SYSTEMS-BASED APPROACHES TO IMPROVING MEDICATION ADHERENCE

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About SIAPS

The Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program works to ensure access to quality pharmaceutical products and effective pharmaceutical services through systems strengthening approaches to achieve positive and lasting health outcomes. SIAPS is funded by the US Agency for International Development (USAID) and is implemented by Management Sciences for Health. For more information, visit www.SIAPSprogram.org.

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Key Words

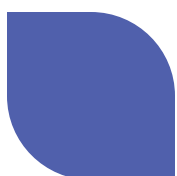medication adherence, health systems, medicines, macro, meso, micro

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ACRONYMS

AIDS	acquired immunodeficiency syndrome
AMI	Amazon Malaria Initiative
APTS	Auditable Pharmaceutical Transactions and Services
ARV	antiretroviral
ART	antiretroviral therapy
CBIA	community-based interactive approach
CBTSP	community-based treatment support program
DM	diabetes mellitus
DOT	directly observed treatment
DOTS	directly observed treatment short course
DTP	drug therapy problem
EDT	electronic dispensing tool
EML	essential medicines list
EWI	early warning indicator
FDC	fixed-dose combination
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
HIV-DR	HIV drug resistance
HSS	health systems strengthening
INRUD-IAA	International Network for the Rational Use of Drugs Initiative on Adherence to Antiretrovirals
MOHSS	Ministry of Health and Social Services [Namibia]
MSH	Management Sciences for Health
PFSA	Pharmaceutical Fund and Supply Agency [Ethiopia]
RAVREDA	Amazon Network for the Surveillance of Antimalarial Medicine Resistance
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SMS	short message service
SPS	Strengthening Pharmaceutical Systems
STG	standard treatment guideline
TB	tuberculosis
USAID	US Agency for International Development
WHO	World Health Organization

01 INTRODUCTION

OVERVIEW

Today's advances in pharmaceutical development mean that more often than not, a medicine exists that will help patients recover from minor injuries, prevent or treat infections and other acute diseases, or manage a long-term health condition. With the shift from a disease landscape that focuses on the treatment of acute and short-term illnesses to one that faces an increasing burden of chronic diseases that may require life-long medicine use, the role of medicines in ensuring a healthy population is more important than ever.

However, as former Surgeon General C. Everett Koop noted, medicines "don't work in patients who don't take them."[1] Even when medicines are available, patients may not take them as directed. In other words, they may not adhere to the treatment prescribed to them.

This problem is surprisingly widespread. Several studies have estimated that in developed countries, only approximately 50% of patients who suffer from chronic diseases take their medicines as directed.[2] Although data are limited, adherence likely presents a greater challenge in low- and middle-income countries given the widespread resource and capacity challenges faced by most health systems.[3]

While much research has focused on the role of the patient, adherence is ultimately determined by many factors and barriers that interact at different levels. These include social and economic factors, factors related to the disease and treatment, and factors related to the health system itself. There is growing recognition that strong health systems help to create an enabling environment that makes it easier for patients to follow the treatment prescribed by their provider.[4] However, few comprehensive, system-based approaches (i.e., those in which the patient, health care provider, community, health facilities, and health system are all recognized) have been adopted.

PURPOSE OF THIS DOCUMENT

This document suggests a health systems strengthening (HSS) approach to addressing medication adherence issues, with a particular emphasis on its application in low- and middle-income settings. Chapter 2 reviews the importance of considering health systems in improving medication adherence and introduces a system-based framework, while Chapters 3–5 discuss approaches, interventions, and activities that span the health system as described at the macro, meso, and micro levels and provide implementation examples.

Specifically, the objectives of this document are to:

- Provide a rationale for HSS approaches to address challenges related to medication adherence

- Describe appropriate adherence strategies and tools with an emphasis on those that are relevant for resource-limited settings

This document is primarily intended for policy makers, program managers, government stakeholders, implementing partners, donors, and health managers involved in improving medication adherence. However, as the World Health Organization's (WHO) publication *Adherence to long-term therapies: Evidence for action* notes, "adherence is a multidimensional issue where different health care actors' efforts meet." Therefore, this document also includes relevant information for health care providers, opinion leaders, advocates, community networks, and consumer organizations.

DEFINING ADHERENCE

Compliance, adherence, and concordance all describe how well a patient is able to follow a regimen or recommendations from a health care provider. Although these terms are used interchangeably at times, *adherence* is the most widely accepted term. WHO defines adherence as "the extent to which a person's behavior—taking medication, following a diet, or executing lifestyle changes—corresponds with agreed recommendations from a health care provider."[5] While the definition of adherence includes a health care provider's dietary or behavioral recommendations, for the purposes of this document, we use the term adherence to primarily refer to the extent to which a person takes medication as prescribed by their health care provider, which is also known as *medication adherence*.[6]

Medication non-adherence occurs when patients are unable to take medication or do not adhere to treatment as directed by a health care provider. There are two broad categories of non-adherence. *Primary non-adherence* occurs when patients do not get their initial prescriptions filled, while *secondary non-adherence* occurs when patients do not to take their medicines as recommended.[7] Secondary non-adherence can be further delineated into unintentional and intentional non-adherence. In the former, patients want to follow their treatment regimen but cannot because of barriers that are beyond their control. In the latter, patients voluntarily decide to stop or change their treatment regimen.[8] Non-adherence can also refer to patients who take too much medication (overuse) or use medicines inappropriately, without a prescription, or when medicine use is not indicated (misuse).

Patients can vacillate between unintentional and intentional non-adherence based on a variety of factors, including whether cues for action, such as reminders to take medicine, are in place; the patient's health motivation; and the patient's perception of his or her susceptibility to the illness, the severity of

Table 1. Types of Non-adherence and Example Barriers

Type of Non-adherence		Example Barrier to Adherence
PRIMARY Prescription not filled		Medication cost
SECONDARY Medicines not taken as recommended	**Unintentional** Stops or changes regimen due to barriers beyond patient's control	Travel
	Intentional Patient voluntarily stops or changes regimen	Adverse medicine reaction

the illness, the benefits of treatment, and the barriers to adherence.

Because many medicines, especially those used for long-term or chronic conditions, are usually taken outside a health facility and away from the supervision of a health care provider, adherence is often measured through indirect methods that can introduce measurement biases and errors. The most common ways of measuring adherence include pill counting, electronic monitoring, and self-reporting.[9]

THE EFFECT OF ADHERENCE ON HEALTH

Non-adherence to medicines and treatment regimens is a critical modifier of treatment efficacy, the achievement of optimal health outcomes, and ultimately, the effectiveness of health systems.[10] The effects of non-adherence are particularly relevant for chronic and long-term health conditions, including human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), tuberculosis (TB), diabetes, hypertension, depression, and other chronic conditions for which medicines must be taken over long periods as a part of effective disease management.[11] Chronic diseases are the leading cause of death worldwide, and the global burden is expected to increase, especially in developing countries where 79% of all chronic disease deaths occur.[12]

The Challenge of Non-adherence

For patients, non-adherence may lead to a number of negative health outcomes (box 1). For example, patients with hypertension who take their medicines less than 20% of the time are twice as likely to be hospitalized as those who take their medicines at least 80% of the time.[13] Similarly, several studies of diabetes patients have shown that non-adherence to treatment leads to suboptimal health outcomes and significantly increases mortality rates.[14,15]

Box 1. Potential Patient-level Outcomes of Medication Non-adherence

- Worsening the overall course of illness
- Decreasing a patient's responsiveness to treatment
- Increasing the risk of treatment failure and relapse
- Increasing the risk of antimicrobial resistance
- Increasing the risk of toxicity or of dependence on medicines (in cases of overuse)
- Increasing the likelihood of adverse effects (in cases of misuse)

Non-adherence is a challenge in every country, regardless of income; however, weak health systems, limited resources, and shortages of qualified health professionals in low- and middle-income countries are additional barriers to adherence. In some countries, the percentage of non-adherent patients is greater than the percentage of adherent patients, which makes it critical for policy makers, program managers, and health providers to consider and account for non-adherence in planning, implementing, and care giving.[16]

Particular populations that are at an increased risk for medication non-adherence include the elderly, marginalized or underserved populations, children, and adolescents.[17] These populations face unique barriers to adherence that should be addressed in health systems and by providers. Studies have shown that between 40% and 75% of elderly people do not take their medications at the right time or in the right amount.[18] This may be the result of having multiple health conditions, taking multiple medications, receiving care from multiple providers, and/or having physical or cognitive issues. Additional unique barriers are faced by children (who require an adult to

remember and appropriately administer medications); adolescents (who experience many social, physical, and psychological changes as they become older); and marginalized populations (which may face additional economic, social, or stigma-related barriers to adherence).

Beyond the consequences for individuals, non-adherence also negatively impacts the larger health system. Medication non-adherence contributes to medicine waste and can lead to additional medicines being prescribed and/or additional laboratory tests, visits to health care providers, and hospitalizations. It can also lead to treatment failure and the development of antimicrobial resistance. Non-adherence also results in a heavy financial burden for health systems and governments, contributing 57% of the avoidable costs due to suboptimal medicine use.[19]

Better Adherence, Better Health, Lower Health Care Costs

Access to medicines and advances in biotechnologies alone are not sufficient to bring about good treatment outcomes. Strong systems to monitor and improve medication adherence are also critical.[20] A systematic literature review by Boswell et al., found that adherence to medication positively affected the health outcomes of patients suffering from 12 diseases that were reviewed, including cardiovascular diseases, diabetes, and mental illnesses.[21] Several studies have also demonstrated that better medication adherence reduces emergency visits, hospital admissions, the overall number of medicines prescribed, and mortality rates.[22,23]

In addition, improved adherence reduces health care costs. For example, 4.6% of to-

tal global health expenditures, or USD 269 billion, could be eliminated through better medication adherence.[24] The following examples provide additional evidence of the effect of adherence on health care costs.

- A pharmacy-based, in-person management program yielded a return of about USD 3 for each USD 1 invested.[25]

- For patients with diabetes, hypertension, hypercholesterolemia, or congestive heart failure, hospitalization rates and health care costs were significantly lower for those with high medication adherence.[26]

- For patients with diabetes, every 10% increase in adherence has been linked to a 4% decrease in total medical costs.[27]

- A Blue Cross Blue Shield study on medication therapy management reported a 12-fold return on investment from a medication therapy management service. This service included the development of patient medication records, a review of medicine use, collaboration with nurses or physicians, and follow-up.[28]

Because of the significant modifying effect adherence can have on treatment outcomes, it must be a critical consideration for any major global health effort, including creating an AIDS-free Generation, Ending Preventable Child and Maternal Deaths, Protecting Communities from Infectious Diseases, Goal 3 of the Sustainable Development Goals (Good Health and Well Being), and the Global Health Security Agenda.

02 ADHERENCE FROM THE HEALTH SYSTEM PERSPECTIVE

Although significant research has been devoted to assessing ways to help patients adhere to treatment, surprisingly little has focused on the role of the health system in promoting and creating an enabling environment for medication adherence. WHO defines a health system as "all organizations, people and actions whose primary interest is to promote, restore or maintain health." A health system can be viewed through six building blocks or core functions (figure 1): leadership and governance, financing, health workforce, medical products and technologies, information and research, and service delivery.[29] The US Agency for International Development (USAID) uses a similar framework to guide its vision for HSS by referring to system building blocks as HSS core functions.[30] Throughout this document, we refer to these aspects of the health system as core functions.

The core functions act across three levels of the health system (macro, meso, and micro; see box at right) to affect adherence in several different ways, including determining the number, level, and quality of health facilities; distribution of human and financial resources, and availability of systems to collect and use health-related information. Without functioning facilities, available medicines, qualified health personnel, current and accurate information, and other system-level enabling factors, achieving and maintaining adherence becomes difficult even before the patient has received a prescription.

The distinction between the macro, meso, and micro levels is not always clear cut, and each level interacts with and influences the other two.[32] Table 2 provides examples of

THREE HEALTH SYSTEM LEVELS[31]

- The **macro** level refers to the national health care system, where the focus is on policy development and high-level leadership.

- The **meso** level refers to the local health system, where the focus is on organizing and managing health care that responds to local needs and circumstances.

- The **micro** level refers to the interaction of individuals in the health system, including patients, health care providers, and health managers.

predictors of non-adherence at each level of the health system using findings from Nigeria, Ethiopia, Mozambique, South Africa, and Uganda.

Just as each level of the health system influences adherence, the core functions of a health system—service delivery, health workforce, health information system, medical products and technologies, health financing, and leadership and governance— also contribute to creating an environment that is conducive to achieving medication adherence. Taken together across each level of the health system, these core functions make up the environment in which patients

Figure 1. The WHO health system framework

System building blocks

- Leadership/governance
- Health care financing
- Health workforce
- Medical products, technologies
- Information and research
- Service delivery

Access Coverage

Quality Safety

Goals/outcomes

- Improved health (level and equity)
- Responsiveness
- Financial risk protection
- Improved efficiency

Source: World Health Organization. Everybody's Business: Strengthening Health Systems to Improve Health Outcomes. WHO's Framework for Action. Geneva: WHO; 2007.
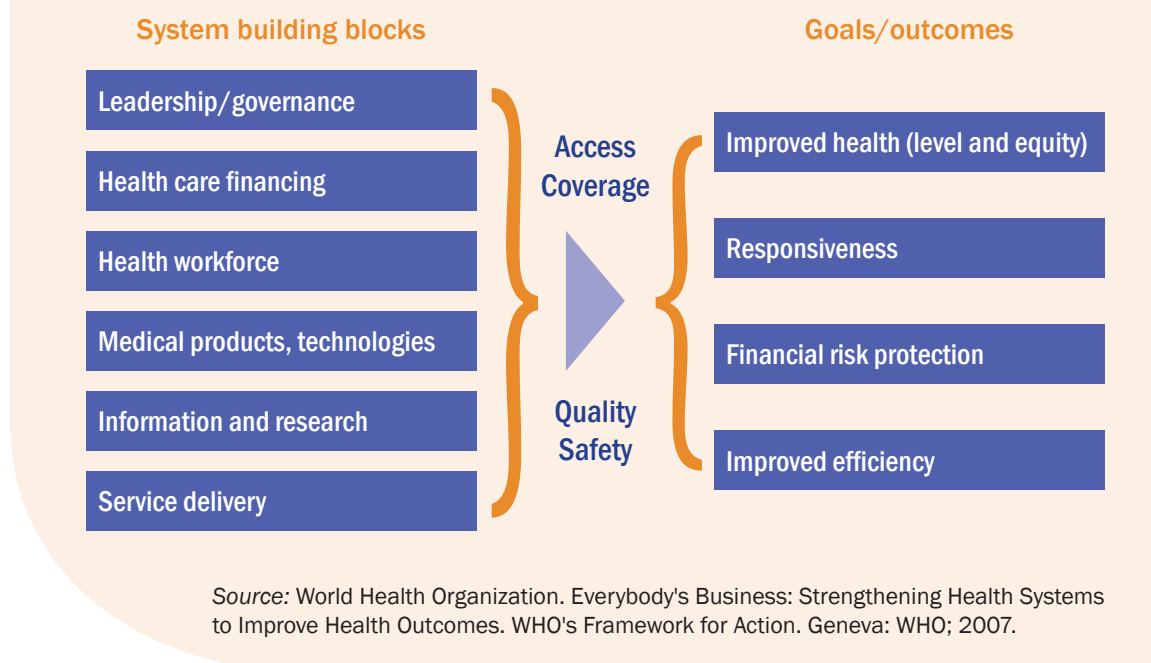
Table 2. Select Predictors of Medication Non-adherence at Each Level of the Health System Based on Studies from Nigeria, Ethiopia, Mozambique, South Africa, and Uganda [33,34,35,36,37, 38,39,40,41,42,43]

Health system level	Predictors of non-adherence
Macro	• Limited health care coordination • Limited access to care and treatment • High medication costs and copayments • Inadequate remuneration and high staff turnover
Meso	• Inadequate communication among health care providers • High patient load and long waiting times • Poorly organized patient tracking and record systems • Little consideration of the patient's financial burden
Micro	• Lack of involvement in the treatment decision-making process • Suboptimal medical literacy • Health beliefs and attitudes concerning the effectiveness of treatment • Lack of motivation • Economic constraints • Lack of social support • Pill burden • Prescribing complex treatment regimens • Ineffective communication between provider and patient • Stigma associated with disease • Patient's formulation preference and acceptability

receive care and ultimately shape many of the determinants that help enable or deter medication adherence.

LEADERSHIP AND GOVERNANCE

While there is growing recognition that the burden of adherence does not rest solely on the patient or provider, there has been relatively little discussion on the extent to which legal frameworks, including legislation, regulations, and national medicine policies, affect medication adherence. Without sufficient funding, resources, or a political commitment provided through high-level governance and leadership structures, the systems that support and create an enabling environment for medication adherence are likely to be neglected, eroded, or nonexistent. The inclusion of medication adherence in a national health strategy or national medicine policy helps direct additional attention, funding, and resources to address both adherence and the many issues that influence it, including medicine availability, equity of health services, human resources for health, and information systems.

HEALTH WORKFORCE/HUMAN RESOURCES

There are many drivers of and contributors to medication non-adherence, but few have a greater direct impact than the interaction between the patient and the provider. Patient counseling, education, and follow-up are all critical in supporting and enabling patients to adhere to their prescribed treatment, as are the upstream determinants that dictate the level, quantity, and distribution of health care providers; how performance and quality are monitored; and the extent to which providers have been trained to address adherence. Addressing human resource shortages, setting quality standards for service delivery, and implementing trainings on adherence all happen at the macro or meso level but

have a direct impact on a provider's ability to support patient adherence at the micro level.

INFORMATION AND RESEARCH

Even when providers are appropriately trained and have sufficient time for patient counseling and other adherence-supporting interventions, many low- and middle-income countries lack the clinical and behavioral tools needed to evaluate or address adherence issues. In addition, patient registers, appointment-keeping systems, and other information systems, which can support better patient follow-up and improve adherence, are often missing or unused in low-resource settings. Additional research is needed both to improve the use of information systems and to look beyond interventions that show positive signals within the constraints of a clinical trial or research study. These interventions should expand operational research into multidimensional, multilevel programs that may contribute to the long-term sustainability of improved adherence.

FINANCING

Financing policies set at the macro or meso level significantly influence adherence levels by determining the affordability of medicines and health services and allocating resources for staffing, information systems, education and training programs, and research. Medicines prices, fee-for-service or copay models for health services, and resources to support the implementation of adherence-related strategies all dictate the capability of both patients and providers to support better medication adherence.

SERVICE DELIVERY

Adherence is also influenced by where patients receive their medicines and how those medicines are provided. Patients may have access only to a small, local drug

shop or they may receive medicines from a trained pharmacist at a health facility or hospital. Access to well-regulated, high-quality pharmaceutical services can help ensure that patients are receiving up-to-date and relevant medication information, foster patient trust in the health system, support patient follow-up, and create an enabling environment for improved medication adherence. At health facilities and hospitals, improved models of care that integrate pharmacists and prescribers as part of the health care team and emphasize pharmacist counseling can help prevent or mitigate medicine use issues, improve team work and collaboration across the health care team, and support better medication adherence.[44] Efforts to improve access to pharmaceutical services, strengthen connections to community resources and groups, improve provider-patient interactions, and simplify medication regimens are all key factors in supporting improved adherence.

MEDICINES AND HEALTH TECHNOLOGIES

Ensuring a continuous supply of and improving access to safe and effective medicines of assured quality helps to improve adherence by reducing stock-outs that can interrupt or dissuade patients from continuing treatment, reducing medication issues associated with substandard or falsified medicines, and ensuring continuity of treatment across providers and facilities. Regulatory systems strengthening is critical to improving key functions that help ensure the safety and quality of medicines. These include product registration, inspection and licensing of pharmacies or drug shops, quality testing, and medicine safety monitoring (also known as pharmacovigilance). Without a strong regulatory system, patients may receive falsified or substandard medicines that have additional side effects, do not effectively treat their condition, or worsen their health. These outcomes negatively impact patient adherence, erode trust in the health system, and contribute to the development of antimicrobial resistance.

Table 3 shows adherence-related efforts according to health system levels and by health system core functions. The relationship between adherence and the core functions of the health system is explored in additional detail in Chapter 3 (*macro* level), Chapter 4 (*meso* level), and Chapter 5 (*micro* level). At the end of each chapter, a case study is provided that explores interventions spanning multiple core functions and health system levels. These case studies encompass a systems-strengthening approach to improving medication adherence in the practical application of an intervention.

Table 3: Adherence-supporting Policies, Strategies, and Interventions According to Health System Core Function and Health System Level

Health system core function	Policies, strategies, and interventions	Health system level (macro, meso, or micro)
Leadership and governance	• Include adherence-supporting statements in national medicine policies and strategies	• Macro
	• Interdisciplinary learning (e.g. from HIV/AIDS programs) to help manage other chronic conditions	• Macro (also meso)
	• Team-based approaches to care	• Meso
Human resources	• Addressing human resource gaps (e.g., through task shifting)	• Macro
	• Systematic capacity building for health providers	• Meso (also macro)

Health system core function	Policies, strategies, and interventions	Health system level (macro, meso, or micro)
Information and research	• Applied research (e.g., assessing new measures of adherence, cost-effectiveness of improving adherence)	• Macro (also meso)
	• Use of appropriate tools, technologies, and techniques to assess and enhance adherence (e.g., appointment systems)	• Meso (also macro)
Financing	• Financing policies that promote medication adherence	• Macro
Medicines and health technologies	• Equitable access to and use of safe and effective medicines of assured quality	• Macro (also meso)
Service delivery	• Improved access to services	• Macro (also meso)
	• Create incentives and enablers	• Macro (also meso)
	• Improved provider-patient relationship and interactions	• Micro
	• Simplified medication regimens	• Micro
	• Patient support at home and in the community	• Micro (also meso)

HEALTH SYSTEMS STRENGTHENING FRAMEWORK TO IMPROVE ADHERENCE

To optimize adherence, multidisciplinary and multilevel approaches are necessary.[45] For an intervention to be truly multilevel, it must consider barriers at all levels of the health care system and across relevant core functions.

To help conceptualize how health system-level intervention can support optimal medication adherence, the USAID-funded Systems for Improved Access to Pharmaceutical and Services (SIAPS) Program developed a framework that depicts health system strategies at the macro, meso, and micro levels to support medication adherence and improve clinical outcomes (figure 2). The framework is encapsulated within the core functions of the health system to reflect how these functions underpin strategies at the macro, meso, and micro levels.

Figure 2. SIAPS health systems-strengthening framework to improve medication adherence
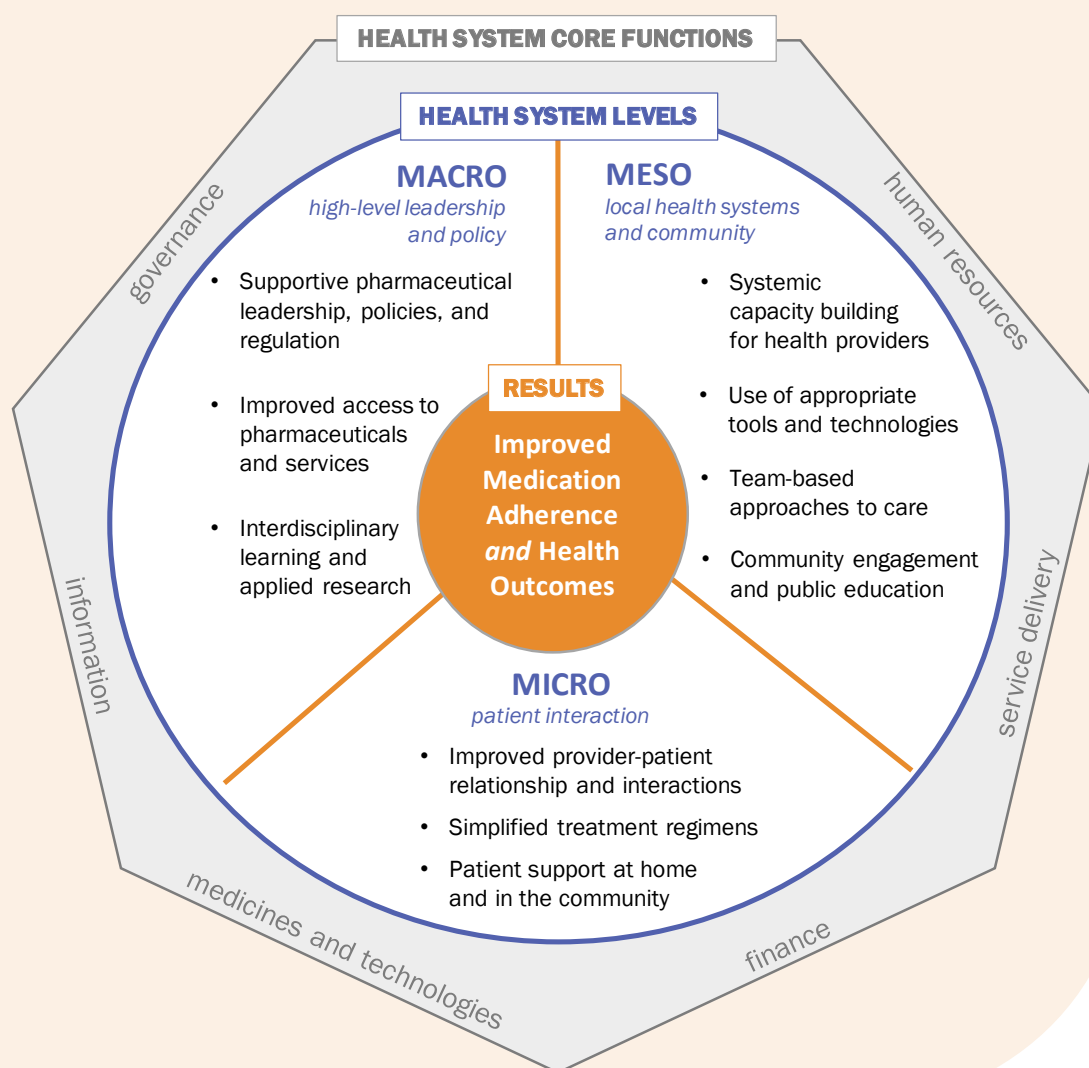
CHAPTER SUMMARY

Although much research has been devoted to helping patients improve individual adherence levels, the systems that support medication adherence have received less attention. A systems-oriented approach requires that the challenge of medication adherence be considered across the three levels of the health system (macro, meso, and micro) and through the lens of each of the core functions of a health system (leadership and governance, health workforce, information and research, financing, service delivery, and medicines and health technologies). By approaching medication adherence from the health systems perspective, interventions go beyond addressing challenges at the patient or provider level and instead are rooted within the larger operating context and aim to create an enabling environment that supports long-term adherence.

03 INITIATIVES AT THE MACRO LEVEL OF THE HEALTH SYSTEM

At the macro level, initiatives to support medication adherence are closely tied to the core functions of governance and medicines and health technologies and primarily focus on improving national policies, guidelines, and regulations that improve medicine availability and use. These initiatives require broad and extensive advocacy and partnerships, improvements to pharmaceutical systems and supply chains, and supportive policies that promote adherence. Financing allocations and policy decisions at the macro level also have a direct impact on factors that influence adherence at the meso and micro levels. In addition, barriers to adherence faced by HIV/AIDS programs and the innovations that were developed as a result can shed light on strategies that may be useful for chronic and noncommunicable diseases. Investing in applied research can also help address adherence-related issues.

MACRO
High-level leadership and policy

- Supportive pharmaceutical leadership, policies, and regulations

- Improved access to pharmaceuticals and services

- Interdisciplinary learning and applied research

enablers, and addressing gaps in human resource skills and allocation can create an enabling environment for improved medication adherence.

SUPPORTIVE PHARMACEUTICAL LEADERSHIP AND POLICIES

The inclusion of adherence and medicine use considerations in high-level policies, strategic plans, and other key governance documents helps foster a common vision and way forward for all stakeholders involved in providing or managing patient care. These high-level commitments from national governing bodies also help to define national health priorities and direct financial and human resources to activities that can help improve adherence. In addition to including adherence-supporting language in national medicine policies and health strategies, developing appropriate financing policies, creating systems for incentives and

Medicine Policies and Other Key Guidance Documents

A *national medicine policy* is a common framework that addresses all aspects of the pharmaceutical sector, including access, quality, and rational use of essential medicines. Including adherence-related statements in key national-level guidance documents helps mandate and drive adherence-related strategies, programs, and activities. The WHO manual on developing and implementing national medicine policies includes language in support of medication adherence.[46] The Afghanistan National Medicines Policy 2014–2019 emphasizes medication adherence at several points in the document.[47] Similarly, the Malaysian National Medicines Policy of 2012 highlights

Figure 3: Informational poster developed by South Africa's National Department of Health to inform patients about a new FDC antiretroviral treatment.
Image credit: South Africa Department of Health

medication adherence as a key area of focus to support health literacy and empower consumers to better manage their medicines.[48] Other national-level policy documents are also critical for paving the way for improved adherence. For example, many countries are beginning to develop national action plans on antimicrobial resistance that may serve as an opportunity to include language on adherence as it relates to efforts to improve medicine quality, dispensing and prescribing practices, and regulatory functions.[49,50] National- or facility-level standard treatment guidelines (STGs), which reflect the recommended treatment course for a variety of medical conditions, can also help promote adherence by standardizing treatments.[51] Up-to-date STGs help ensure that patients receive the most appropriate treatment for their condition. Similarly, essential medicines lists (EMLs) contribute to the selection and use of effective, safe, and cost-effective medicines. Without STGs and EMLs, patient

may be prescribed medications that are more expensive, have more side effects, or are less effective, all of which are key factors that can negatively impact adherence.

Other high-level policy decisions can also create an environment that is conducive to better medication adherence. For example, in South Africa, the National Department of Health made a national policy decision and began rolling out fixed-dose combination (FDC) antiretrovirals (ARVs) to the public sector in 2013 in an effort to reduce pill burden, side effects, and treatment costs. Referred to as *one pill a day*, the FDC is a combination of three ARV medicines—tenofovir, efavirenz, and emtricitabine (figure 3). A meta-analysis conducted by Ramjan et al., found that FDC regimens, such as the one implemented in South Africa, resulted in better adherence and a tendency for greater virological suppression among patients compared to separate tablet regimens.[52]

Financing Policies

Multiple studies have found an inverse correlation between medication adherence and health care costs. For example, one study found that patients with a lower copay were more likely to refill medications for antihypertensive treatment.[53] In a similar study, increases to out-of-pocket expenses doubled the risk of interrupting statin therapy and showed that higher copays were associated with poorer adherence outcomes.[54]

The high costs of medicines and health care, combined with transportation and opportunity costs for clinic visits, are important contributors to non-adherence in developing countries.[55] Because more than 70% of medicine expenditures are paid out-of-pocket in low-income countries, selecting, procuring, and prescribing more affordable generic medicines that meet therapeutic needs can help reduce the financial barriers to adherence.[56,57] Additional evidence has shown that reducing out-of-pocket expenses can improve patients' medicine-taking behavior.[58]

Policies that promote medication adherence by reducing copays or other expenses may be very cost effective.[59] Recent widespread recognition of and growing commitment to universal health coverage is expected to increasingly contribute to improved and affordable access to essential medicines and reduced out-of-pocket expenditures.

One study found that for each dollar increase in a patient's copay, adherence is expected to decrease by 0.4%.[60]

In many low- and middle-income countries, people in rural areas are geographically removed from health services and pharmacies. Accessing these services requires significant time and money, which increases the financial strain and the time away from work and family. Subsidizing travel costs, delivering medicines directly to the community through home-based care models, and establishing neighborhood medicine dispensaries are examples of interventions that could be supported by financing policies to help overcome geographical barriers and improve access to medicines.[61]

Incentives and Enablers

Many health programs and projects have taken the lead in introducing incentives and enablers to motivate both health care providers and patients. An *incentive* is a stimulus or small reward designed to encourage a particular behavior, such as following-up with patients, taking medicine as prescribed, or keeping appointments.[62] For example, a health facility may provide food baskets as an incentive to patients who come to their appointments.[63]

A pilot study in Rwanda found that in antiretroviral therapy (ART) facilities that received financial incentives, health care providers were more motivated and creative in their approaches to ensure that patients kept their appointment dates.[64] In Zambia, a pilot study of food supplementation was implemented to improve ART adherence. Box 2 briefly discusses the key findings of this study.

An *enabler* is something given to a patient or provider that makes it possible, practical, or easy to behave in a certain way. For example, a health facility may provide transportation

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Box 2. A Pilot Study of Food Supplementation to Improve ART Adherence in Lusaka, Zambia[65]

The Zambian Ministry of Health implemented a home-based adherence support program in Lusaka in 2004 as part of a national program to support HIV care and treatment. In this program, patients were assessed for food insecurity at eight government clinics. Four clinics provided patients with monthly rations of micronutrient-fortified oil, maize meal, and beans, while the remaining four did not provide food supplementation.

Findings from the study suggest that providing food supplementation to food-insecure adults initiating ART improves adherence. Adults who received food supplementation were 50% more likely to be adherent than were those in the control group.

In the context of a home-based adherence support program, this study demonstrated that it is feasible to provide low-cost, locally available foods to food-insecure adults initiating ART, and doing so may improve medication adherence. Food insecurity is a reality for many ART patients in resource-limited settings, and nutrition should be considered a key component of integrated HIV care and treatment.

vouchers to make it easier for people to keep their appointments.[66] Other examples include:

- In the Czech Republic, vouchers worth 4 to 5 euros are offered to homeless and other vulnerable populations after a TB diagnosis. As a result of this program, case detection among the homeless population receiving incentives was five times higher than among the general homeless population.[67]

- A pilot program in Romania provided patients with travel support to attend a TB clinic for one year. Adherence increased to 95% during the program and decreased to 80% after the program ended.[68]

Incentives and enablers should be customized to the needs and interests of patients to support adherence. Enablers should be provided to patients as soon as treatment is initiated, and incentives should be used once the patient and provider have established a good relationship. While the evidence base on incentives and enablers is limited, their potential role has been described in literature reviews, surveys, and mapping workshops.[69]

Human Resources and Capacity Building

Many low- and middle-income countries are attempting to scale up chronic and non-communicable disease treatment programs while facing a dearth of qualified health professionals. As a result, country govern-ments are working to develop policies to both address and adapt to human resource shortages through task shifting and other strategies.

WHO defines task shifting as "the rational redistribution of tasks among health workforce teams." Specific tasks are reassigned, where appropriate, from highly

Box 3. Task Shifting Helps Reduce Loss to Follow-up in an HIV Treatment Program in Lusikisiki, South Africa[72,73]

Lusikisiki is considered one of the poorest and most densely populated rural areas of South Africa, where one hospital and 12 clinics serve a population of 150,000. There are only five physicians per 100,000 people, and approximately 50% of all nurs-ing posts are vacant. A lack of support staff burdens nurses with heavy workloads. Because the subdistrict has both a severe shortage of health workers and a high prevalence of HIV, health facilities have integrated HIV treatment into primary health care and adopted task shifting as a way to scale-up treatment.

Lower-level health care workers were given additional responsibilities. At the same time, quality control measures were put in place to ensure appropriate medical oversight. Primary health care nurses and community health workers were trained, mentored, and supervised to keep the ART program running. Nurses, in particular, were trained on HIV management, management of opportunistic infections, ART, and patient management skills (e.g., examining patients, taking histories, and counseling).

Table 4 compares the roles of various categories of health professionals before and after task shifting was introduced. Shifting tasks and providing training and mentoring to support workers has made it possible for the clinic to continue offering HIV services.

Table 4. Traditional and Revised Roles of Health Care Providers in the Lusikisiki Program

Category	Traditional role	Role in the Lusikisiki program
Physicians	Conduct patient consultations, including opportunistic infections, staging, and initiation	Conduct mobile visits to see challenging cases; supervise clinics and mentor nurses and counselors; serve as part of a multidisciplinary team
Pharmacists	Manage medicine supply; oversee prescriptions	Mentor pharmacist assistants
Nurses	Support physicians; conduct voluntary counseling and testing; prepare individuals for ART; monitor ART patients; collect data; manage medicine supply; supervise community caregivers	Manage opportunistic infections; perform clinical staging; initiate and monitor ART; supervise clinic staff; manage medicine supply; supervise adherence counselors
Adherence counselors	Not used	Prepare individuals for ART; empower ART recipients; run ART support groups; collect data for ART register; mentor community caregivers; track individuals who default
Pharmacist assistants	Not used or have a limited role (dispense medicines only under strict pharmacist supervision at the hospital)	Manage medicine supply; dispense medicines; monitor adherence; identify individuals who default
Community caregivers	Promote health; directly observe treatment (including recall of patients who default)	Run HIV support groups
Support groups, committees, activists, people with HIV/AIDS	Not used	Prepare individuals for and monitor adherence to ART; promote health in the community; recall individuals who default; address bottlenecks; advocate for better service delivery

The number of people utilizing the program nearly doubled over a two-year period. While workloads increased to accommodate more patients, the number of professional nurses (n=30) remained the same. This strategy allowed for the rapid scale-up of ART in a short period and led to positive outcomes. Only 2% of people were lost to follow-up at the clinics, compared to 19% of people at the hospital, where task shifting was not implemented.

trained health workers to those who require less training and fewer qualifications to more efficiently use the available human resources for health.[70] Task shifting has been successfully used in resource-limited settings, such as South Africa (box 3).[71]

IMPROVED ACCESS TO MEDICINES AND PHARMACEUTICAL SERVICES

Access to treatment and care and the availability of medicines both influence medication adherence. Some patients travel long distances to reach a health facility and wait

many hours to be seen by a health care provider. A study in rural India found that more than 50% of patients surveyed traveled more than 200 kilometers to reach a health facility.[74] Likewise, in rural Botswana, patients have reportedly waited up to 12 hours to receive care.[75] Once patients arrive at the health facility or pharmacy, there often is no guarantee that the medicine they need will be in stock or will be of assured quality, which impedes treatment and erodes confidence and trust in the health system.[76]

Of 91 low- and middle-income countries surveyed in 2008, 34% had experienced at least one stock-out of a required ARV medicine.[77]

In addition, according to WHO, 45% of high-burden countries reported stock-outs of first-line TB medicines at the central level in 2007, compared to 9% of these countries in 2006. At the peripheral level, 41% of high-burden countries reported stock-outs of first-line TB medicines in 2007, compared to 27% of countries in 2006.[78]

Government initiatives should aim to improve access to medicines and health services. Potential interventions include:[79,80]

- Strengthening quantification and procurement systems to ensure the availability of medicines

- Establishing or strengthening pharmacovigilance systems to monitor medicine quality, safety, and therapeutic effectiveness[81]

- Setting up mobile care and treatment services to visit patients for whom travel to the clinic is not practical or feasible

- Providing transport coupons or reimbursing travel costs for patients who travel long distances or incur significant financial expense to reach a health facility

- Integrating health services to reduce the need for multiple trips to different facilities

- Dispensing medicines at two or three monthly intervals to reduce the number of times a patient has to travel to the health facility

Box 4: Community Medicine Distribution in Tanzania and Uganda[82]

In 2007, in response to a health care provider shortage, the Ministry of Health in Tanzania began implementing community medicine distribution to help reach ART patients in rural areas, including the Babati District in the northern part of the country. Between hospital visits, patients could visit the mobile clinic to receive medications, contraceptives, and education regarding ART and HIV management. By 2010, nearly 2,500 patients were served via the mobile clinic, and more than 200 health care workers had been trained to support the effort.

The community distribution program expanded to Uganda, where 77 community distribution centers had been established by 2010. The AIDS Support Organization conducted a study in the Ugandan distribution centers and found that only 1% of participants were lost to follow-up. Patients noted that they were able to share their experiences and discuss side effects with their providers, volunteers, and other patients in the mobile clinic. Enlisting the help of HIV-positive patients in the community created awareness about the new service and reduced the stigma of HIV/AIDS.

- Setting flexible clinic hours to accommodate patients who may prefer to come before or after work

Box 4 describes how the expansion of community medicine distribution in Tanzania and Uganda has increased access to HIV/AIDS medicines and information in the community.

To bring health services closer to the community and patients, South Africa developed a decentralized ART distribution system by supporting treatment down-referral. The USAID-funded Strengthening Pharmaceutical Systems (SPS) Program worked with the South African Government and other stakeholders to refer stable ART patients from hospitals to primary health care clinics while maintaining a centralized dispensing unit at the hospital.[83] Based on the prescriptions, pharmacists at the hospital's central dispensing unit prepare packages of medicines for individual patients that are delivered to the clinic closest to that patient.

In addition to reducing the patient load for the hospital's pharmaceutical service, this strategy also reduces transportation costs for patients and brings services closer to a patient's home. To support this transition, SPS helped develop policies and procedures for down-referral and a computerized dispensing system at the central dispensing unit. At the clinic, health care providers dispense the ARVs and review treatment progress. The clinic then returns progress reports and uncollected medication to the hospital. The system worked so well for ART patients that it was expanded to include patients needing long-term treatment for mental illnesses and other chronic diseases.

In Uganda, Tanzania, and Liberia, efforts to accredit drug shops have increased the availability of medicines in rural areas, where the nearest health facility may be several hours away. In Uganda, the Accredited Drug Seller Initiative, with support from the Bill and Melinda Gates Foundation, was able to broaden access to family planning services by training 479 drug sellers to improve counseling to women, provide supportive supervision, and increase the use of patient registers. The program increased access to family planning services for 12,000 family planning clients in four districts between July 2012 and May 2013. During that time, more than 7,191 cycles of oral contraceptives were dispensed. In addition, a baseline evaluation showed that at the start of the intervention, 70% of accredited drug sellers carried oral contraceptives. By the end of the intervention, that number rose to 93%.[84]

INTERDISCIPLINARY LEARNING AND APPLIED RESEARCH

As models of care shift from management of acute diseases to those that can better accommodate and manage long-term chronic conditions, learning from previous program implementation efforts and conducting additional research will be necessary to advance the most effective and sustainable models of care.

Interdisciplinary Learning

HIV/AIDS programs in many countries have already been adapting to long-term treatment requirements to support major control efforts such as the 90-90-90 initiative, which aims to ensure that by 2020, 90% of people living with HIV will know their status, 90% of those diagnosed will receive sustained ART, and 90% of all people on ART will achieve viral suppression. These and other efforts offer distinct learning opportunities and can provide potential best practices.

The response to the HIV/AIDS epidemic has provided treatment and care to millions of people around the world. This response was backed by activism, country leadership, donor funding, community engagement, and health worker empowerment.[85] Several programmatic strategies were employed to deliver clinical services to millions of people in need (table 5). The dedicated resources

and intense focus on advancing AIDS treatment and intervention programs around the world offer ample opportunity to translate the lessons learned to other diseases that face similar challenges and barriers to adherence.[86,87,88,89]

Table 5. Programmatic Strategies for Tackling HIV/AIDS[90]

Strategy	Description
Multidisciplinary teams	• Establish multidisciplinary teams and add new health worker cadres • Enhance counseling, adherence support, patient education, and community outreach • Transform professional hierarchies, strengthen patient-provider relationships, and facilitate task shifting
Family-focused care	• Set up colocated, coscheduled appointments for family members • Coordinate adult and pediatric providers serving the same household • Link family medical records • Reach out to family members not yet engaged in care
Support for adherence and retention	• Establish appointment systems and onsite medical records • Enhance pharmacy systems and documentation • Institute patient support groups and defaulter tracking • Implement peer education
Involvement of people living with HIV, civil society, and stakeholders	• Mobilize communities • Generate demand • Engage civil society • Provide peer educators or supporters • Generate broad-based support for HIV services and new resources to tackle health threats
Monitoring, evaluation, and program design	• Establish explicit targets and publicly report results • Introduce new data collection systems and cadres • Track indicators (e.g., cohort retention rates, interim outcomes, end points) • Maximize accountability and enable stakeholders to assess performance and compare facilities and partners
Task shifting	• Add new health worker cadres, such as counselors, peer educators, and data clerks • Leverage the skills of existing cadres by redefining scopes of practice
Community- and home-based care	• Establish a continuum of care from the hospital to the health center, community-based resources, and finally home-based care and support • Engage community-based organizations to provide counseling and care services • Train laypeople to support adherence and outreach • Engage associations of people living with HIV in community and encourage patient involvement
Health systems strengthening	• Implement disease-specific interventions designed to minimize a negative impact on other health programs and/or to support health systems more broadly

The lessons learned from HIV/AIDS programs can enhance the development of initiatives to prevent, manage, and treat chronic conditions in resource-limited settings.[91] Table 6 provides examples of innovations that have strengthened HIV/AIDS service delivery and can help to promote adherence.

Applied Research

There is a growing body of evidence that enables better understanding of medication adherence, but more research is needed to address systems-level determinants and sustainability as well as issues in daily practice, particularly in resource-limited settings. Health program planners, policy makers, and governments need to invest in research to identify effective, valuable interventions.

Potential areas of investigation include: [93,94,95,96,97]

- Standardized and uniform reporting measures of adherence

- New strategies to improve medication adherence

- The cost-effectiveness of medication adherence improvement interventions

- The influence of micro-, meso-, and macro-level health system factors on medication adherence

Table 6. Examples of HIV/AIDS Program Innovations[92]

Health system elements	Innovations
Stewardship	• Transparent targets • National framework and coordinating authority • Centralized monitoring and evaluation • Decentralized models of service
Financing and payments	• Performance-based financing • Elimination of user fees • Insurance schemes
Human resources	• Training and mentoring • Task shifting/sharing • Engaging people living with HIV
Infrastructure	• Renovations and repairs of clinical, counseling, laboratory, and pharmacy space
Commodities/supply chain	• Strengthening of procurement systems
Information/data	• Onsite medical records • Electronic medical records
Clinical services	• Family- and patient-focused care • Adherence counseling and support • Comprehensive primary care for people living with HIV
Provider and patient behaviors	• Multidisciplinary care teams • Use of counselors and peer educators • Adherence and psychosocial support • Stimulating demand for services

Table adapted from Rabkin M and El-Sadr WM. 2011. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases.

- Improved approaches to sustainable adherence management

- The long-term effects of electronic reminders on medication adherence

- The role of community leaders (e.g., parents, local officials, religious leaders) in influencing medication adherence

- Enlisting local structures (e.g., street committees, microcredit organizations) to enhance medication adherence

- The practicality and effectiveness of scaling up potentially promising interventions in large populations of patients

- The impact of incentives, reimbursements, and other provider and payer behaviors on adherence

- Pharmaceutical efforts to simplify regimens and improve adherence (e.g., polypills, longer-acting formulations)

Operational research supported by USAID in the Amazon region of South America between 2005 and 2009 highlights how conducting adherence studies informed policies for promoting adherence to malaria treatment. The Amazon Malaria Initiative (AMI) and the Amazon Network for the Surveillance of Antimalarial Medicine Resistance (RAVREDA) were established in 2001 to improve malaria control and treatment in countries of the Amazon Basin, including Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, and Suriname.

Resistance to antimalarial medicines was identified in the Amazon region in the late 1990s. In response, RAVREDA-AMI set out to improve the availability of antimalarial medicines and ensure their appropriate use by prescribers and patients. In 2004, studies of adherence from Colombia, Bolivia, and Ecuador demonstrated poor adherence

Figure 4. Graphic illustration of medicine instructions introduced by Ecuador's National Malaria Control Program

to treatment for uncomplicated malaria, particularly to the 14-day treatment regimen. The results helped to stimulate the demand for additional adherence assessments.

As a result, a standard protocol for assessing adherence to antimalarial treatment regimens for *P. falciparum* and *P. vivax* was developed. This methodology allowed studies across time and countries to be compared. Subsequent studies evaluating adherence were conducted in Brazil, Colombia, and Ecuador between 2005 and 2006. In Ecuador, findings from these studies prompted Ecuador's National Malaria Control Program to introduce a graphic illustration of the medicine instructions to show how many and which pills to take each day, how to use coblisters, and to provide staff training to improve adherence to treatment regimens (figure 4).

Similar studies in other countries led to the introduction of FDCs, prescriber checklists, and the use of media or materials at the community level to raise awareness.[98]

IMPROVING TREATMENT ADHERENCE TO TB MEDICINES IN BRAZIL[99]

TB is the fourth leading cause of infectious disease deaths in Brazil. In 2003, the government of Brazil declared TB an official public health priority and committed funding to combat its spread. Over the next nine years, Brazil's budget for TB control increased 14-fold.

The government of Brazil also introduced the Directly Observed Treatment Short Course (DOTS) to encourage adherence to TB treatment and implemented several additional initiatives aimed at providing incentives or enablers to support greater adherence. These initiatives included providing free passes for public transportation, a free meal to patients who show up to take their medication in direct observation therapy, and FDC regimens. The FDC, also known as 4-in-1, reduces the number of pills that patients must take.

The USAID-funded Rational Pharmaceutical Management Plus and SPS programs provided technical assistance to the government to promote the appropriate use of TB medicines in accordance with STGs and to make the transition to FDC regimens nationwide. Guidance, reference materials, and procedures for transitioning to the new FDC regimen were developed, including guidelines for determining quantification needs, monitoring prescriptions and treatment adherence, handling medicines, dispensing, and placing medicine orders. Targeted support was also provided to the DOTS Expansion and Supervision program for the state of Rio de Janeiro to strengthen DOTS within the community, establish transport logistics for supervision and regular data collection, develop the on-the-job capacity of health professionals in FDC management and rational medicine use, and support patient follow-up.

Brazil has since made considerable progress in controlling the TB epidemic. Between 1999 and 2010, the treatment dropout rate fell from 14% to 7%, nearly achieving the WHO target of 5%.

Efforts in Brazil illustrate how multilevel, multisectoral initiatives are required to improve treatment adherence. At the macro level, high-level policy decisions from the government and subsequent and sustained financial commitments paved the way for implementation changes at the meso level, which built the capacity of health professionals, strengthened supply chains for TB medicines, and bolstered information systems. These system-level changes supported improvements at the service delivery level, including ensuring the continuous availability of medicines and health care providers to better track and follow-up with patients who might otherwise be lost to follow-up.

CHAPTER SUMMARY

Decisions made at the policy level, delineated in key strategy documents, and implemented through strong leadership and standardized guidelines influence how well providers are able to support and address adherence issues with their patients and can directly affect a patient's ability to adhere to treatment. These policy decisions and implementation actions can facilitate the introduction of easier formulations, such as FDCs; may lower financial costs associated with care, such as user fees; and help determine how many health providers are available and appropriately trained to address adherence. The lessons learned from HIV/AIDS treatment programs, for example, can help guide initiatives to improve adherence, although additional operational research must also continue.

04 INTERVENTIONS AT THE MESO LEVEL OF THE HEALTH SYSTEM

Interventions at the meso level of the health system emphasize the local organization and management of the health care environment in which patients receive care. Cutting across all health system core functions, particularly human resources, information, and service delivery, meso-level interventions can improve adherence and health outcomes and include providing the proper training and tools to health care providers, engaging with communities, developing functional information and monitoring systems, and promoting team work across multidisciplinary teams. Building local capacity, expanding the use of information systems, and enhancing access to quality health care and pharmaceuticals are all central to addressing adherence at the meso level.

MESO
Local health systems and community

- Systemic capacity building for health providers
- Use of appropriate tools and technologies
- Team-based approaches to care
- Community engagement and public education

SYSTEMIC CAPACITY BUILDING FOR HEALTH PROVIDERS

Adherence initiatives are only effective when systemic capacity building efforts are instituted and providers at many different levels of the health workforce are equipped with the appropriate knowledge, skills, and tools (figure 5). Incorporating adherence-related topics into pre- and in-service training and strengthening the role of pharmacists in pharmaceutical care are important strategies to support medication adherence.

Competency-based Pre- and In-service Trainings

In a study of European medicine, pharmacy, and nursing institutions, 20% reported an absence of specific content on how to assess medication adherence in their curriculum.[100] To ensure that all health care providers have standard competencies in recognizing the signs of non-adherence and delivering interventions to encourage adherence, medication adherence should be incorporated into training curricula for all health care professionals, including physicians, nurses, and pharmacists.[101] Training in adherence management should address information on adherence, the clinical decision-making process, and behavioral tools for health professionals—in other words, knowledge, thinking, and action (figure 6). In addition, an emphasis should be placed on ongoing professional education and training so that health professionals continue to build their knowledge and skills in the workplace.[12]

Health professionals need a wide range of competencies to effectively manage and support medication adherence. Table 7 presents a common curriculum to guide education and training. It can be adapted

Figure 5. Systemic capacity building for improving medication adherence.
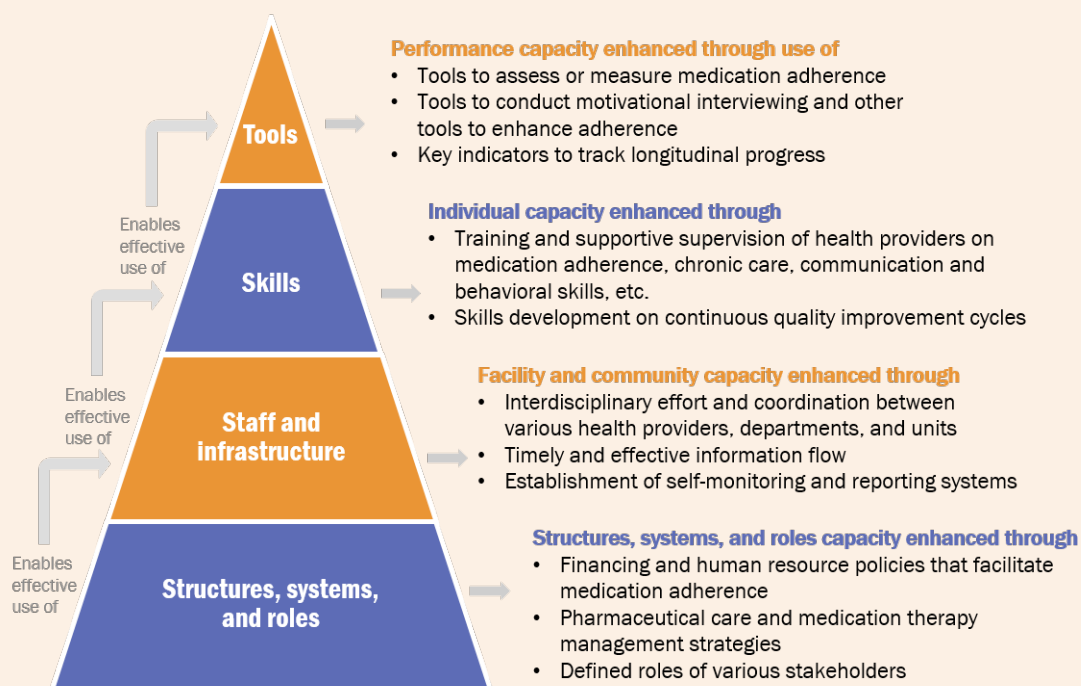
Adapted from Potter C, Brough R. 2004. Systemic capacity building: A hierarchy of needs.

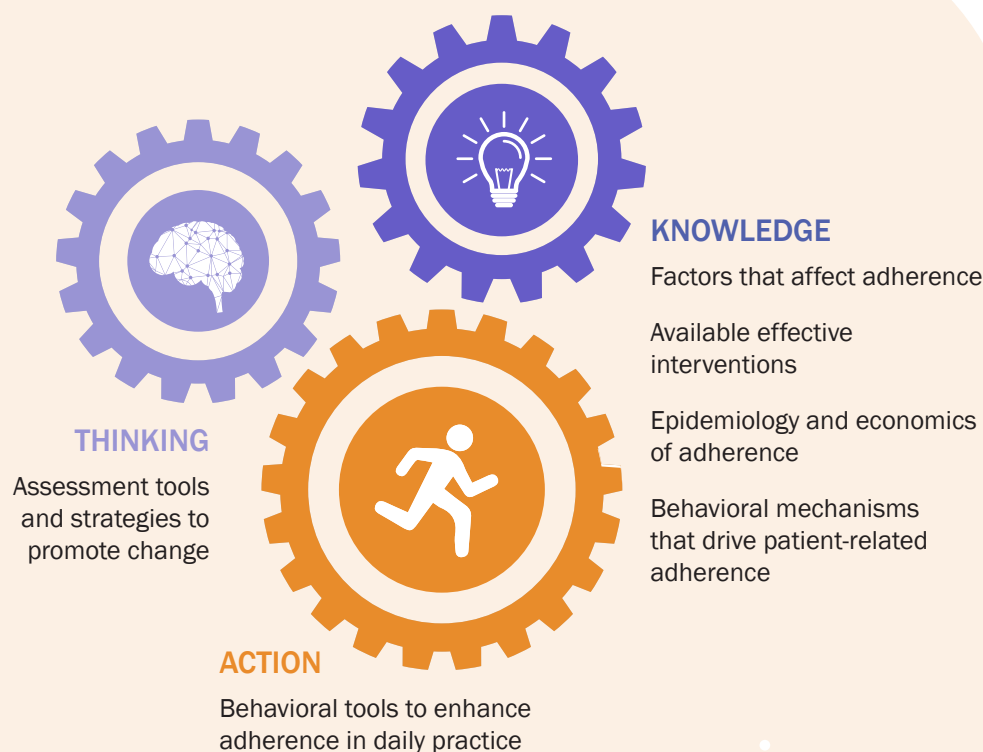### Table 7. A Common Curriculum for Managing and Supporting Medication Adherence[103]

Competency area	Learning outcomes	Educational content Theory, evidence, best practice, and techniques
Communicating with patients about medication	1. Practice active listening 2. Help patients understand and meaningfully interpret the information they receive	• Promoting effective, patient-centered communication, including non-verbal communication, in relation to medications • Reflecting on and developing communication skills
	1. Define and agree on the purpose of the patient consultation 2. Demonstrate up-to-date knowledge of the area of practice and wider health and social services	• Preparing for and managing patient consultations • Maintaining up-to-date professional knowledge and skills to support medication adherence • Developing strategies and policies aimed at managing and supporting adherence • Working in partnership to support patients in medication adherence

Table 7. Continued

Competency area	Learning outcomes	Educational content Theory, evidence, best practice, and techniques
Managing and supporting medication adherence	1. Treat each patient as an individual 2. Discuss the illness and all treatment options 3. Determine the most appropriate strategy with the patient 4. Support the patient with taking medicine	• Understanding the patient's current circumstances, previous experiences, beliefs, and behavior • Discussing current symptoms, management, and health outcomes related to treatment options, including no treatment • Discussing and agreeing with the patient on a preferred treatment option • Recognizing signs of non-adherence • Identifying reasons for and causes of non-adherence and barriers to future adherence • Managing adherence by providing effective practical support • Providing information and feedback and helping to monitor adherence throughout treatment

Adapted from: Final Report of the Ascertaining Barriers for Compliance Project, 2012.

Figure 6. Topics for training in adherence management

KNOWLEDGE

Factors that affect adherence

Available effective interventions

Epidemiology and economics of adherence

Behavioral mechanisms that drive patient-related adherence

THINKING

Assessment tools and strategies to promote change

ACTION

Behavioral tools to enhance adherence in daily practice

Adapted from World Health Organization.
Adherence to Long Term Therapies: Evidence for action; 2003.

for different levels of study and incorporated into existing training curricula.

Strengthening the Role of Pharmacists

Despite their frequent interaction with patients, pharmacists are underutilized in efforts to improve adherence. Pharmacists are critical in expanding the counseling and medication management support provided by other health care professionals.[104] A Cochrane Review of 12 studies (of which 7 were from low- and middle-income countries) found that pharmacist-provided nondispensing services (including adherence counseling) were effective in achieving improvements in patient outcomes.[105]

Pharmacists can initiate interventions to improve adherence, including:

- Sending out refill reminders several days before the patient's dispensing date

- Conducting medication therapy management,[106] which includes reviewing medication therapy, developing medication records, implementing medication-related action plans, providing referrals, collaborating with nurses and physicians, and following up with patients

Studies of pharmacist-led interventions in primary care settings in primarily high-income countries have consistently resulted in positive outcomes, demonstrating an improvement in adherence of up to 35%.[107] In the United Kingdom, national guidelines and policies have expanded the professional scope of pharmacists to include support for patient

Box 5: Promoting Patient-centered Clinical Pharmacy Services in Ethiopia[108]

Many countries are facing an increasing burden from chronic communicable and non-communicable diseases. Providing effective, long-term care for these diseases requires clinical pharmacy services to be strengthened to accommodate more robust patient counseling and adherence support as a part of a shift from product-focused services to one that emphasizes patient-centered pharmaceutical care. To respond to this need, SIAPS and its predecessor, USAID-funded SPS, collaborated with the Pharmaceutical Fund and Supply Agency (PFSA) and Jimma University in Ethiopia to design and implement an in-service training program to introduce patient-centered pharmacy services in hospitals by enhancing the role of pharmacists in patient care. After developing the curriculum, training materials, and a series of implementation tools, SIAPS worked with local universities to train more than 150 pharmacists in 65 hospitals.

Of the 43 hospitals sampled during an assessment conducted by the PFSA and SIAPS in 2015, 41 (95.3%) had started providing ward-based clinical pharmacy services in which the pharmacists worked with multidisciplinary care teams, 29 (70.7%) pharmacy departments had developed an annual action plan for clinical pharmacy services, and clinical pharmacy interventions were being documented in 36 (87.8%) hospitals. Document reviews from 31 hospitals showed that 8,257 drug therapy problems (DTPs) had been identified by pharmacists since the initiation of the service in August 2012. Pharmacists were able to intervene in 87% of the 8,257 DTPs and their recommendations had an 88% acceptance rate by the multidisciplinary teams.

The government's policy support and strong commitment, coupled with collaboration among stakeholders (government, universities, and hospitals) to build the local capacity of training institutions, enabled the successful start-up of clinical pharmacy services in Ethiopia.[109]

adherence. Box 5 shows a successful service initiated in a resource-constrained country.

USE OF APPROPRIATE TOOLS AND TECHNOLOGIES

Supporting medication adherence requires an assessment of the degree of patient adherence, followed by the use of appropriate strategies, tools, and techniques to improve adherence. This section discusses tools and techniques to help assess and improve adherence.

Measuring Adherence

Assessing medication adherence should be a routine part of clinical care. The appropriate use of adherence measurement tools offers insight into patient behavior that cannot be captured through health outcome monitoring alone.[110] These tools enable effective treatment planning, guide decisions to change treatment recommendations, and improve patient-provider interactions.

An ideal adherence measurement tool is reliable and objective and provides a continuous record of medicine-taking behavior.[111]

Medicine is usually taken in the privacy of the home, so nearly all methods of measuring adherence are indirect and therefore subject to error. Common methods of measurement include pill counts, pharmacy refill records, self-report measures, appointment attendance, and electronic monitoring.[112] Taking the local context into consideration, health care organizations should determine which tools would be most relevant and feasible in their setting and implement them in a system-based manner. To enhance the institutionalization of the tools, the organization's leadership team should invest in training, monitoring, and ongoing improvement plans for the use of the tools.

Table 8 offers a list of the select measurement methods that are available, along with the advantages and disadvantages of each.

Standardized measures of adherence include dispensing data in pharmacy records, self-report data in medical records, and attendance logs. Such data can be collected systematically from facilities in resource-limited settings to determine performance over time and between facilities.[117]

An important resource on adherence measurement is the adherence indicator survey

manual developed by the International Network for Rational Use of Drugs Initiative on Adherence to Antiretrovirals (INRUD-IAA), which describes how to measure adherence in ART facilities. The manual helps program managers to assess how a facility is currently performing, how it is doing over time, how its performance compares to that of other facilities, and the effectiveness of interventions to improve adherence. The adherence survey tools and manual can be accessed at https://sites.google.com/a/msh.org/inrud-archive/arv-adherence-project/adherence-survey-tools-and-manual. These methods have been nationalized by country HIV programs.

Table 8. Direct and Indirect Methods for Measuring Patient Adherence[113,114,115,116]

Method	Description	Advantages	Disadvantages
Directly observed therapy (box 6)	A health care worker directly observes a patient taking medicine	• Most accurate	• Patients can hide pills in mouth and discard them • Not very practical for routine use
Biochemical measurement	Measures the level of the medicine, metabolite, or a biological marker present in a patient's blood or urine	• Direct • Sensitive	• Expensive • Not practical for routine use • Findings can be misleading and are influenced by a variety of individual factors, including diet, absorption, and rate of excretion • Only reflects recent medication consumption • Variations in metabolism and medicine taking behavior around visits can give a false impression of adherence
Pharmacy refill records	Shows the frequency of prescription refills over a specific period	• Noninvasive • Easy to obtain data • Economical	• No information on patterns of medicine taking (e.g., timing, patterns of doses) • Does not record actual consumption • Does not account for pill dumping or pill sharing • Requires consistent access to all pharmacy data, significant back-end programming for calculations, and a closed pharmacy system • Unstable over shorter intervals
Pill count	A health care worker counts the number of pills that remain in the patient's medication bottles or vials at the end of a designated period	• Easy to use • Quantifiable • Inexpensive	• Does not record actual consumption • Does not account for pill dumping, moving pills to another container, or hoarding pills • Time consuming • Requires a separate recording process in the pharmacy that is often not part of routine dispensing operations

Table 8. Continued

Method	Description	Advantages	Disadvantages
Medication events monitoring system	A medicine container with a microprocessor built into the lid that records the date and time each time it is opened	• Noninvasive • Accurate and sensitive • Provides continuous, real-time measurement • Provides information on behavior patterns	• Expensive • Does not record actual consumption • Not practical for everyday use • Cannot be used for medicines that are not in bottles • Requires return visits and downloading data from medication vials • Subject to mechanical malfunction • Data can be falsified if patient opens bottle but does not take the medicine
Tracking appointment attendance	Health care providers track appointment attendance against expected prescription refill times	• Can assess adherence trends over time	• Indirect method • Requires detail record keeping and follow-up
Self report	The patient provides answers on medication use (e.g., via patient diary, questionnaire, Likert scale, or interview)	• Brief • Easy to use • Economical	• Highly susceptible to distortion, falsification, and/or recall bias • Can be time consuming

Appointment-keeping Systems

Many health facilities in resource-limited settings have large patient loads, weak community linkages, shortages of skilled staff, and a lack of efficient systems for tracking patients and tools to improve adherence. These strains on the health system make it difficult for health facilities to identify patients who miss their appointmets.[121] Research conducted by INRUD-IAA in Kenya, Rwanda, Tanzania, and Uganda demonstrated that simple appointment systems are easy to set up and can be used as a basic method to regularly monitor adherence in health facilities. An appointment system can immediately highlight nonattendance and is an easy way to assess facility performance.[122]

For example, in Kenya, the following interventions were implemented over a one-year period to improve appointment keeping and adherence monitoring in ART facilities:[123]

● Implementing a patient appointment register to track clinic attendance (figure 7)

● Modifying the national routine patient monitoring card

● Training health service providers on basic adherence concepts

● Conducting supervisory visits to support facility teams

The results of this intervention have important implications for improving the quality of care. Findings show that the appointment

Figure 7. Patient appointment register for tracking clinic attendance in Kenya. *Photo credit: Susan Njogo*

register was a useful tool for monitoring adherence and helped health workers quickly identify defaulters. Monitoring appointments identifies patients who require extra support for adherence and strengthens adherence monitoring practices and health system performance.[124] A separate study in Uganda showed that high-performing health facilities have well-organized patient tracking and record systems, often with trained record assistants.[125] In Ethiopia, efforts to follow up via phone calls to patients who missed their appointments (a total of 259 patients) resulted in 92% (237) being reached and 65% (155) of those returning for treatment.[126]

The importance of monitoring adherence in chronic treatment programs is well established, and the easiest method is to monitor appointment attendance rates.[127,128] Many lessons in monitoring and evaluation can be drawn from HIV/AIDS programs and applied to other chronic disease programs. HIV programs have introduced new data collection systems, cadres of the workforce, and state-of-the-art approaches for using data to improve the quality of care at the facility level.[129]

Technologies to Improve Adherence

Forgetfulness is one of the most commonly reported barriers to long-term treatment adherence. Simple interventions to improve a patient's ability to remember to take

medication can aid in maintaining medication adherence. Reminders are based on behavioral learning theory, which posits that behavior depends on internal or external cues. Repetitive environmental cues, therefore, can change the behavior of patients to support better adherence.[130]

Reminders may be delivered in a variety of ways, including mobile phones, pagers, and pillbox alarms.[131] Electronic reminders are particularly useful as they can be programmed to be sent automatically and do not require any additional effort from health care providers.[132] Because mobile devices are so readily incorporated into daily routines, they are a particularly effective way of reaching patients.

Mobile health, or *mHealth*, is the use of mobile phones to improve health outcomes and is emerging as a promising approach to improve quality and efficiency in health care. [133,134] mHealth interventions are inexpensive and convenient; promote privacy and confidentiality; can be used to reach rural populations; and help overcome barriers related to poor transportation, infrastructure, and stigma.[135]

A number of studies have assessed the effectiveness of mobile text messaging as a method to improve ART adherence. Evidence suggests that short message service (SMS) messages, sent at weekly intervals, are effective for enhancing adherence to ART and improving viral load suppression.[136] Daily SMS reminders, however, do not significantly improve medication adherence among HIV patients.[137] The short-term effectiveness of electronic reminders, particularly SMS reminders, has been consistently demonstrated; however the long-term effects of electronic reminders are less-well known.[138]

Mobile phones can also be used to improve adherence to treatment for malaria, TB, and noncommunicable diseases.[139] Box 7 describes the use of *On Cue* SMS messages in South Africa that remind patients to take their TB medicines. This service is meant to accom-

pany DOT and is recommended for patients who have been stabilized on a regimen.[140,141]

Box 8 describes the SIMpill Medication Adherence System, an innovative electronic reminder device that was originally developed to detect real-time non-adherence to TB treatment.[144]

It should be noted that a mobile phone-based intervention can only be successful if messages are developed in the local language.[145] Also, while mobile reminders are effective, they should complement, rather than replace, social support from family, friends, and the community.[146]

Telephone counseling is another way electronic devices can be used to support patient adherence. Box 9 describes a simple telephone counseling intervention among non-adherent patients taking five or more medicines for chronic disease.

A variation of telephone monitoring was studied in patients in the United States and Mexico in which health care providers watched patients take each dose of medicine via video. Patients used mobile phones to record themselves taking their medications and send the videos to their prescribers. This study found high adherence rates, and 92% of participants stated a preference for video-DOT over traditional, in-person DOT.[151]

Tools to Improve Adherence

Pillboxes, medication diaries, and pill charts are examples of aids that health providers can share with their patients to encourage treatment adherence.[152]

- A **pillbox** is a container for storing medication with dividers for each day. This aid makes it easier for patients to remember to take their doses correctly and allows them to monitor their own adherence. Patients who cannot read or who are very ill may need help filling their pillboxes correctly. Patients may also experience greater stigma and

Box 7. On Cue SMS Service in South Africa[142,143]

Achieving optimal adherence to TB medicines is a challenge in Cape Town, South Africa. DOT is considered the primary method for monitoring adherence, but this can often be a source of stress for the health care team. *On Cue* utilizes SMS text messages to remind patients of upcoming doses for their TB regimen. Given that 71% of the South African population has a mobile device, using cell phones to promote adherence was especially useful in this region.

The *On Cue* database stores each patient's contact information and sends a text message reminding patients to take their medication. The messages can be personalized and sent in various languages. SMS saves money and time for patients who do not have to pay for transportation to a clinic. In addition, patients do not consider mobile phone use intimidating and are not shy about asking family and friends for help. Among the 221 patients who participated in the program, there was a 62.4% cure rate and a 72.9% treatment success rate.

Creators of this program emphasize, however, that this service is only meant to be an auxiliary program to DOT. In addition, the *On Cue* service is recommended for patients who have been stabilized on a regimen. The pilot program only enrolled patients after one month of DOT to monitor for adverse effects and complications.

discrimination because the use of a pillbox may unintentionally disclose a patient's health status.

- A **medication diary** is a notebook used by patients to record the time and date of medication intake, missed doses, and reasons for missed doses. This aid can serve as a valuable record of issues that patients may encounter.

- A **pill chart** is used to visually display the color, shape, name, and dosage for each medication. Pill charts are used by health care providers during counseling. They are particularly useful for patients who are not literate.

Adherence-enhancing techniques or tools need to be further developed for real-world, real-time use, and available tools need to be more widely utilized.[153] Beyond these tools, treatment guidelines and medicine formularies that promote simple, convenient, and cost-effective pharmacotherapy should be available in all health facilities.

Monitoring Adherence through Early Warning Indicators

As part of its global strategy to prevent and monitor HIV medicine resistance, WHO recommends that national ART programs conduct population-based monitoring of HIV drug resistance using early warning indicators (EWIs). Relevant EWIs include ART prescribing practices, patients lost to follow-up at 12 months, patient retention on first-line ART, on-time ARV medicine pick-ups, medicine supply continuity, and viral-load suppression at 12 months.[154]

Box 10 explains how using EWIs to approximate medication adherence is helpful for identifying patients who are at risk of developing resistance to HIV treatment and for improving facility performance. Data on EWIs can be used to tailor interventions to the needs of high-risk patients.

Job Aids for Health Care Providers

Although it has been shown that printed materials alone do not change behavior, they can be useful when used in combination with

Box 8. A Real-time Wireless Tool for Detecting Non-adherence[147,148]

SIMpill, a London-based medication technology company, developed the SIMpill® Medication Adherence System, a real-time wireless pill bottle that monitors a patient's medication schedule and intake. The pill bottle contains a SIM card that, when opened, automatically delivers an SMS message to a central server indicating that a dose has been taken. If no SMS is received at the designated time, the patient has not taken his or her dose. If the patient does not take his or her medication as prescribed, the wireless pill bottle sends a text message to the patient's mobile phone. If the patient does not respond, the server contacts a caregiver who can then follow-up with the patient. Similarly, when the patient takes his or her medication at an incorrect time, he or she receives a warning message.

This innovative tool evolved from a one-year pilot project implemented in South Africa in 2006 to reverse low adherence rates to TB medication in the Western Cape. In 2005, South Africa had a 71% DOTS success rate. A total of 155 TB patients at three clinics in the Cape Town area used the SIMpill for 10 months. After the intervention was introduced, medication adherence stabilized between 86% and 92%, and the treatment success rate was 94%.

more complex interventions.[155] Checklists, instruction cards, worksheets, wall charts, and other handy and practical materials can serve as effective job aids for health care providers. Box 11 describes a country-level example of several educational strategies for providers in Ethiopia.

TEAM-BASED APPROACHES TO PATIENT CARE

Providing the necessary information to help patients manage their health is best achieved through collaboration among providers.[156] Adopting a multidisciplinary or team-based approach to health care is valuable and contributes to the concept of pharmaceutical care.

Pharmaceutical care is "the responsible provision of medication-related care designed to achieve health outcomes aimed at improving and/or maintaining a patient's quality of life."[157] It is a patient-centered and system-oriented approach that emphasizes direct interaction with patients, provider accountability, and achievement of optimal health outcomes. It also fosters a collaborative team

Box 9. Reducing Mortality through Telephone Counseling[149,150]

When taken as prescribed, medicines for chronic conditions reduce morbidity and mortality. However, patients who are prescribed multiple medications have low levels of adherence—only approximately 50% of patients with chronic conditions who receive more than one prescribed medicine are fully adherent. When a patient receives counseling, the health care provider thoroughly describes the advantages and disadvantages of each prescribed medicine, its dose, and the timing of intake. Counseling is a two-way dialogue in which the patient is invited to learn and ask questions, and his or her values and beliefs are respected and reinforced.

A team of researchers in Hong Kong set out to determine whether telephone counseling can improve medication adherence. A total of 442 patients who were taking five or more medicines for a chronic disease participated in a two-year randomized controlled trial. At enrollment, 236 patients were classified as adherent. Approximately half of the 442 patients were randomly assigned to a telephone counseling group, and the remaining half to a control group. Patients assigned to the intervention group received a call from a hospital pharmacist at the midpoint between clinic visits throughout the study period to discuss misconceptions, side effects, the importance of adherence, and important aspects of self-care. Each call lasted approximately 10 to 15 minutes, and pharmacists would remind patients of their next clinic visit. Patients assigned to the control group were not called.

The benefits of regular telephone counseling for patients taking multiple medicines were manifold. When compared to the control group, fewer patients in the intervention group who were non-adherent at enrollment remained non-adherent at the end of the study (18% versus 7%). Of the patients who were adherent at enrollment, 81% of the intervention group remained compliant, while only 58% of the control group remained compliant. In addition, telephone counseling was associated with a 41% reduction in the risk of death. This study demonstrated that having a pharmacist conduct periodic telephone counseling with non-adherent patients who were taking five or more medicines for chronic disease improved medication adherence and reduced mortality.

Box 10. Implementing a Routine HIV Drug Resistance EWI Monitoring System

HIV drug resistance (HIV-DR) poses a significant threat to global health. According to WHO, nearly 4% of people living with HIV have resistance to first-line treatment. In settings where medicine stock-outs are frequent, this rate nearly quadruples. The number of people presenting with primary and secondary HIV-DR around the world is expected to grow as the number of people receiving ART increases.

To preserve the future effectiveness of ART, WHO recommends the HIV-DR EWI strategy, which is a comprehensive approach to HIV-DR surveillance, monitoring, and prevention. HIV-DR EWIs assess the extent to which a national ART program is detecting and minimizing the risk of the emergence of HIV-DR and optimizing patient care. With this strategy, treatment programs can monitor the quality of their services and carry out immediate corrective actions as problems are identified. Management Sciences for Health (MSH) developed an electronic dispensing tool (EDT) to help pharmaceutical providers accurately dispense medicines by collecting, managing, and generating the necessary data. The SPS program, implemented by MSH, developed a clinical algorithm to measure adherence in resource-limited settings that was incorporated into the EDT. With this feature, the EDT has the unique ability to generate data on four WHO-recommended HIV-DR EWIs.

The value of the EDT in producing information on HIV-DR EWIs was demonstrated in Namibia, where SIAPS provided technical assistance to develop and implement reporting on EWIs. SIAPS also collaborated with WHO through Tufts University to conduct an annual data abstraction from the EDT national database. Data were imported into the WHO electronic EWI abstraction tool, and values were calculated for each indicator at each site. The data were then validated using patient care booklets and the electronic patient management system and analyzed for site- and national-level indicators. Failure to reach EWI targets indicated a need for additional resources, staff training, or review.

In Namibia, the EWI intervention has led to valuable recommendations and several achievements, including improving the accuracy of data abstraction, engaging sites on standard dispensing practices, enhancing site collaboration in ART service delivery, boosting the use of the EDT in facilities, analyzing adherence in each facility, and conducting service quality assessments in poorly performing sites.

All of Namibia's 50 ART sites are currently involved in quarterly and annual monitoring and review of EWIs at the national level. EWIs that are monitored include on time pill pick-up, retention in care, pharmacy stock-outs, and dispensing practices. The ART retention rate improved from 87% in March 2012 to 95.3% in September 2014, and on-time pill pick-up improved from 73% to 86% for the same period. Program managers have acted on the recommendations from the reports to enhance compliance to guidelines and minimize the risk of HIV-DR development.

Similarly, staff in ART clinics across Kenya monitor patient adherence using the upgraded EDT. The tool has been successfully adapted and rolled out at 380 sites. The records of more than 80% of the 600,000 patients on ART in Kenya are maintained using the EDT.

environment in which the patient, health care provider, and other members of the health care team each have a role to play in improving the patient's health and well-being. A multidisciplinary approach encourages open communication and shared responsibility and engages all parties throughout the continuum of care.[158] For an example of how pharmaceutical care was implemented in Ethiopia, see box 12 and box 5.

Team work respects the goals of both patient and provider and encourages two-way communication about medicine use at every opportunity.[159] A team-based approach also includes training pharmacists to provide patient education; place reminder phone calls; use adherence monitoring tools; and, with office staff, assess non-adherence. Health teams share information to deliver consistent support for adherence and prioritize adherence support through service provision and health system design.[162]

In summary, the goal of team work is to achieve treatment adherence and good clinical outcomes for a patient who is being supported by different health care providers with various roles within a single health care setting.

Box 11. Medication Adherence Initiatives in Ethiopia

In Ethiopia, SPS and SIAPS embarked on several initiatives for health care providers and patients with the goal of improving treatment adherence.

Pediatric Antiretroviral Medicines: Prescribing and Dispensing Aid was developed under SPS and revised under SIAPS. This job aid is a useful resource and quick reference for health care providers to enhance ART adherence and co-trimoxazole use among children. It contains information such as medicine name, frequency of administration, available dosage forms and strengths, a guide on dose calculations by weight, the one-time dose by weight range, medicines that should not be co-administered with regimens, common side effects, medicine-food interactions, and additional information helpful in prescribing and dispensing ARVs and co-trimoxazole to pediatric patients. Service providers receive a brief orientation on using the chart.

Pocket-size booklets on ART adherence entitled *Antiretroviral Side Effects: Recognition and Management by Fixed-Dose Combination (FDC) Regimen* were printed in simplified Amharic and distributed to health facilities providing ART treatment for patient use. Patients receive this adherence aid during medicine pick-up and counseling. The purpose of the booklet is to assist patients in recognizing FDC ARV side effects, manage those side effects at home or before visiting health care providers, and differentiate side effects and comorbidity. The booklet also has space to document encounters. These materials are believed to help educate and empower patients as they manage ART and assist health care providers in providing counseling and improving treatment adherence.

Finally, an electronic version of the *Operational and Ongoing Antiretroviral Treatment Adherence Counseling Aid* was prepared and shared with regional pharmaceutical associates and other stakeholders. This operational adherence counseling aid assists health professionals in providing services, enhancing patient adherence, and conducting mentoring activities.

Box 12. Fostering Team-based and Patient-centric Care through Clinical Pharmaceutical Care

Studies have shown that when health care is provided through a multidisciplinary team, the quality of care increases.[160] However, in many low- and middle-income countries, health care providers may work in silos and miss out on the benefits of collaboration. In 2011, a rapid assessment conducted by SPS indicated that the practice of pharmaceutical care in Ethiopia was minimal.[161] Pharmacists were unlikely to be involved in any type of direct patient care, including care meetings, ward rounds, or prevention of potential medication and treatment issues. Only approximately one-third of pharmacists were found to have access to any patient information at all.

Acting on the findings of the assessment, SIAPS and the Ministry of Health worked to develop an in-service training program to provide pharmacists with the knowledge and skills required to carry out basic pharmaceutical care activities. The curriculum and training manuals were developed and piloted with 21 pharmacists from 21 hospitals throughout Ethiopia. As part of the curriculum, pharmacists were placed in a three-week ward rotation where they attended clinical rounds, reviewed patient charts, and discussed patient treatment plans with the clinical team.

These pharmacists now contribute to multidisciplinary ward rounds, help identify medicine therapy problems, and provide remedial suggestions to clinicians. The clinical pharmacy service has enhanced team work and the practice of pharmaceutical care in the participating hospitals.

COMMUNITY ENGAGEMENT AND PUBLIC EDUCATION

Interventions at the meso level of the health system focus on strengthening treatment and care services for patients. Connecting with community resources leads to more positive adherence outcomes.

Adequate social support is associated with better health outcomes and health behaviors. Family, friends, and community members can provide physical, social, and emotional support. Social support makes a person feel a sense of belonging, care, and value. Specifically, social support provides social acceptance, emotional and informational support, and help with daily tasks.[163] Research has suggested that social support may lead to lower rates of depression and, consequently, greater self-efficacy and confidence among patients.[164,165] In addition, community support initiatives can address the shortage of nurses and doctors, further increasing the effectiveness and efficiency of treatment efforts.[166]

Community support initiatives alleviate the pressure on health systems and staff, improve coverage of health services in communities, and address the psychosocial needs of patients receiving long-term treatment for chronic conditions. Types of community support providers identified in ART-related activities include:[167]

- **Community health worker:** A nonprofessional cadre of health workers who undertake short course training and work within their own communities to complement and support the services provided by other health workers

- **Community care coordinator:** A person living with HIV or AIDS who is trained to perform the tasks of a community health worker

- **Peer health worker:** A community health worker who is HIV positive and whose role is to conduct adherence counseling and provide health education and psychosocial support

- **Field officer:** A trained lay worker who supports medicine delivery and monitors patients

- **Health extension worker:** An individual recruited from the community and trained to manage operations of health posts, conduct home visits and outreach services to promote preventive health care, refer cases to health centers, and follow-up on referrals

- **HIV/AIDS lay counselor:** An individual who manages HIV testing, provides pre-ART training and ART adherence support, identifies patients eligible for ART, and tracks defaulting ART patients

- **DOT for ART observer:** A community member close to the patient who directly monitors daily medication intake

- **Adherence supporter:** An individual who promotes healthy behaviors, provides HIV/AIDS and ART-related knowledge and develops skills, and promotes adherence by providing psychosocial support

- **Home-based care volunteer:** A community member trained to provide ART adherence counseling and perform a wide range of home-based care activities

The community can play an active role in nurturing positive behavioral change during the treatment process. Community-based programs have the benefit of addressing the physical and psychosocial needs of patients and their families. In Malawi, a minimum care package of community support in rural areas has been associated with improved ART outcomes. This package of support includes home-based care, support to family caregivers, adherence counseling, and defaulter tracing.[168]

The community-based treatment support program (CBTSP) model was developed for people living with HIV in resource-limited settings of sub-Saharan Africa. The model stresses that to have a better quality of life and optimal health outcomes, people living with HIV/AIDS in resource-limited settings should have access to clinical services and community-based support. CBTSP relies on the involvement of government, private-sector, and community-based organizations to manage disease, offer psycho-social support, and encourage patient self-management. The package of community-based services includes home-based care, food security, psychosocial support, buddy programs, medicine literacy tools, prevention education, orphan care, referrals for counseling and testing, income-generating activities, and other services. Like other community-based care models, CBTSP has a positive effect on HIV patients' overall health, quality of life, treatment adherence, and clinical outcomes in resource-limited settings.[169]

In Mozambique, HIV programs encourage the use of treatment partners to improve adherence for patients receiving highly active antiretroviral therapy (HAART). In this peer-support model, treatment partners provide ongoing social support and encouragement to patients on HAART. As in the community-based DOT model, treatment partners are selected by the patient and may be a spouse, family member, or friend.[170] A 2009 study found that treatment partners positively affected a patient's ability to achieve high adherence to HAART in an urban setting in Mozambique.[171]

Community-based programs have been successfully conducted at a moderate cost for people with chronic conditions in a variety of settings and have the additional advantage of reducing the amount of time health professionals need to care for patients with chronic conditions.

MINIMIZING BARRIERS TO EFFECTIVE PHARMACEUTICAL SERVICES IN ETHIOPIA

Ethiopia has improved its primary health care service delivery nationwide and made great strides in combatting TB and HIV; however, the country has not made sufficient progress in terms of pharmaceutical services—a patient's last point of care. Expiry and stock-outs are common, leaving patients without needed medications. Nationally, stock-outs lasted, on average, 99.2 days per year in public health facilities and 99 days in regional drug stores. According to the fourth National Health Sector Development Program (2010/11–2014/15), only 68% of patients were given adequate information on dispensed medicines, 35% of health facilities encountered stock-outs of essential medicines, and 8% of stock was wasted due to expiry. Inconsistent medicine availability, not receiving adequate information regarding medicine, and poorly organized pharmacy operations are all major barriers to medication adherence.

Building on the efforts of predecessor programs, SIAPS collaborated with local stakeholders to develop the Auditable Pharmaceuticals Transactions and Services (APTS) intervention, which seeks to improve the transparency and accountability of pharmaceutical transactions, develop and deploy pharmacy staff effectively, gather and track accurate information, and improve the customer's pharmacy experience. While the program was not directly targeted at improving adherence, local stakeholders recognized that by systematically improving pharmacy operations, many barriers to patient adherence would also be reduced.

Although many interventions were implemented through the APTS initiative, key activities that supported improved patient care, patient satisfaction, and reduced barriers to adherence included:

- **Developing and enacting regulations.** SIAPS supported actions taken by regional governments to develop, enact, and popularize legislation to establish and adopt APTS. The resulting legislation defined pharmaceutical management systems and the roles and responsibilities of different bodies and improved practices related to transparency and accountability.

- **Workforce adjustment.** To operate efficiently and provide quality patient care, facilities implementing APTS worked with government bodies to identify, recruit, and deploy the appropriate number and mix of pharmacy-related staff.

- **Infrastructure improvement and reorganization of pharmacy units.** Renovations to pharmacy infrastructure and space allowed for increase visit efficiency and patient confidentiality.

- **Medicines availability and tracking.** Improved tracking of medicines helped reduce stock-outs, minimize waste, and improve transparency

As of August 2016, APTS has been implemented at 50 hospitals, all of which have completely redesigned their physical infrastructure to create a space for greater efficiency and service quality. Changes to the pharmacy layout improved patient convenience at service delivery points and shortened wait times. Private counseling spaces helped to improve confidentially and facilitate open communication between patients and providers.

In addition, the improvements in medicine management and tracking improved medicine availability. In most hospitals, the availability of key medicines increased from 65% to more than 95%, nearly reaching the national health sector development goal of 100% availability of essential medicines.[172]

Finally, while the national baseline for patient satisfaction is 74.4%, three sites that were among the first to implement APTS (Axum, Felege Hiwot, and Debre Markos hospitals) reported upwards of 90% patient satisfaction based on exit interviews. Notably, APTS helped one hospital to more than double its reported patient satisfaction (the hospital's baseline was 40%).

The APTS package of interventions has helped to reshape the environment in which patients receive care and treatment at the meso level of the health system. Increased transparency and accountability achieved through leadership, stewardship, and governance helped to improve medicine availability and facilitated a better experience for patients needing medication. Tools that helped to collect data and use information for decision-making reduced medicines expiry and waste, while efforts to build the capacity of health workers to counsel patients contributed to service delivery through responsiveness, confidentiality, and patient-centered care. With legal frameworks and guidelines in place at the macro level, APTS helped to strengthen the systems that influence the relationship between patient and provider at the micro level.

CHAPTER SUMMARY

Shaped by legislation and policies at the macro level, the meso level of the health system comprises local health systems that dictate the environment in which patients receive care. The extent to which health providers are appropriately trained and equipped with tools, facilities and infrastructure promote privacy and team-based approaches to care, and communities are engaged and educated on adherence helps create an enabling environment for patients to remain adherent to medication and treatment.

05 INTERVENTIONS AT THE MICRO LEVEL OF THE HEALTH SYSTEM

Interventions at the micro level of the health system focus on creating enabling conditions that empower patients to better manage their own health. While interventions at the micro level are generally focused on the service delivery building block of the health system, this level also sees the culmination of efforts at the macro and meso levels and is where the results of system-based interventions are felt most strongly. This chapter describes the micro level initiatives illustrated in the SIAPS framework for strengthening systems to improve medication adherence. Encouraging patients to take ownership of their health begins with improving patient-provider interactions, simplifying treatment regimens, and supporting patients at home and in the community.

MICRO
Provider-patient interaction

- Improved provider-patient relationship and interactions

- Simplified treatment regimens

- Patient support at home and in the community

PROVIDER-PATIENT RELATIONSHIPS AND INTERACTIONS

There are several ways to enhance patient-provider interactions and promote adherence. These include communicating and interacting appropriately, promoting partnerships and shared decision-making, using educational and behavioral strategies, and improving patients' self-management skills.

Appropriate and Effective Communication

A positive, supportive environment in which a patient can speak openly, ask questions, and voice concerns helps to encourage better adherence. Elements that help foster effective communication and interaction include offering appropriate counseling services, practicing effective communication skills, maintaining confidentiality, and encouraging health literacy and patient empowerment.

"Misunderstandings about the patient's disease and medicines occur in 80% of consultations between doctors and patients."[173]

- **Offer appropriate counseling services.** In low- and middle-income countries, a dispenser spends an average of less than one minute with a patient, and only approximately 50% of patients ever receive instructions on how to take their medicines.[174] Ensuring that health care providers take the time to explain why a medicine is being provided, how to take it appropriately, and what to expect from medicine use can help mitigate non-adherence before it starts. [175] Patient counseling about recommended medicines

should include an explanation of which medicine is being prescribed, administration and dosing instructions, potential side effects, strategies for remembering to take medicines, additional resources to help maintain adherence, and other topics relevant to the patient's needs.[176,177]

- **Practice effective communication skills.** Using effective verbal and nonverbal communication skills allows health care providers to gain insight into patient behavior. For example, actively engaging patients in a productive conversation elicits information about medicine-taking behavior, helps providers assess any information gaps, and provides patients with an opportunity to ask questions. Providers should ask their patients about their concerns and practice active listening, a communication technique that relies on focused attention to verbal and nonverbal messages to understand what the patient is saying. Successful communication requires that providers remain neutral when listening to patient concerns and offer simple, nonjudgmental responses. To build patient trust and, in turn, improve adherence, health care providers should offer encouragement by acknowledging their patients' strengths and successes.[178]

- **Maintain confidentiality.** A common problem faced by health facilities in resource-limited settings is inadequate space for confidential counseling. Without a safe, private space for patients to receive their medicines and counseling, they may feel too embarrassed or insecure to ask questions.

- **Encourage health literacy.** Low health literacy is associated with poor health outcomes across all disease categories.[180] To ensure that patients with low health literacy understand everything they need to know about their medicines, providers should consider using a combination of verbal, written, visual, and other methods of communication that present and reinforce information in a simple manner. One such method is the teach-back approach, also known as the ask-tell-ask approach. In this approach, health care providers prompt patients to repeat the most important points about their medicines.[181]

- **Encourage patient empowerment.** Ensuring that patients feel comfortable asking their health care provider questions helps clarify treatment information before a problem occurs. One method to empower patients to ask questions is to have *"Questions to Ask"* posters or brochures available to patients in the waiting room, exam room, pharmacy, or bathroom. These materials give patients an idea of the types of questions to ask. For example, SIAPS developed patient awareness

Box 13. Ensuring a Confidential Space to Receive Medication Counseling[179]

In 2003, the government of Kenya initiated ART at four health facilities in the Coast Province to treat and care for people living with HIV. New private counseling booths were constructed at pharmacy windows to create a confidential and secure environment. Pharmacy staff were trained on rational medicine use and given tips on how to provide medication counseling to ART patients. Having access to counseling booths enabled pharmacy staff to improve the quality of counseling for ART patients and apply these skills to counseling patients on other medicines.

Figure 8. A poster that can help patients assess whether they may be experiencing side effects from treatment. *Image credit: SIAPS Program*

posters on potential side effects of anti-tuberculosis medicines (figure 8).[182]

Partnerships and Shared Decision-making

Shared decision-making is a valuable process and has been shown to improve patient adherence and lead to better clinical outcomes.[183,184] By using this patient-centered approach, health care providers and patients can openly explore the available evidence about treatment options as well as the patient's beliefs and views about those options. Patients can actively participate in making their treatment decisions rather than passively accepting their health care provider's recommendations. This technique promotes partnerships and places value on the views of both patients and health care professionals.

Through this process of shared decision-making, a personalized treatment plan can emerge. Together, health care providers and patients should set specific, measurable, achievable, realistic, and timely goals. Providers should offer continuous support to help their patients achieve these goals.

Behavioral Strategies

Offering patients information on what medicines they are taking and why, what to expect from each medicine, possible side effects, and how to manage those side effects will keep them well-informed. Information alone, however, is not the solution. Behavioral interventions can motivate and encourage patients to follow their treatment plan. Behavioral interventions also provide a unique opportunity because behavior is more readily changed than are other characteristics that can negatively influence adherence, such as environmental or socio-economic factors.

Motivational interviewing is a "directive, client-centered counseling style for eliciting behavior change by helping clients to explore and resolve ambivalence."[185] Rooted in the readiness to change model,* this counseling technique focuses on the patient's decision-making process.

In motivational interviewing, health care providers work with patients to enable the transition from unhealthy to healthy behaviors by openly discussing the rationale for the treatment, the patient's fears, desired outcomes, and social pressures.[186]

Motivational interviewing, which emphasizes patient choice and options, goes a step beyond traditional counseling in several ways (table 9).

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* The readiness to change model, also known as the stages-of-change model, states that individual's progress through five stages of behavior change (precontemplation, contemplation, preparation, action, maintenance). This model is used to understand and predict intentional behavior change and can be used as a guide to interact with patients and tailor treatment to their needs.

Table 9. Traditional Counseling versus Motivational Interviewing

Traditional counseling	Motivational interviewing
The provider is the expert.	The provider develops a partnership with the patient.
The provider assumes that the patient lacks knowledge.	The provider exchanges information to facilitate an informed decision.
The provider tells the patient what to do and hopes that the patient will follow instructions.	The patient has the right to decide on his or her own care.
The provider provides definitive information, and instructions are presumed to be nonnegotiable.	The provider provides information to the patient to show the discrepancy between the present behavior and the goal.
The provider dictates health care behavior.	The provider and patient negotiate behavior and reach an agreement.
The goal is to motivate the patient.	The goal is to encourage motivation and elicit the patient's commitment to behavioral change.
The provider expects respect from the patient.	The provider must earn the patient's respect.

Adapted from ONS. 2009. *Tools for Oral Adherence Toolkit.*

Motivational interviewing requires time and practice.** However, it shares a number of similarities with active listening. When a health care provider is discussing medicine use and adherence with a patient, he or she should:

- **Express empathy** to understand the patient's perspective and create a comfortable and open environment

- **Support self-efficacy** to help the patient maintain his or her motivation to change

- **Value the patient's perspective**

- **Develop discrepancy** to help patients understand that their current behavior is not helping them reach their goals

Self-management Skills

Self-management increases patient confidence in managing personal health, enables patients to make well-informed decisions about their treatment, encourages patients to articulate their needs, and inspires healthy choices. Self-management skills are particularly valuable for patients with chronic conditions who must learn to maintain their behavior over a long period of time, usually without continuous supervision. The following are key components of self-management:[187]

- Give patients information about their condition, medicine, and support groups

- Teach patients specific self-management skills

- Promote healthy behavior

- Help patients develop problem-solving skills

- Address patients' emotional and psychosocial issues related to their condition

- Schedule regular follow-up visits or calls with patients

- Encourage patients to actively manage their condition

** The National Heart Foundation of Australia developed the Motivational Interviewing Professional Development Kit to help health professionals adopt this skill. For more information, visit www.heartfoundation.org.au.

The "Five As" can guide providers as they help their patients self-manage their conditions: [188]

- **Assess**: Find out about the patient's health-related beliefs, behavior, and knowledge.

- **Advise**: Give patients specific information related to their disease and medicines. Outline the benefits of the recommended treatment.

- **Agree**: Set achievable goals based on the patient's needs and confidence in his or her ability to achieve the goals.

- **Assist**: Help patients create a self-management road map. Address possible barriers to self-management and identify strategies and aids to overcome these barriers.

- **Arrange**: Specify a plan for follow-up with the patient.

Self-management can be strengthened by using memory aids, such as special pillboxes, telephone reminders, or alarms.[189] Technology is increasingly being used to remind patients to take their medicine, as explained in Chapter 4.

SIMPLIFY TREATMENT REGIMENS

Research shows that adherence improves when fewer medicines are taken less frequently.[190,191] In other words, frequent dosing and complex treatment regimens make a patient less likely to adhere to treatment.[192] Studies have shown that the greatest improvement in adherence is observed when the frequency of dosing decreases from three times to two times per day.[193] To improve adherence, health care providers should select the simplest and most convenient treatment available that is suited to a patient's clinical needs. Prescribing FDCs, which combine two or more medicines into a single tablet or capsule, and prepackaging

medicines (e.g., blister packs) can simplify treatment regimens.[194,195]

A meta-analysis by Claxton et al., showed an inverse correlation between dosing frequency and adherence. Adherence was 79% for once-daily dosing, 69% for twice-daily, 65% for three times per day, and 51% for four times per day.[196] Each extra daily dose, therefore, corresponded to a roughly 10% decrease in adherence.[197] Box 14 further explores how FDCs can help simplify regimens and increase patient adherence to medication.

Prepackaging medicines can improve appropriate prescribing by health professionals and the patients' ability to understand and adhere to the recommended treatments.[198] Several studies have shown that prepackaging improves patients' adherence to antimalarial medication.[199] In addition, prepackaging may also potentially reduce errors and contamination of products during dispensing.[200]

SUPPORT PATIENTS AT HOME AND IN THE COMMUNITY

Supportive social relationships with family, friends, peer groups, and communities, both formal and informal, increase a patient's confidence in following treatment recommendations. Social support has proven effective in improving long-term adherence to treatment for diabetes, hypertension, HIV/AIDS, and other chronic conditions.[202] Common approaches to supporting patients at home and in the community include making arrangements for peer-to-peer support, linking patients with community support organizations, and setting up follow-up visits.

Medication Support Groups and Peer-to-peer Counseling

Support interventions can take place one on one or in a group setting. Medication groups and peer support groups are two examples

of successful community-based programs. Community-based programs encourage peers to share experiences, provide comprehensive medical information, and empower patients to take responsibility for their own care.[203]

Peer counselors act as role models for others with the same disease or condition and are visible in the community. They raise awareness and act as a bridge between patients and the health system. As such, they should be recognized as an important part of the health care team.

By sharing their personal experiences, peer counselors help patients become more confident in their treatment. In the case of HIV/AIDS, having a peer counselor also encourages patients to disclose their HIV status and confront the fear of stigma.[204]

The *community-based interactive approach* (CBIA) is an active self-learning method that empowers patients to explore and assess information about their treatment. Box 15 describes how this approach was used in hospitals in Indonesia to promote education and encourage treatment adherence among patients with diabetes.

Patient Support Organizations

Patient support organizations provide patients with opportunities to share their beliefs, views, and experiences with other patients, and they can motivate patients to self-manage their chronic conditions. They are generally supported by community health professionals and keep patients actively engaged and informed. Patient organizations may be owned and managed by a health care provider, directly owned by patients but organized and supported by health care providers, or independent.[207]

Appropriate Patient Follow-up

Patient follow-up is a critical component of improving adherence. A patient can visit his

or her provider regularly, or follow-up visits may take place in the patient's home.

Home visits, or the buddy system, engage a confidante to support the patient in following his or her treatment regimen. During home visits, a buddy may remind the patient to take his or her medicine on time; help the patient keep appointments; or provide any needed emotional, social, and logistical support. This approach is low cost and can lead to excellent adherence.[208,209]

Box 16 describes Zambia's prevention, care, and treatment partnership program, which aimed to support adherence among people living with HIV.

Box 16. Zambia Prevention, Care, and Treatment Partnership Program [210]

The government of Zambia has rolled out HAART to improve viral suppression, delay the progression of the disease, and decrease HIV-related deaths. However the country suffers from a shortage of health care workers, which has impeded efforts to roll out ART in resource-limited settings.

To bridge the human resources gap, Family Health International's USAID-funded Zambia Prevention, Care, and Treatment Partnership Program trained community volunteers as adherence support workers to help people living with HIV remain on treatment. Modules included technical information on ART and adherence, techniques for relationship building, counseling skills, and documentation.

Between March 1 and April 4, 2007, adherence support workers worked alongside doctors and nurses and were supervised by professional health care workers. They provided education, psychosocial support, and referrals to HIV patients and conducted community visits to track patients who missed their clinic appointments. The intervention resulted in:

- A decrease in loss to follow-up of new clients from 15% to 0%

- An increase in reporting of side effects to clinicians by patients

- An increase in patient self-efficacy, positive attitudes toward ART adherence, and hope

- An improvement in quality services due to reduced workload among facility staff

This intervention demonstrated that the responsibility for adherence counseling can be transferred to lay providers without compromising quality. Adherence support workers, who are critical role models, effectively educate and conduct follow-up visits with people living with HIV.

IMPROVING HEALTH LITERACY FOR BETTER ADHERENCE TO ARVS IN NAMIBIA

The rollout of ART in Namibia has been successful in recent years; by 2008, more than 75,000 people living with HIV/AIDS were on ART. However, educational materials on ART were inadequate. With little accurate information on what to expect or how to manage challenges associated with ART, program planners recognized that patients would be less inclined to adhere to treatment.

In response, a comprehensive audio-visual ARV treatment literacy and adherence improvement program was launched in 2009 to empower the general public to learn more about ART. The initiative, developed by the Ministry of Health and Social Services (MOHSS) and Catholic Health Services, aimed to ensure that patients, treatment supporters, family members, and the wider community are well informed; improve adherence to ARV treatment in Namibia; and minimize resistance to ARVs.

In collaboration with BroadReach Health Care and Catholic Health Services, USAID-funded SPS provided technical support to develop patient-based ARV treatment literacy communication tools. The package of tools comprised a pictorial flip chart, posters, and a series of videos produced in English, Afrikaans, Oshindonga, Oshikwanyama, Thimbukushu, and Ngciriku-Rumanyo. The aim of these materials was to standardize messages used for ARV treatment counseling. The materials focused on four priority themes: (1) preparing to start ARV therapy, (2) starting ARV therapy, (3) alcohol and adherence, and (4) long-term adherence to ARV therapy. Each video was 8 to 10 minutes long and featured Namibians at home or at a health care facility sharing their experiences on ART.

The videos and flips charts were piloted at six health facilities in six regions. Following the pilot, an evaluation was conducted to assess the change in ART knowledge between pilot sites and control sites. This evaluation demonstrated the intervention's effectiveness in improving both ART knowledge and the efficiency of the counseling process. The MOHSS approved the roll-out of the ART treatment literacy tool from the six pilot sites to health facilities across Namibia. As part of the country-wide roll-out plan, the treatment literacy approach was incorporated into the Medicines Adherence Counseling curriculum.

At the micro level, interventions such as improving health literacy can positively impact adherence to medication; however, as in Namibia, such interventions are most effective when supported by policy decisions at the macro level and institutionalized changes at the meso level (e.g., changes to the preservice curriculum).

CHAPTER SUMMARY

The relationship between provider and patient at the micro level of the health system is where the health system core functions culminate in the interactions and experience of patients with health care providers and the health system. In addition to macro- and meso-level interventions that help to form the environment in which patients seek care, interventions that aim to improve the patient-provider relationship, simplify treatment regimens, and support patients at home and in the community can amplify adherence efforts.

Medication non-adherence is a global problem that contributes to poor health outcomes, increased cost, and reduced quality of life for patients. Beyond negative consequences for individuals, poor adherence also affects nearly every aspect of the health care system and can exacerbate the development of antimicrobial resistance.

While medicine coverage has rapidly increased in some parts of the world, there has been little focus on developing standardized and system-based strategies for monitoring and improving adherence. Poor adherence goes beyond patients; it is a multidimensional challenge that requires multidimensional solutions. Interventions to promote adherence should address barriers at all three levels of the health system: micro, meso, and macro. Each of these levels interacts with and influences the other two. Effective adherence interventions require addressing all three aspects of the health system to change the knowledge, attitudes, and skills of patients, health care providers, and policy makers as well as the health care environment in which these individuals interact.

The **macro level** refers to high-level governance and leadership, typically at the national level, where the focus is on policy development and strategy. Increased focus on adherence at the macro level helps to align stakeholders around a common vision and supports additional financial allocations for adherence-related interventions. Leadership and policy initiatives at the macro level may target the expansion of human resources for health, the provision of incentives and enablers, improved access to pharmaceuticals and services, and financial policies that support adherence. Knowledge gained from managing HIV/AIDS treatment programs, along with new forays into applied research, should be utilized to improve the management of other chronic conditions.

The **meso level** refers to the local health system, where the focus is on organizing and managing health care that supports and enables patients to remain adherent to their medication. Including medication adherence topics in pre- and in-service training curricula ensures that all health providers have appropriate competencies for supporting patient adherence. Once in the workplace, health providers should have access to the necessary tools and techniques to measure and improve patient adherence. Minimizing potential barriers to care, including long wait times, overburdened staff, and a lack of private consultation rooms, is also critical at the meso level. Creating an environment that takes into account the needs of the patient combined with improved patient-provider interactions at the micro level helps to eliminate barriers to medication adherence. Interventions at this level should also promote collaboration among various health care professionals and ensure that all members of the health care team are supporting patient adherence and promoting pharmaceutical care.

Adherence interventions at the **micro level** aim to improve patients' knowledge, skills, and behaviors that are necessary to manage their medications well. This goal requires that providers develop strong active listening skills so that they are cognizant of the patient's beliefs and preferences. It

also requires providers to promote patient-centered care through shared decision-making between the patient and provider and through behavioral programs that assist patients in making the behavior changes necessary to adhere to their treatment plan. These efforts should be complemented by provider selection of simple, convenient, and cost-conscious therapy, as well as setting up necessary follow-up visits to ensure that the original therapy plan is working for the patient and allows for adjustments as needed. Finally, interventions at the micro level can bolster patient adherence through social support systems such as peer-to-peer counseling and linking to patient-support organizations.

The SIAPS adherence framework depicted in figure 2 shows the three levels of the health system and adherence interventions available at each. The strongest interventions are those that target all three levels and multiple core functions of the health system. Such multilevel interventions bring complementarity in action and support better outcomes. In addition, each core function of the health system influences the environment in which patients seek care and receive treatment and therefore affects how well the health system supports patient adherence.

The health system determines patient access to care, resources, and information. Without functioning facilities, available medicines, appropriate tools and techniques, adequate counseling, and guidance from skilled health professionals, achieving and sustaining adherence over the long term will continue to be a major challenge. A systems-based approach is critical to achieve comprehensive, institutionalized, and sustainable results. Improving adherence is cost effective for the health system; improves patient outcomes and quality of life; and contributes to USAID priority goals, such as AIDS Free Generation, Ending Preventable Child and Maternal Deaths, and Protecting Communities from Infectious Diseases.

REFERENCES

1   Ho PM, Bryson CL, Rumsfeld JS. Medication Adherence: Its Importance in Cardiovascular Outcomes. Circulation. 2009;119:3028–3035.

2   World Health Organization. Adherence to Long Term Therapies: Evidence for action. Geneva: WHO; 2003.

3   Ibid.

4   Ibid.

5   Ibid.

6   Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353:487–497.

7   Ibid.

8   Clifford S, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the Necessity-Concerns Framework. J Psychosom Res. 2008; 64(1):41–6.

9   IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

10   Ibid.

11   WHO. Innovative Care for Chronic Conditions; 2002.

12   WHO. World Health Report 2002: Reducing risks, promoting health life.

13   Muszbek N, Brixner D, Benedict A et al. The economic consequences of noncompliance in cardiovascular disease and related conditions: A literature review. Int J Clin Pract. 2008; 62:338–351.

14   Currie C, Peyrot M, Morgan C et al. The impact of Treatment Noncompliance on Mortality in People with Type 2 Diabetes. Diabetes Care. 2012; 35(6):1279–1284.

15   Rhee M, Slocum W, Ziemer D et al. Patient adherence improves glycemic control. Diabetes Educ. 2005; 31(20):240–50.

16   World Health Organization. Adherence to Long Term Therapies: Evidence for action. Geneva: WHO; 2003.

17   Richardson R et al. Learning curve. Hypertension: Catch them when they're older. Nursing Times. 2000; 96:42–43.

18   National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan; 2007.

19   IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

20   World Health Organization. Adherence to Long Term Therapies: Evidence for action. Geneva: WHO; 2003.

21   Boswell KA, Cook CL, Burch SP et al. Associating Medication Adherence with Improved Outcomes: A Systematic Literature Review. Am J Pharm Benefits. 2012; 4(4) e97–108.

22   Akinbosoye OE, Taitel MS, Grana J et al. Improving Medication Adherence and Health Care Outcomes in a Commercial Population through a Community Pharmacy. Population Health Management; 2016.

23   Ruppar TM, Cooper PS, Mehr DR, Delgado JM, Dunbar-Jacob JM. Medication adherence interventions improve heart failure mortality and readmission rates: Systematic review and meta-analysis of controlled trials. J Am Heart Assoc. 2016; 5:e002606.

24   IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change. 2012.

25   Ibid.

26   Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care. 2005; 43:521–530.

27   Shenolikar RA, Balkrishnan R, Camacho FT, Whitmire TJ, Anderson RT. Comparison of medication adherence and associated health care costs after introduction of pioglitazone treatment in African Americans versus all other races in patients with type 2 diabetes mellitus: A retrospective data analysis. Clin Ther. 2006; 28(8):1199–1207.

28   IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

29   Everybody's Business: Strengthening Health Systems to Improve Health Outcomes. WHO's Framework for Action. Geneva: WHO; 2007.

30   USAID. USAID's Vision for Health System Strengthening: 2015-2019. Available at: https://www.usaid.gov/sites/default/files/documents/1864/HSS-Vision.pdf.

31   World Health Organization. Innovative care for chronic conditions: building blocks for action: global report. Geneva: WHO; 2002.

32   Ibid.

33   Osterberg L, Blaschke T. Drug therapy; adherence to medication. New Engl J of Med. 2005; 353(5):487–497.

34   Joyner-Grantham J et al. Self-reported influences of hopelessness, health literacy, life style action, and patient inertia on blood pressure control in a hypertensive emergency department population. Am J Med Sci. 2009; 338(5):368–372.

35   Uzochukwu et al. Determinants of non-adherence to subsidized antiretroviral treatment in Southeast Nigeria. Health Policy and Planning. 2009; 24:189–196.

36   Brunner R et al. Predictors of adherence in the Women's Health Initiative Calcium and Vitamin D Trial. Behav Med. 2009; 34(4):145–155.

37   Kip E, Ehlers V, Wal van der D. Patients' adherence to antiretroviral therapy in Botswana. J Nurs Scholarsh. 2009; 41(2):149–157.

38   Brown MT, Bussell JK. Medication Adherence: WHO Cares? Mayo Clinic Proc. 2011; 86(4):304–314.

39   Chalker J. Measuring adherence using paper-based facility records: Methods of the INRUD initiative for improving antiretroviral adherence in Africa [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

40   Gordon K, Smith F, Dhillon S. Effective chronic disease management: Patients' perspectives on medication-related problems. Patient Educ Couns. 2007; 65(3):407–415.

41   Bowry AD et al. A Systematic Review of Adherence to Cardiovascular Medications in Resource-Limited Settings. Journal of General Internal Medicine. 2011; 26(12):1479–91.

42   Obua et al. Multiple ART programs create a dilemma for providers to monitor ARV adherence in Uganda. The Open AIDS Journal. 2011; 5: 17–24.

43   Yap AF, Thirumoorthy T, Kwan YH. Medication adherence in the elderly. Case Report. J Clin Gerontology Geriatrics. 2016; 7:64–67.

44   Leguelinel-Blanche G, Dubois F, Bouvet S, Rou-marson C et al. Improving Patient's Primary Medication Adherence: The Value of Pharmaceutical Counselling. Medicine (Baltimore). 2015; 94(41):e1805.

45   National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan; 2007.

46   World Health Organization. How to develop and implement a national drug policy, 2nd edition. Geneva: WHO; 2001.

47   Afghanistan National Medicines Policy 2014–2019, Afghanistan Ministry of Public Health; 2014.

48   Malaysian National Medicines Policy, 2nd edition. Ministry of Health, Malaysia; 2012.

49   WHO, FAO, OIE. A Manual for Developing National Action Plans. Version 1. February 2016. Available at: http://apps.who.int/iris/bitstream/10665/204470/1/9789241549530_eng.pdf?ua=1.

50   WHO. Global Action Plan on Antimicrobial Resistance. 2015. Available at: http://www.wpro.who.int/entity/drug_resistance/resources/global_action_plan_eng.pdf.

51   SIAPS. Developing, Implementing, and Monitoring the Use of Standard Treatment Guidelines: A SIAPS How-to Manual. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health; 2015.

52   Ramjan R, Calmy A, Vitoria M et al. Systematic review and meta-analysis: Patient and program impact of fixed-dose combination antiretroviral therapy. Trop Med Int Health. 2014; 19:501–513.

53   Ho PM, Bryson CL, Rumsfeld JS. Medication Adherence: Its Importance in Cardiovascular Outcomes. Circulation, 2009; 119: 3028–3035.

54   Ibid.

55   World Health Organization. Adherence to Long Term Therapies: Evidence for action; 2003.

56   Holloway K, van Dijk L. The World Medicines Situation 2011: Rational Use of Medicines. 3rd ed. Geneva: WHO; 2011.

57   Management Sciences for Health. MDS-3: Managing Access to Medicines and Health

Technologies. Arlington, VA: Management Sciences for Health; 2012.

58   Agency for Healthcare Research and Quality (AHRQ). Medication Adherence Interventions: Comparative Effectiveness. Closing the Quality Gap: Revisiting the State of the Science. AHRQ Pub. No. 12-E010-1; 2012.

59   Ibid.

60   Matsui D. Medication adherence issues in patients: Focus on cost. Clinical Audit 5. 2013; 33–42.

61   Tuller et al. Transportation costs impede sustained adherence and access to HAART in a clinic population in Southwestern Uganda: A qualitative study. AIDS Behav. 2010; 14:778–784. DOI 10.1007/s10461-009-9533-2.

62   Centers for Disease Control and Prevention. Self-Study Modules on Tuberculosis: Module 9 – Patient Adherence to Tuberculosis Treatment Reading Material; 2012. Available at: http://www.cdc.gov/tb/education/ssmodules/module9/ss9reading3.htm.

63   Management Sciences for Health. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA: Kumarian Press: 33.11; 2011.

64   Nyamusore et al. Effects of patient tracking systems and providers incentives on patient appointment keeping [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

65   Adapted from Patel A, Hirschhorn L, Fullem A, Ojikutu B, Oser R. Adult Adherence to Treatment and Retention in Care. Arlington, VA: USAID | AIDSTAR-ONE PROJECT, Task Order 1.

66   Management Sciences for Health. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA: Kumarian Press: 33.12; 2011.

67   Ibid; 33.11.

68   Ibid; 33.11.

69   Ibid; 31.15.

70   Wouters et al. Impact of community-based support services on ART program delivery and outcomes in resource-limited countries: A synthetic review. BMC Health Services Research. 2012; 12:194.

71   Bedelu M, Ford N, Hilderbrand K, Reuter H. Implementing antiretroviral therapy in rural communities: The Lusikisiki model of decentralized HIV/AIDS care. Journal of Infectious Diseases. 2007; 196(Supplement 3):S464.

72   Ibid.

73   Zachariah R, Ford N, Philips M, Lynch S, Massaquoi M, Janssens V, Harries AD. Task shifting in HIV/AIDS: Opportunities, challenges and proposed actions for sub-Saharan Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2009; 103(6):549–558.

74   Cauldbeck MB et al. Adherence to Anti-Retroviral Therapy among HIV Patients in Bangalore, India. AIDS Research and Therapy. 2009; 6:7.

75   Hardon AP et al. From Access to Adherence: The Challenges of Antiretroviral Treatment: Studies from Botswana, Tanzania and Uganda. Geneva: WHO; 2006.

76   Patel A, Hirschhorn L, Fullem A, Ojikutu B, Oser R. Adult Adherence to Treatment and Retention in Care. Arlington, VA: USAID | AIDSTAR-ONE PROJECT, Task Order 1.

77   World Health Organization. Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector. Geneva: WHO; 2009b.

78   World Health Organization, Stop TB Partnership. Falling Short: Ensuring Access to Simple, Safe and Effective First-Line Medicines for Tuberculosis; 2010.

79   Uzochukwu BSC, Onwujekwe OE, Onoka AC, Okoli C, Uguru NP, Chukwuogo OI. Determinants of non-adherence to subsidized antiretroviral treatment in Southeast Nigeria. Health Policy and Planning. 2009; 24:189–196.

80   Kagee A, Remien RH, Berkman A, Hoffman S, Campos L, Swartz L. Structural barriers to ART adherence in Southern Africa: Challenges and potential ways forward. An International Journal for Research, Policy and Practice. 2011; 6:1, 83–97.

81   Strengthening Pharmaceutical Systems (SPS). Supporting Pharmacovigilance in Developing Countries: The Systems Perspective. Submitted to the US Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

82   IRIN. EAST AFRICA: Community HIV drug distribution improves adherence. Available at: http://www.irinnews.org/report/89757/east-africa-community-hiv-drug-distribution-improves-adherence.

83   Mabirizi D, Embrey M, Saleeb S, Aboagye Nyame F. Pharmaceutical System Strengthening Interventions to Improve Access to Antiretroviral Treatment. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program;
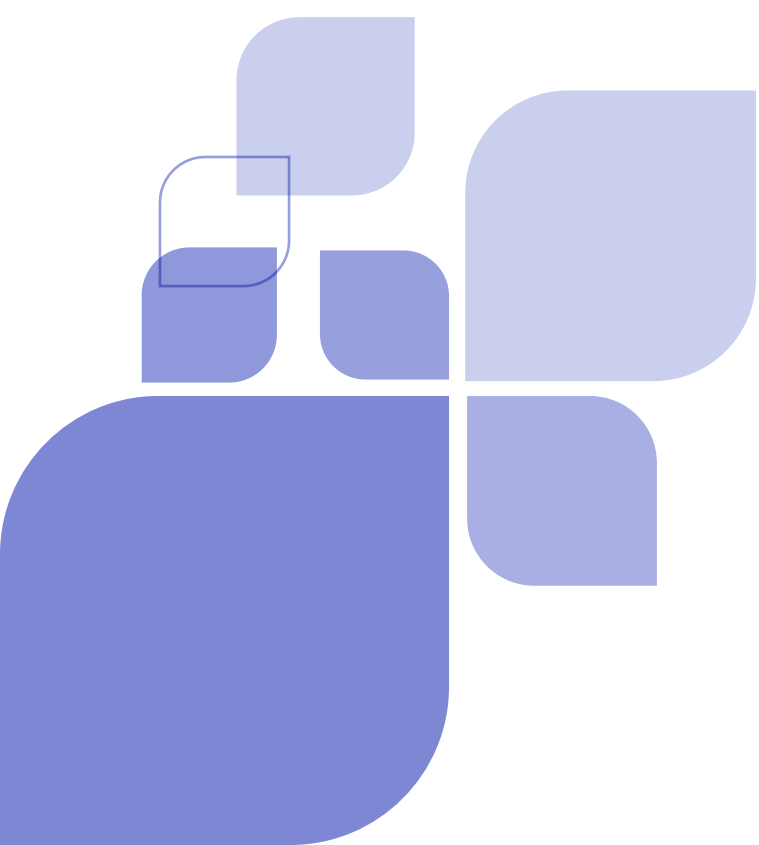
Arlington, VA: Management Sciences for Health; 2014.

84 Drug Seller Initiatives. Increasing Access to Family Planning Commodities through ADS in Liberia, Tanzania, and Uganda. Available at: http://www.drugsellerinitiatives.org/publication/increasing-access-to-family-planning-commodities-through-ads-in-liberia-tanzania-and-uganda/.

85 Rabkin M, El-Sadr WM. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases. Global Public Health. 2011; 6(3):247–256.

86 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

87 Embrey M, Hoos D, Quick J. How AIDS funding strengthens health systems: progress in pharmaceutical management. J Acquir Immune Defic Syndr. 2009; 52:S34–S37.

88 Chalker J, Wagner A, Tomson G, Johnson K, Wahlstrom R, Ross-Degnan D. Appointment systems are essential for improving chronic disease care in resource-poor settings: Learning from experiences with HIV patients in Africa. Int Health. 2013; 5:163–165.

89 Rabkin M, El-Sadr WM. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases. Global Public Health. 2011; 6(3):247–256.

90 Reproduced from Rabkin M, El-Sadr WM. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases. Global Public Health. 2011; 6(3):247–256.

91 Ibid.

92 Ibid.

93 Ho PM, Bryson CL, Rumsfeld JS. Medication Adherence: Its Importance in Cardiovascular Outcomes. Circulation. 2009; 119: 3028–3035.

94 ABC Project. Ascertaining Barriers for Compliance: policies for safe, effective and cost-effective use of medicines in Europe. Final Report of the ABC Project; 2012. Available at: http://www.abcproject.eu/.

95 Vervloet M, Linn AJ, van Weert JCM et al. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: A systematic review of the literature. J Am Med Inform Assoc. 2012; doi:10.1136/amiajnl-2011-000748.

96 Kagee A, Remien RH, Berkman A, Hoffman S, Campos L, Swartz L. Structural barriers to ART adherence in Southern Africa: Challenges and potential ways forward. An International Journal for Research, Policy and Practice. 2011; 6:1, 83–97.

97 Seabury SA, Gupta CN, Philipson TJ et al. Understanding and Overcoming Barriers to Medication Adherence: A Review of Research Priorities. J Manag Care Pharm. 2014; 20(8):775–83.

98 Management Sciences for Health/Amazon Malaria Initiative. Systematization of Studies of Adherence to Antimalarial Treatment Conducted from 2004 to 2009 in Countries of the Amazon Basin. Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health; 2010.

99 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

100 ABC Project. Ascertaining Barriers for Compliance: policies for safe, effective and cost-effective use of medicines in Europe. Final Report of the ABC Project; 2012. Available at: http://www.ABCproject.eu.

101 Ibid.

102 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

103 ABC Project. 2012. Final Report of the ABC Project. Ascertaining Barriers for Compliance Project. June. Available at: http://abcproject.eu/img/ABC%20Final.pdf.

104 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

105 Pande S, Hiller JE, Nkansah N, Bero L. The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilization and costs in low- and middle-income countries. Cochrane Database Syst Rev. 2013; 20(2).

106 American Pharmacists Association and National Association of Chain Drug Stores Foundation. Medication Therapy Management in Pharmacy Practice: Core Elements of an MTM Service Model; 2008. Available at: http://www.pharmacist.com/sites/default/files/files/core_elements_of_an_mtm_practice.pdf.

107 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

108 SIAPS. Technical Program Update on Promoting the Rational Use of Medicines, March 2015. Available at: http://siapsprogram.org/wp-content/

uploads/2015/03/RMU-TechUp-date-Mar2015.pdf.

109 Pharmaceuticals Fund and Supply Agency (PFSA) and Systems for Improved Access to Pharmaceuticals and Services (SIAPS). National Assessment on the Implementation Status of Clinical Pharmacy Service at Public Hospitals in Ethiopia. Addis Ababa: PFSA and SIAPS; 2016.

110 World Health Organization. Adherence to Long Term Therapies: Evidence for action; 2003.

111 Lam WY, Fresco P. Medication Adherence Measures: An Overview. Biomed Res Int. 2015; 217047.

112 Nachega et al. HIV treatment adherence, drug resistance, virologic failure: Evolving concepts. Infectious Disorders – Drug Targets. 2011; 11: 167–174.

113 Osterberg L, Blaschke T. Drug therapy; adherence to medication. New Engl J of Med. 2005; 353(5):487–497.

114 National Heart Foundation of Australia. Improving adherence in cardiovascular care: A toolkit for health professionals; 2011.

115 Oncology Nursing Society (ONS). Tools for Oral Adherence Toolkit; 2009.

116 Ross-Degnana D, Pierre-Jacques M, Zhan F et al. Measuring adherence to antiretroviral treatment in resource-poor settings: The clinical validity of key indicators. BMC Health Services Research. 2010; 10:42.

117 Chalker J. Measuring adherence using paper-based facility records: Methods of the INRUD initiative for improving antiretroviral adherence in Africa [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

118 Zhang HY, Ehiri J, Yang H et al. Impact of Community-Based DOT on Tuberculosis Treatment Outcomes: A Systematic Review and Meta-Analysis. PLOS ONE. 2016; 11(2):e0147744.

119 Karumbi J, Garner P. Directly observing people with TB take their drugs to help them complete their treatment. Cochrane Review; 2015.

120 Yin J, Yuan J, Hu Y, Wei X. Association between Directly Observed Therapy and Treatment Outcomes in Multidrug-Resistant Tuberculosis: A Systematic Review and Meta-Analysis. PLOS ONE. 2016; 11(3):e0150511.

121 Njogo S. Improving appointment keeping and adherence monitoring in ART facilities in Kenya: Views of providers and patients [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

122 Chalker J. Measuring adherence using paper-based facility records: methods of the INRUD initiative for improving antiretroviral adherence in Africa [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

123 Njogo S. Improving appointment keeping and adherence monitoring in ART facilities in Kenya: Views of providers and patients [PPT]. Presented at the Third International Conference on Improving Use of Medicines; 2011 Nov 14–18; Antalya, Turkey.

124 Ibid.

125 Obua et al. Multiple ART programs create a dilemma for providers to monitor ARV adherence in Uganda. The Open AIDS Journal. 2011; 5:17–24.

126 Systems for Improved Access to Pharmaceuticals and Services. Systems for Improved Access to Pharmaceutical Services Annual Report: Project Year 4, October 2014–September 2015. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health; 2015.

127 Chalker et al. Measuring adherence to antiretroviral treatment in resource-poor settings: the feasibility of collecting routine data for key indicators. BMC Health Services Research. 2010; 10:43. Available at: http://www.biomedcentral.com/1472-6963/10/43.

128 Chalker J, Wagner A, Tomson G, Laing R, Johnson K, Wahlstrom R, Ross-Degnan D, on behalf of INRUD-IAA. Appointment systems are essential for improving chronic disease care in resource-poor settings: Learning from experiences with HIV patients in Africa. Int. Health. 2013; 5(3):163–165. Available at: http://inthealth.oxfordjournals.org/content/5/3/163.full.pdf+html.

129 Rabkin M, El-Sadr WM. Why reinvent the wheel? Leveraging the lessons of HIV scale-up to confront non-communicable diseases. Global Public Health. 2011; 6(3):247–256.

130 Vervloet M, Linn AJ, van Weert JCM et al. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: A systematic review of the literature. J Am Med Inform Assoc. 2012; doi:10.1136/amiajnl-2011-000748.

131 Patel A, Hirschhorn L, Fullem A, Ojikutu B, Oser R. Adult Adherence to Treatment and Retention in Care. Arlington, VA: USAID | AIDSTAR-ONE PROJECT, Task Order 1.

132 Vervloet M, Linn AJ, van Weert JCM, et al. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: A systematic review of the literature. J Am Med Inform Assoc. 2012; doi:10.1136/amiajnl-2011-000748.

133 Thirumurthy H, Lester RT. M-health for health behavior change in resource-limited settings: Applications to HIV care and beyond. Bull World Health Organ. 2012; 90:390–392.

134 DiStefano MJ, Schmidt H. mHealth for Tuberculosis Treatment Adherence: A Framework to Guide Ethical Planning, Implementation, and Evaluation. Glob Health Sci Pract. 2016; 4(2):211–221.

135 Sharma P, Agarwal P. Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection: RHL commentary. The WHO Reproductive Health Library; Geneva: World Health Organization; 2012.

136 Ibid.

137 Pop-Eleches, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: A randomized controlled trial of text message reminders. AIDS. 2011; 25(6): 825–834.

138 Vervloet M, Linn AJ, van Weert JCM, et al. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature. J Am Med Inform Assoc. 2012; doi:10.1136/amiajnl-2011-000748.

139 Thirumurthy H, Lester RT. M-health for health behavior change in resource-limited settings: applications to HIV care and beyond. Bull World Health Organ. 2012; 90:390–392.

140 Bridges.org. Evaluation of the On Cue Compliance Service Pilot: Testing the Use of SMS Reminders in the Treatment of Tuberculosis in Cape Town, South Africa; 2005.

141 Interactive Research and Development (IRD). mHealth to Improve TB Care; 2012. Available at: http://www.stoptb.org/assets/documents/resources/publications/acsm/mHealth%20to%20Improve%20TB%20Care.pdf.

142 Thirumurthy H, Lester RT. M-health for health behavior change in resource-limited settings: applications to HIV care and beyond. Bull World Health Organ. 2012; 90:390–392.

143 Bridges.org. Evaluation of the On Cue Compliance Service Pilot: Testing the Use of SMS Reminders in the Treatment of Tuberculosis in Cape Town, South Africa; 2005.

144 Barclay E. Text Messages Could Hasten Tuberculosis Drug Compliance. The Lancet. 2009; 373(9657):15–16.

145 Vervloet M, Linn AJ, van Weert JCM, et al. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature. J Am Med Inform Assoc. 2012; doi:10.1136/amiajnl-2011-000748.

146 Kelly, Giordano. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: A randomized controlled trial of test message reminders. AIDS Correspondence. 2011; 25(8):1137.

147 Barclay E. Text Messages Could Hasten Tuberculosis Drug Compliance. The Lancet. 2009; 373(9657):15–16.

148 African Strategies for Health Project. Case Study from the mHealth Database: SIMpill Medication Adherence Solution. Management Sciences for Health; 2012. Accessed: 28 July 2016. Available at: http://www.africanstrategies4health.org/uploads/1/3/5/3/13538666/simpill_medication_adherences_solution.pdf.

149 Laufs U, Rettig-Ewen V, Böhm M. Strategies to improve drug adherence. European Heart Journal. 2010; doi:10.1093/eurheartj/ehq297.

150 Wu et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: Randomized controlled trial. BMJ. 2006; doi:10.1136/bmj.38905.447118.2F.

151 Garfein R, Collins K, Munoz F, Moser K, Cerecer-Callu P, et al. High Tuberculosis Treatment Adherence Obtained Using Mobile Phones for Video Directly Observed Therapy: Results of a Binational Pilot Study. Journal of Mobile Technology in Medicine. 2012;1:4S:30.

152 Patel A, Hirschhorn L, Fullem A, Ojikutu B, Oser R. Adult Adherence to Treatment and Retention in Care. Arlington, VA: USAID | AIDSTAR-ONE PROJECT, Task Order 1

153 Nachega et al. HIV treatment adherence, drug resistance, virologic failure: Evolving concepts. Infectious Disorders – Drug Targets. 2011; 11: 167–174.

154 Sigaloff et al. Early Warning Indicators for Population-Based Monitoring of HIV Drug Resistance in 6 African Countries. Clinical Infectious Diseases. 2012; 54(S4):S294–9.

155 Rowe AK, Rowe SY, Peters DH, Holloway KA, Chalker J, Ross-Degnan D. "Health Care Provider Performance Review: A systematic review of strategies to improve health worker performance in low- and middle-income countries. Preliminary results." USAID. Ronald

Reagan Building, Washington, DC. 31 March 2015. Seminar and Demonstration.

156 Starr, Sacks. Improving outcomes for patients with chronic disease: The medication adherence project (MAP). Toolkit and training guide for primary care providers and pharmacists; 2010.

157 Systems for Improved Access to Pharmaceuticals and Services (SIAPS). Enhancing Health Outcomes for Chronic Diseases in Resource-Limited Settings by Improving the Use of Medicines: The Role of Pharmaceutical Care. Submitted to the U.S. Agency for International Development by the SIAPS Program. Arlington, VA: Management Sciences for Health.

158 National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan; 2007.

159 Ibid.

160 Yarnall KSH, Østbye T, Krause KM, et al. Family Physicians as Team Leaders: 'Time' to Share the Care. Preventing Chronic Disease. 2009; 6(2): A59. Available at: www.cdc.gov/pcd/issues/2009/apr/08_0023.htm.

161 Geremew E, Worku F, Tadeg H, Ejigu E, Mekonnen N. Building Local Capacity for Clinical Pharmacy Service in Ethiopia through a Holistic In-Service Training Approach. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health; 2014.

162 ABC Project. Ascertaining Barriers for Compliance: policies for safe, effective and cost-effective use of medicines in Europe. Final Report of the ABC Project; 2012. Available at: http://www.abcproject.eu/.

163 Stubbs et al. Treatment partners and adherence to HAART in Central Mozambique. AIDS Care. 2009; 21(11):1412–1419.

164 Ibid.

165 Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ, Safren SA. Depression and diabetes treatment nonadherence: A meta-analysis. Diabetes Care. 2008; 31(12):2398–2403.

166 Wouters et al. Impact of community-based support services on ART program delivery and outcomes in resource-limited countries: A synthetic review. BMC Health Services Research. 2012; 12:194.

167 Ibid.

168 Kabore et al. The effect of community-based support services on clinical efficacy and health related quality of life in HIV/AIDS patients in resource limited settings in sub Saharan Africa. AIDS PATIENT CARE and STDs. 2010; 24 (9) DOI:10.1089/apc.2009.0307.

169 Ibid.

170 Stubbs et al. Treatment partners and adherence to HAART in Central Mozambique. AIDS Care. 2009; 21(11):1412–1419.

171 Ibid.

172 SIAPS. SIAPS Annual Report: Project Year 4, October 2014–September 2015. Submitted to USAID by the SIAPS Program. Arlington, VA: Management Sciences for Health; 2015.

173 Britten N, Stevenson FA, Barry CA, et al. Misunderstandings in prescribing decisions in general practice: Qualitative study. BMJ. 2000; 320:484–488.

174 Holloway K, van Dijk L. The World Medicines Situation 2011: Rational Use of Medicines. 3rd ed. Geneva: WHO; 2011.

175 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

176 Starr, Sacks. Improving outcomes for patients with chronic disease: The medication adherence project (MAP). Toolkit and training guide for primary care providers and pharmacists; 2010.

177 National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan; 2007.

178 Starr, Sacks. Improving outcomes for patients with chronic disease: the medication adherence project (MAP). Toolkit and training guide for primary care providers and pharmacists; 2010.

179 Management Sciences for Health. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA: Management Sciences for Health; 2012.

180 Starr, Sacks. Improving outcomes for patients with chronic disease: the medication adherence project (MAP). Toolkit and training guide for primary care providers and pharmacists; 2010.

181 Brown MT, Bussell JK. Medication Adherence: WHO Cares? Mayo Clinic Proc. 2011; 86(4): 304–314.

182 Systems for Improved Access to Pharmaceuticals and Services. Preventing and Minimizing Risks Associated with Antituberculosis Medicines to Improve Patient Safety. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health; 2013.

183 IMS Institute for Healthcare Informatics. Advancing the responsible use of medicine: Applying levers for change; 2012.

184 Starr, Sacks. Improving outcomes for patients with chronic disease: The medication adherence project (MAP). Toolkit and training guide for primary care providers and pharmacists; 2010.

185 National Heart Foundation of Australia. Improving adherence in cardiovascular care: A toolkit for health professionals; 2011.

186 Laufs U, Rettig-Ewen V, Böhm M. Strategies to improve drug adherence. European Heart Journal. 2010; doi:10.1093/eurheartj/ehq297.

187 National Heart Foundation of Australia. Improving adherence in cardiovascular care: a toolkit for health professionals; 2011.

188 Ibid.

189 Management Sciences for Health. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA: Management Sciences for Health. 2012;33.12.

190 Laufs U, Rettig-Ewen V, Böhm M. Strategies to improve drug adherence. European Heart Journal. 2010; doi:10.1093/eurheartj/ehq297.

191 Matsui D. Medication adherence issues in patients: Focus on cost. Clinical Audit. 2013; 5 33–42.

192 Ibid.

193 Uzochukwu BSC, Onwujekwe OE, Onoka AC, Okoli C, Uguru NP, Chukwuogo OI. Determinants of non-adherence to subsidized antiretroviral treatment in Southeast Nigeria. Health Policy and Planning. 2009; 24:189–196.

194 Management Sciences for Health. MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA: Management Sciences for Health. 201; 33.8.

195 Laufs U, Rettig-Ewen V, Böhm M. Strategies to improve drug adherence. European Heart Journal. 2010; doi:10.1093/eurheartj/ehq297.

196 Matsui D. Medication adherence issues in patients: Focus on cost. Clinical Audit. 2013; 5 33–42.

197 Brown MT, Bussell JK. Medication Adherence: WHO Cares? Mayo Clinic Proc. 2011; 86(4):304–314.

198 Management Sciences for Health. Building Local Coalitions for Containing Drug Resistance: A Guide. Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health; 2011.

199 Fuangchan A, Dhippayom T, Kongkaew C. Intervention to Promote Patients' Adherence to Antimalarial Medication: A Systematic Review. Am J Trop Med Hyg. 2014; 90(1): 11–19.

200 Lauwo JA, Hombhanje FW, Tulo SP et al. Impact of pre-packaging antimalarial drugs and counselling on compliance with malaria treatment at Port Moresby General Hospital Adult Outpatient Department. P N G Med J. 2016 Mar-Jun; 49(1-2):14–21.

201 Bangalore S, Kamalakkannan G, Parkar S, Messerli FH. Fixed-dose combinations improve medication compliance: A meta-analysis. Am J Med. 2007; 120: 713–719.

202 World Health Organization. Adherence to Long Term Therapies: Evidence for action; 2003.

203 Ibid.

204 Gusdal et al. Peer counselors' role in supporting patients' adherence to ART in Ethiopia and Uganda. AIDS Care. 2011; 23(6):657–662.

205 Hartayu et al. Improving of Type 2 Diabetic Patients' Knowledge, Attitude, and Practice Toward Diabetes Self-Care by Implementing Community-Based Interactive Approach – Diabetes Mellitus Strategy. BMC Research Notes. 2012; 5:315.

206 Hartayu et al. Improving Diabetic Patients' Adherence to Treatment Program by Using Community-Based Interactive Approach Diabetes Mellitus (CBIA-DM) Strategy in Hospital-Based Patients Community [PowerPoint presentation]. International Conference on Improving the Use of Medicines; 2011.

207 World Health Organization. Adherence to Long Term Therapies: Evidence for action; 2003.

208 Birbeck GL et al. Antiretroviral Adherence in Rural Zambia: The First Year of Treatment Availability. The American Journal of Tropical Medicine and Hygiene. 2009; 80(4):669–74.

209 Nam SL et al. The Relationship of Acceptance or Denial of HIV-Status to Antiretroviral Adherence among Adult HIV Patients in Urban Botswana. Social Science & Medicine. 2008; 67(2):301–10.

210 Torpey KE et al. Adherence Support Workers: A Way to Address Human Resource Constraints in Antiretroviral Treatment Programs in the Public Health Setting in Zambia. PLOS One. 2008; 3(5):e2204.