAPCO) in Ethiopia. Similarly, NCD cluster (Department of Health), NCD Prevention and Control Unit (Ministry of Health), NCD section (Disease Control Division/Ministry of Health) and NCD focal unit (Ministry of Health) are the NCD mechanisms in South Africa, Sri Lanka, Malaysia and Ethiopia respectively.

Strategic information

Monitoring and Evaluation along with innovative research are the key HIV and NCD strategic areas in all the case countries. The three types of monitoring activities evident in this study are patient/clinical/monitoring, disease/risk factor/ monitoring and program monitoring. As all these forms of monitoring are driven by the national programs, their stages of implementation are different for HIV/AIDS and NCDs in the case countries. But the NCD monitoring can learn from HIV monitoring. A study conducted in Ethiopia revealed that patient monitoring systems developed for HIV/AIDS programs could be adapted for NCDs.[42]

Monitoring and evaluation systems

The Health information system (HIS) in each of the case countries supports strategic, management and operational decisions in the entire health sector. The HIS is a result of combined efforts of many stakeholders including the Ministry of Health and National statistical offices. M&E units in the NCM of HIV/AIDS response coordinate the M&E of National Strategic Plans (NSP) using the concept of *one*

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national M&E framework. The HIV/AIDS M&E system is inter-linked with national HIS. Despite the presence of NCD strategic plans in all the case countries, the development of M&E frameworks for NCDs is at early stage. South Africa has yset ten targets to be achieved by 2020. Sri Lanka's strategic plan states indicators and their means of verification.

The flow of M&E data in the case countries is as follows. In Sri Lanka's HIV response, all reporting units report directly to the Strategic Information Management (SIM) unit of National STD/AIDS control program. In Malaysia, the Malaysian AIDS Council (MAC) coordinates the report from Civil Societies and NGOs and reports to the National AIDS Program Secretariat at Minstry of Health. All government sectors directly report to the secretariat. In Ethiopia, government sectors report to Federal HIV/AIDS Prevention and control office while other implementors report to relevant structures at their level of implementation. In South Africa, Health facilities report to District AIDS councils, which report to provincial AIDS councils, which further report to SANAC. Government and civil society sectors will be reporting within their established structures at the different levels

Both national HIV/AIDS and NCD M&E systems need to draw data from national health information system. The performance of HIV/AIDS and NCD M&E systems is therefore directly related to national HIS. Similarly, interventions designed to strengthen HIV/AIDS and NCD M&E systems will directly contibute to the national HIS. Both HIV/AIDS and NCD M&E systems need to invest on national HIS. The requirements of HIV/AIDS and NCD M&E systems shound fit with the capacity of the national HIS. HIV/AIDS indicators are well included in the National HIS of the countries. However, the current National HIS in the case countries are not responsive to NCD related indicators. Hypetension rate and Mental Health case load are captured in South African District Health Barometer. Hospital statistics in Sri Lanka has indicators on NCDs.

Surveillance, surveys and registry

ANC-based HIV sentinel surveillance, Behavioral Survey Surveillance (BSS) and Demographic Health Surveys (DHS) are the common forms of HIV/AIDS surveillance and surveys in the case countries. AIDS case reporting is also among the mechanisms used to monitor the status of the HIV/AIDS Epidemic. Surveillance systems for NCDs are at different stages in the case countries. Malaysia, Sri Lanka and South Africa have reported the existence of cancer registry and NCD risk factor surveillance. Both cancer registry and surveillance of NCD risk factors were not available in Ethiopia. South Africa has prepared a plan for comprhensive NCD surveillance. In the intrim, South African Health and Nutrition Examination Survey is expected to provide relevant information. Ethiopia has conducted NCD situatiobal assessment and is looking forward to conduct a baseline assessment of NCDs. There are generally three forms of NCD surveillance considered: risk factor surveillance (bio-behavioral), disease surveillance and case registry/reporting. The eligible population groups vary but the two M&E systems can learn from each others – especially methods and techniques. Some general population surveys like DHS, in some countries, adress both HIV/AIDS and NCDs. In South Africa, a chronic disease register has been produced for implementation in public health facilities to ensure that NCDs are detected early and managed approproately.

In Malaysia, the National Health and Morbidity survey for NCD risk factors will be conducted every four years. Several NCD indicators are also included in the performance indicator sets of Ministry of Health. The National Diabetes registry is established to obtain epidemiological and clinical data of diabetes patients receiving treatment in healthcare facilities throught malaysia. It involves electronic collection of data and is made available online.

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Table 5. Summary of the parallels and differences between national responses to HIV/AIDS and non-communicable diseases.

	HIV/AIDS	Both HIV/AIDS and NCDs	NCDs
Policy response	3rd or 4th strategic period. Policy priorities are quality and sustainability. Sector, population, program specific policies.	Have responsible policy making bodies and national policy framework. Both are included in sector-wide policy frameworks.	At early stage. Advocacy and instituting systems are priorities. Disease, risk factor specific policies.
Prevention	Youth and MARPs focused; aim to reduce transmission; purpose is chaning sexual behavior; more sensitive context; human rights, equity and justice as interventions.	Prevention approaches; intervention dimensions; affecting individual decision is the ultimate goal. Mostly outside the health sector.	Adult focused; aims to reduce risk; purpose is to change lifestyle; less sensitive context; regulatory measures as interventions.
Treatment	Coverage higher. Ensuring universal coverage and impoving quality are the strategic priorities indicated in the policy frameworks.	Need strong health systems; multidisciplinary health treams; adjacent prevention; long duration of monitoring and follow up. Adherence is key.	Coverage low. Increasing availability and accessibility of treatment services is the main priority.
Care and support	Orphan and vulnerable children are concerns; co-infections more common; stigma and discirmination is a concern.	Ensuring continuum of care, control of disease, prevention of complications and provision of integrated services.	Comorbidities are more common; mostly associated with ageing/aged care;
Cross-cutting	Strengthening HIV/AIDS specific (technical and analytical capacity) and sector-wide structures (for management and implementation).	Strengthening of sector-wide structures; mainstreaming in to sectors; community empowerment; partnership and cooperation	Strengthening NCD specific structures (technical and analytical capacity)
Institutional arrangement	Most of government sectors involved; many NGOs and CSOs involved in implementation; well established NCM; better funded.	Involves both state and non-state actors as well as partners; a multi-sectoral coordinating structure is existing.	Limitted government sectors involved; CSOs involved in advocacy; NCM at early phase; low funding.
Monitoring and evaluation	Target population are ANC mothers, youth, and MARPs; stronger evidence base; priorities are ensuring quality and utilization of evidence	Draws data from national Health information system; risk factors and disease surveillance as well as case registry	Target population are adults; weak evidence base; priorities are ensuring NCD responsive information systems

NCD, non-communicable diseases.

Discussion

HIV/AIDS and NCD epidemics have many commonalities. Both HIV/AIDS and common NCDs have slow pace of progression. HIV/AIDS has a long asymptomatic stage. The asymptomatic stage lies between primary HIV infection and the development of AIDS.[43] The risk of many NCDs is set during development of a person. Nutritional imbalance and exposure to environmental chemicals during development can increase NCD risk later in life.[44] Most NCDs are associated with long-term and persistent exposure to the risk factors. Many NCDs also have *pre-disease* stages that may last for a number of years.[45] Moreover, combinations of major NCDs and infections can interact adversely. Co-morbidities in HIV/AIDS and NCDs are also of great clinical and public health importance.[46]

In the early period, infectious disease, like HIV/AIDS, and NCDs were perceived to be largely different. But with the advent to treatment, HIV/AIDS has now turned out to be a chronic disorder, like many of the common NCDs. As both are chronic diseases, the response interventions to HIV/AIDS and NCDs share many similarities. Prevention strategies of both HIV/AIDS and NCDs are targeted at modifying known risk behaviours. Treatment and care interventions focus on controlling disease progression and improving quality of life through better adherence to treatment, frequent monitoring of biomarkers, and provision of social support.[47] National responses to HIV/AIDS and NCDs are at different stages of maturity. As a result of this, the level of attention and priority given to HIV/AIDS and NCDs during the past three decades in developing countries are very different. These differences have shaped all the components of national response in different ways. In this regard, National responses to HIV/AIDS are at a higher level of maturity and thus the focus of HIV/AIDS policies are quality and sustainability. As a result of early stages of development, the current focuses of NCD policies are advocacy and instituting appropriate institutional systems. Though differences in stages of maturity of programs are recognized, NCD programs can learn a lot from the experiences of HIV programs. The programmatic responses to HIV/AIDS and NCDs are comprised of prevention, treatment, care and support and cross-cutting interventions. The main target population groups and the contents of interventions show higher level of differences than the approaches and models used in the delivery of interventions in the cases countries. Of great importance is the overlap between cross-cutting interventions of both HIV/AIDS and NCDs that mainly aim for strengthening sector-wide structures. In this regard, cross-cutting interventions are potential areas of integration.

Regarding instututional mechanisms, both HIV/AIDS and NCDs involve muti-sectoral and whole of goverment and whole of society efforts. Both require a country response coordinating mechanism at national level. The nature and complexity of the coordination mechanisms, however, are different. National HIV/AIDS response coordination mechanisms have the characteristics of *agency* while those of NCDs have the characteristics of *network*. This difference has an important implication in the integration of HIV and NCD responses with the overall health system inteventions.

The models and methods of strategic information of national responses to HIV/AIDS and NCDs share many similarities though the contents and priorities of the strategic information section of the responses have many essential differences. A summary of the parallels and differences between national responses is shown in Table 5.

Information outlets for HIV/AIDS in the case countries include AIDS resource centers, websites of National Coordinating Mechanims, and telephone-based help/talk lines, and State and private media. Information outlets for NCDs are mainly websites of civil society organizations engaged in NCD advocacy activities. Most of the avaialble information about NCDs is related to the magnitude of the problems and their risk factors. Information about the responses to NCDs are very limitted.

Emphasis is given to NCD specific and HIV/AIDS specific M&E system and the sector-wide M&E system in all the case countries. The main priorities of HIV/AIDS M&E systems in the case countries is to strengthen existing M&E systems in health facilities and to incorporate new systems for community-based monitoring and reporting. By doing this, the quality of HIV/AIDS information is expected to be improved. Among the M&E priorities is instituting a culture of evidence-informed decision making *i.e.* the use of evidence for policy and programs.

In comparison, the main M&E priorities related to NCDs is making the national HIS responsive to NCDs. These include incorporating NCDs in to national HIS, promoting the generation and utilization of NCD related evidence and instituting new methods of NCD monitoring and evaluation (*e.g.* surveillances, registry systems) as an integral part of national HIS.

The findings of this study have important implications for policy and practice. The main implication is the coordination of national responses to HIV/AIDS and NCDs in order to reduce duplication and overlap and maximize synergy and efficiency. This study has identified essential areas of focus for integrated response. One of these is the cross-cutting interventionns that focus on strengethining health systems.

There are some limitations associated with this study. Firstly, this study is limited to the context of four purposively selected case countries. The countries have heterogeneous epidemiological and socio-economic contexts. Thus, the study findings are only analytically generalizable. Secondly, the analysis focuses on national level (macro-level) responses and may not reflect meso and micro-level situations in the case countries. Moreover, exploration of the differences between case countries was beyond the scope of this study. Thirdly, the study is limited to the five broader thematic areas and information extraction is limited to these thematic areas only. Besides, limitations related to data availability and quality as well as the *value-nature* of the analysis methods should be taken in to consideration in the interpretation of the findings.

Conclusions and Recommendations

While the *content* characteristics of HIV and NCD policies are different, the *process* characteristics involved are largely similar. The *operational* characteristics of programmatic response to HIV and NCDs are similar. But the *internal constituents* of the programmatic response are different. Though both HIV and NCDs require both a multi-sectoral response and a coordination mechanism, the models and complexity of coordination are different. Strategic information frameworks for HIV/AIDS and NCDs employ similar methods. However, the indicators, targets and priorities are different. In general, the parallels between the national responses between HIV/AIDS and NCDs are largely in process characteristics and the differences are in content characteristics. The differences in the nature of the diseases and the level of maturity of the responses explain the major differences. It will be wise to consider the parallels identified in this study as initial areas of focus for integrated response to HIV/AIDS and NCDs in low- and middle-income countries. We also recommend further and more detailed exploration of similarities and differences between the responses to HIV/AIDS and NCDs in specific countries.

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Chapter 7

Developing action model for integration of responses to HIV/AIDS and NCDs

CHAPTER 7 OVERVIEW

Having generated evidence on the four forms of inter-relationships between HIV/AIDS and NCDs (Convergence, Linkage, Co-occurrence and Parallels), chapter 7 applies this evidence for the development of action model, a systematic approach, for the integration of health system responses to HIV/AIDS and NCDs in the context of developing countries. Using the evidence presented in the previous four chapters along with inputs for additional trans-disciplinary literature review, we developed an action model using progressive and iterative qualitative model development techniques. The resulting model has five underpinning principles, five key processes and a nine-step action cycle. This chapter presents the model development process and the resulting model. The model is expected to help as a guide for system level integration of responses to HIV/AIDS and NCDs. Parts of the model can also be adapted to local contexts.

Citations

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Publication Declaration

Monash University

Declaration for Thesis Chapter 7

Declaration by candidate

In the case of Chapter 7, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Wrote the proposal, collected the data, analysed the data, wrote the manuscript, revised the manuscript.	75%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Julian Elliott	Supervised & reviewed the study	NA
Geoffrey Setswe	Supervised & reviewed the study	NA
Brian Oldenburg *	Supervised & reviewed the study	NA

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature		**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

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Developing an Action Model for Integration of Health System Response to HIV/AIDS and Noncommunicable Diseases (NCDs) in Developing Countries

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Abstract

Introduction: Although there are several models of integrated architecture, we still lack models and theories about the integration process of health system responses to HIV/AIDS and NCDs.

Objective: The overall purpose of this study is to design an action model, a systematic approach, for the integration of health system responses to HIV/AIDS and NCDs in developing countries.

Methods: An iterative and progressive approach of model development using inductive qualitative evidence synthesis techniques was applied. As evidence about integration is spread across different fields, synthesis of evidence from a broad range of disciplines was conducted.

Results: An action model of integration having 5 underlying principles, 4 action fields, and a 9-step action cycle is developed. The **INTEGRATE** model is an acronym of the 9 steps of the integration process: 1) Interrelate the magnitude and distribution of the problems, 2) Navigate the linkage between the problems, 3) Testify individual level co-occurrence of the problems, 4) Examine the similarities and understand the differences between the response functions, 5) Glance over the health system's environment for integration, 6) Repackage and share evidence in a useable form, 7) Ascertain the plan for integration, 8) Translate the plan in to action, 9) Evaluate and Monitor the integration.

Conclusion: Our model provides a basis for integration of health system responses to HIV/AIDS and NCDs in the context of developing countries. We propose that future empirical work is needed to refine the validity and applicability of the model.

Keywords: HIV/AIDS, Noncommunicable diseases, integration, model, health system response

1. Introduction

Integration is a dynamic and multidimensional concept. It may mean different things to different people. For some, integration is a polarized concept and for others it is a continuum. In Health systems, the term has been widely used to describe the bringing together of different components of the healthcare system. Integration is 'a framework – a lens that can be systematically applied to better link units…it is a means to tackle fragmentation, duplication and gaps' (Armitage, Suter, Oelke, & Adair, 2009). Though it could apply to any function/process in the health system, integration is commonly applied to service delivery to ensure *continuity* of services and thereby to effectively address patient needs (D.L. Kodner & Spreeuwenberg, 2002). The working definition of "integrated care" by the World Health Organization (2008) is "The management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system" This definition implies that integration is a function of both the management and the delivery of health services, and its purpose is to ensure continuity of services that is essential to address client needs.

Integration is a means to an end rather than an end by itself (D.L. Kodner, 2009). Based on its different

dimensions considered ('integration compact'- See figure 1), there are different classifications of integration in a health system. According to the axis of the health system, integration could be *horizontal or vertical*. Depending on the level of health system where it occurs, integration could be *strategic* (upstream/Macro level), *managerial* (Midstream/Meso level) or *Operational* (Downstream/Micro level). Integration could also be partial or full; specific or generalized; strong or weak; localized or universal. Integration may also be classified based on the foci of integration, the units that are going to be integrated. Besides, integration can be internal (e.g. intra-program), external (inter-program), across stakeholders, across levels and with sector-wide responses.

Integration can be approached from a perspective of clinical model, business model, workforce model or community model (Karakusevic, 2010). Most of the currently existing integration models focus on the architecture of *output* of integration, the configuration of an integrated whole, and how it works (Lloyd & Wait, 2013). Some model address principles of successful health system integration (Armitage et al., 2009). Other studies addressing issues related to strategies of integration indicate how two services can be integrated (Dudley & Garner, 2011). There are many forms of health system integration models: System level (Lukas et al., 2002; Markoff, Finkelstein, Kammerer, Kreiner, & Prost, 2005; Miller, 2000), service level (Batterham et al., 2002; Byrnes, 1998; King & Meyer, 2006; O'Connell, Kristjanson, & Orb, 2000; Weiss, 1998; Wulsin, Sollner, & Pincus, 2006) and progressive models (Boon, Verhoef, O'Hara, & Findlay, 2004; Gillies, Shortell, Anderson, Mitchell, & Morgan, 1993; Leatt, Pink, & Guerriere, 2000; Leutz, 1999). Most of these models are service level models that focus on integration outputs rather than integration processes.

Health Systems in developing countries, especially in Sub-Saharan Africa, have been fighting the HIV/AIDS epidemic during the past three decades. Subsequently, several policies, programs, and systems have been developed to mitigate the impacts of this epidemic. As a result, the HIV/AIDS epidemic in those settings is stabilizing. However, the epidemic of Noncommunicable diseases (NCDs) is rapidly increasing in these countries. As HIV/AIDS and NCDs share many characteristics, an integrated approach could be a more effective and efficient alternative to curb the tide of the two epidemics. Given the political recognition of the need for integrated approach and the resource constraints in developing countries, there is an urgent need for evidence-based models for integrating the responses to HIV/AIDS and NCDs.

However, to the knowledge of the authors, there is no systematic and systemic model that could guide the *process* of integrating two or more health system response functions like that of HIV/AIDS and NCDs. Therefore, this study was designed to develop an action model, a step-by-step approach, for the integration of health system responses to HIV/AIDS and NCDs in the context of developing countries. The new model is expected to be useful for assessment, strategy development, healthcare management and in refinement of existing strategies related to integration.

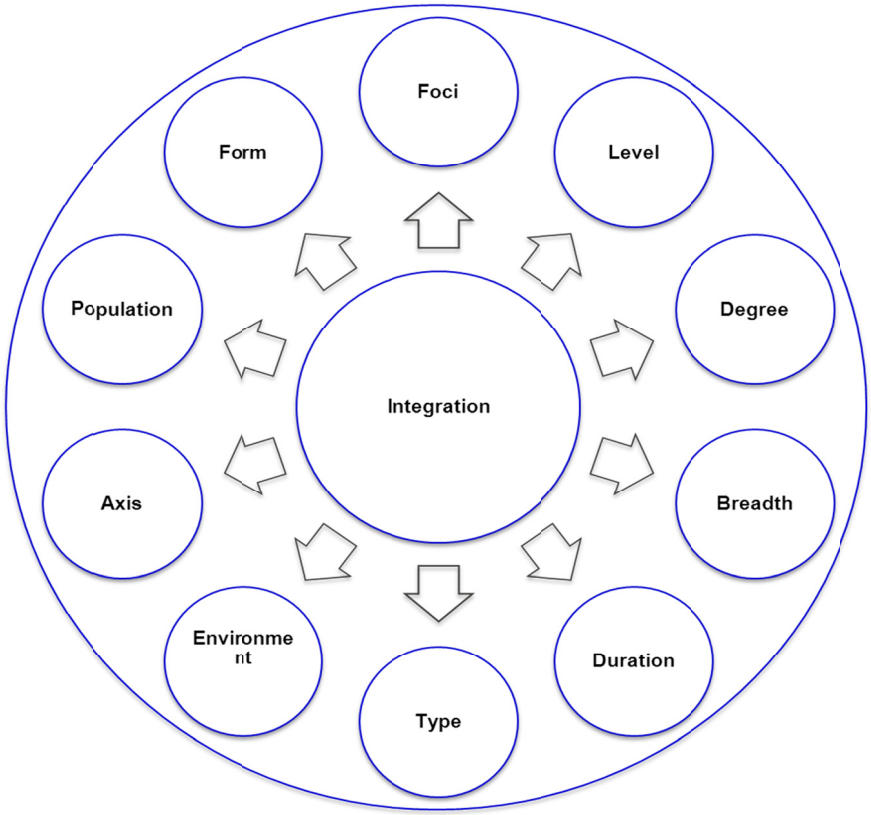

Figure 1. The 'integration compact'

2. Model Development Methods

Multiple stages and steps were involved in this study. We began this study by carrying out a *scoping review* of the literature to explore the rationale for integrating the responses to HIV/AIDS and NCDs in developing countries (T. Nigatu, 2012). This initial review revealed that analysis of the *connections* between HIV/AIDS and NCDs is essential to establish the need for an integrated response. Accordingly, we conducted analyses and synthesis of the connections between HIV/AIDS and NCDs at three levels: Population, Disease and Individual level. After the analysis of the connections, it became evident that an additional dimension, analysis of the relationships between the responses to the HIV/AIDS and NCDs, is essential to identify the eligible functions for integration. Accordingly, we conducted a qualitative analysis of the similarities and differences between responses to HIV/AIDS and NCDs case study approaches. Further exploration of evidence from integration of HIV/AIDS and reproductive health services in developing countries yielded an additional factor important for our model development process. This was the role of organizational/system *environment*. In this study, we described the major 'environmental' factors that should be considered in the integration process.

Following the generation of evidence for integration, the next logical step is communication. In order for evidence to better inform decisions, it needs to be *repackaged* in to a more simple and understandable form. By adopting concepts from knowledge translation models, we included this important step in to our model. Finally, we used the PIE (Plan, Implement and Evaluate) model of integration management for the rest of the steps. We detailed the application of all the steps in using the HIV/AIDS and NCD integration as a working example.

In overall, this model development process was *iterative* and *progressive*. We used descriptive, integrative and configurative evidence synthesis techniques at different levels. We considered the model to be *cyclical* rather than *linear*. The primary information sources during the design of the model were the sub-studies conducted as part of a larger research project and additional trans-disciplinary literature review.

3. The INTEGRATE Model for Integration

Integration consists of a series of steps that *integration managers* should implement to arrive at an effective integration of functions. If *integration managers* use a systematic process of integration, there will be a higher chance of successful integration as compared to the use of fragmented and unsystematic processes of integration.

This article describes a model for integration process of health system response functions of HIV/AIDS and Noncommunicable diseases using the acronym INTEGRATE. Each letter of the acronym INTEGRATE stands for a step in the action cycle that needs to be carried out before proceeding to the next step. The nine steps in the INTEGRATE Model are shown in the figure below.

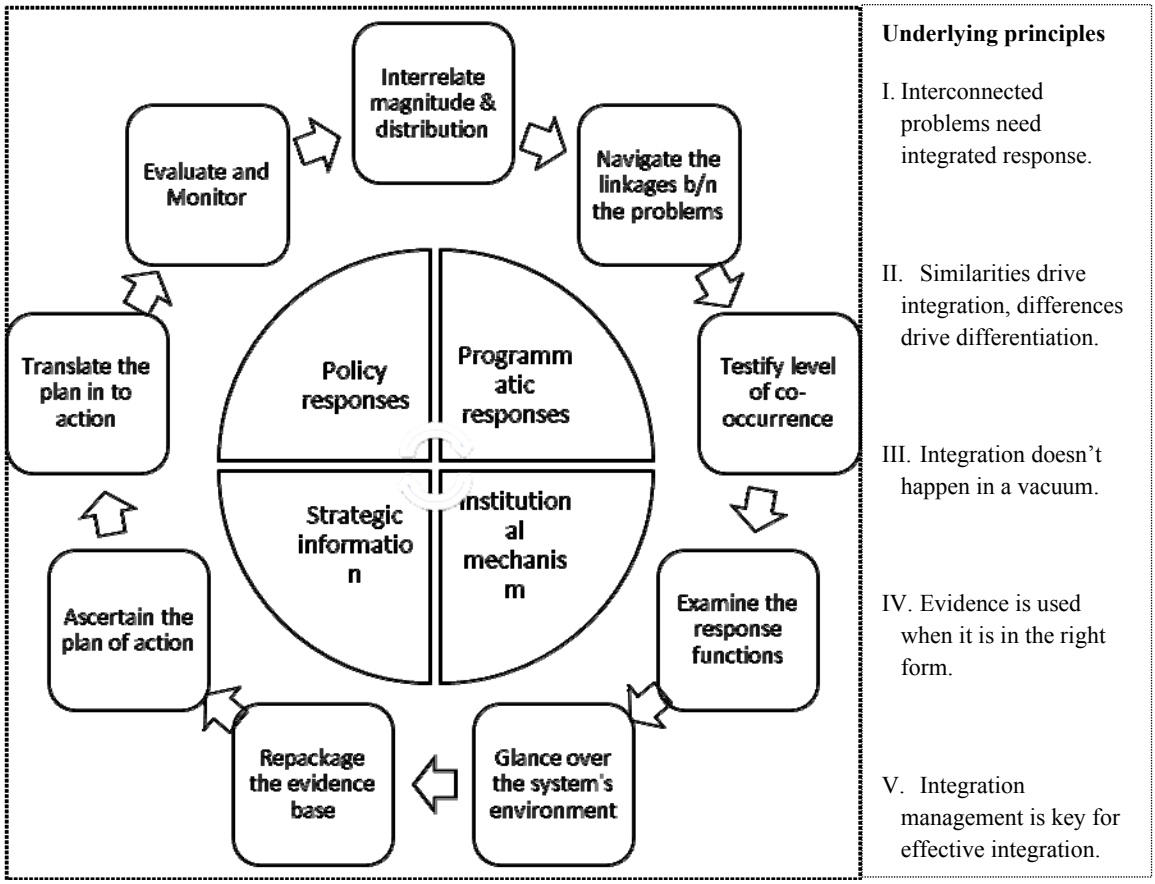

Figure 2. **INTEGRATE**: Integration action model with 5 principles, 4 action fields and a 9-step action cycle

As described in the above figure, the resulting action model has five underpinning principles, five key processes, four action fields and a nine-step action cycle. These principles, key processes and steps are illustrated in the following sections.

3.1 Interconnected Problems Need Integrated Response

Key process I: Analyze connections between the problems

As it is the case for many other management functions, integration starts with understanding of HIV/AIDS and NCDs, more specifically the connections between them. Using the *syndemic* theory and ecological model, analysis of the connection between HIV/AIDS and NCDs can be conducted at three levels: Population, Problem and Individual levels.

Step 1: Interrelate the magnitude and distribution of the problems

Interrelating the magnitude and distribution (by person, place and time) of HIV/AIDS and NCDs at *population* level is essential to identify epidemiological overlaps between the problems. Evidence from population level overlap informs overall policy approaches and priorities. It also informs the need for a more detailed analysis. The magnitude of HIV/AIDS and NCDs can be interrelated at point in time (in a cross-sectional manner), across time (in a time-series manner), across different geographic settings, and across different segments of a population. The interrelationships between *patterns and trends* of HIV/AIDS and NCDs across different dimensions could be explored using a cluster analysis, trend analysis and correlational analysis techniques.

In the analysis of epidemiological *overlap* between HIV/AIDS and Diabetes (considered as a prototype NCD) in

developing countries, Diabetes was found to have higher prevalence and HIV was found to have higher disability-weight-adjusted prevalence. Diabetes had an increasing trend while HIV had a stabilizing trend. Countries with high diabetes prevalence tend to have lower HIV prevalence. Four clusters of countries were identified from the cluster analysis of the patterns in the prevalence of HIV/AIDS and Diabetes (Haregu, Elliott, Setswe, & Oldenburg, 2013).

Step 2: Navigate the linkage between the problems

At disease level, analysis of the *linkage* between HIV/AIDS and NCDs and plotting the linkage in to a framework is important for better understanding the interconnections between the diseases. This evidence is essential for a coordinated response to public health problems as well as in developing the content of intervention packages. The *linkage* between HIV/AIDS and NCDs has direct or indirect pathways and is based on both *risk* and *severity*.

In the development of a public health framework for the epidemiological linkage between HIV/AIDS and the common NCDs (Cardiovascular disease, cancer, Diabetes and chronic obstructive pulmonary disease), six major pathways of linkage were found. These were direct cause-effect relationship, common underlying/background factors, lifestyle factors, treatment effects, common complications, and other disease conditions (T. Nigatu, Setswe, Elliott, & Oldenburg, 2012). Apart from these, similarities in disease characteristics are also important.

Step 3: Testify individual level co-occurrence of the problems

The third level in the analysis of the connections between HIV/AIDS and NCDs is their level of co-occurrence - (Comorbidity and Multimorbidity). This is analysis of individual level co-occurrence of the health problems. This evidence is important in planning and resource allocations. As most health systems in developing countries can't afford to assign more than a single health care provider (team) to manage a patient with comorbidity and patients in those settings have the right to receive all the healthcare services they need from a single service delivery point, analysis of magnitude of co-occurrence of HIV/AIDS and NCDs is important to design effective strategies that can address the needs of multi-morbid patients.

Perspectives, constructs, and methods in the measurement of comorbidity and multimorbidity are detailed elsewhere (Haregu, Oldenburg, Setswe, & Elliott, 2012). In our analysis of the magnitude of comorbidities of common NCDs among HIV positive people, we have documented evidence of increased risks of cancer and cardiovascular diseases and the absence of evidence of increased risk of diabetes (Haregu, Oldenburg, Setswe, Elliott, & Nanayakkara, 2012; T. Nigatu, Oldenburg, Elliott, Setswe, & Woldegiorgis, 2013). Anti-retroviral treatment (ART) is associated with decreased magnitude of NCD comorbidity among HIV+ people (Islam, Wu, Jansson, & Wilson, 2012).

3.2 Similarities Drive Integration, Differences Drive Differentiation

Key process II: Examine the similarities and differences between responses

Step 4: Examine the similarities and understand the differences between response functions

After establishing the need for integrated response through analysis of connections between HIV/AIDS and NCDs, the next step is to identify eligible units for integration by examining similarities and differences between response functions. This step has four sub-steps.

3.2.1 Identify the Response Functions (i.e. Action Fields)

How health systems are responding to HIV/AIDS and NCDs? What constitutes a Health system response to HIV/AIDS and NCDs? What are the major processes/functions in a health system response? There are different classifications of the functions of a health system including the WHO Health system framework (World Health Organization). Qualitative analysis of the similarities and differences between responses to HIV/AIDS and NCDs revealed four inter-related categories of functions (Haregu, Oldenburg, Elliott, & Setswe, 2013).

These were *policy* related functions, *program* related functions, institutional arrangement/*coordination/* related functions, and *strategic information* related functions. Analysis of parallels and differences between the national responses to HIV/AIDS and NCDs yielded a fifth additional category which was labelled as *management* related functions. The functions under these major categories are shown in the table below.

Table 1. List of major functions in a health system response

Categories	Functions	Description of the functions
Policy	Leadership	High level political commitment
	Policy advising	Providing inputs for policy making
	Policy making	Formulation of policies
	Governance	Overseeing policy implementation processes
Program	Prevention	Measures taken to prevent disease
	Treatment	Services provided to control/treat disease
	Care & support	Services provided to improve quality of life
	Health System Strengthening	Interventions that improve system capacity
Management	Planning	Strategic and annual planning
	Implementation	Overseeing implementation of national programs
	Resource Mobilization	Securing resources needed for programs
	Multisectoral. Coordination	Coordination of multiple actors/sectors
Strategic information	Patient Monitoring	Monitoring the progress of patients
	Disease Monitoring	Monitoring of disease/epidemic patterns
	Program Monitoring &Evaluation	Monitoring and Evaluation of national programs
	Dissemination of information	Communication of findings of M&E

The scope and details of the above functions would vary across the three levels of the health system: Strategic (Macro), Managerial (Meso) and Operational (Micro). When one goes upwards in a health system, programmatic/technical/ functions get more *specialized* and administrative functions get more *converged*. In the process of integration, these functions/processes are integrated to arrive at an integrated whole.

3.2.2 Set Parameters to Compare Response Functions

Once the functions relevant for integration management are identified, the next step is to assess the relational similarities (and differences) between these functions. The basic question then will be 'what parameters should be used to assess the similarities between response functions?' These are the comparators, instruments for comparison. Below is a list of possible comparators. Although all these comparators may not apply to each and every function, the list is believed to include most of the relevant comparators.

Table 2. List of possible parameters for assessing the similarities between functions

Parameters (similarity in what?)	Descriptions
Operational characteristics	Nature and technical complexity
Timing of the functions	Time and frequency (when and how often)
Actors/performers	The skills/expertise/speciality required
Methods/tools	Models and approaches used
Targets/users	The characteristics of the customers/users
Results/outputs	The attributes of the end products
Input requirements	Financial and non-financial requirements
Levels in the system	Levels of health system where the functions happen
Lines of accountability	Command and communication chains
Monitoring Modalities	Monitoring requirements (formats, schedules etc)
Priorities and interests	Accorded priorities and vested interests

3.2.3 Rate the Degree of Similarity/Difference between the Response Functions

In a health system response to a HIV/AIDS and NCDs, it is possible for some functions to be more or less integrated than others. Though any set of functions can be assessed for degree of similarity and thus be eligible for integration management, the practice is common for parallel functions (e.g. treatment of HIV and Treatment of NCD, rather than treatment of HIV and Prevention of NCD). The degree of similarity between response functions can be rated using either a dichotomous or a likert-type scale. Below is a five point likert-type scale for rating two functions using the parameters identified in the above steps. The scores can be summed up to get a single summary score.

Who should rate the similarities? We propose two approaches: 1) The *deliberative* approach where a panel of experts, preferably from the concerned functions, deliberate on the similarities and provide an agreed up on score; 2) The *investigative* approach where an investigator assess the similarity between the functions and give a score based on the findings.

3.2.4 Determine the Strategic Importance of the Similarities/Differences

In addition to the degree of similarity, the importance (strategic, managerial, economical and operational) of the similarities and differences between functions is essential for integration. Finally, the examination of similarities/differences should come up with short list of functions that can undergo the integration process.

Table 3. Rating similarity between two functions using the assessment parameters

SN	Parameters for similarity (Similar in what?)	Degree of Similarity (How much similar?)				
		Very Low (1)	Low (2)	Medium (3)	High (4)	Very High (5)
1	Technical characteristics					
2	Priorities/premises					
3	Actors/performers					
4	Methods/tools					
5	Targets/users					
6	Results/outputs					
7	Settings/contexts					
8	Stages of Maturity					
9	Lines of accountability					
10	Monitoring Modalities					
	Total score					

3.3 Integration Doesn't Happen in a Vacuum!

Key process III: Scan the health system environment for integration

Step 5: Glance over the Health system's environment for integration

As integration happens in the real environment, the other major factor that is important for integration is the health system environment, the set of forces surrounding the health system that have the potential to affect the way it operates and its access to scarce resources. These include *internal* environment – internal to the units to be integrated (e.g. healthcare workers, managers, healthcare settings), the *task* environment (e.g. patients/clients, other actors, partners, donors, pressure groups), and the *external* environment (Political, Economic, Socio-cultural and Technological factors).

Among the prominent system factors in the context of developing countries is motivation among policy makers, health managers and providers for integration. *Acceptability* of the level of integration by target users is also important. Other important elements are capacity for integration, external influences of different stakeholders on integration and the impacts of integration on important stakeholders.

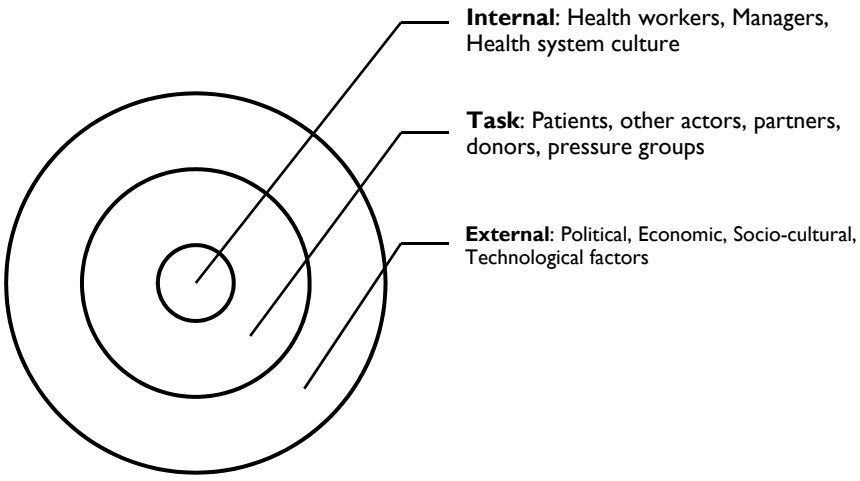

Figure 3. Elements of Health system environment

3.4 Evidence is Used Only When it is in the Right Form

Key process IV: Repackage evidence for integration

Step 6: Repackage and share evidence in a usable form

In Health systems integration, the focus has primarily been on structures. Though equally important systems level integration of functions has received little attention (Burns et al., 2001; Fawcett & Cooper, 2001). For system level integration of health system responses, different integration strategies need to be employed at multiple levels (D. L. Kodner, 2002). Similarly, multiple processes have to be used to ensure successful integration. Integration strategies at *system* level and *service* level are different (Dodds et al., 2004). *System level* strategies relate to administrative linkages between partners, shared philosophy statement, and role enhancement of certain provider groups (Wilson, Rogowski, & Popplewell, 2003). Accordingly, evidence for system level integration should be communicated to different audience at multiple levels. As different audience have different interests, the evidence needs to be repackaged before it gets disseminated.

Evidence repackaging is the presentation of evidence in a more understandable, readable, acceptable and usable form. The contents of the evidence obtained from the analyses in the above steps would indicate the need for integration, eligible functions for integration, various factors that would affect integration, *desired* level of integration, *existing* level of integration and the *gaps* between the desired and existing levels of integration. Purpose-driven packaging of evidence can facilitate effectiveness of communication.

The content of evidence relevant to integration can be repackaged based on the models of integration. The model for system level integration depends on the required level of integration, and resources available for conducting the integration process and executing the integrated functions. The following are examples of models of integrating functions: a *causal model* of organizational performance and change (Burke & Litwin, 1992), a *3-dimensional model* developed based on key dimensions of an integrated health system (Conrad & Shortell, 1996), a *linear model* developed to measure outcomes (Lukas, et al., 2002), and the Relational Systems *Change Model* developed based on psychological development (Markoff, et al., 2005).

Moreover, evidence about integration of functions could also be repackaged based on desired types of integration: Virtual (networked) integration, vertical (hierarchical) integration, horizontal (same level) integration, functional integration, clinical integration, and physician integration. In general, repackaging of integration related evidence should consider the audience, the content, the purpose and the method of communication.

3.5 Integration Management is Key to Effective Integration

Key process V: Manage integration

Step 7: Ascertain the plan of integration

Levels of integration can be considered as parts of a continuum. There are several models of levels of integration that are developed based on health service integration (Heath, Wise Romero, & Reynolds, 2013; Suter et al.,

2007). It is possible to assume that there is always some level of integration between two functions. Identifying the existing level of integration between two functions is the first task at this step. The next task is determining the desired level of integration between the functions. This will be the aim of the integration process.

Integration managers should develop a detailed Policy/Strategy/*Plan of integration* that describes the components of responses are going to be integrated, the existing and the desired level of integration, the strategies to be used, the resource requirements, and the benefits and the risks of the integration. This will serve as a roadmap for the overall integration process. Assessment of local and global *experiences* and *best practices* relevant to the integration is essential. Communication and coordination (e.g. through consultative meetings with relevant stakeholders) is very crucial at this stage. Measurable objectives should be developed and agreed up on. Contextual factors, like personal preferences and urgency of the problem and interests of the various stakeholders involved may affect the planning and implementation integration. The required level of system integration will also depend on the type of interdependence (pooled, sequential, or reciprocal) in the structure of the systems (Peters, 1998). The resulting integration plan needs to be aligned with existing policies and strategies.

Evidence about HIV-NCD integration in the literature

1. Cervical Cancer screening in to HIV services (Sneden, Huchko, Cohen, & Yamey)
2. Gestational Diabetes screening in to HIV treatment/PMTCT (Gonzalez-Tome et al., 2008)
3. HIV/AIDS, Diabetes, and Hypertension services in to a chronic disease clinic (Janssens et al., 2007)
4. Leveraging HIV programs to support diabetes services (Rabkin et al., 2012)
5. Integrating smoking cessation in to HIV care -(Drach et al.)
6. Integrating HIV/AIDS and Alcohol (Bryant, Nelson, Braithwaite, & Raoch, 2010)

The selection of approach of integration depends of local contexts. For instance, policy integration of HIV/AIDS and NCDs can be realized in terms of one policy governing both HIV/AIDS and NCDs or a special policy guiding the integration of HIV/AIDS and NCD responses. Policy statements that support the integration of HIV/AIDS and NCD responses could also be included in both HIV/AIDS and NCD policy documents. Such policies/strategies could guide integration at program, management and information levels.

Table 4. Possible levels of integration of response functions

S.N.	Levels	Description of levels
1	Communication	Exchange of information, keep up to date
2	Consultation	Informing actions and consulting for actions
3	Coherence	Ensuring that there are no contradictions in actions
4	Consensus	Recognizing interdependence and ensuring harmonization
5	Coordination	Helping each other but not changing the basic way of doing business
6	Cooperation	Helping each other in specific ways
7	Collaboration	Working together/jointly on mutual interests
8	Co-location	Functions co-located to be under the same space/facility
9	Coalition	Performing functions with the same team with role difference
10	Combination	Transforming functions in to a single merged practice

Step 8: Translate the plan to action

The action fields for Health system response are identified as policy response, programmatic response, institutional mechanism, and strategic information. The integration strategies to be used can vary based on both the action field and the desired level of integration. The common system level strategies in the implementation of health system integration include patient engagement and participation, well-developed performance

management system, well-functioning information system, cohesive organizational culture, relationship development, right sizing and controlled growth, and sound financial management. The level, type and combination of strategies required are highly contextual and have to be geared towards better outcomes. System level integration may begin at any level. But it must extend to all other levels. Integration between two functions could be at the development of a plan, implementation of activities and at Monitoring and Evaluation of a program.

Successful implementation of integration requires time, sufficient resources and a defined, multi-model intervention. A formal Strategic plan with measurable objectives, time lines, responsibilities, and outcomes is essential. Structural changes and resource sharing along with sufficient attention to relationships are required at all levels of a system. Flexibility of leadership is essential to adapt to the changes. Development and execution of strategies is progressive. Never expect to "finish" the integration – Integration is an on-going process (Contandriopoulos, Denis, Touati, & Rodriguez, 2003; Vanderbent, 2005).

Barriers to effective integration are categorized in to *specialization* barriers and *political* barriers. In contrast, mechanisms that facilitate the implementation of integration include standardization (work, output, skill and norms), direct supervision, coordinated planning, and mutual adjustment. The suitability of the mechanism of integration depends on task *complexity* and task *interdependence* (Barki & Pinsonneault, 2005).

Step 9: Evaluate and Monitor the integration

Evidence related to evaluation of integration is related to the following constructs: Configuration, Effectiveness, Efficiency, Synergy and impact. *Configurations* are forms of alignment between strategy, structure, processes and environment. Measurement of integration (the level/intensity of integration of integrated system – the actual degree of integration between functions) often refers to configuration. Integrated policies, integrated programs, integrated management, integrated organizational structures and integrated monitoring and evaluation systems are the outputs of strategic level integration. The changes in configurations are expected to reduce *complexity* but may increase *connections*. Configurations in most models of degree of integration consider a continuum extending from full segregation through a number of intermediate forms to full integration (Ahgren & Axelsson, 2005).

Effectiveness of integration refers to the achievement of the intended goals of the integration. There is a difference between the achievement of the goals of the health system (impact) and the achievement of the goals of integration (effectiveness). The change in *performance* of a system that could be attributed to the integration process is the effect of the integration. Accordingly, integration effectiveness can be measured at community, integration/network and organization levels (Provan & Milward, 2001). The stakeholder groups and effectiveness criteria are different among these levels.

Synergy among the integrated functions is another important *proximal* outcome of integration. Synergy in the context of integrated functions means the "combined effect" of multiple functions as compared to the sum of the effect of the independent functions. Synergy among functions is influenced by resources, partnership characteristics, relationship among partners and external environment (Lasker, Weiss, & Miller, 2001).

Efficiency of integration is often related to the financial performance in the process of achievement of the intended outcomes of the health system. However, efficiency of integration should be viewed from a broader perspective. In Health system context, efficiency refers to how well healthcare resources are used to obtain health improvements. This comprises of two components: *Technical* efficiency (whether functions are performed with the least amount of inputs) and *allocative* efficiency (whether a set of technically efficient functions is chosen to yield the greatest possible outcome) (Peacock, Chan, Mangolini, & Johansen, 2001).

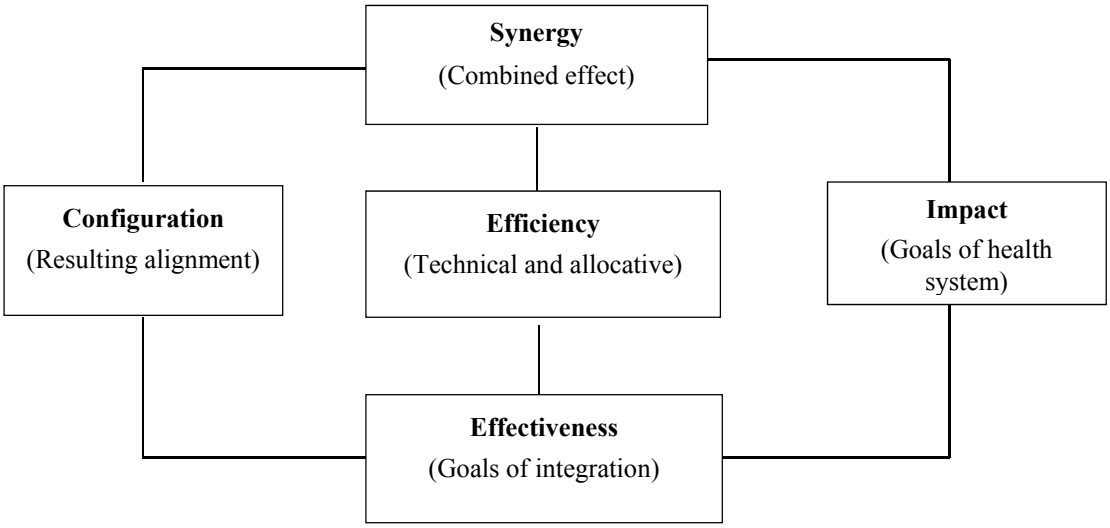

Figure 4. A framework for Evaluation of integration

The widely used measurement tool for integration is the *Balanced Score Card* (BSC). BSC is appropriate to evaluate both the implementation and impact of integration (Kaplan & Norton, 1993). The second measurement tool is the *clinical microsystem assessment* tool (Peacock et al., 2001). This tool is primarily designed for the clinical system. The third tool is the *scale of functional integration* which is validated for several forms of integration (Nelson et al., 2002).

4. Conclusion

Developing countries are facing a double-burden of HIV/AIDS and Noncommunicable diseases. As the intersection between HIV/AIDS and NCDs is significantly high, an integrated response can maximize synergy and improve efficiency of the responses. The need for integrated response is therefore clear.

Integration is an iterative, dynamic and complex process. Using synthesis of evidence from various fields, we have developed an action model that could guide the integration of health system responses to HIV/AIDS and NCDs in developing countries. The model has 5 underpinning principles, 5 key processes and 9 steps. It could serve as a step-wise framework for systematic integration of health system responses to HIV/AIDS and NCDs in the context of developing countries. Although this model is prepared as an action cycle, users may use the steps out of sequence, as appropriate, depending on their context. The model can be a good basis for the development tools that could be used to operationalize the different steps stated in this model.

This model is developed based on synthesis of best available evidence about integration of responses to HIV/AIDS and NCDs. The principles and the steps developed in this action model could be adapted to other disease conditions in similar contexts. This action model is conceptually enriched through a review of literature from different disciplines. However, it hasn't yet been empirically tested. Besides, the steps in this model are stated as general guiding statement and are not operationalized in to specific tasks and activities.

Therefore, we propose that future empirical work is needed to refine the validity and applicability the model. The model should also be translated in to tools that facilitate its application to meet the intended purpose. Further research work is also needed to refine this model.

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A GUIDING TOOL FOR INTEGRATION

A tool to guide the process of integrating Health system responses to Public Health problems

An integrated model of health system responses to public health problems is considered to be the most preferable approach. Accordingly, there are several models that stipulate what an integrated architecture should look like. However, tools that can guide the overall process of integration are lacking.

This tool is designed to guide the entire process of integration of Health system responses to major public health problems. It is developed by taking in to account the contexts of health systems of developing countries. The evidence base for the development of the model was chronic diseases - HIV/AIDS and NCDs. System level horizontal integration of health system responses were considered in the development of this tool.

This tool is based on the 'Analysis – Synthesis – Action' continuum. It considers integration as a *spiral* rather than a *linear* process. The target users of this tool are health policy makers, health care managers and health policy and systems researchers. These users may use this tool out of sequence based on their context and needs. As this tool is generic in its nature, users should adapt it to their own health system context, public health problems, and responses considered for integration.

This tool was developed based on an action model of integration presented elsewhere. It builds up on the best available evidence. It combines theoretical, empirical and practical evidence. It is worth noting that there are several other models that address the different components of this tool. This tool presents a unique consolidation of the translation of these models in a form of a guiding tool along with essential new elements. The contents of this tool are conceptually validated and were enriched using inputs from expert consultations.

This tool is divided in to five major sections:

I. Analysing the connections between *problems*
II. Examining similarities between *responses*
III. Scanning the *environment* for integration
IV. Repackaging Evidence for *communication*
V. Managing *integration*

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SECTION I: PROBLEMS - ***Analysing the connections between the problems***

P1	Convergence	Overlaps between the problems (Population level)
P2	Linkage	Linkages between the problems (Disease level)
P3	Co-occurrence	Co-occurrence of the problems (Individual level)

SECTION II: RESPONSES - ***Examining similarities between responses***

R1	Responses	The different elements of the response that are of interest
R2	Comparators	The attributes of the responses used for comparison
R3	Degree	The strength of similarities between responses
R4	Importance	The relative importance of the similarities

SECTION III: ENVIRONMENT- ***Scanning the environment for integration***

E1	Motivation	Interest for integration among important actors
E2	Capacity	Managerial, technical & institutional capacity for integration
E3	Acceptability	Acceptability of integrated approach key role players
E4	Influence	The reaction of important stakeholders towards integration
E5	Impacts	The effect of the integration on important stakeholders

SECTION IV: COMMUNICATION - ***Repackaging evidence for integration***

C1	Audience	The target audience of the evidence (who)
C2	Purpose	The objective of communicating evidence (why)
C3	Content	The evidence to be communicated (what)
C4	Method	Methods of communicating the evidence (How)

SECTION V: INTEGRATION - ***Managing integration***

I1	Planning	Developing the plan of integration
I2	Implementation	Translating the plan in to action
I3	Evaluation	Evaluating the outputs, outcomes and impacts

SECTION I: PROBLEMS- *Analysing the connections between the problems*

P1. Convergence between the problems

Definition: Understanding population level (epidemiological) overlap between the distributions of two public health problems is important to inform overall policy approaches that address the problems. Considering the Ecological model, Epidemiological overlap between two diseases has three dimensions: Population groups, Geographic settings, and time.

Population groups: Segments of the population based on different factors.
Geographic settings: Different places within a certain county/region.
Time: A point or a period of time of interest.

Task 1: *Population groups*: To assess overlap between two problems in terms of the population groups, use the following 3x3 Tool and assign different population groups/segments in to the cells.

Tool 1: A 3X3 matrix for relating the population groups affected by two problems

		Magnitude of Problem B		
		High	Medium	Low
Magnitude of Problem A	High			
	Medium			
	Low			

Task 2: *Geographic settings*: To assess overlap between two problems in terms of the geographic settings, use the following 3x3 Tool and assign different geographic settings in to the cells.

Tool 2: A 3X3 matrix for relating geographic settings affected by two problems

		Magnitude of Problem B		
		High	Medium	Low
Magnitude of Problem A	High			
	Medium			
	Low			

Note: Cut-off points that differentiate between *high, medium and low* (In task 1 and 2) are relative and highly dependent on local contexts. Thus, these are left to the users of this tool. Groups/settings assigned to 'High-High' will be the most likely focus of integration. *Cluster analysis* could be used if actual values are available.

Task 3: *At a point in time*: To assess concurrence between the two problems in terms of their magnitude (at a defined population and place) at a point in time, use the following 3x3 Tool and assign the magnitude of the problems in to the cells. The *average* magnitude to be used for comparison could be national prevalence (for sub-

national considerations) or global prevalence (for national considerations). When both problem A and Problem B have high magnitude, the need for integrated response is more likely to be higher.

Tool 3: A 3X3 matrix for relating the magnitude of two problems at a point in time

		Magnitude of Problem B		
		High	Average	Low
Magnitude of Problem A	High			
	Average			
	Low			

Task 4: *Time-trend*: To assess epidemiological overlap between two problems in terms of their trend (of magnitude) across time (at a defined population and place), use the following 3x3 matrix and assign the trends in the magnitude of the problems in to the cells.

Tool 4: A 3X3 matrix for relating time-trends of two problems

		Time-trend of problem B		
		Increasing	Stabilized	Decreasing
Time-trend of Problem A	Increasing			
	Stabilized			
	Decreasing			

A *trend-line* would be important to assess the presence of overlapping trends. When both problems have an increasing trend, the need for integrated response becomes more likely. The time period for the trend needs to be set based on relevance and availability of data. Trends without a defined pattern may be treated in a different way. *Correlational analysis* could also be used in such cases.

***Note*:** The assessment of overlaps between the two problems is based on ecological model and thus is subjected to ecological fallacy.

P2. Linkage between the problems

Definition: Information about the inter-relationships between problems is important to inform the *content* of interventions packages. The linkage between two problems takes two forms: *Risk* and *Severity*. *Risk* is when the presence of problem A affects the probability of occurrence of problem B and/or vice versa. *Severity* is when the presence of problem A affects the severity of problem B and/or vice versa.

Task: To assess the linkage between two problems in terms of risk and severity, compare the risk and severity in the *sub-populations* with that of the general population. The following tool summarizes the risk and severity of a problem in the

sub-populations, along with a three-point scale, as compared to that of the general population.

Tool 5: Matrix for rating linkage between two problems

	Greater	**Similar**	**Lower**
Risk of problem B among A+ as compared to general population			
Risk of problem A among B+ as compared to general population			
Severity of problem B among A+ compared to general population			
Severity of problem A among B+ compared to general population			

When data are available, it would be preferable to use *quantitative* measures of risk and severity to demonstrate actual levels. The greater the risk and severity of the problems in the sub-populations (as compared to the general population), the higher is the need for integrated response.

P3. Co-occurrence of the problems

Definition: Evidence about the magnitude of co-occurrence of two problems in an individual is useful to inform planning and resource allocation. Co-occurrence of two diseases can be expressed in two forms: *Co-morbidity* (when there is an index disease) and *Multimorbidity* (when there is no index disease).

Task: To explore the magnitude of co-occurrence of two problems, compare the prevalence of each problem among those having the other with that of the general population (for comorbidity); and the prevalence of both diseases in the population to prevalence that would otherwise occur by chance. The following tool summarizes these measures.

Tool 6: Matrix of classifying levels of co-occurrence of two problems

	Greater	**Similar**	**Lower**
Prevalence of A among B+ as compared to prevalence of A (P_A)			
Prevalence of B among A+ as compared to prevalence of B (P_B)			
Prevalence of AB in general population as compared to (P_A*P_B)			

In situations where actual prevalence values are available, they can be used for the comparison. The greater the prevalence of comorbidity and multimorbidity, the higher the need for integrated response.

Note: At the end of Section I, you would establish the need for integration from the problems' perspective.

SECTION II: RESPONSES - *Examining similarities between responses*

R1. Define response

Definition: A health system response to a public health problem contains several components at different levels. At upstream (Macro) level are *strategic* functions including policy making, leadership and governance. At mid-stream (Meso) level are *management* functions like planning, coordination, resource mobilization etc. At down-stream (Micro) level are *operational* functions such as service provision, data collection etc. Within each of the elements of the response, several functions and structures are involved.

An effort of integration may involve all or some of these functions/structures. Some processes may require a stronger integration than others. One possible method to establish this is by analysing the *similarities* between parallel processes (e.g. Treatment of A and Treatment of B). This is based on the assumption that a higher level of similarity predicts a stronger need for integration. Analysis of similarities between the responses to problem A and Problem B starts with defining the functions of interest that constitutes a response.

Task: Depending on the intended focus and type of integration, *identify and describe* the elements of the response that could be the *possible candidates* for integration. The scale of the details of these functions would vary based on the level of the health system. An example of list of core functions and their description is presented in the following tool.

Tool 7: List of major functions that constitute response to health problems

Categories	Functions	Description of the functions
Policy	Leadership	High level political commitment
	Policy advising	Providing inputs for policy making
	Policy making	Formulation/approval of policies
	Governance	Overseeing policy implementation processes
Program	Prevention	Measures taken to prevent disease
	Treatment	Services provided to control/treat disease
	Care & support	Services provided to improve quality of life
	System Strengthening	Interventions that improve system capacity
Management	Planning	Strategic and annual planning
	Implementation	Overseeing implementation of programs
	Resource Mobilization	Securing resources needed for programs
	Multisectoral. Coordination	Coordination of multiple actors/sectors
Strategic information	Patient Monitoring	Monitoring the progress of patients
	Disease Monitoring	Monitoring of disease/epidemic patterns
	Program M&E	Monitoring and Evaluation of programs
	Dissemination	Communication of findings of M&E

R2. Identify comparators

Definition: Once the response functions, the possible candidates for integration, are defined, the next step will be to assess the similarities between the parallel functions. Assessment of similarity between two functions requires comparators – parameters that are used to compare two functions.

Task: Identify parameters/attributes of the functions that could be used to compare two processes in order to identify similarities and differences. A list of possible parameters is given below.

Tool 8: List of potential parameters that may be used to assess similarity

Parameters	**Descriptions**
Operational characteristics	Nature and technical complexity
Timing of the functions	Time and frequency (when and how often)
Actors/performers	The skills/expertise/speciality required
Methods/tools	Models and approaches used
Targets/users	The characteristics of the customers/users
Results/outputs	The attributes of the end products
Input requirements	Monetary and non-monetary requirements
Levels in the system	Levels of health system where the functions happen
Lines of accountability	Command and communication chains
Monitoring Modalities	Monitoring requirements (formats, schedules etc)
Priority and interests	Accorded priorities and vested interests

R3. Rate degree of similarity:

Definition: The degree of (relational) similarity is the extent to which a pair of parallel response functions [e.g. Prevention of A and Prevention of B] shares common parameters/attributes. The most appropriate and applicable set of parameters should be used for the rating. The rating scale may vary from dichotomous scale to a higher point likert scales.

Task: Using a selected set of parameters, rate the degree/strength of similarities between a pair of parallel functions. A sample template for rating the similarity between program related functions of problem A and Problem B is given below.

Tool 9: Matrix for rating degree of similarity of parallel functions

Pairs of parallel functions (*These are examples only, add more to this list*)	**Degree of similarity**		
	Low	**Medium**	**High**
Prevention [of A and B]			
Treatment [of A and B]			
Care & support [of A and B]			
Health System Strengthening [of A and B]			

R4. Determine importance of similarities

Definition: In addition to the degree of similarity, the importance of similarity is also essential. The importance of the similarities between a pair of parallel functions can be viewed from four major perspectives:

Policy – the strategic importance of the similarity for policy purpose
Management – the importance of the similarity for decision making
Economic – the importance of the similarity in efficient use of resources
Practice – the importance of the similarity for program implementation

Task: Determine the relative importance of the similarities between a pair of parallel functions by considering the policy, management, economical, and practice perspectives.

Tool 10: Matrix for rating relative importance of similarity between parallel functions

Similarity between (*These are examples only, add more to this list*)	**Relative importance**		
	Low	**Medium**	**High**
Prevention [of A and B]			
Treatment [of A and B]			
Care & support [of A and B]			
Health System Strengthening [of A and B]			

Note: At the end of this section, an initial short-list of possible candidates (for integration) of response functions would be reached. Though higher degrees of similarity and higher relative importance of the similarity could be the mainstay of the selection, this will also depend of judgement by the responsible body.

SECTION III: ENVIRONMENT- *Scanning the environment for integration*

After establishing the need for integration [section I] and identifying candidate functions/structures for integration [section II], the third phase is assessing whether the environment is enabling/conducive for integration. This is conducted using environmental scanning. In principle, three components of the environment need to be considered: Internal (Staffs, Managers, Organizational set up), Task-related (patients, competitors i.e. other actors, partners, donors, pressure groups), and External (Political, Economic, Socio-cultural and Technological factors). From the perspective of integration, the following themes are important.

E1. Motivation for integration

Definition: Interest among managers and staffs (of Unit A and Unit B) to integrate the relevant functions/structures and operate in an integrated approach.
Task: Assess whether policy makers, managers and staffs of unit A and unit B are interested to integrate the respective functions and thereby operate in an integrated approach.

Tool 11: Matrix for rating levels of motivation towards integration

Major actors	**Levels of Motivation**		
	Low	**Medium**	**High**
Policy makers			
Managers			
Practitioners			

E2. Capacity for integration

Definition: Capacity to integrate (for managers) and capacity to operate in an integrated approach (for staffs and institution/infrastructure).
Task: Assess the capacity (managerial, technical and institutional) to integrate the functions and operate in an integrated approach.

Tool 12: Matrix for rating levels of capacity for integration

Capacity dimensions	**Levels of capacity**		
	Low	**Medium**	**High**
Managerial capacity			
Technical capacity			
Institutional capacity			

E3. Acceptability of integration

Definition: The extent to which the integrated approach is acceptable to the end users (patients, donors, governments) of the processes or the arrangements.

Task: Assess whether an integrate approach is acceptable to end users of the functions.

Tool 13: Matrix for rating levels of acceptability of integration by end users

Important stakeholders	**Levels of acceptability**		
	Low	**Medium**	**High**
Service users/customers (e.g. patients)			
Funding agencies (donors)			
Governing bodies (including government)			

E4. Influences on integration

Definition: The effects (reactions) of important stakeholders and their activities on integration process. Influences may be negative, neutral or positive.

Task: Assess the possible reactions of other important stakeholders towards the integrated approach.

Tool 14: Matrix for classifying anticipated reactions of stakeholders

Important stakeholders	Anticipated reactions		
	Negative	**Neutral**	**Positive**
Stakeholder 1			
Stakeholder 2 (*add rows for more stakeholders*)			

E5. Implications of integration

Definition: The possible effects (impacts) of the integration on important stakeholders and their business. This may also be positive, neutral or negative.

Task: Assess how the integration of the functions/structures might affect other important stakeholders.

Tool 15: Tool for classifying anticipated impacts of integration on stakeholders

Important stakeholders	**Anticipated impacts**		
	Negative	Neutral	Positive
Stakeholder 1			
Stakeholder 2 (*add rows for more stakeholders*)			

SECTION IV: COMMUNICATION - *Repackaging evidence for integration*

All the preceding sections of this tool were designed for *generating* important evidence about the need for integration, identifying the appropriate candidate functions/units for integration and assessing the conduciveness of health system environment for integration. The evidence generated need to be repackaged in a form that can better inform decisions related to integration. This section has the following parts.

C1. The audience (WHO)

Definition: Integration may mean different things for different people. Policy makers, Managers, Healthcare providers, patients, and researchers have different views about integration. Repackaging evidence of integration needs to take in to account these views and interests.

Task: Clearly state the target audience, their views, and their interests in relation to integration.

C2. The purpose (WHY)

Definition: Repackaging of integration related evidence should be targeted towards achieving a clearly defined purpose. The purpose is usually *instrumental* – for practical applications. In some instances, however, it may be *symbolic* – to confirm decisions, policies and practices.

Task: Clearly state the purpose(s) of the communication of evidence about integration.

C3. The content (WHAT)

Definition: What needs to be included in the communication package depends on the purpose and the audience of the communication.

Task: Prepare the content of communication product – the knowledge/evidence that is going to be communicated.

C4. The method (HOW)

Definition: The method of communication may be selected based on knowledge about the interests of the audience. It may be in the form of printed materials, electronic materials, audio-visuals, conference presentations etc.

Task: Decide on the method of communication and appropriate communication product.

Tool 16: A matrix of four major elements of evidence communication

Purpose	Audience	Content/Message	Method

SECTION V: INTEGRATION - *Managing integration*

Once the evidence about integration is effectively communicated, responsible bodies are expected to make decision about the integration. The translation of that decision in to action should be systematic, with steps involving planning, implementation, Monitoring and Evaluation.

I1. Planning integration

Definition: Integration should be a well-planned process. Integration planning needs to consider the parts and the parties that are going to be integrated. Depending on its extent, integration planning may address a range of tasks:

Task 1: Select the *foci* of integration (units/functions that are going to be integrated). These may include functions/structures relevant to policy, institutional arrangement, management, program, and information.

Task 2: Formulate the Goals/objective of the integration

Task 3: Determine baseline (the existing) and the target (the desired level) of integration for each foci of integration. The following tool could be used.

Tool 17: The ten levels of integration

Levels of integration	Communication	Consultation	Coherence	Consensus	Coordination	Cooperation	Collaboration	Co-location	Coalition	Combination
Baseline level										
Target level										

Task 4: Identify Strategies/Mechanisms to be used to achieve objective of the integration.

Task 5: Estimate the Cost/resources required for implementing the strategies

Task 6: Weigh the benefits and risks that might be associated with the integration

Define the key elements of integration plan and prepare *the plan*.

I2. Implementing integration

Definition: This step is about the application of the integration plan in to action. It involves operationalization of integration plan in to implementation plan and carrying out activities as per the implementation plan. The implementation of integration plan, therefore, involves:

Task 1: **Operationalization**: Deciding who will do what & when–*implementation plan*

Task 2: **Implementation**: Translating the implementation plan in to action

Task 3: **Coordination**: Synchronizing activities and actors

Task 4: **Supervision**: Supervising and taking corrective action

Task 5: **Monitoring**: Measuring progress and comparing against the plan

I3. Evaluating integration

Definition: As any other performance improvement initiative, integration should be evaluated. The key constructs that are usually important in the evaluation of integration are the following:

Configuration: The alignment/arrangement of functions/structures.

Task 1: Describe the alignment of the processes before and after integration and explain the differences in the integration architecture.

Synergy: The combined effect of the integrated whole.

Task 2: Measure performance of the integrated architecture (after integration) and compare it with the sum of performance of the units (before integration).

Efficiency: Technical and allocative efficiency.

Task 3: Calculate the unit cost per performance units before and after the integration and describe the differences.

Effectiveness: The extent to which the objectives of integration are met.

Task 4: Determine the level of achievement of the stated objectives of the integration (as stated in the integration plan).

Impact: The extent to which the objectives of the health system are achieved.

Task 5: Determine the difference between the level of achievements of the objectives of the health system before and after the integration.

Tool 18: Major constructs for evaluation of integration

Indicators for	**Before integration**	**After integration**	**Change**
Level of integration			
Systems' performance			
Cost performance units			
Objectives of integration			
Goals of Health system			

Summary of the aims of the sections:

Section I: Establishes the need for integration

Section II: Identifies possible candidate functions for integration

Section III: Scans the health system environment for integration

Section IV: Ensures effective communication of evidence

Section V: Helps systematic management of integration

CHAPTER 8

Rationale, Policies and Models for HIV-NCD integration in developing countries

CHAPTER 8 OVERVIEW

Having explored the inter-relationships between HIV/AIDS and NCDs, and developed a model and tool for integration of responses to HIV/AIDS and NCDs, chapter 8 summarizes the basic rationale for integrated HIV-NCD response. It also illustrates the policy bases for integrated response to HIV/AIDS and NCDs in developing countries. Moreover, it reiterates HIV-NCD integration with existing practical experiences from different countries.

It is assumed that summarizing the rationale, policy bases and existing examples of HIV-NCD integration will fine-tune the evidence base towards policies and practical actions relevant to HIV-NCD integration. This 'digest' has also taken in to account the realities of what works in the ground from review of existing experiences in HIV-NCD integration. In this regard, it summarizes and synthesises evidence from three perspectives: Research perspective (justifications for integration), policy perspective (policies supporting integration) and practice perspective (existing experiences from integration).

By elucidating these perspectives, this chapter consolidates the overall evidence and lines of argument towards integrated response to HIV/AIDS and NCDs in the context of developing countries.

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Publication Declaration

Monash University

Declaration for Thesis Chapter 8

Declaration by candidate

In the case of Chapter 8, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Wrote the proposal, collected the data, analysed the data, wrote the manuscript, revised the manuscript	75%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Julian Elliott	Supervised & reviewed the study	
Geoffrey Setswe	Supervised & reviewed the study	
Brian Oldenburg *	Supervised & reviewed the study	

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work*.

Candidate's Signature	[redacted]	**June 30, 2014**
Main Supervisor's Signature	[redacted]	**June 30, 2014**

*Note: Where the responsible author is not the candidate's main supervisor, the main supervisor should consult with the responsible author to agree on the respective contributions of the authors.

Rationale, Policies and Models of HIV-NCD integration in Developing countries: *A Qualitative Synthesis*

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Abstract

Introduction: HIV/AIDS and NCDs are major public health problems in developing countries. An integrated approach of response to these problems is recommended. However, the evidence base for such approach is both limited and fragmented.

Objectives: To consolidate evidence related to the rationale, the policy basis and models of HIV-NCD integration in order to better inform decisions related to the integration of health system responses to HIV/AIDS and NCDs in the context of developing countries.

Methods: Analytical review of evidence related to the *rationale* for HIV-NCD integration, the policy basis for HIV-NCD integration, and models of HIV-NCD integration was conducted. As the evidence-base for HIV-NCD integration is very limited, *a purposive* and *targeted* search of the literature was used. Information was extracted using an abstraction tool. The extracted information was then aggregated and undergone qualitative synthesis under pre-defined themes.

Results: There is strong epidemiological, Clinical and Management related evidence base relevant to the rationale for the integration of health system responses to HIV/AIDS and NCDs in developing countries. Global declarations and strategies are in favour of integrated health system response to HIV/AIDS and NCDs. Types of models of HIV-NCD integration that were 'tested' in the context of developing countries vary by contexts, disease combinations, types of services, and number of disease conditions involved. Despite these variations, all the models for which outcomes are available indicated that the integrated approach was feasible, effective, efficient and acceptable.

*Conclusions***:** Consolidated evidence about the rationale, policy bases and existing models of HIV-NCD integration from developing countries strongly favors integrated response. However, this is limited in breadth and depth. Therefore, more evidence is needed to better inform decisions related to the practicalities of HIV-NCD integration.

Key words*: Integration, HIV/AIDS, NCDs, Developing countries*

INTRODUCTION

Communicable diseases are still the leading causes of morbidity and mortality in many low-and-middle income countries. Communicable diseases, maternal and child health problems, and injuries are still profoundly impacting on the health and economic development of those countries (1-3). Globally, an estimated 35.3 million people were living with HIV in 2012. Since the beginning of the epidemic, almost 70 million people have been infected with the HIV virus and about 35 million people have died of AIDS. Sub-Saharan Africa remains to be the most severely affected, with nearly 5% of adults living with HIV and accounting for 69% of the people living with HIV worldwide (4).

The current trend is, however, shifting towards Noncommunicable diseases. These diseases kill more than 36 million people each year. About four-fifth of these deaths occur in low and middle income countries. More than 25% of all NCD deaths occur before age of 60; and 90% of these premature NCD deaths occur in low and middle income countries. The four common NCDs (Cardiovascular diseases, Cancers, Diabetes, and chronic respiratory diseases) which share four common risk factors (unhealthy diet, insufficient physical activity, tobacco use, and harmful use of alcohol) account for around 80% of all NCD deaths (5). In Sub-Saharan Africa, where average age at death has risen by less than 10 years, Noncommunicable diseases account less than 50% of all health years lost (6).

Using indigenous resources and external funding support, a lot has been invested to curb the tides of the communicable disease epidemics, like HIV/AIDS, Malaria and Tuberculosis, in many low-and-middle income countries. However, major challenges still remain for the fight against these culprits (7). While the agenda of communicable diseases is still unfinished, low and middle income countries need to prioritize the fight against Noncommunicable diseases.

Along with the emergence of Noncommunicable Diseases (NCDs) as a major public health challenge in low-and-middle income countries, there is a consistent conversation about *integrated response,* a strategy through which key actors and their actions are well synchronized to address health needs (1). Inferring from the chronic nature of both HIV/AIDS and NCDs, there is a tendency to build bridges between HIV/AIDS and NCDs programs (8). Similarly, motivated by the anticipated efficiency in the use of limited resources and potential synergy of programs, there is an intention to move towards integrated response to HIV/AIDS and NCDs (9).

However, the evidence-base to support the argumentation is very limited and fragmented.

Though most of HIV/AIDS related evidence is from actual implementation of interventions, the majority of the NCD-related evidence focuses on analysis and presentation of the magnitude of the specific NCDs and their risk factors, mostly from developed countries (10, 11). Other components of the evidence are about the factors that are associated with high or low prevalence of NCDs and their risk factors. The overall volume of evidence on NCDs is low and most of it is about characterizing the problems.

A recent study about evidence for NCDs indicated that the overwhelming body of evidence for NCDs is from developed countries. Evidence about NCDs in low-and-middle income countries is very limited (12). As a result, experts recommend that NCD response have to learn from the HIV/AIDS response. On the other hand, efforts attempting to put in to practice the existing NCD policies and strategies in to action are often challenged by resource constraints (13). One possible solution to this challenge is the integration of NCD services with other programs, such as HIV/AIDS (14).

From health services point of view, there are a few disease and service specific attempts to integrate NCD services in to HIV/AIDS programs in low-and-middle income countries. These efforts used different models in different settings for different combinations of disease entities. With these premises, this study is designed to consolidate evidence related to the rationale, the policy basis and models of HIV-NCD integration in order to better inform decisions related to the integration of health system responses to HIV/AIDS and NCDs in the context of developing countries. The envisaged study answers three essential questions:

- What are the fundamental reasons behind considering HIV-NCD integration in developing countries?
- How much emphasis is given by existing global & national policies to HIV-NCD integration?
- What models of HIV-NCD integration have so far been considered in the context of developing countries?

METHODS

We conducted an *interpretive qualitative synthesis* of evidence related to the *rationale* for HIV-NCD integration, the policy basis for HIV-NCD integration, and models of HIV-NCD integration at global level. In this review, we limited NCDs in to the four common NCDs - Cardiovascular diseases, Cancers, Diabetes, and chronic respiratory diseases. As the evidence-base for HIV-NCD integration is very limited, we conducted *a purposive* and *targeted* search of the literature using search terms relevant to HIV/AIDS, NCDs (including the four specific NCDs) and integration. Information sources explored include electronic databases (Embase and Medline), general search engine (Google) and websites of different global organizations including WHO, UNAIDS, and the NCD alliance. We also explored the most recent national HIV/AIDS and NCD strategic plans of four purposively selected countries for contents relevant to integration. In all cases, we limited the inclusion of references to those published after 2006.

Using an abstraction tool, information was extracted from the selected sources. The extracted information was then aggregated and undergone qualitative synthesis under pre-defined themes. Evidence related to rationale for HIV-NCD integration was categorized based on the basic foundations of argumentation. Evidence relevant to policy bases for HIV-NCD integration was categorized and summarized based on the major anchors of the HIV/AIDS and NCD response: global HIV/AIDS and NCD declarations, strategies and action plans. Evidence addressing models of HIV-NCD service integration in developing countries was categorized according to the types of models of integration considered. Information in each category was presented using narrative summaries. Finally, evidence from the three dimensions was consolidated using *interpretive* synthesis.

RESULTS

The rationale for HIV-NCD integration

Critical scrutiny of the evidence about the rationale for the integration of Health system responses to HIV/AIDS and Noncommunicable diseases revealed five major reasons relevant to HIV-NCD integration. These are illustrated below.

Similarities in disease Characteristics

Chronicity is a key characteristic of both HIV/AIDS and the common NCDs. These disease entities have gradual development and slow progression. In the era of anti-retroviral treatment, HIV has turned out to be a chronic disease of infectious origin

(15, 16). Therefore, a chronic disease management model is applicable for the prevention and control of both HIV/AIDS and NCDs.

Epidemiological Convergence

Epidemiological evidence suggests that low-and-middle income countries bear the highest burden of both HIV/AIDS and NCDs (17, 18). This is as a result of high population size, increasing life expectancy and rapidly changing lifestyles that resulted in increase of NCD in countries which have an already high HIV prevalence. As a result, the main focus of global HIV and NCD prevention and control efforts are in low and middle income countries. Overlapping problems require coordinated responses. In this regard, HIV-NCD integration is an important policy issue.

Linkage between the diseases

The existing **l**inkages between HIV/AIDS and NCDs are strategically important (19). HIV and NCDs are connected both in terms of risk of development of disease, and severity of progression of disease: HIV increases the risk of developing NCDs, and NCDs aggravate the severity of HIV disease (20). Therefore, the development and implementation of intervention packages need to consider the linkages between HIV/AIDS and NCDs. Integrated response required well-aligned intervention packages. Therefore, connection between HIV and NCDs could be considered as an important driver of integrated response.

Level of co-occurrence

Due to the connection between HIV/AIDS and NCDs, co-occurrence of the diseases in an individual, comorbidity, is common. Evidence about levels of comorbidity is essential for planning and management of multi-morbid cases (21). Because of the effects of HIV disease itself, HIV treatment effects and increasing age, the HIV positive population is at a higher risk of NCDs than the general population (22). HIV patients having NCDs need comprehensive services that have continuity. This goal is achieved through integration. Health systems in low and middle income countries could also maximize efficiency by integrating HIV/AIDS and NCD services, especially for individuals with comorbidity.

Commonalities between responses

Health system responses to HIV/AIDS and NCDs share many similarities. Long-term treatment, regular (biomedical) monitoring, good adherence to treatment and associated lifestyle modifications are the essential elements of management of both

disease conditions. Multi-sectoral, whole-of government and whole of society efforts are key to the responses to both public health challenges (23, 24). The lessons and experiences gained from HIV programs could be used for NCD programs. Many of the health system *challenges* (organizing and delivering adequate prevention services; chronic treatment and care; addressing the social and environmental determinants of these health issues; and reaching people without access to services) are also common to both HIV and NCDs (25). In order to ensure that commonalities result in synergy rather than duplication, integration of response is needed.

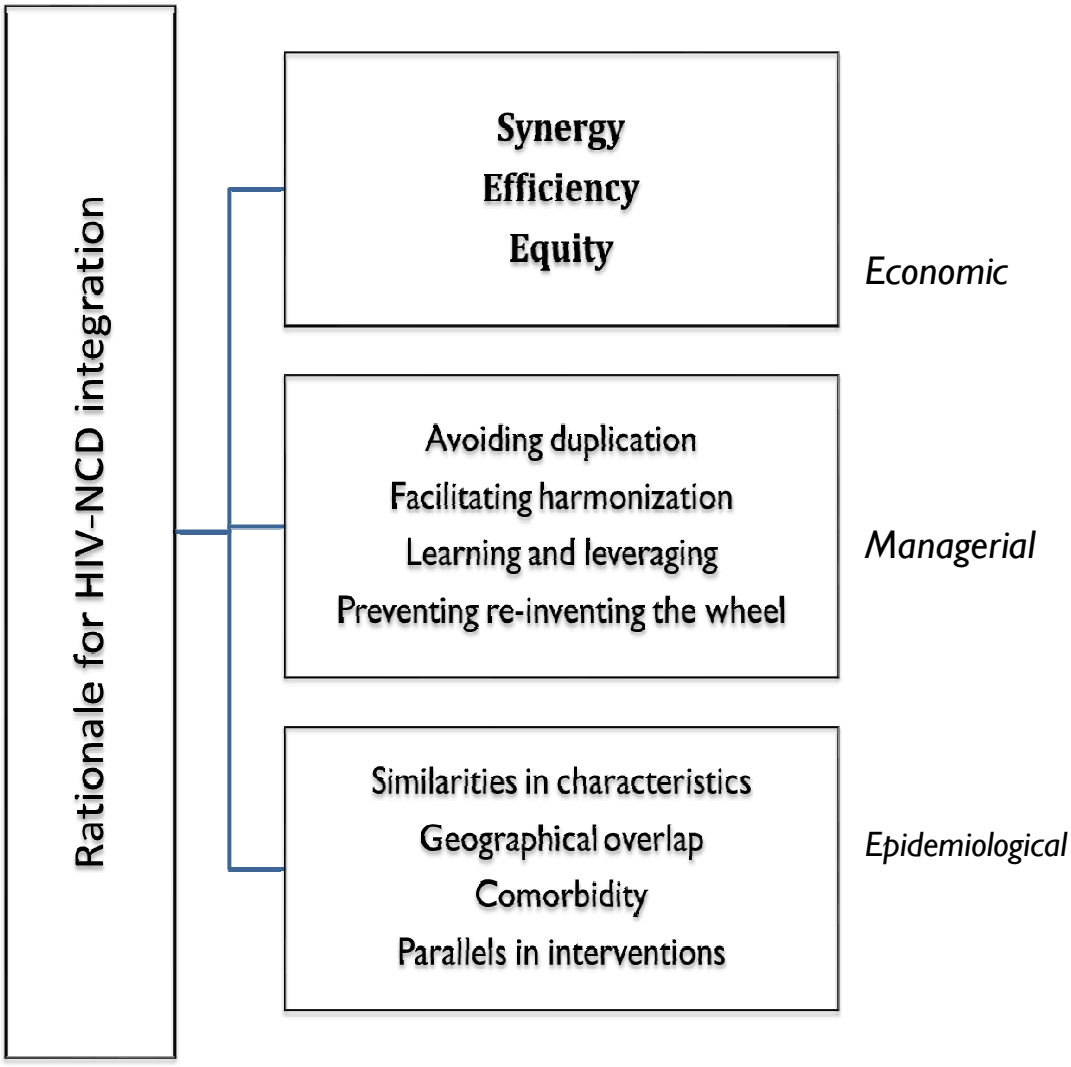

Fig 1. Three levels of rationale for HIV-NCD integration

The policy bases for HIV-NCD integration

Exploration of the policy bases for integration of the responses to HIV/AIDS and NCDs indicated that almost all existing global Health, HIV/AIDS and NCD policy statements and strategies favour the integration of responses to HIV/AIDS and NCDs. Findings from the main global HIV, NCD, and Health policies are summarized below.

HIV/AIDS Declaration 2011

This declaration emphasizes on the achievement of Millennium Development Goals (MDGs). It recognises the importance of integrating HIV/AIDS prevention, treatment, and care and support services with efforts that are important to achieve MDGs. The declaration also emphasizes on the integration of high impact HIV interventions in to the activities of different sectors. Integrating HIV response in to primary healthcare, including Maternal and Child Healthcare, is also highlighted. Besides, the integration of Tuberculosis, hepatitis, and food and nutrition support interventions in to HIV response in underscored (26). HIV-NCD integration is implied in throughout this declaration. The declaration is generally in favour of integrated response, both within HIV programs and with other programs.

Global Health Sector strategy on HIV/AIDS 2011-2015

One of the main themes in this strategy is about attaining better integration of HIV programs with other health programs (which include NCDs). Providing comprehensive and integrated services for key populations is among the core elements of the strategy. Linking programs and integrating HIV in to other health services is highlighted. The strategy also states that HIV programs have assisted in integrating chronic disease management in resource limited settings. As per the strategy, promoting the linkage between HIV and other priority health programs (including NCDs) is among the WHO contributions. Among the recommended country actions is strengthening the management of both HIV and Noncommunicable and chronic diseases. Maximizing synergy across other programs (including NCDs) is also among WHO's optimizing activities (27).

UNAIDS strategy 2011-2015

This strategy supports the strengthening of Health systems to deliver decentralized and integrated services. TB/HIV integration and leveraging services for the elimination of vertical transmission of HIV at antenatal, delivery and child health services is underlined. In line with the declaration, the strategy also articulates the

integration of HIV response with other health and development efforts; integration of HIV with primary healthcare; integration of HIV treatment programs with food and nutrition support, maternal and child health services, sexual and reproductive health services and nutritional support, drug dependence treatment services. Integration of prevention and treatment of HIV, TB, hepatitis (B and C), malaria, congenital syphilis is also among the strategic issues. To address women's right in the context of HIV, integration of HIV with sexual and reproductive health programs is among the strategic issues (28). This strategy doesn't specifically call for HIV-NCD integration. However, there is a report about how to leverage HIV experience for NCDs prepared by UNAIDS (29). Furthermore, in *a letter of agreement*, WHO and UNAIDS agreed to collaborate for joint activities in areas of advocacy, technical cooperation, and strategic information. Moreover, *Treatment 2015* considered the integration of HIV counselling with NCD screening (30).

UN Declaration on NCDs, 2011

Article 27 of United Nations general assembly political declaration on the prevention and control of NCDs unequivocally states "Note with concern the possible linkages between non-communicable diseases and some communicable diseases, such as HIV/AIDS, and call to integrate, as appropriate, responses for HIV/AIDS and non-communicable diseases and, in this regard, for attention to be given to people living with HIV/AIDS, especially in countries with a high prevalence of HIV/AIDS and in accordance with national priorities." Additional articles in the same declaration re-iterate this call by recommending learning from experiences in the field of HIV/AIDS and integration of Sexual and Reproductive Health (SRH) and Maternal and Child Health (MCH) programs with NCDs at primary healthcare level (31).

Global Action plan on NCDs 2013-2020

Based on this action plan, one of the priority actions for member states is "to review existing HIV/AIDS programs for opportunities to *integrate* in to them service delivery for the prevention and control of NCDs." The NCD action plan also reaffirms "*integrating* NCD programmes or palliative care with HIV care programmes would bring mutual benefits since both cater to long-term care and support as a part of the programme and also because Noncommunicable diseases can be a side-effect of long-term treatment of HIV infection and AIDS." According to this action plan, support roles related to *integration* are provisionally given to UNAIDS and UNDP (32).

National HIV/AIDS policy frameworks

Analysis of recent National HIV/AIDS strategy frameworks from the four purposively selected countries found various directions. HIV/AIDS strategy framework of **Ethiopia** emphasizes of the integration of HIV/AIDS interventions with other (Health) programs (33). The national HIV Strategic plan of **Sri Lanka**, which is developed more recently than the others, also underlines the integration of HIV/AIDS programs in to the activities of different sectors (34). In **Malaysia**, one of the focus of the HIV/AIDS strategy framework is "Strengthening priority health services through increased integration of HIV service delivery (35)." The National HIV/AIDS Strategy framework of **South Africa** go further and calls for integration of the screening of common NCDs and their risk factors with outreach HIV counselling and testing programs (36). HIV/AIDS strategic frameworks of all four countries give due consideration for the integration of different components of HIV/AIDS response.

National NCD policy frameworks

National NCD strategy frameworks on the other hand underscore integrated NCD response (i.e. integration of the responses to specific NCDs) and integration of NCD response in to the Health and other related systems. For instance, one of the objectives of the National NCD strategic plan of **Malaysia** is to integrate prevention and control of such diseases into policies across all government departments. This NCD strategic plan was meant to *integrate* the various frameworks, strategies and action plans addressing specific risk factors and particular diseases into a holistic and definitive approach to NCD prevention and control (37). Similarly, the National NCD strategic framework of **Sri Lanka** aims to integrate prevention and control of NCDs into policies across all government ministries and private sector organisations. It also facilitates the provision of integrated preventive, curative, rehabilitative and palliative services at each level of service delivery (38).

The NCD strategic framework of **Ethiopia** values NCD response as an integral part of primary health care and Health Extension Program. In this line it aims to establish a program for surveillance of chronic disease risk factors, as an integral part of the communicable disease surveillance and response system (39). Based on the principle of Integrated Chronic Disease Management Model, the NCD strategic framework of **South Africa** aims to integrate NCDs in to the re-engineering of primary Health care in that country. This framework explicitly states the integration of HIV testing and NCD screening (40).

In general, three forms of integration are addressed by the above mentioned policy frameworks. These are integration of HIV/AIDS and NCD responses into the health system, integration within HIV/AIDS or NCD response (intra-), and integration between HIV/AIDS and NCD responses (inter-). The degree of emphasis given for these forms of integration is indicated in the following table.

Table 1: Degree of policy support given to the three forms of integration

	Policy frameworks	**"In to" health system**	**"Within" HIV or NCD**	**"Between" HIV and NCD**
Global	Health	+++	+	+
	HIV/AIDS	++	+++	+
	NCD	+++	+++	+++
National	Health	+++	+	+
	HIV/AIDS	++	+++	+
	NCD	+++	++	+/++

Existing Models of HIV-NCD integration

Evidence about models of HIV-NCD integration is very limited. There are no controlled or randomized evaluation studies. Our review identified a few feasibility studies from low-and-middle income countries. All these studies were are limited to specific settings and contexts within those countries. The findings from these studies and projects are summarized below.

Integrating cervical cancer screening in to HIV services

There are many small scale studies reporting on the integration of Cervical Cancer screening in to HIV programs in different countries including **Cote D'ivoire, Kenya, Mozambique, Zambia, Botswana, Nigeria, Ethiopia, Tanzania** and **Guyana** (41-47). All these initiatives involve the use of Visual inspection with Acetic acid (VIA) as a screening method. The studies were conducted between 2007 and 2012. In all the studies, integration of cervical cancer screening in to HIV services was reported to be feasible, effective, efficient and acceptable. The challenges faced were related to capacity and loss to follow up.

Chronic Disease Clinic

This model used full integration of HIV and NCD services in to a chronic disease clinic in **Cambodia** (48). HIV, Hypertension and diabetes care and treatment services were integrated. The newly established chronic disease clinics were at provincial hospitals and were supported by external funding but gradually taken by Ministry of Health. The service delivery in the clinics had strong emphasis on outpatient consultations. After implementation over three years, it was proved that integration of HIV and NCDs is feasible, effective, efficient and acceptable in that context.

Adapting HIV strategies, systems and tools for Diabetes

This model was about leveraging HIV programs to support diabetes services. It was implemented in **Ethiopia** and **Swaziland** (49). A project was implemented to evaluate the feasibility and effectiveness of adapting HIV program-related tools and systems for patients with Diabetes. The project was based on gaps in diabetes response in settings with better HIV response systems. The intervention package included *strategies, systems and tools* adapted from HIV clinic and applied to diabetes services to outpatient department. The outcomes have illustrated that "countries which have successfully scaled up HIV services have already learned profound lessons about the delivery of chronic care. Using these locally owned and contextually appropriate resources may be an efficient and effective way to 'jumpstart' NCD programs and to strengthen health systems to support longitudinal services for all."

Rapid Multi-disease testing screening

This model involved leveraging rapid community-based HIV testing campaigns for NCDs in rural **Uganda**. The study tested the feasibility and diagnostic yield of integrating NCD and communicable diseases in to rapid HIV testing and referral campaign. The multi-disease campaign included provision of diagnostic, preventive, therapeutic and referral services for HIV, Malaria, Tuberculosis, Hypertension and Diabetes at a point-of-care. The campaign demonstrated the feasibility of integrating hypertension, diabetes and communicable diseases into HIV/AIDS initiatives (9). In another similar integrated screening for HIV, TB, Diabetes and Hypertension in a mobile unit in **South Africa**, a high yield but low level of linkage to care was reported (50).

Integrating cardiovascular disease screening in to HIV services

This model is a pilot project in **Kenya**. The pilot program offers Cardiovascular disease (CVD) screening for people attending healthcare facilities for HIV prevention

and treatment (51). HIV Service providers were trained to screen CVD risk factors using adapted behaviour materials and job aids. Counselling and referral linkage are offered for clients in need. Ministry of Health and National AIDS and STI control program were engaged. It is reported that the recent strategic plan now calls for integration of HIV and CVD screening because of the inspiration of this project.

Integrated Chronic Disease Management Model

In response to the quadruple burden of health problems, **South African** Department of Health (DOH) introduced a Health System Framework to strengthen the response to NCDs: the Integrated Chronic Disease Management Model (ICDM). The model is for chronic diseases, both NCDs and communicable disease, notability HIV and Tuberculosis (52, 53). The model is based on re-engineering of the primary healthcare process. Results are yet to be reported.

Integrating NCD risk factor and HIV/AIDS interventions

The integration of substance abuse treatment - Smoking cessation and alcohol abuse prevention – is studied in the developed world. A study conducted in **Botswana** recommended the integration of alcohol abuse and HIV prevention efforts (54). The importance of smoking cessation interventions in HIV care are underscored by a study from **Nepal** (55). Evidence on the integration of physical activity and Nutritional interventions among PLHIV in developing countries is limited.

These models are centred on four focal points: Problem, People, Process, Patient, and patient (Fig 2). These points are not mutually exclusive.

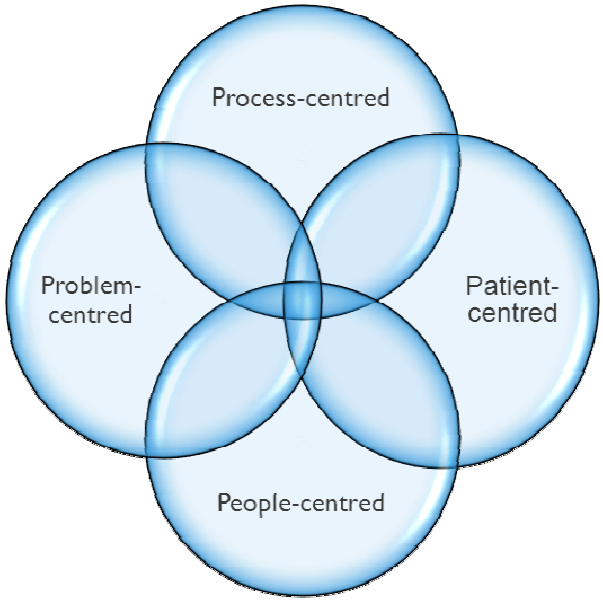

Fig 2. Categories of HIV-NCD service integration models.

DISCUSSION

Summary of the evidence

There is strong epidemiological, Clinical and Management related evidence base about the rationale for the integration of health system responses to HIV/AIDS and NCDs in developing countries. However, the relevance of this evidence base varies based on the 'balance' between the burden of HIV/AIDS and NCDs in different countries (56). The evidence strongly supports integration for high HIV and high NCD burden contexts where the 'doses' of the responses are proportional.

Global HIV/AIDS declarations and strategies are in favour of integrated health system response in general though these have not been specifically articulated in terms of HIV-NCD integration. Additional position statements, however, explicitly state HIV-NCD integration as a preferred approach for developing countries. On the other hand, the NCD declaration and action plan unequivocally adopted integrated approach, including that with HIV, as a primarily preferred strategy. The priorities of National strategies seem to vary based on epidemiological profiles. The actual implementation of these policies and strategies should also focus on integrated approaches.

Models are limited to Health Services integration, mostly for HIV and one NCD. The types of models of HIV-NCD integration that were 'tested' in the context of developing country vary by country contexts, disease combinations, types of services, and number of disease conditions involved. Despite these variations, all the models for which outcomes are available indicated that the integrated approach was feasible, effective, efficient and acceptable.

Implications of the evidence

The overall evidence suggests that there exists a strong rationale and a well-founded policy basis for integration of the responses to HIV/AIDS and NCDs in developing countries. The presence of various models of integration reflects the differences in the health system environment and disease epidemiology among different countries. Moreover, integration of different services at a single site can be expensive (57). Therefore, context specific models which promote stronger interactions among HIV/AIDS and NCD actors and sectors are needed.

Limitations of the study

There are three major limitations associated with this evidence synthesis study. First, there is limited evidence about HIV-NCD integration both in terms of scope and generalizability of the evidence. Second, the existing evidence is limited to small scale feasibility studies in largely different contexts. There were no large scales or randomized and/or controlled evaluations. Third, for some of the models, data on effectiveness outcomes are yet to be available in the near future.

CONCLUSIONS

Consolidated evidence is essential for informed decision making. For most of policy and practice related decisions, comprehensive evidence addressing rationale, policy and models of action is very useful. This synthesis has consolidated the evidence base about the rationale, policy bases and existing models of HIV-NCD integration in the context of developing countries. This will be useful inform the implementation of policies related to HIV-NCD integration. However, the overall evidence in this arena is limited and more context specific evidence is needed to better inform decisions related to HIV-NCD integration.

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Chapter 9

Discussion

CHAPTER OVERVIEW

Having analysed the interrelationships between HIV/AIDS and NCDs and developed a model for the integration of health system responses to HIV/AIDS and NCDs, this chapter discusses the research findings and their implications for blah, blah, blah….. This chapter has four sections. The first section summarizes how the research was undertaken and the major findings. The second section addresses the key outputs of the PhD research. This is followed by a discussion of the major limitations associated with the PhD research. The final section discusses implications of the finding for future policy, practice and research.

Introduction

HIV/AIDS and Noncommunicable diseases are currently the major public health threats of the low-and middle income countries, especially Sub-Saharan Africa. HIV/AIDS affects more than 34 million people worldwide, causing more than 1 million deaths ever year (1). Accordingly, HIV/AIDS remained to be the priority area of healthcare interventions during the past three decades (2). As a result of their rapid emergence, NCDs are now becoming among the priorities of the health systems of many low – and middle income countries. NCDs cause about 36 million deaths every year globally. Of these deaths, 80% occur in low- and middle income countries (3). With the unfolding epidemics of NCDs as a major threat to economic development, the UN General Assembly adopted a landmark political declaration on the prevention and control of NCDs. This declaration has important implications for policy and practices of the prevention and control of NCDs (4). This declaration acknowledges the existence important inter-relationships between HIV/AIDS and NCDs and proposes the integration of responses to HIV/AIDS and NCDs as appropriate to country contexts. However, the evidence base to inform the implementation of this proposal is limited. This study was therefore conducted to generate evidence that could contribute to filling this evidence gap.

With the aforementioned rationale, this research focused on two overarching constructs relevant to HIV/AIDS and NCDs: inter-relationships and integration. A total of seven constructs (four under inter-relationships and three under integration) are addressed in this research. The overall research, considered to be relevant to Health Policy and health systems in low and middle income countries, applied

multiple and mixed methods with emerging research designs used at different stages. It followed the constructivist paradigm of evidence synthesis and qualitative research. The overall research yielded important outputs from the various sub-studies. These research outputs and their implications for policy, practice and research are discussed in this chapter. The important limitations associated with the overall research are also outlined to facilitate better understanding and interpretation of the results.

Key outputs

This PhD research yielded important evidence about the inter-relationships between HIV/AIDS and NCDs at various levels; a public health framework that explains disease-level linkages between HIV/AIDS and NCDs; and an action model that could guide possible integration of the responses to HIV/AIDS and NCDs in the context of developing countries. These research outputs are summarized under the following sub-sections.

Evidence about inter-relationships and integration

This PhD research has generated relevant evidence about the *Epidemiological overlap* (convergence) of HIV/AIDS and NCDs epidemics in developing countries using correlational and cluster analysis of the prevalence of HIV and Diabetes. It was found that, with the rapidly emerging epidemic of NCDs and stabilizing epidemic of HIV/AIDS in low- and middle income countries, there is a moderately negative correlation between the prevalence trends of HIV/AIDS and NCD epidemics in these countries. Cluster analysis of joint pattern of HIV and Diabetes prevalence has

yielded four clusters of countries. The four cluster of countries, based on their proximity in the joint patterns of HIV/AIDS and Diabetes prevalence, respectively, were Medium-Low, Very Low –Medium, Low-High, and High-Low. This analysis has shown a great variability among clusters of countries in their joint patterns of HIV/AIDS and NCDs (5).

Systematic reviews of the prevalence and incidence of NCD comorbidity among PLHIV provided better insights in to the levels of *co-occurrence* of HIV/AIDS and the common NCDs at individual level. Comorbidity studies from developing countries were mostly prevalence studies. Analysis of the prevalence of NCD comorbidities among PLHIV has found out that, in the era of antiretroviral treatment, cardiovascular abnormalities and pre-cancerous lesions are more prevalent among PLHIV than the general population. However, the existing evidence doesn't favour of higher prevalence of Diabetes and Metabolic syndrome among PLHIV as compared to the general population. Besides, there exists a difference between the forms of cardiovascular problems among PLHIV and what are commonly considered as cardiovascular diseases in the NCD epidemiology. The cardiovascular abnormalities among PLHIV are often related to myopathy and neuropathy whereas the traditional cardiovascular diseases are often vascular origin. As there is very limited research about the prevalence of chronic respiratory diseases among PLHIV, our analysis was not able to explore this area (6, 7).

By using qualitative content analysis and synthesis techniques, this PhD research has also explored the *similarities and differences* between Global and National level health

system responses to HIV/AIDS and NCDs. Analysis on five major thematic areas of health system response (i.e. policy response, programmatic response, institutional arrangement, coordination mechanism and strategic information) has indicated that the responses to HIV/AIDS and NCDs are more similar in approach and models than in technical content and implementation instruments. Analysis of strategic level HIV/AIDS and NCD responses from four case countries (South Africa, Malaysia, Sri Lanka and Ethiopia) has revealed the existence differences in the level of similarities and differences between national HIV/AIDS and NCD responses across countries. This seems to be related to the epidemiological profile of HIV/AIDS and NCDs in these countries (8, 9). This evidence gives a clue that the level of similarities may be modulated by the level of overlap between the two epidemics.

Regarding evidence relevant to HIV-NCD integration, an interpretive synthesis of the *rationale, policies and models* of HIV-NCD integration in developing countries was conducted. General Health policies, HIV/AIDS policies and NCD policies vary in the ways they address HIV-NCD integration. While general health policies focus on integrating HIV and NCD responses in to the overall health system, HIV policies give more emphasis on integration within HIV programs. NCD policies, on the other hand, give more weight to integration among NCD programs (among disease-specific programs) and integrating NCDs response in to the health system. HIV-NCD integration received more attention in the policies of high HIV prevalence countries which are also facing a rapidly increasing burden of NCDs.

It was found that HIV-NCD integration is underpinned by three major ultimate drivers: Synergy, Efficiency, and Equity. These ultimate drivers emanated from intermediate drivers: the need to avoid duplication and re-invention of the wheel; and to promote leverage and learning from program experiences. The intermediate drivers are grounded on immediate drivers: similarities between disease characteristics, convergence of the epidemics, linkages between diseases, magnitude of co-occurrence and the parallels in responses.

Key examples of HIV-NCD integration in the context of developing countries identified in this research include integrating cervical cancer screening in to HIV services in many African countries; Chronic Disease Clinic in Cambodia; adapting HIV strategies, systems and tools for Diabetes in Ethiopia and Swaziland; rapid Multi-disease testing screening in Uganda; integration of cardiovascular disease screening in to HIV services in Kenya; and Integrated Chronic Disease Management Model in South Africa. Further analysis has shown that these models are centred on four focal points: Problem, People, Process, Patient, and patient

A Public Health Framework for Linkage

The thematic research synthesis in this PhD research was conducted to explore the linkages (disease level inter-relationships) between HIV/AIDS and the common NCDs and to develop a generic public health framework that best explains these linkages. The public health framework developed in this research depicts two types of linkages (direct and indirect linkages), two forms of linkages (risk related and severity related linkages) and two directions of linkages (unidirectional and bi-

directional linkages) between HIV/AIDS and the common NCDs. Five major pathways of linkages along with five connecting nodes were also identified and explained. All elements of the linkages are configured in to the public health framework that could serve as a useful tool for public health policy, practice and research that address disease-level inter-relationships between HIV/AIDS and NCDs (10).

An action model for integration

Another output of this PhD research was an *action model* for the integration of Health system responses to HIV/AIDS and NCDs in developing countries. Inductive, progressive, and iterative model development techniques were used in this phase of the research. It is worth noting that the main aim was to develop an action model, a systematic approach for the integration process rather than a model of integration, (i.e. for the integrated architecture). Accordingly, utilizing the evidence from analysis of strategic inter-relationships between HIV/AIDS and NCDs along with additional literature review about integration of health system responses, an action model with five underlying principles/assumptions, four action fields, five key processes and a nine-step action cycle was developed (11). The model has undergone conceptual validation using further literature review that aimed to refine the key processes and steps in the action cycle. Peer-review of the model has also yielded relevant inputs for further refinement of this model.

A guiding tool for integration

By adopting the principles of "Analyse – Synthesize –Act" continuum, the action model developed to guide the integration of health system responses to HIV/AIDS and NCDs was operationalized in to a *Guiding tool*. The tool presents a unique combination of the translation of evidence of integration in a form of a guiding tool along with essential new elements. The contents of this tool were conceptually validated and were enriched using inputs from expert consultations. The guiding tool has five major sections. Drawn from the evidence of inter-relationships, the first section guides the analysis of the inter-relationships between the public health problems, HIV/AIDS and NCDs. The second section, drawn from analysis of parallels, helps examine similarities between health system responses to HIV/AIDS and NCDs. The third section, drawn from strategic management, is useful for scanning the health system's environment for possible integration of responses. The fourth section, adapted from knowledge management principles, is about the actions that have to be done to repackage and communicate evidence relevant for integration to decision-makers. The final section is about the management of integration (i.e. planning, implementation, and evaluation of integration). Under each section, constructs, definitions and tasks are identified and explained to facilitate better understanding and simpler adaptation by possible users.

Table 2: A summary of major outputs of the PhD research

Output	**Brief Description**
Evidence	Information about Epidemiological overlap, levels of co-occurrence, parallels in responses, HIV-NCD integration.
Framework	A Public Health Framework that illustrates the various types, forms, and pathways of linkages between HIV and NCDs.
Action Model	A model that presents a systematic approach for the integration of health system responses to HIV/AIDS and NCDs in the context of developing countries.
A Guiding Tool	A conceptually validated tool that operationalizes the action model in to tasks and activities.

Limitations

There are some limitations associated with the overall research and individual studies as well. The main limitations associated with this PhD research are highlighted below.

1. Analysis of health system responses in this research mainly focuses on Macro-*level* (Global and National) of Health Systems. Thus, the findings are directly relevant at this level. Even though evidence is drawn from lower levels of health system, and could potentially inform on some aspects, the findings may not fully reflect the detailed realities at meso- and micro levels of health systems.
2. Regarding its breadth, this research gave more emphasis on analysis of inter-relationships and parallels between the responses to HIV/AIDS and NCDs

rather than on the detailed epidemiological characteristics of the problems (HIV/AIDS and NCDs) themselves. Analysis of the inter-relationships was also seen with the lens of integration of responses. Thus, descriptions of the magnitude, distribution and determinates of HIV and NCD across geographic regions, demographic characteristics of populations and time were used for the purpose of setting the context only.

3. In its analysis of inter-relationships between HIV/AIDS and NCDs, this PhD research has aimed at four areas of inter-relationships (Convergence, co-occurrence, linkage and parallels) between HIV/AIDS and NCDs; and three aspects of integration of responses (Action model, a guiding tool, and evidence consolidation) to HIV/AIDS and NCDs. In the analysis of responses, the focus was limited to five response themes of health system responses (Policy response, programmatic response, institutional mechanism, coordination mechanism and strategic information).
4. Throughout the research, analysis efforts were aimed at comparing different attributes between HIV/AIDS and NCDs. *Comparisons* among NCDs (diseases, risk factors, interventions) and different HIV programs (prevention, care and treatment) were not the primary focuses of this research. In the analysis of national responses, the main emphasis has been on the comparison of HIV and NCD responses in the selected countries. Comparison of HIV and NCDs responses between countries was not the main focus in this research. Besides, there was no intention to evaluate the effectiveness of HIV/AIDS and NCD responses in the selected countries.

5. Due to feasibility issues, only conceptual *validation* of the proposed guiding tool for integration was considered. The guiding tool for integration underwent conceptual validation and enrichment through literature review and expert review. Empirical validation of the tool was not possible in the life cycle of this research.
6. There were some problems of completeness in the data and information used in the assessment of national responses to HIV/AIDS and NCDs. In this research, information available in the public domain along with a few key informant interviews was used to assess health system responses to HIV and NCDs. A more detail analysis of each case country, using field observations and interviews with a wider range of stakeholders would result in a more detailed understanding of these findings.

Besides the aforementioned limitations, there are also some limitations associated with the specific studies reported in this research. Table 3 summarizes these limitations.

Table 3: Limitations associated with specific studies of this PhD research

SN	Study	Summary of the limitations
1	Epidemiological patterns of HIV/AIDS and NCDs	Risk of ecological bias, Diabetes used as a prototype NCD may not necessarily reflect the total NCD burden
2	Epidemiological Linkage between HIV/AIDS and NCDs	A generic public health framework of linkages considers NCD as an entity. Linkage between HIV and individual NCDs may have some variations from this framework
3	Epidemiology of comorbidities between HIV/AIDS and NCDs	Due to the absence of well-designed cohort studies, the study of the incidence of NCD comorbidities in HIV utilized studies from developed countries. Prevalence studies had low sample sizes.
4	Parallels/similarities and differences between responses to HIV/AIDS and NCDs	The analysis of parallels and differences focused on macro (strategic) level of health systems. Meso (managerial) and micro (operational) levels need further evidence.
5	Developing action model for integration of responses	The action model provides a systematic approach of integration. It is not a model of integration by itself. It presents the process of integration rather than integration architecture.
6	Preparation of a guiding tool for integration	This is a guiding tool. It serves as a guide only. The tasks and activities need to be adapted to specific contexts.
7	Rationale, policies and models of HIV-NCD integration	Evidence is limited to small scale feasibility studies in largely different contexts. There were no large scales or randomized and/or controlled evaluations

Implications

Implications for policy

The findings of the overall PhD research have three important implications for *policy.* Firstly, future policy processes (policy formulation, implementation and evaluation) need to take in to account the *inter-relationships* between HIV/AIDS and NCDs as these forms the basis for effective policies. Secondly, sector-wide policies in the low- and middle income countries need to give a *balanced* attention to HIV/AIDS and NCDs. According the appropriate level of priority to HIV/AIDS and NCDs will ensure equity in the allocation of resources and provision of services. Thirdly, there exists a clear need for *integrated* HIV/AIDS and NCD policies. Sector-wide, disease-specific, NCD-specific, and risk factor specific policies at different levels have to be well aligned. In addition to these policy implications of the overall research, specific studies included in this thesis have also their own implications for policy.

The moderately negative correlation between the prevalence trends of HIV and Diabetes in developing countries suggests rapidly increasing burden of NCDs and slowly stabilizing burden of HIV/AIDS. In this regard, greater policy attention is needed to curb the tide of the NCD epidemic and sufficient policy attention is needed to sustain and maintain the rate of decline of HIV/AIDS. The output of the cluster analysis, clusters of countries, implies that countries in the same cluster has relatively similar joint epidemiological patterns of HIV/AIDS and NCDs and can share important policy implementation lessons.

The public health framework for the linkage between HIV/AIDS and NCDs demonstrates the existence of complex but epidemiologically important linkages between HIV/AIDS and NCDs which are expressed in terms of comorbidity and multimorbidity. This evidence about linkages infers that interventions for HIV could have effects on NCDs and vice versa. Inter-linked problems require inter-linked solutions. Therefore, the design, implementation and evaluation of NCD policies need to take in to account the spill over effects of these policies on HIV and vice versa. Consideration of coherence among HIV and NCD policies is vital in this context. This is mainly important for coordination of responses to HIV and NCDs.

The existence of strategic parallels between health system responses to HIV/AIDS and NCDs implies that there are important policy formulation and implementation lessons that the NCD response in low and middle income countries could learn from the 30 years of experience of HIV/AIDS response. As both HIV/AIDS and NCD interventions share the same service delivery platform of the general health system, evidence of the parallels can be strategically used to avoid possible duplication of efforts. Instead, health systems can re-align these parallels in a synergistic manner. On the other hand, the presence of some key differences between the responses to HIV/AIDS and NCDs implies for the need to maintain the integrity of both HIV/AIDS and NCD responses. Hence, integration of the responses to HIV/AIDS and NCDs needs to consider integrity of the responses; and avoid complete/full integration or merging of the interventions as these may have detrimental effects to the effectiveness of both HIV/AIDS and NCD policies.

Implications for practice

Evidence about inter-relationships between HIV/AIDS and NCDs implies essential areas of learning, and leveraging of responses to avoid the re-invention of the wheel, fragmentation of response and duplication of efforts in the delivery of HIV/AIDS and NCD services. There are many lessons the NCD services can learn from the rich experience of HIV services in low and middle income countries. As the degree of similarities between the responses to HIV/AIDS and NCDs is strong, integration of interventions and services needs to be an area of focus for future HIV/AIDS and NCD programs. Integrated strategy will maximize synergy and improve efficiency of the response for both HIV/AIDS and NCDs programs.

Two major areas of concern are the prevention of NCDs among people living with HIV and the management of HIV positive patients having NCD comorbidity. Due to the effects of the HIV itself, the side effects of anti-retroviral treatment, and increasing age of PLHIV, their risk of developing NCDs has increased dramatically. Therefore, integrating NCD screening in to HIV/AIDS treatment and care services could contribute to the aversion of the increasing burden of NCDs among PLHIV through early diagnosis and treatment. Integration of screening for cancers, cardiovascular conditions and diabetes for PLHIV would be some of the examples.

As to the management of HIV positive people with NCD comorbidity, integration of HIV/AIDS and NCD services would provide patients with a seamless service delivery system to navigate through. Given, the limited human resources for health in low and middle income countries, integration enables efficient utilization of multi-skilled health workers who can delivery both HIV and NCD services at a

single point of service delivery for HIV+ patients with NCD comorbidity. On the contrary, the absence of these integrated services would mean a 'disease-focused' approach rather than 'people-focused' one, where lives saved from HIV may be lost due to NCDs.

An implication of the similarities between HIV/AIDS and NCD responses to practice is that the strategies and tools developed for HIV/AIDS could be adapted to the prevention and control of NCDs. Such strategies and tools include effective behavioural change communication (BCC) strategies and tools, inter-linked patient monitoring strategies and tools, and the global and national HIV/AIDS epidemic monitoring tools and frameworks. Adapting these strategies and tools in to the NCD context has dual advantages. First, these strategies and tools have been applied in low and middle income settings and are proven to be effective. Second, adaptation of the tools and the strategies saves cost as compared to the development of new strategies and tools. Application of the tools and strategies will also be simpler for health workers who have already been using the same tools and strategies for decades. This is one of the ways that the previous investment on HIV/AIDS can be leveraged to address the rapidly increasing burden of NCDs in those settings.

Implications for research

This research has investigated the strategic inter-relationships between HIV/AIDS and NCD responses at multiple levels and galvanized the evidence base for the integration of health system responses to HIV/AIDS and NCDs. The presence of strategic inter-relationships between HIV/AIDS and NCDs and existence for

indicative evidence for integration implies the importance of expanding the breadth and depth of future research in this area.

The analysis of convergence involved the prevalence of HIV/AIDS and Diabetes. Diabetes was considered as a prototype NCDs. Given the limited prevalence data on the other NCDs, and the fact that the common NCDs share common risk factors; the analysis of convergence sounds well. However, whether the evidence of convergence between HIV/AIDS and Diabetes also apply for HIV/AIDS and other NCDs needs further research. The level of convergence will also change as the magnitude of HIV/AIDS and NCDs changes across time. Thus, future updating of the evidence about the convergence is also needed.

The public health framework for the linkages between HIV/AIDS and the common NCDs could be considered as a useful tool to facilitate the conceptualization and design of research and evaluation studies related to HIV/AIDS and NCDs. The framework presents possible linkages from synthesis of research-based evidence. Though the framework is useful as an initial guide for research, the strength and the relative practical importance of these linkages needs further research.

In the study of NCD comorbidities among HIV positive people, incidence studies from the developing countries were limited despite 90% of HIV positive people are living in these countries. Most of the prevalence studies had small sample size and were conducted in health facility settings. Evidence from incidence studies on comorbidities of NCDs in HIV patients in low and middle income countries, where

the HIV burden is high, is needed. Moreover, large scale, more representative or multi-country, prevalence studies of NCD comorbidities in HIV infection in Sub-Saharan Africa are also needed. The extent to which evidence about incidence of NCD comorbidities in HIV infection from the developed world could be useful in the context of developing countries also needs further research.

As the analysis of parallels between the responses to HIV/AIDS and NCDs in this research has focused national and global levels, evidence about the parallels and differences at technical level of health systems is needed in order to inform possible service integration or coordination. Besides, this research included only four countries. Inclusion of more countries in to a similar analysis could broaden and deepen the evidence base about the parallels between responses to HIV/AIDS and NCDs.

In the consolidation of evidence about the integration of the responses to HIV/AIDS and NCDs in developing countries, it was found that the available studies and projects were small scale feasibility studies. The findings from these studies indicated that HIV-NCD integration is feasible, acceptable and effective. However, larger randomized and controlled trials/evaluations are needed for the scale up of HIV-NCD integration practices in developing countries.

The action model of integration and its guiding tool for integration developed in this research are at their early stage of development. These need further refinement

through empirical testing in health systems of low and middle income countries. Therefore, further research is needed to refine the contents and to evaluate the applicability of these tools in specific contexts of low- and middle income countries. The model and tools could also be potentially useful in guiding the integration of responses between other chronic diseases. Future research could also take in to account extend the model and the tool beyond HIV/AIDS and NCDs.

Conclusions

The strength of inter-relationships between HIV/AIDS and NCDs and the similarities between the responses to these conditions require integration of the responses as appropriate to specific local contexts. In addition to generating evidence relevant to HIV-NCD integration, this PhD research has yielded three important research outputs – a public Health Framework for linkage, an action model of integration, and a guiding tool for integration. Further research is needed to refine these research outputs and to test their applicability in specific country contexts.

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