HIV, Tuberculosis, and Non-Communicable Diseases:

What is known about the costs, effects, and cost-effectiveness of integrated care?

Supplemental Digital Content: Technical Appendix

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Introduction

The attached article describes an agenda to investigate the epidemiology, screening, treatment, quality of life, costs, and cost-effectiveness associated with the management of non-communicable diseases (NCDs) in people living with HIV (PLHIV) in low- and middle-income countries (LMICs). As data continue to emerge regarding specific NCDs among PLHIV, a close examination of the most prevalent NCDs among the general population in LMICs offers insight into the NCDs whose treatment is likely to exert the greatest impact when integrated into HIV care.

Methods

We examined data from the Global Burden of Disease Study 2010 (GBD 2010).[1] The dataset with "GBD 2010 Results by Cause 1990-2010" presents results sorted by cause of death, region, year, age, and sex.[2] For all adults (ages 15+) in Latin America, Sub-Saharan Africa, and Southeast Asia, we summed the total number of years of life lost (YLL) for each cause of death and reported the 10 NCD causes of death that resulted in the greatest total number of YLL (Table A1). Because the main attached article discusses HIV and tuberculosis (TB) in addition to NCDs, Table A1 also includes mortality due to HIV and TB. Other communicable diseases, such as malaria, are excluded.

To contextualize the burden of NCDs in LMICs, we derived the total population at risk in each region of interest by summing the populations of each country in 2010 based on data from the International Monetary Fund.[3] For Table A1, broad categories were used that include similar, more specific causes of death provided by the GBD 2010. Table A2 details the specific causes of death from the GBD 2010 that were combined for each broader category used in Table A1.

Table A3 was also generated from data provided by the GBD 2010. With its data visualization tools, we adapted a heat map of top risk factors for each region of interest.[4,5] Risk factors were ranked by YLL (i.e., a ranking of 10 denotes a risk factor that results in the lowest YLL) and colored on a gradient scale to highlight these rankings: 10 (green) to 5 (yellow) to 1 (red).

Table A4 displays the relationship between selected risk factors and the most common causes of death from Tables A1, A2, and A3, and outlines screening and treatment options. An "X" denotes when a risk factor is associated with a specific cause of death.[4] Hepatitis B, hepatitis C, and human papillomavirus (HPV) have also been added as risk factors in Table A4 because screening and treatment options are available. A color scale is used to delineate the comparative costs of implementing each screening and treatment strategy: green (lowest cost), yellow (moderate cost), and red (highest cost). Costs for screening and treatment were obtained through literature searches not restricted to HIV-infected populations. These references are cited with the screening and treatment interventions in Table A4. Additionally, not all interventions for risk factors or causes of death are medical interventions. Blue cells indicate opportunities to decrease YLL that are best addressed by public health interventions rather than medical interventions.

Results

Cardiovascular disease (CVD) is the leading cause of death among NCDs (Table A1). CVD accounts for 9% of YLL in Sub-Saharan Africa, 26% in Southeast Asia, and 22% in Latin America. Cancer and other chronic illnesses such as diabetes and chronic kidney disease are also major causes of death in LMICs. Mortality due to violence and the lack of home and motor vehicle safety are also top causes of mortality in resource-limited settings and should be included in discussions regarding high-yield targets for risk reduction. In 2005, HIV represented 18% of all YLL in LMICs: 29% in Sub-Saharan Africa, 4% in Southeast Asia, and 4% in Latin

America. By 2010, the percentage of YLL due to HIV had fallen to 14% for LMICs (regional breakdown in Table A1), demonstrating the decreasing burden of HIV and relative increasing burden of NCDs in LMICs over the past decade.

Table A3 displays risk factors ranked by YLL. Dietary risks, alcohol use, and physiological factors such as high blood pressure, high fasting plasma glucose, and high body-mass index are among the highest factors for YLL in all three regions.

Table A4 shows that many of the risk factors shown in Table A3, such as alcohol use, tobacco use, dietary risks, and high blood pressure, are risk factors for multiple NCDs and therefore potentially high-impact targets for risk reduction strategies. Screening and treatment of risk factors is relatively less costly than screening and treatment of NCDs. Table A3 demonstrates the importance of early detection and treatment of risk factors; interventions such as surgery and dialysis are often more costly after NCDs have developed. Additionally, management of risk factors, rather than a focus on one disease at a time, can reduce the risk of multiple NCDs.

Table A1. Years of life lost by non-communicable disease in three regions of the world in low- and middle-income countries among the general population.[1,4]

	YEARS OF LIFE LOST (%)			
Cause of Death	**Total LMIC**	**Sub-Saharan Africa**	**Southeast Asia**	**Latin America**
Cardiovascular disease	16.31	9.16	25.54	22.20
HIV*	14.38	24.13	3.72	3.63
Home safety	5.91	4.56	3.86	12.28
Motor vehicle safety	5.80	5.13	6.48	6.64
Tuberculosis*	5.54	5.78	8.46	0.87
Cancer	5.18	2.78	7.91	7.70
Diabetes	2.91	1.68	4.16	4.41
Cirrhosis	2.83	1.85	3.72	4.16
Chronic kidney disease	1.82	0.82	2.52	3.45
Mental health	1.69	1.20	2.09	2.40
Chronic obstructive pulmonary disease	1.53	0.78	2.21	2.57
Malnutrition	1.28	2.13	0.30	0.40
All other	34.82	40.00	29.03	29.29
Total YLL (2010)	**326,648,605**	**170,911,645**	**90,548,896**	**65,188,064**
Population Size	**2,030,260,000**	**873,156,000**	**610,491,000**	**546,613,000**

*Denotes communicable disease.

LMICs, low- and middle-income countries; YLL, years of life lost.

Table A2. Components of broader categories for causes of death for years of life lost in low- and middle-income countries.

Broad Category	Global Burden of Disease Specified Cause of Death
Cardiovascular disease	Hemorrhagic and other non-ischemic stroke
	Ischemic stroke
	Ischemic heart disease
	Hypertensive heart disease
	Other cardiovascular and circulatory disease
	Cardiomyopathy and myocarditis
	Rheumatic heart disease
Home safety	Assault by firearm
	Assault by sharp object
	Assault by other means
	Mechanical forces (firearm)
	Falls
	Fire, heat, and hot substances
Motor vehicle safety	Motorized vehicle with three or more wheels
	Motorized vehicle with two wheels
	Pedestrian injury by road vehicle
	Road injury other
	Other transport injury
	Pedal cycle vehicle

Table A2 (Continued) Components of broader categories for causes of death for years of life lost in low- and middle-income countries.

Broad Category	Global Burden of Disease Specified Cause of Death
Cancer	Cervical
	Colon
	Breast
	Prostate
	Bladder
	Trachea, bronchus, and lung
	Liver cancer from hepatitis B
	Liver cancer from hepatitis C
	Liver cancer from alcohol use
	Other liver cancer
Cirrhosis	Cirrhosis of the liver from hepatitis B
	Cirrhosis of the liver from alcohol use
	Cirrhosis of the liver from hepatitis C
	Other cirrhosis of the liver
Chronic kidney disease	Chronic kidney disease due to diabetes mellitus
	Chronic kidney disease due to hypertension
Mental health	Self-harm
Malnutrition	Protein-energy malnutrition

Table A3. Ranking of years of life lost by risk factors in three regions of low- and middle-income countries among the general population, adapted from Lim S., *et al*., Lancet 2012.[4]

	Ranking		
Risk Factor	**Sub-Saharan Africa**	**Southeast Asia**	**Latin America**
Dietary risks	6	1	1
High blood pressure	5	2	2
Alcohol use	4	7	3
Smoking	7	3	5
Household air pollution	2	4	9
High fasting plasma glucose	>10	5	6
Suboptimal breastfeeding	3	10	>10
High body-mass index	>10	8	4
Childhood underweight	1	>10	>10
Physical inactivity	>10	6	7
Ambient PM pollution	10	9	>10
Occupational risks	>10	>10	10
High total cholesterol	>10	>10	8
Sanitation	9	>10	>10
Vitamin A deficiency	8	>10	>10

Green-Yellow-Red color denotes the range in years of life lost due to a risk factor (Green: 10, the lowest YLL; Red: 1, the highest YLL).

Abbreviations: PM, particulate matter.

Table A4. Relative costs and effectiveness of screening and treatment strategies for non-communicable diseases and their common risk factors.*

	Risk Factor															
Cause of Death	Dietary risks	High blood pressure	Alcohol use	Smoking	Household air pollution	High fasting plasma glucose	High body-mass index	Childhood underweight	Physical inactivity	Ambient PM pollution	High total cholesterol	Occupational risks	Hepatitis B and C*	Human papillomavirus*	Screening	Treatment
Cardiovascular disease	X	X	X	X	X	X	X		X	X	X				Stress tests[6-10]	Revascularization, risk factor modification
Home safety			X												Survey	PHI
Motor vehicle safety			X												Survey	PHI
Diabetes	X		X	X		X	X		X						Glucose[11,12]	Medications
Cirrhosis			X										X		INR, albumin, liver biopsy[13]	Supportive care/liver transplant
Chronic kidney disease	X	X				X	X								Creatinine/UA	Dialysis
Mental Health			X												Survey[14]	Medications, psychotherapy[15]
Chronic obstructive pulmonary disease				X	X					X		X			Spirometry[16]	Medications, smoking cessation[17]
Malnutrition								X							Anthropometric[18-20]	Food support, micronutrients

Table A4 (Continued) Relative costs and effectiveness of screening and treatment strategies for non-communicable diseases and their common risk factors.

		Risk Factor															
	Cause of Death	Dietary risks	High blood pressure	Alcohol use	Smoking	Household air pollution	High fasting plasma glucose	High body-mass index	Childhood underweight	Physical inactivity	Ambient PM pollution	High total cholesterol	Occupational risks	Hepatitis B and C*	Human papillomavirus*	Screening	Treatment
Cancer	Bladder				X											UA/biopsy	Surgery, chemotherapy[21]
	Breast	X		X				X		X						Mammogram	
	Cervical				X										X	Pap, VIA[22]	
	Colon and rectum	X		X	X			X		X						Colonoscopy	
	Kaposi sarcoma															Biopsy	
	Liver (hepatocellular carcinoma)			X	X									X		AFP/US	
	Prostate	X														PSA/biopsy	
	Trachea, bronchus, and lung	X			X	X					X		X			Chest X-ray	
Screening			Blood pressure[10]	Survey	Survey		Glucose[11,12]	Anthropometric[18-20]	Anthropometric[18-20]			Cholesterol		Serology[23-25]	Pap, VIA[22]		
Treatment		PHI	Medication, diet[26]	Counseling[17]	Smoking cessation program[17]	PHI	Medications	Diet, counseling[11,12]	Food support, micronutrients	PHI	PHI	Diet medication[11,12]	PHI	Vaccine, medications[27,28]	Vaccine[22]		

***The table notes the relationship between the 10 most common NCD causes of death in LMICs and multiple risk factors. Each "X" notes where there is a relationship. The two screening and treatment columns on the right show what tests and treatments are available for each cause of death. The two screening and treatment rows at the bottom highlight where there are tests and treatments for the risk factors. To reflect relative costs of the interventions, the disease test and treatments are shown in light green/yellow/red/blue and the risk factors tests and treatments in darker green/yellow/red/blue.**

Green, lowest cost; yellow, moderate cost; red, highest cost; blue, public health interventions.

PHI, public health intervention; INR, international normalized ratio; PM, particulate matter; UA, urinalysis; VIA, visual inspection with acetic acid; AFP, alpha fetoprotein; US, ultrasound; PSA, prostate-specific antigen.

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