

Chapter 16

Integrated Public Health and Health Service Delivery for Noncommunicable Diseases and Comorbid Infectious Diseases and Mental Health

Matthew Magee, Mohammed Ali, Dorairaj Prabhakaran, Vamadevan S. Ajay, and K. M. Venkat Narayan



INTRODUCTION

The co-occurrence of noncommunicable diseases and communicable diseases raises important challenges to the integration of public health and care delivery for more than one morbidity. Effective integration requires assessing needs, designing integrated systems, leveraging existing infrastructure, and addressing resource challenges through creative organizational and technological strategies.

This chapter uses the example of diabetes as a prototypical noncommunicable disease and highlights the urgent need for integrated approaches to addressing three key comorbidities in patients with diabetes: mental health disorders, tuberculosis, and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). We explore the epidemiology of joint burdens, risk factors, and prognoses of these co-occurring conditions. We summarize the available evidence and address the challenges of integrating public health and health services for persons jointly affected by diabetes and the three comorbidities. We focus on a case study for integrating care for diabetes and mental health disorders. Finally, we address gaps in data regarding combined

burdens and effectiveness and cost-effectiveness of integrated interventions and make recommendations for closing those gaps.

GLOBAL BURDEN OF COEXISTING DIABETES WITH DEPRESSION, TUBERCULOSIS, AND HIV/AIDS

Diabetes and Mental Health

Joint Burdens

Mental illnesses, especially depression, occur more commonly in people with other chronic illnesses (Patel, Chatterji, and others 2011; Poongothai and others 2010; Poongothai and others 2011; Raval and others 2010). A study of 245,404 participants from 60 countries showed that, although one-year prevalence of depression based on codes in the 10th edition of the *International Statistical Classification of Diseases and Related Health Problems* was 3.2 percent, between 9.3 percent and 23.0 percent of participants with one or more chronic illnesses had comorbid depression. Adjusting for all other socioeconomic conditions and comorbidities, depression remained the most important contributor to

Corresponding author: Matthew Magee, Division of Epidemiology and Biostatistics, School of Public Health, Georgia State University, Atlanta, Georgia, United States; mjmagee@gsu.edu.

self-reported poor health scores in these persons (Moussavi and others 2007). In a large meta-analysis, depression was twice as common in people with diabetes than in those without the disease (Anderson and others 2001); up to 50 percent of patients with cancer suffer from depression or anxiety (Massie 2004).

Mental illnesses may be risk factors for the development of chronic diseases. Depression has been shown to be a risk factor for type 2 diabetes (Carnethon and others 2007; Golden and others 2004; Knol and others 2006; Llorente and Urrutia 2006). Depression increases the risk independent of smoking, physical activity, alcohol intake, C-reactive protein, and other factors associated with both depression and diabetes (Carnethon and others 2007). Depression may induce hypothalamic-pituitary-adrenal axis dysregulation and adverse autonomic nervous system dysfunction (Carnethon and others 2003). Both short- and long-term activation of sympathetic nervous systems suppress beta-cell function and insulin secretion, which may contribute to the increased risk for type 2 diabetes (Everson-Rose and others 2004). This bidirectional relationship makes comorbid diabetes-depression challenging to prevent and treat.

Individual and Societal Risk Factors

Mental illnesses are generally multifactorial. Mood disorders such as depression are related to different demographic, economic, contextual, psychological, and biological factors (Patel and others 1999; Patel and others 2009). In many cases, the confluence of vulnerabilities, stressors, and timing results in psychological distress and illness.

Prognosis and Outcomes

People with comorbid chronic and mental illnesses report worse health status and more burdensome symptoms; they have a higher risk of end-organ complications, relapse of depression (Lustman, Griffith, Freedland, and Clouse 1997), disability, and mortality.

Biologically, depression is linked to systemic inflammatory (Frohlich and others 2000; Konsman, Parnet, and Dantzer 2002) and endothelial (Laghrissi-Thode and others 1997; Musselman and others 1996) processes that perpetuate atherosclerosis and heighten the risk for cardiovascular disease (Joynt, Whellan, and O'Connor 2003; Rugulies 2002). A meta-analysis of depression and cardiovascular disease reported that persons with clinical depression had 2.7 (95 percent confidence interval [CI] 1.6–4.4) times the risk of coronary heart disease compared with those without depression (Rugulies 2002).

These poor outcomes may be mediated by behavioral or pathophysiological processes. For example, depression adversely affects self-care for diabetes (Beverly and

others 2012; Gonzalez and others 2008; Llorente and Urrutia 2006; Sridhar and Madhu 2002) and worsens glycemic control (Lustman, Anderson, and others 2000) and quality of life (Egede, Grubaugh, and Ellis 2010; Sridhar 2007). People with depression are twice as likely to smoke (Lasser and others 2000) and are less likely to engage in protective physical activity (Roshanaei-Moghaddam, Katon, and Russo 2009).

Mental illnesses, particularly depression, are the leading risk factors for suicide (Whiteford and others 2013); mental illnesses also increase the risk for other health outcomes and mortality. People with diabetes and depression have twice the risk of intensive care unit admissions and longer hospital stays than do those without depression (Davydow and others 2011). Comorbid depression is associated with up to three times higher risk of mortality in people with diabetes or chronic kidney disease (Bot and others 2012; Lin and others 2009; Sullivan and others 2012; Young and others 2010).

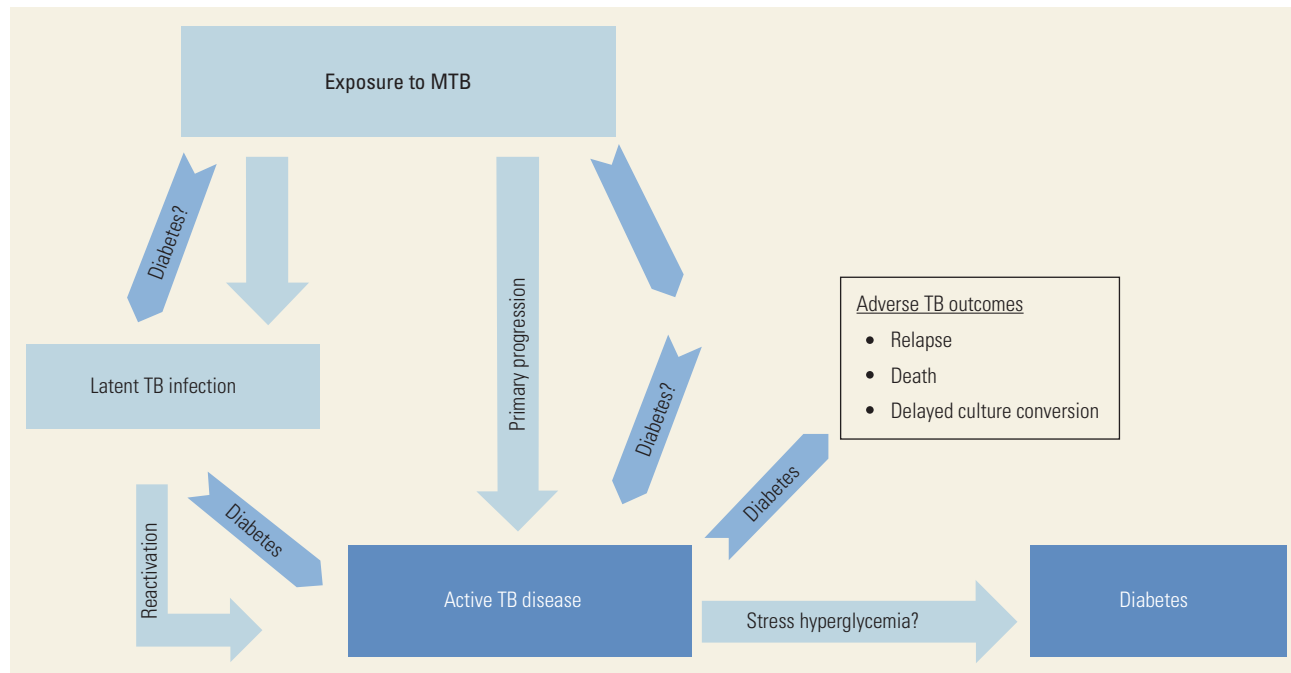
Diabetes and Tuberculosis

Each year, nearly 9 million people develop active tuberculosis; nearly 2 million die from tuberculosis-related causes, accounting for 2 percent of deaths from infectious diseases (WHO 2012). More than 95 percent of all tuberculosis cases occur in low- and middle-income countries (LMICs); an estimated 2 billion people have *Mycobacterium tuberculosis* complex infection and are at risk for developing the active disease (Nelson and Williams 2007). Diabetes prevalence (currently 366 million and estimated to reach 570 million by 2030) and diabetes cause-specific mortality (1.3 million deaths in 2010) are expanding (IDF 2013). The anticipated increases in diabetes-associated burdens will occur disproportionately in LMICs, where tuberculosis is likely to remain endemic for the foreseeable future (Magee, Blumberg, and Narayan 2011).

The increasing coprevalence has heightened public health interest in the intersection of diabetes and tuberculosis in individuals. Diabetes increases the chance of developing active tuberculosis by approximately threefold (Jeon and Murray 2008). Both in vivo and in vitro studies suggest that diabetes may affect vulnerability to *Mycobacterium tuberculosis* infection by altering cytokine signaling related to both innate and adaptive immune responses (figure 16.1) (Martinez and Kornfeld 2014; Restrepo and Schlesinger 2013).

Tuberculosis may increase the risk of diabetes. Chronic inflammation that results from major infections such as tuberculosis can induce stress-related hyperglycemia (Kapoor and Harries 2013), and active tuberculosis disease can worsen existing hyperglycemia and insulin resistance. However, older studies that have documented changes in

Figure 16.1 Tuberculosis Infection and Disease States and Effects of Diabetes Mellitus



Note: MTB = *Mycobacterium tuberculosis*; TB = tuberculosis. Arrows including “diabetes” indicate a hypothesized increased risk due to diabetes; “?” indicates a hypothesis without substantial epidemiologic data.

glucose tolerance during and after tuberculosis treatment report that a high proportion of newly diagnosed tuberculosis patients with hyperglycemia or diabetes return to normal blood glucose levels after tuberculosis treatment (WHO 2011). Additional research is needed to differentiate the impact of tuberculosis on the risk of incident diabetes (versus new diagnosis of previous diabetes) and to describe glycemic trajectories before, during, and after tuberculosis treatment.

An increased proportion of new tuberculosis cases is attributed to diabetes—an estimated 15 percent or 1.4 million annual cases (Lonnroth, Roglic, and Harries 2014). The struggle to reduce the incidence of tuberculosis and diabetes has resulted in an increased global burden of people experiencing both diseases. The co-occurrence of these two pandemics illustrates a new epidemiological phenomenon in which chronic diseases occur simultaneously with infectious diseases not only in the same population but also in the same individuals (Magee, Blumberg, and Narayan 2011).

Joint Burdens

The annual global incidence of tuberculosis is concentrated among 22 high-burden countries, all LMICs. In 2011, an estimated 82 percent (7.1 million) of all incident tuberculosis cases (8.7 million) occurred in these

countries; 37 percent (3.2 million) were in China and India (WHO 2012). Historically, national programs in the high-tuberculosis-burden countries have not routinely conducted surveillance of diabetes among patients with tuberculosis. Similarly, diabetes care guidelines have not traditionally incorporated recommendations for tuberculosis screening in diabetic patients.

In 2009, the International Union Against Tuberculosis and Lung Disease and the World Health Organization (WHO) recognized the need for bidirectional screening and initiated pilot screening programs in China and India. In India, more than 8,000 tuberculosis patients from third-level clinics and tuberculosis units were screened for fasting blood glucose; 13.4 percent had diabetes by the WHO standard classification (table 16.1) (Kumar and others 2013). The prevalence of diabetes in patients with tuberculosis was consistently higher in South India than in North India; this difference partially reflects the geographic and age distribution of diabetes in India, but it is also likely attributable to increased screening in South India (Kumar and others 2013). A similar pilot screening program in 2011 in China detected 12.3 percent prevalence of diabetes among 8,886 patients with tuberculosis who were screened in urban and rural regions (Li and others 2012). Although data are not widely available and considerable geographic variation exists, the prevalence of

Table 16.1 Prevalence of Tuberculosis, Diabetes Mellitus, and Co-Occurring Tuberculosis and Diabetes Mellitus in Select High-Burden Countries

Location	Study	2011 National Tuberculosis Incidence ^a	2011 National Diabetes Prevalence ^b		Diabetes Prevalence in Patients with Tuberculosis	
		Number (thousands)	Number (thousands)	%	Number	%
India	Kumar and others 2013	2,200	61,258	8.3	1,084/8,109	13.4
China	Li and others 2012	1,000	90,045	9.3	1,090/8,886	12.3
Indonesia	Alisjahbana and others 2007	450	7,293	4.7	94/634	14.8
Pakistan	Jawad and others 1995	410	6,349	6.7	21/106	19.8
South Africa	—	500	1,947	6.5	—	—

Source: Based on WHO 2012.

Note: — = not available.

a. Unadjusted estimates in adults ages 20–79 years (IDF 2011).

b. IDF 2013.

diabetes among tuberculosis patients in most LMICs is likely to be greater than the prevalence of diabetes in the nontuberculosis population.

Individual and Societal Risk Factors

In LMICs, especially in regions where the prevalence of HIV/AIDS is low, diabetes may be responsible for a large proportion of incident tuberculosis cases, and this proportion is projected to increase. Using standard attributable fraction formulas, Stevenson, Forouhi, and others (2007) estimated that 15.1 percent of adult incident tuberculosis cases (141,548 cases) in India in 2000 could be attributed to diabetes. Even though the increased risk of developing active tuberculosis is much lower in diabetic patients than in HIV/AIDS patients, the high prevalence of diabetes is an important factor that inhibits global progress in reducing tuberculosis incidence.

Prognosis and Outcomes

The burden of diabetes on tuberculosis control extends beyond an increased risk of active tuberculosis. Observational studies that compared patients with both conditions to tuberculosis patients without diabetes have reported important differences in clinical manifestations of tuberculosis. Although standardized measures of clinical tuberculosis severity are not widely used in epidemiology, studies reported clinical symptoms of tuberculosis among tuberculosis-diabetes patients that are characteristic of greater severity. Examples of important measures of clinical severity at baseline include positive acid-fast bacilli (AFB) sputum smear grade

(Mac Kenzie and others 2011; Wallis and others 2000), cough with blood (hemoptysis), extent of bacterial involvement according to chest radiographs (Holtz and others 2006; Ralph and others 2010; Stout and others 2010; Wallis and others 2000), and presence of multidrug-resistant tuberculosis (Holtz and others 2006). Greater initial disease severity among tuberculosis-diabetes patients may increase the duration of treatment, require more human and financial resources, and lead to poor tuberculosis treatment outcomes.

More studies that have compared AFB smear status and grade characteristics of tuberculosis patients at the time of diagnosis demonstrated an association between diabetes and the more infectious, smear-positive forms of tuberculosis (table 16.2) (Stevenson, Critchley, and others 2007). Previous studies comparing tuberculosis symptoms at time of presentation also reported more cough (Restrepo and others 2007; Singla and others 2006) and hemoptysis (Restrepo and others 2007; Singla and others 2006; Wang and others 2009) in tuberculosis patients with diabetes than in tuberculosis patients without diabetes. Studies that examined radiographic findings in tuberculosis-diabetes patients and in tuberculosis patients without diabetes have documented important differences (Dooley and Chaisson 2009). Several studies have demonstrated that tuberculosis-diabetes patients had greater lower-lung involvement and more cavitory lesions compared with tuberculosis patients without diabetes (table 16.3); these radiographic characteristics are associated with misdiagnosis of tuberculosis and treatment failure.

Table 16.2 Acid-Fast Bacilli Smear Positivity among Tuberculosis Patients with and without Diabetes Mellitus at Time of Tuberculosis Diagnosis

Location	Study	Tuberculosis-diabetes patients (N)	Tuberculosis-only patients (N)	AFB smear + tuberculosis-diabetes (%)	AFB smear + tuberculosis only (%)
Turkey	Bacakoglu and others 2001	92	92	72.8	91.3
Saudi Arabia	Singla and others 2006	187	505	65.2	54.1
Indonesia	Alisjahbana and others 2007	94	540	29.8	38.9
Mexico	Restrepo and others 2007	607	2,804	96.8	94.9
Texas, United States	Restrepo and others 2007	401	1,040	64.9	50.9
Taiwan, China	Wang and others 2009	74	143	68.9	53.8
Baltimore, MD, United States	Dooley and others 2009	42	255	54.8	41.2
Taiwan, China	Chang and others 2011	60	132	88.3	59.1

Source: Based on Ruslami and others 2010.

Note: AFB = acid-fast bacilli.

Table 16.3 Chest X-Ray Findings among Tuberculosis Patients with and without Diabetes Mellitus

Location	Study	Diabetes-tuberculosis patients (N)	Tuberculosis-only patients (N)	More lower-lung involvement among diabetes-tuberculosis patients	More cavitory lesions among diabetes-tuberculosis patients
Turkey	Bacakoglu and others 2001	92	92	No	No
Mexico	Perez-Guzman and others 2003	192	130	Yes	Yes
Saudi Arabia	Singla and others 2006	187	505	Yes	—
Indonesia	Alisjahbana and others 2007	94	540	—	No
Texas, United States	Restrepo and others 2007	401	1,040	—	Yes
Saudi Arabia	Al-Tawfiq and Saadeh 2009	57	78	—	No
Taiwan, China	Wang and others 2009	74	143	Yes	Yes
Baltimore, MD, United States	Dooley and others 2009	42	255	—	Yes
Taiwan, China	Chang and others 2011	60	132	—	Yes
Portugal	Carreira and others 2012	123	123	Yes	No
Mexico	Jimenez-Corona and others 2013	313	758	—	Yes

Sources: Based on Dooley and others 2009; Ruslami and others 2010.

Note: — = not available.

The prevalence of multidrug-resistant tuberculosis among tuberculosis-diabetes patients has not been extensively examined. In general, studies examining multidrug-resistant tuberculosis in patients with and without diabetes have not reported an association between diabetes and drug-resistant tuberculosis (Alisjahbana and others 2007; Chang and others 2011; Singla and others 2006; Stevenson, Critchley, and others 2007), although important exceptions exist (Bashar and others 2001; Fisher-Hoch and others 2008). Several studies have found consistent associations with clinical manifestations in tuberculosis-diabetes patients, but previously mentioned studies were all observational in design, and the quality of key study metrics, such as diabetes status, was highly variable.

Increased risk of poor clinical outcomes among tuberculosis-diabetes patients is an additional burden conferred by the confluence of the two diseases. Most observational studies that compare tuberculosis treatment outcomes in patients with and without diabetes indicate slower sputum culture conversion time (Guler and others 2007; Restrepo and others 2008) and increased risk of treatment failure (Ponce-de-Leon and others 2004), death (Faurholt-Jepsen and others 2013), or relapse (Zhang, Xiao, and Sugawara 2009) among tuberculosis-diabetes patients.

A meta-analysis estimated that, compared with tuberculosis patients without diabetes, the effect of diabetes on the risk ratio (RR) for death among tuberculosis-diabetes patients was 1.89 (95 percent CI 1.52–2.36) (Baker and others 2011); however, this RR estimate was not adjusted for important confounders such as age and HIV/AIDS status (Baker and others 2011). The same meta-analysis also estimated a greater risk of tuberculosis relapse among tuberculosis-diabetes patients than among tuberculosis patients without diabetes (RR 3.89; 95 percent CI 2.43–6.23). Studies examining the effect of tuberculosis on diabetes outcomes are notably lacking.

Diabetes and HIV/AIDS

Joint Burdens

As a result of longer life expectancy, persons living with HIV/AIDS experience prolonged exposure to traditional and HIV/AIDS-specific risk factors for metabolic disorders, including diabetes.

The prevalence of diabetes among persons with treatment-naïve HIV/AIDS (patients who previously have not received care for HIV/AIDS) varies considerably by geographic region and is distributed similarly to trends in diabetes prevalence in general populations. In high-income countries (HICs), the prevalence of diabetes in patients with HIV/AIDS ranges from 1.9 percent to

14.9 percent (table 16.4) (Brown and others 2005; Butt and others 2009; Mondy and others 2007), similar to the national prevalence of diabetes among those ages 20 years or older (11.3 percent). The prevalence of diabetes is lower in LMICs than in HICs. A study from South Africa found that 3.4 percent of HIV/AIDS treatment-naïve patients had diabetes (Dave and others 2011); a multicountry study from South America reported diabetes prevalence from 0.8 percent to 6.5 percent in patients with HIV/AIDS (Cahn and others 2010). Although diabetes prevalence is lower in LMICs than in HICs, the absolute number of persons with both diabetes and HIV/AIDS is greater in LMICs because of the higher burden of HIV/AIDS.

Few studies have compared the incidence of diabetes among patients with HIV/AIDS to the incidence of diabetes in HIV-negative persons. A study in the United States from 1999 to 2003 reported that the adjusted incidence of diabetes was 4.1 times greater among patients with HIV/AIDS than among patients without HIV/AIDS (Brown and others 2005). However, a study in Denmark from 1999 to 2009 found no differences in diabetes incidence when comparing patients with and without HIV/AIDS (Rasmussen and others 2012).

Individual and Societal Risk Factors

The same well-established risk factors for diabetes mellitus in the general population are also associated with increased risk of diabetes in patients with HIV/AIDS. Older age; obesity (both body mass index and waist circumference); lifestyle factors; close relatives with a history of diabetes; hypertension; low levels of high-density lipoprotein cholesterol; and, for women, a history of gestational diabetes are all associated with diabetes in persons both with and without HIV/AIDS (Kalra and Agrawal 2013; Tebas 2008). Patients with HIV/AIDS who have lipodystrophy and recently had CD4 counts below 200 cells per microliter are at increased risk of developing diabetes (Petoumenos and others 2012).

Among patients with HIV/AIDS, certain antiretroviral medications are associated with the development of diabetes. Many of the agents associated with diabetes incidence were part of earlier generations of antiretrovirals and are no longer commonly used. Protease inhibitors—specifically indinavir, ritonavir, and amprenavir—are associated with increased risk of diabetes. Protease inhibitors directly affect glucose uptake by inhibiting the transport function of insulin in adipose tissue and lead to hyperglycemia (Murata, Hruz, and Mueckler 2000).

Cumulative exposure to reverse transcriptase inhibitors, specifically stavudine and efavirenz, is associated with increased dysglycemia in HIV-infected persons. A large Danish population-based cohort study reported

Table 16.4 Incidence and Prevalence of Diabetes Mellitus in Patients with and without HIV/AIDS from Large Observational Cohort Studies

Study	Study	Study years	Location	HIV-positive diabetes prevalence (%) ^a	HIV-positive diabetes incidence ^b	HIV-negative diabetes incidence ^c	Adjusted incidence ratio	Antiretroviral treatment and diabetes association ^d
MACS	Brown and others 2005	1999–2003	United States	13.9	4.7	1.4	4.1 (1.9–9.2)	Ritonavir
WIHS	Tien and others 2007	2000–06	United States	11.2	2.9	2.0	1.2 (0.7–1.9) ^e	Lamivudine
DHCS	Rasmussen and others 2012	1996–98	Denmark	—	0.5	0.2	3.2 (1.4–7.4)	Stavudine
DHCS	Rasmussen and others 2012	1999–2009	Denmark	—	0.4	0.4	1.0 (0.8–1.3)	Stavudine
NTUH	Lo and others 2009	1993–2007	Taiwan, China	2.5	1.3	—	—	Zidovudine
SHCS	Ledergerber and others 2007	2000–06	Switzerland	1.9	0.4	—	—	Stavudine and didanosine, stavudine and lamivudine, and didanosine and tenofovir
D:A:D	De Wit and others 2008	1999–2007	Multiple	2.9	0.6	—	—	Stavudine, zidovudine, and didanosine
VACS	Butt and others 2009	2002–04	United States	14.9	—	—	—	—

Note: — = not available; D:A:D = Data Collection on Adverse Events of Anti-HIV Drugs study; DHCS = Danish HIV Cohort Study; HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome; MACS = Multicenter AIDS Cohort Study; NTUH = National Taiwan University Hospital study; SHCS = Swiss HIV Cohort Study; VACS = Veterans Aging Cohort Study; WIHS = Women's Interagency HIV Study.

- a. Prevalence of diabetes mellitus at cohort baseline unless otherwise noted.
- b. Unadjusted rate per 100 person-years for HIV-positive persons on antiretroviral treatment.
- c. Unadjusted rate per 100 person-years for HIV-negative persons from study's comparison group.
- d. Among HIV-infected persons, any antiretroviral drugs associated with increased risk of incident diabetes.
- e. Hazard ratio.

higher diabetes incidence (RR 1.8, 95 percent CI 1.2–2.8) in patients with HIV/AIDS who were ever exposed to stavudine compared with those who were never exposed to stavudine (Rasmussen and others 2012). A study of 849 patients with HIV/AIDS in South Africa showed that exposure to efavirenz was associated with dysglycemia (odds ratio 1.7, 95 percent CI 1.2–2.5) even after controlling for age, gender, and CD4 count (Dave and others 2011).

Globally, infection with hepatitis C virus (HCV) is frequently prevalent in persons who inject drugs. Unsterile injection of drugs is also a common transmission route for HIV; many persons with HIV/AIDS also have coprevalent HCV. Chronic HCV infection is associated with increased risk of diabetes. A meta-analysis of 10 cohort studies, mainly retrospective studies from Italy and the United States, reported a 67 percent increase in the rate of incident diabetes in persons with HCV

compared with persons without HCV (White, Ratziu, and El-Serag 2008).

Prognosis and Outcomes

Few studies have examined the prognosis or treatment outcomes of patients with HIV/AIDS and diabetes. Among patients with HIV/AIDS, having diabetes increases the risk of peripheral lipoatrophy and greater waist-hip ratio; these are likely to be intermediate factors on the causal path to poor HIV/AIDS treatment outcomes, including cardiovascular disease, renal disease, and mortality (Kalra and Agrawal 2013; Tebas 2008).

Among patients with HIV/AIDS, coprevalent diabetes is predictive of cardiovascular disease. In the Data Collection on Adverse Effects of Anti-HIV Drugs study, a large multinational prospective cohort study, diabetes was associated with increased hazards of cardiovascular disease (hazard ratio [HR] 1.9, 95 percent CI 1.6–2.4),

coronary heart disease (HR 1.9, 95 percent CI 1.5–2.4), and myocardial infarction (HR 2.3, 95 percent CI 1.7–3.0) (Friis-Moller and others 2010). Chronic kidney disease, including progression to end-stage renal failure, is also more common among patients with HIV/AIDS and diabetes than among patients with diabetes alone.

A study from Malawi compared kidney function in patients with HIV/AIDS and diabetes to patients with diabetes alone. Those with co-occurring HIV/AIDS and diabetes were significantly more likely to have albuminuria than patients with diabetes alone (48.0 percent and 33.3 percent, respectively) (Cohen and others 2010). In the United States, a cohort of veterans was followed to determine rates of progression to chronic kidney disease. Compared with patients without HIV/AIDS or diabetes, the rate of progression to chronic kidney disease was greater in patients with diabetes only (HR 2.48, 95 percent CI 2.19–2.80) and with HIV/AIDS only (HR 2.80, 95 percent CI 2.50–3.15) and greatest among those with both HIV/AIDS and diabetes (HR 4.47, 95 percent CI 3.87–5.17) (Medapalli and others 2012). Acute renal failure is also associated with diabetes among patients with HIV/AIDS. A 2003 cohort of hospitalized patients in New York was analyzed to determine risk factors for the development of acute renal failure. The study reported that patients with HIV/AIDS and diabetes were more likely to have acute renal failure (odds ratio 1.3, 95 percent

CI 1.1–1.5) than patients with HIV/AIDS only (Wyatt and others 2006).

OPPORTUNITIES AND CHALLENGES TO INTEGRATION

Integration of Care

The rise of chronic noncommunicable diseases worldwide has presented new challenges for most health systems, particularly in LMICs. Vertical approaches alone that have proved quite successful in combating communicable diseases may not be feasible and cost-effective in treating noncommunicable diseases, given their chronic nature and the continued long-term care required. Insufficient empirical evidence exists to estimate the efficacy or cost-effectiveness of applying communicable disease approaches to noncommunicable disease care.

A search of existing literature on collaborative care returned 1,097 published studies, of which 246 were related to integration. Only seven studies reviewed were related to integration of diabetes care with care for HIV/AIDS, tuberculosis, or depression. Table 16.5 summarizes the observational and case studies of integrated care; table 16.6 summarizes the randomized trials.

Although efficacious and cost-effective preventive and curative solutions exist, timely and sustained

Table 16.5 Examples of Integrated Service Programs from Low- and Middle-Income Countries

Location	Study	Integrated services	Objective	Outcome
Siem Reap and Takeo, Cambodia	Janssens and others 2007	<ul style="list-style-type: none"> HIV: HAART Diabetes: metformin and glibenclamide Hypertension: antihypertensive protocol 	<ul style="list-style-type: none"> Drug adherence Lifestyle changes Self-management of diseases 	<ul style="list-style-type: none"> HIV/NCD integration feasible Services gained efficiency Low patient loss to follow-up
Rural Rwanda	van Olmen 2011	<ul style="list-style-type: none"> Chronic renal disease screening in patients with HIV/AIDS, hypertension, and diabetes 	<ul style="list-style-type: none"> Screening for serum creatinine or proteinuria in high-risk patients at noncommunicable disease clinics 	<ul style="list-style-type: none"> Algorithms for outpatient management of kidney disease and mild hyperkalemia
Manzini, Swaziland	Church and others 2015	<ul style="list-style-type: none"> Counseling and testing integrated with family planning, pregnancy counseling, and promotion of condom use 	<ul style="list-style-type: none"> Improved efficiency of two-care systems in high HIV/AIDS-prevalence setting 	<ul style="list-style-type: none"> Integration not fully achieved Organizational factors limited capacity to implement integration
Western Kenya	Ouma and Pastakia 2010	<ul style="list-style-type: none"> Shared electronic medical records systems for patients with HIV/AIDS, tuberculosis, and diabetes Home glucose monitoring 	<ul style="list-style-type: none"> Enhanced diabetes care in rural setting with high HIV/AIDS and tuberculosis burden 	<ul style="list-style-type: none"> Observed reductions in glycated hemoglobin Insulin doses adjusted based on standardized protocols

Note: HAART = highly active antiretroviral therapy; HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome; NCD = noncommunicable disease.

Table 16.6 Randomized Controlled Trials of Integrated Care for Diabetes and Depression

Location	Study	Design	Integration summary
Hong Kong SAR, China, public hospital	Chan and others 2014	Randomized trial JADE+PEARL	After one year, patients with type 2 diabetes receiving integrated care with peer support had similar proportions achieving glycosylated hemoglobin targets and self-reported depression scores compared with controls.
Washington, United States, primary care clinic	Katon and others 2010b	Randomized trial with medically supervised nurse	After one year, patients with type 2 diabetes and coexisting depression receiving care in coordination with primary care nurses had better glycosylated hemoglobin and depression scores compared with controls.
Washington, United States, primary care clinic	Katon and others 2004	Randomized trial Pathways case management	After one year, patients with type 2 diabetes and coexisting depression receiving care in coordination with case management had improved depression scores but similar glycosylated hemoglobin levels compared with controls.

Note: JADE = Joint Asia Diabetes Evaluation; PEARL = Peer Support, Empowerment, and Remote Communication Linked by Information Technology.

delivery of these interventions is a major challenge. Meeting this challenge requires concurrently strengthening the health systems and integrating efforts to address both communicable and noncommunicable diseases synergistically under the umbrella of primary health care (Atun and others 2010). Given the increased global prevalence of several noncommunicable diseases and the health system burdens they have created, the WHO and the United Nations High-level Meeting on Non-Communicable Diseases have called for health system strengthening and integration as essential pathways.

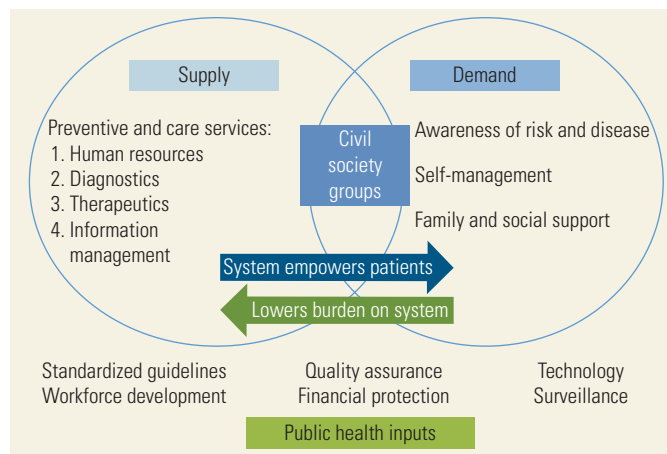
Noncommunicable diseases often have shared risks or coexist with communicable diseases, thereby increasing the risk or adverse impact of each other. Such interconnections provide a clear rationale for implementing common prevention, screening, management, and follow-up strategies within health systems. Table 16.5 presents examples of three programs that have integrated health services in LMICs to improve the efficiency of care.

Proposed Pathways for Integration

A potential framework for conceptualizing integration includes engaging civil society groups to meet the supply of and demand for public health systems (figure 16.2). Inputs into this framework include standardized guidelines, workforce development, quality assurance, financial protection, technology, and disease surveillance.

The information, education, and communication strategies used by communicable disease programs could be expanded to include messages about preventing and controlling noncommunicable diseases. Bidirectional screening (Jeon and others 2010) with common management guidelines could be another potential pathway

Figure 16.2 Macrolevel Framework for Integration of Noncommunicable and Communicable Disease Health Systems



to integrating health care services. Maternal and child health programs could be similarly engaged, using existing structures and personnel to assess blood pressure, blood glucose, and cardiovascular risk, as well as to promote risk reduction measures and management. Simple nonlaboratory risk assessment could be promoted across programs, particularly those that entail multiple contacts with health personnel.

Optimizing available human resources by sharing tasks and shifting care to community health workers is another pathway that merits consideration for strengthening health systems and integrating communicable and noncommunicable disease services. Data on the effectiveness of nonphysician health care workers in chronic disease care, although limited, are summarized in chapter 17 of this volume (Joshi and others 2017).

Strategies for Integration

Integration requires multiple strategies:

- *Diverting health workers from redundant programs.* This approach requires reassessing the continuing relevance of existing health programs from which health workers could be diverted. For example, where control programs for guinea worm, leprosy, or other neglected tropical diseases have eradicated diseases, the trained manpower from these control programs may be redeployed.
- *Retraining and imparting multiple skills to the workforce in existing health programs.* In many countries, health care professionals encounter patients with noncommunicable diseases who are more proactive in their health-seeking behavior than patients with existing diseases. Patient management requires coordinated care, which demands teamwork and skills. The health care workforce needs to be up to date with the explosive growth of knowledge and technologies and with their application to care delivered in health facilities, homes, and communities (Frenk and others 2010). Training approaches need to be restructured to include a new set of core competencies for noncommunicable disease care that includes patient-centered care, partnering, quality improvement, information and communication technology, and public health perspectives (Pruitt and Epping-Jordan 2005).
- *Expanding and reorienting the health system to prevent, detect, and care for chronic diseases, with particular focus on nonphysicians.* The existing health system needs to be expanded and reoriented to deliver chronic disease care. An integrated chronic care model includes multiple components, such as patient self-management support, delivery system design, decision support, clinical information systems, community resources, and multisector collaboration (WHO 2013). Of these components, self-management support, delivery system design, and decision support have been shown to be effective. However, large-scale population-based studies in LMICs that attempt to implement such models are essential. For cost-effectiveness, early results are inconclusive; costs, savings, and benefits need to be studied in more detail (Busse, Schreyögg, and Smith 2008). Integrated chronic care models need to be built around nonphysician health cadres that are also adapted to the resource constraints in LMICs (Katon and others 2010a, 2010b).

The most effective integration mechanisms will likely depend on the structure of the health system in each setting. For example, in some countries the provision of clinical care for diabetes or mental health may be outsourced to nongovernmental agencies or private

service providers, whereas in other countries integrated care coordination could be used by government health systems.

CASE STUDIES OF SUCCESSFUL MODELS OR MODELS WORTHY OF EVALUATION

Prevention

Addressing societal risk factors to prevent depression will be important, but the literature and empirical data in this area are extremely limited (Lund and others 2011). General goals in trying to prevent depression include the following:

- Increasing engagement in health promotion activities
- Increasing self-efficacy in the areas of decision making, conflict management, and positive thinking
- Increasing resilience and self-esteem.

These goals may be achieved through a variety of approaches (for example, education, mental health promotion, violence prevention) and settings (for example, schools, homes, workplaces). However, more robust and context-specific data are needed before those approaches can be recommended widely.

Treatment and Barriers

Strong evidence indicates that management of depression with pharmacotherapy, psychotherapy, or both is effective and cost-effective. However, most LMICs have barriers to care in both the supply of and the demand for mental health services (Collins and others 2011; Wang, Simon, and Kessler 2003).

Many similarities exist between mental illnesses and chronic diseases with regard to treatment approaches and barriers to care. For example, mental health and cardiometabolic diseases are chronic, complex, progressive, and costly (Unutzer and others 2009); identification is a key step toward initiating clinical care and self-care; and for both conditions, behavioral activation and motivation are critical for adherence to management plans. Care for both conditions is hampered by major patient- (Egede and Osborn 2010), provider-, and system-level barriers, all of which interact (Balabanova and others 2009). These similarities, as well as the synergistic effects of these conditions (Golden and others 2008; Mezuk and others 2008; Pan and others 2012), offer opportunities to identify and integrate care platforms that efficiently address both sets of conditions.

Integrated care models address barriers to care by leveraging existing facilities, infrastructure, and human resources.

Integrated care can be based in primary care settings or specialist care settings. In primary care, the approach involves decentralizing management of mental illnesses and chronic diseases through structured, collaborative care, and using nonmedical personnel to augment care (Gilbody and others 2006). The goal is to leverage common infrastructure to detect and manage all diseases, whether comorbid or single, in the same location with the same resources (Kolappa, Henderson, and Kishore 2013).

Comprehensive care requires targeting symptoms of depression and hopelessness with medications and behavioral therapies, improving self-management through empowerment, helping patients adopt health-promoting behaviors, and optimizing treatment intensification by health care providers to improve chronic disease care. Integrated care may offer synergistic benefits by managing depression and chronic diseases together. Optimizing therapy for control of depression, glucose, blood pressure, and cholesterol together is associated with better depressive outcomes than focusing on depression alone (Katon and others 2004; Katon and others 2010a; Lustman, Freedland, and others 2000; Lustman, Griffith, Clouse, and others 1997; Lustman and others 1998); exercise, weight loss, and better glyce-mic control decrease depressive symptoms in people with both diabetes and depression (Blumenthal and others 1999; Testa and Simonson 1998; Wing, Phelan, and Tate 2002).

Studies evaluating models of care that incorporate structured, collaborative care approaches to managing patients with comorbid diseases have shown significantly enhanced responses to treatment of depression, as well as enhanced medical control of diabetes. Randomized controlled trials demonstrated that interventions that included collaborative care with primary health care via enhanced education or nurse case management lead to improvements in adherence and follow-up, reductions in depressive symptoms, and better control of diabetes and cardiovascular risk factors (Katon and others 2004; Katon and others 2010a; Simon and others 2007).

These complex care delivery interventions require resource investments, and studies evaluating the cost-effectiveness of these interventions have noted that the investment costs are offset by savings for future medical care (Shidhaye, Lund, and Chisholm 2015; Simon and others 2001; Simon and others 2007). In HICs, collaborative care models have been adopted by health care providers, payers, and some health agencies (Kates and Craven 2002; Meadows 1998).

There are, however, few or no data regarding collaborative care models from LMICs. Models of care that have been evaluated in LMICs involve using non-medical personnel to deliver mental health services,

particularly depression care, in primary care settings. In India (Patel and others 2010; Patel, Weiss, and others 2011), lay counselors were trained to manage cases and deliver psychotherapy, with step-up to antidepressant drugs provided by primary care physicians under the supervision of mental health specialists. Compared with usual care, this intervention was associated with a 30 percent reduction in the prevalence of mental health disorders, 36 percent reduction in suicidal attempts or plans, fewer days missed from work, and less psychological morbidity among public facility attendees over the year. In Chile (Araya and others 2003; Araya and others 2006), nonmedical health workers helped deliver patient care that included psychoeducation in groups, structured follow-up, and antidepressant medications, where indicated. After a six-month follow-up, 70 percent of intervention participants experienced a significant reduction in depressive symptoms, compared with 30 percent of usual care participants. However, these interventions were focused on mental illness and not on coexisting chronic and mental illnesses.

CONCLUSIONS

Longer life expectancy and growing prevalence of chronic diseases are associated with an increase in coexisting mental and physical morbidities—particularly chronic diseases and comorbid depression. This coexistence exacerbates health and economic impacts on patients, families, communities, and countries.

Given the similarities in the course of disease and barriers to care, as well as the adverse interactions, integrated care that combines mental health management with cardiometabolic risk reduction may provide efficient opportunities to reduce morbidity and to improve physical and social functioning (Katon and others 2010b; McGregor, Lin, and Katon 2011). The goals of collaborative care are to improve patient-centered self-care and adherence, provider accountability, teamwork in clinical settings, and relapse prevention. Achieving all of these goals will help strengthen health systems.

At least four important gaps in knowledge and information regarding the co-occurrence of diseases need to be addressed:

- Expanding current global disease surveillance systems for collection of information on comorbid conditions to enhance the ability to prioritize which co-occurring diseases should be addressed with greatest intensity
- Providing additional studies to clarify the effects of co-occurring diseases on the prognosis of each illness

Table 16.7 Public Health Integration Recommendations

Health system recommendations	Research recommendations
<ul style="list-style-type: none"> • Establish disease surveillance for comorbid conditions • Implement bidirectional screening programs • Retrain health care workers for multiple disease skill sets • Reorient systems to the prevention of comorbid conditions 	<ul style="list-style-type: none"> • Expand research on etiologic prognosis of comorbid diseases • Identify efficacious therapies for patients with co-occurring diseases • Evaluate intervention cost-effectiveness

- Providing data to determine the effectiveness of interventions to address the confluence of diseases and effective management of two diseases simultaneously
- Determining the cost-effectiveness of interventions to improve disease outcomes for individuals with co-occurring diabetes and HIV/AIDS.

National health programs and public health agencies need to address the emerging co-occurring diseases. However, funding gaps are likely to arise, and identifying additional resources will be a challenge. Funding agencies historically committed to the control of infectious diseases also need to promote efforts to gather data, implement interventions, and test integrated prevention and treatment programs for both communicable and noncommunicable diseases (table 16.7). Expanding the growing list of global health priorities to include the integration of care is likely to lead to primary prevention, improved disease prognosis, and enhanced knowledge regarding implementation sciences and health care delivery.

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046 to US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126 to US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

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