

Section I

SECTION I

Setting the scene

Chapter I

C H A P T E R I

Defining Adherence

1. What is adherence? 17
2. The state-of-the-art measurement 18
3. References 19

1. What is adherence?

Although most research has focused on adherence to medication, adherence also encompasses numerous health-related behaviours that extend beyond taking prescribed pharmaceuticals. The participants at the WHO Adherence meeting in June 2001 (1) concluded that defining adherence as “the extent to which the patient follows medical instructions” was a helpful starting point. However, the term “medical” was felt to be insufficient in describing the range of interventions used to treat chronic diseases. Furthermore, the term “instructions” implies that the patient is a passive, acquiescent recipient of expert advice as opposed to an active collaborator in the treatment process.

In particular, it was recognized during the meeting that adherence to any regimen reflects behaviour of one type or another. Seeking medical attention, filling prescriptions, taking medication appropriately, obtaining immunizations, attending follow-up appointments, and executing behavioural modifications that address personal hygiene, self-management of asthma or diabetes, smoking, contraception, risky sexual behaviours, unhealthy diet and insufficient levels of physical activity are all examples of therapeutic behaviours.

The participants at the meeting also noted that the relationship between the patient and the health care provider (be it physician, nurse or other health practitioner) must be a partnership that draws on the abilities of each. The literature has identified the quality of the treatment relationship as being an important determinant of adherence. Effective treatment relationships are characterized by an atmosphere in which alternative therapeutic means are explored, the regimen is negotiated, adherence is discussed, and follow-up is planned.

The adherence project has adopted the following definition of adherence to long-term therapy, a merged version of the definitions of Haynes (2) and Rand (3):

the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.

Strong emphasis was placed on the need to differentiate adherence from compliance. The main difference is that adherence requires the patient's agreement to the recommendations. We believe that patients should be active partners with health professionals in their own care and that good communication between patient and health professional is a must for an effective clinical practice.

In most of the studies reviewed here, it was not clear whether or not the "patient's previous agreement to recommendations" was taken into consideration. Therefore, the terms used by the original authors for describing compliance or adherence behaviours have been reported here.

A clear distinction between the concepts of acute as opposed to *chronic*, and *communicable* (infectious) as opposed to *noncommunicable*, diseases must also be established in order to understand the type of care needed. Chronic conditions, such as human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS) and tuberculosis, may be infectious in origin and will need the same kind of care as many other chronic noncommunicable diseases such as hypertension, diabetes and depression.

The adherence project has adopted the following definition of chronic diseases:

"Diseases which have one or more of the following characteristics: they are permanent, leave residual disability, are caused by nonreversible pathological alteration, require special training of the patient for rehabilitation, or may be expected to require a long period of supervision, observation or care" (4).

2. The state-of-the-art measurement

Accurate assessment of adherence behaviour is necessary for effective and efficient treatment planning, and for ensuring that changes in health outcomes can be attributed to the recommended regimen. In addition, decisions to change recommendations, medications, and/or communication style in order to promote patient participation depend on valid and reliable measurement of the adherence construct. Indisputably, there is no "gold standard" for measuring adherence behaviour (5,6) and the use of a variety of strategies has been reported in the literature.

One measurement approach is to ask providers and patients for their subjective ratings of adherence behaviour. However, when providers rate the degree to which patients follow their recommendations they overestimate adherence (7,8). The analysis of patients' subjective reports has been problematic as well. Patients who reveal they have not followed treatment advice tend to describe their behaviour accurately (9), whereas patients who deny their failure to follow recommendations report their behaviour inaccurately (10). Other subjective means for measuring adherence include standardized, patient-administered questionnaires (11). Typical strategies have assessed global patient characteristics or "personality" traits, but these have proven to be poor predictors of adherence behaviour (6). There are no stable (i.e. trait) factors that reliably predict adherence. However, questionnaires that assess specific behaviours that relate to specific medical recommendations (e.g. food frequency questionnaires (12) for measuring eating behaviour and improving the management of obesity) may be better predictors of adherence behaviour (13).

Although objective strategies may initially appear to be an improvement over subjective approaches, each has drawbacks in the assessment of adherence behaviours. Remaining dosage units (e.g. tablets) can be counted at clinic visits; however, counting inaccuracies are common and typically result in overestimation of adherence behaviour (14), and important information (e.g. timing of dosage and patterns of missed dosages) is not captured using this strategy. A recent innovation is the electronic monitoring device (medication event monitoring system (MEMS)) which records the time and date when a medication container was opened, thus better describing the way patients take their medications (9).

Unfortunately, the expense of these devices precludes their widespread use. Pharmacy databases can be used to check when prescriptions are initially filled, refilled over time, and prematurely discontinued. One problem with this approach is that obtaining the medicine does not ensure its use. Also, such information can be incomplete because patients may use more than one pharmacy or data may not be routinely captured.

Independently of the measurement technique used, thresholds defining “good” and “poor” adherence are widely used despite the lack of evidence to support them. In practice, “good” and “bad” adherence might not really exist because the dose–response phenomenon is a continuum function.

Although dose–response curves are difficult to construct for real-life situations, where dosage, timing and others variables might be different from those tested in clinical trials, they are needed if sound policy decisions are to be made when defining operational adherence thresholds for different therapies.

Biochemical measurement is a third approach for assessing adherence behaviours. Non-toxic biological markers can be added to medications and their presence in blood or urine can provide evidence that a patient recently received a dose of the medication under examination. This assessment strategy is not without drawbacks as findings can be misleading and are influenced by a variety of individual factors including diet, absorption and rate of excretion (15).

In summary, measurement of adherence provides useful information that outcome-monitoring alone cannot provide, but it remains only an estimate of a patient’s actual behaviour. Several of the measurement strategies are costly (e.g. MEMS) or depend on information technology (e.g. pharmacy databases) that is unavailable in many countries. Choosing the “best” measurement strategy to obtain an approximation of adherence behaviour must take all these considerations into account. Most importantly, the strategies employed must meet basic psychometric standards of acceptable reliability and validity (16). The goals of the provider or researcher, the accuracy requirements associated with the regimen, the available resources, the response burden on the patient and how the results will be used should also be taken into account. Finally, no single measurement strategy has been deemed optimal. A multi-method approach that combines feasible self-reporting and reasonable objective measures is the current state-of-the-art in measurement of adherence behaviour.

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Chapter II

CHAPTER II

The magnitude of the problem of poor adherence

1. A worldwide problem of striking magnitude 24
2. The impact of poor adherence grows as the burden of chronic diseases grows worldwide 24
3. The poor are disproportionately affected 25
4. References 30

1. A worldwide problem of striking magnitude

A number of rigorous reviews have found that, in developed countries, adherence among patients suffering chronic diseases averages only 50% (17,18). The magnitude and impact of poor adherence in developing countries is assumed to be even higher given the paucity of health resources and inequities in access to health care.

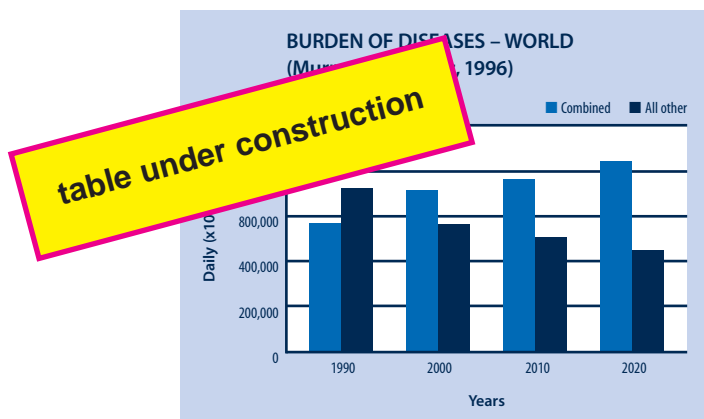
For example, in China, Gambia and the Seychelles, only 43%, 27% and 26%, respectively, of patients adhere to their antihypertensive medication regimen (19–22). In developed countries, such as the United States, only 51% of the patients treated for hypertension adhere to the prescribed treatment (23). Data on patients with depression reveal that between 40% and 70% adhere to antidepressant therapies (24). In Australia, only 43% of the patients take their asthma medication as prescribed all the time and only 28% use prescribed preventive medication (25). In the treatment of HIV and AIDS, adherence to antiretroviral agents varies between 37% and 83% depending on the drug under study (26,27) and the demographic characteristics of patient populations (28). This represents a tremendous challenge to population health efforts where success is determined primarily by adherence to long-term therapies.

Although extremely worrisome, these indicators provide an incomplete picture. To ascertain the true extent of adherence, data on developing countries and important subgroups, such as adolescents, children and marginal populations are urgently required. A full picture of the magnitude of the problem is critical to developing effective policy support for efforts aimed at improving adherence.

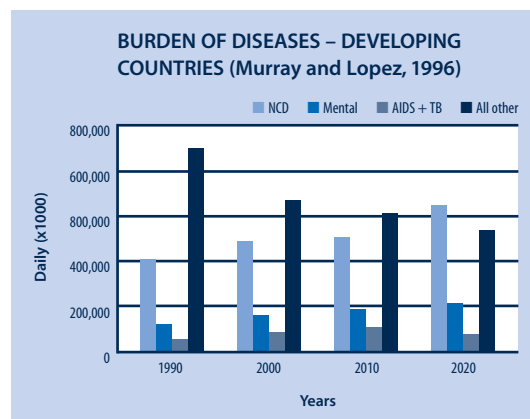
In developed countries, adherence to long-term therapies in the general population is around 50% and much lower in developing countries.

2. The impact of poor adherence grows as the burden of chronic diseases grows worldwide

Non-communicable diseases, mental health disorders, HIV and AIDS and tuberculosis, *combined* represented 54% of the burden of all illness worldwide in 2001 (13) and will exceed 65% of the global burden of disease in 2020 (Fig. 1) (14). Contrary to popular belief, noncommunicable diseases and mental health problems are also prevalent in developing countries, representing as much as 46% of the total burden of disease for the year 2001 (13), and predicted to rise to 56% by 2020 (Fig. 2) (14).



Source: reference (30) – DALY



Source: reference (xx) – AIDS + TB, acquired immunodeficiency syndrome and tuberculosis; DALY, xxxx; NCD, noncommunicable diseases

3. The poor are disproportionately affected

When we are sick, working is hard and learning is harder still. Illness blunts our creativity, cuts out opportunities. Unless the consequences of illness are prevented, or at least minimized, illness undermines people, and leads them into suffering, despair and poverty.

Kofi Annan, Secretary-General of the United Nations on the occasion of the release of the Report of the Commission on Macroeconomics and Health, in London, 20 December 2001.

There is a two-way interdependent relationship between economic poverty and chronic disease. Many of the world's poor, despite regional differences in geography, culture and commerce, experience the same discouraging cycle: being healthy requires money for food, sanitation and medical care, but to earn money, one must be healthy. The lack of adequate care for chronic conditions forces poor families to face a particularly heavy burden of caring for their loved ones that undermines the development of their most basic roles. Women are particularly "taxed" by the lack of a health care system that deals effectively with chronic diseases (15-17). Competing needs in populations suffering from chronic poverty undermine efforts to address the needs of patients requiring long-term care, including the problem of adherence to medications and therapies.

Poor adherence compounds the challenges of improving health in poor populations, and results in waste and underutilization of already limited treatment resources.

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Chapter III

C H A P T E R I I I

How does poor adherence affect policy-makers and health managers?

1. Diabetes 29
2. Hypertension 31
3. Asthma 32

There is strong evidence that many patients with chronic illnesses including asthma, hypertension, diabetes and HIV and AIDS, have difficulty adhering to their recommended regimens. This results in less than optimal management and control of the illness. Poor adherence is the primary reason for sub-optimal clinical benefit (1,2). It causes medical and psychosocial complications of disease, reduces patients' quality of life, and wastes health care resources. Taken together, these direct consequences impair the ability of health care systems around the world to achieve population health goals.

The conclusions of research in this area are unequivocal – adherence problems are observed in all situations where the self-administration of treatment is required, regardless of type of disease, disease severity and accessibility to health resources. While it may seem to be a simple issue, many factors contribute to adherence problems. Although some of these factors are patient-related, the characteristics of the disease and its treatment, and attributes of the health care system and service delivery also have great influence. Adherence problems have generally been overlooked by health stakeholders, and as a result have received little direct, systematic, intervention. Three prevalent chronic diseases, diabetes, hypertension and asthma provide compelling illustrations of different facets of these issues.

1. Diabetes

Poor adherence to the treatment for diabetes results in avoidable suffering for the patients and excess costs to the health system. The CODE-2 study (Cost of Diabetes in Europe – type 2) found that, in Europe, only 28% of patients treated for diabetes achieved good glycaemic control (3,4). The control of diabetes requires more than just taking medicine. Other aspects of self-management such as self-monitoring of blood glucose, dietary restrictions, regular foot care and ophthalmic examinations have all been shown to markedly reduce the incidence and progression of complications of diabetes. In the United States, less than 2% of adults with diabetes perform the full level of care that has been recommended by the American Diabetes Association (5). Poor adherence to recognized standards of care is the principal cause of development of complications of diabetes and their associated individual, societal and economic costs.

The CODE-2 study was done in countries with nearly full access to medicines. The picture in developing countries, where many fewer patients have their diabetes well-controlled, is cause for even greater concern.

Patients with diabetes usually have co-morbidities that make their treatment regimens even more complex. In particular, other commonly associated diseases such as hypertension, obesity and depression are themselves known to be characterized by poor rates of adherence, and serve to further increase the likelihood of poor treatment outcomes (6,7).

The combined health and economic burden of diabetes is huge and increasing. The CODE-2 study showed that the total cost of treating more than 10 million patients with type 2 diabetes in the countries studied was approximately \$29 billion, which represents an average of 5% of the total health care expenditure in each country. The overall cost to the health care system of treating patients with type 2 diabetes is on average over 1.5 times higher than per capita health care expenditure, an excess cost-burden of 66% over the general population. Furthermore, that cost increases 2- to 3.5-fold once patients develop preventable microvascular and macrovascular complications. Hospitalization costs, which include the treatment of long-term complications such as heart disease, account for 30–65% of the overall costs of the disease – the largest proportion of costs.

The direct costs of complications attributable to poor control of diabetes are 3–4 times higher than those of good control. The indirect costs (production losses due to sick leave, early retirement and premature death) are of approximately the same magnitude as these direct costs. Similar findings have been reported in other studies (8–10). Clearly, if health systems could be more effective in promoting adherence to self-management of diabetes, the human, social and economic benefits would be substantial.

2. Hypertension

It is well known that high blood pressure increases the risk of ischaemic heart disease 3- to 4-fold and of overall cardiovascular risk by 2- to 3-fold (11). The incidence of stroke increases approximately 3-fold in patients with borderline hypertension and approximately 8-fold in those with definite hypertension (12). It has been estimated that 40% of cases of acute myocardial infarction or stroke are attributable to hypertension (13–15).

Despite the availability of effective treatments, studies have shown that in many countries less than 25% of patients treated for hypertension achieve optimum blood pressure (16). For example, in the United Kingdom and the United States, only 7% and 30% of patients, respectively, had good control of blood pressure (17) and in Venezuela only 4.5% of the treated patients had good blood pressure control (18). Poor adherence has been identified as the main cause of failure to control hypertension (50–56). In one study, patients who did not adhere to beta-blocker therapy were 4.5 times more likely to have complications from coronary heart disease than those who did (26). The best available estimate is that poor adherence to therapy contributes to lack of good blood pressure control in more than two-thirds of people living with hypertension (27).

Considering that in many countries poorly controlled blood pressure represents an important economic burden (e.g. in the United States the cost of health care related to hypertension and its complications was 12.6% of total expenditure on health care in 1998) (28), improving adherence could represent for them an important potential source of health and economic improvement, from the societal (29), institutional (30) and employers' point of view (31,32).

3. Asthma

Research worldwide has documented poor adherence to treatments for asthma although there are large variations between countries (64). Rates of nonadherence among patients with asthma range from 30% to 70%, whether adherence is measured as percentage of prescribed medication taken, serum theophylline levels, days of medication adherence, or percentage of patients who failed to reach a clinically estimated adherence minimum (34). Evidence shows that adherence rates for the regular taking of preventive therapies are as low as 28% in developed countries (35,36).

Adherence is also a serious problem in particular populations such as children and adolescents. In adolescents, adherence to prescribed pulmonary medication may be as low as 30% in general practice (37). The complexity of optimum routine management of the disease – almost one hundred per cent self-managed – results in reduced adherence (38).

Failure to adhere to a regular self-management plan for asthma (including the regular taking of preventive therapies) results in poor asthma control which has clinical consequences, such as exacerbation of asthma, and decreased quality of life for the patients, as well as economic consequences, such as increased hospitalization and emergency department visits, resulting in unnecessarily high costs of health care.

There is a large variation between countries in the costs associated with asthma, but there are several outstanding commonalities: the total cost of asthma as a single condition currently comprises up to 1 to 2 per cent of health care expenditures; hospitalization and emergency care are consistently, disproportionately high, and there is a nearly 1:1 relationship between direct and indirect costs. The available data suggest that this distribution of excess costs is attributable to nonscheduled acute or emergency care, indicating poor asthma management and control (39). Such data highlight the significant cost of hospital care for asthma, compared to the costs of the more frequently used and less costly outpatient and pharmaceutical services.

Economic studies consistently show that the costs incurred by an adult with poorly controlled asthma are higher than those for a well-controlled patient with the same severity of disease. For severe asthma, it has been estimated that the savings produced by optimal control would be around 45% of the total medical costs (39). Poorer adherence to medication among elderly patients with moderate-to-severe asthma was associated with a 5% increase in annual physician visits, whereas better adherence was associated with a 20% decrease in annual hospitalization (40). This represents a significant potential cost saving to society in addition to the improvement in the quality of life and productive output of the affected individuals.

To the individual with asthma, or his or her family, the costs of asthma can be immense. For example, studies have demonstrated that the average amount spent by a family on medical treatments for children with asthma in the United States ranged between 5.5 and 14.5% of family income (41). In India, a study in the state of Andhra Pradesh estimated that the average expenditure for asthma treatment was about 9% of per capita income (42).

The above discussion shows that when asthma is not well controlled, it is likely to affect the social functioning of a country, impairing not only child development and education but also causing disruption in job training or ongoing employment for millions of adults worldwide.

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