

ADHERENCE TO LONG-TERM THERAPIES

Evidence for action



World Health Organization 2003

ADHERENCE TO LONG-TERM THERAPIES

Evidence for action



World Health Organization 2003

Adherence to long-term therapies : evidence for action.

1. Patient compliance 2. Long-term care 3. Drug therapy - utilization 4. Chronic disease - therapy
5. Health behavior 6. Evidence-based medicine I. WHO Adherence to Long Term Therapies Project
II. Global Adherence Interdisciplinary Network.

ISBN 92 4 154599 2

(NLM classification: W 85)

© World Health Organization 2003

All rights reserved.

Publications of the World Health Organization can be obtained from Marketing and Dissemination, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 2476; fax: +41 22 791 4857; email: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to Publications, at the above address (fax: +41 22 791 4806; email: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

Printed in Switzerland.

All correspondence should be sent to the author. Eduardo Sabaté, World Health Organization, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland (sabatee@who.int). Requests for free electronic copies (pdf format only) should be sent to: adherence@who.int

Preface

Over the past few decades we have witnessed several phases in the development of approaches aimed at ensuring that patients continue therapy for chronic conditions for long periods of time. Initially the patient was thought to be the source of the “problem of compliance”. Later, the role of the providers was also addressed. Now we acknowledge that a systems approach is required. The idea of compliance is associated too closely with blame, be it of providers or patients and the concept of adherence is a better way of capturing the dynamic and complex changes required of many players over long periods to maintain optimal health in people with chronic diseases.

This report provides a critical review of what is known about adherence to long-term therapies. This is achieved by looking beyond individual diseases. By including communicable diseases such as tuberculosis and human immunodeficiency virus/acquired immunodeficiency syndrome; mental and neurological conditions such as depression and epilepsy; substance dependence (exemplified by smoking cessation); as well as hypertension, asthma and palliative care for cancer, a broad range of policy options emerges. Furthermore, this broader focus highlights certain common issues that need to be addressed with respect to all chronic conditions regardless of their cause. These are primarily related to the way in which health systems are structured, financed and operated.

We hope that readers of this report will recognize that simplistic approaches to improving the quality of life of people with chronic conditions are not possible. What is required instead, is a deliberative approach that starts with reviewing the way health professionals are trained and rewarded, and includes systematically tackling the many barriers patients and their families encounter as they strive daily to maintain optimal health.

This report is intended to make a modest contribution to a much-needed debate about adherence. It provides analysis and solutions, it recommends that more research be conducted, but critically acknowledges the abundance of what we already know but do not apply. The potential rewards for patients and societies of addressing adherence to long-term therapies are large. WHO urges the readers of this report to work with us as we make the rewards real.

Derek Yach
January 2003

Acknowledgements

This report was edited by Eduardo Sabaté, WHO Medical Officer responsible for coordinating the WHO Adherence to Long-term Therapies Project, Management of Noncommunicable Diseases Department.

Deep appreciation is due to Rafael Bengoa, who envisioned the project and shaped the most crucial elements of the report, Derek Yach, who provided consistent support, intellectual stimulation and leadership to the project and Silvana De Castro, who provided valuable assistance with the many bibliographical reviews and with the writing of specific sections of this report.

Special appreciation goes to the scientific writers who provided their ideas and the material for the report. Their dedication and voluntary contributions have been central to this work. Thanks are also due to all the participants from WHO and the Global Adherence Interdisciplinary Network (GAIN) who by their continuous involvement and input during the planning, resource collection and writing phases of this project have given breadth and depth to the report.

Special thanks go to Steve Hotz for his intellectual support and hard work in helping to integrate the information on behavioural knowledge and its practical implications. Several international professional associations, in particular the International Society of Behavioural Medicine, the International Council of Nurses, the International Union of Psychological Sciences, the International Pharmaceutical Federation, and the World Organization of Family Doctors have played an important role in providing moral support and valuable input to the report.

Thanks are also due to Susan Kaplan, who edited the final text, and Tushita Bosonet, who was responsible for the artistic design.

The production of this report was made possible through the generous financial support of the governments of United Kingdom, Finland and Netherlands.

Scientific writers

The scientific writers who were invited to contribute to the report are recognized scientists in adherence-related issues. Their contributions were made voluntarily and have been incorporated following the directions of the editor of the report. All of them signed a Declaration of Interest. They are listed below in alphabetical order by topic. (Team leaders are indicated with an asterisk.)

Asthma

Bender, Bruce • Head • Pediatric Behavioral Health, National Jewish Medical and Research Center • USA

Boulet, Louis-Philippe • Professor • Laval University, Laval Hospital • Canada

Chaustre, Ismenia • Attending Physician and Professor • “JM de los Ríos” Children’s Hospital • Venezuela

Rand, Cynthia* • Associate Professor • Johns Hopkins University • USA

Weinstein, Andrew • Researcher and Clinical Practitioner • Christiana Medical Center • USA

With the active support of the WHO-NMH/MNC/Chronic Respiratory Diseases unit

Behavioural mechanisms

Hotz Stephen* • University Research Fellow • University of Ottawa • Canada

Kaptein, Ad A. • Head • Psychology unit, Leiden University Medical Centre • The Netherlands

Pruitt, Sheri • Director of Behavioral Medicine • Permanente Medical Group • USA

Sanchez Sosa, Juan • Professor • National University of Mexico • Mexico

Wiley, Cynthia • Professor of Pharmacoepidemiology • University of Rhode Island • USA

Cancer

De Castro, Silvana* • Technical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

Sabaté, Eduardo • Medical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

With the active support of the WHO-NMH/MNC/Program on Cancer Control unit

Depression

Peveler, Robert* • Head • Mental Health Group, Community Clinical Sciences Division, School of Medicine, University of Southampton • England

Tejada, Maria Luisa • Clinical practitioner • Hospital of Nyon • Switzerland

With the active support of the WHO-NMH/MSD/Mental and behavioural disorders unit

Diabetes

Karkashian, Christine* • Dean • School of Psychology, Latina University • Costa Rica

Schlundt, David • Associate Professor of Psychology • Vanderbilt University • USA

With the active support of the WHO-NMH/MNC/Diabetes unit

Epilepsy

Avanzini, Giuliano • President • International League against Epilepsy • Italy

de Boer, Hanneke M. • Global Campaign Co-Chair • The International Bureau for Epilepsy/Stichting Epilepsie Instellingen Nederland • the Netherlands

De Castro, Silvana* • Technical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

Engel, Jerome Jr • Global Campaign Co-Chair • International League against Epilepsy and Director of the Seizure Disorder Center, University of California at Los Angeles School of Medicine • USA

Lee, Philip • President • International Bureau for Epilepsy • Ireland

Sabaté, Eduardo • Medical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

With the active support of the WHO-NMH/MSD/Epilepsy unit, the International League Against Epilepsy and the International Bureau for Epilepsy

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)

Chesney, Margaret A.* • Professor of Medicine • University of California at San Francisco, Prevention Sciences Group • USA

Farmer, Paul • Director • Partners in health • Harvard University • USA

Leandre, Fernet • Director • Zanmi Lazante Health Care • Haiti

Malow, Robert • Professor and Director • AIDS Prevention Program, Florida International University • USA

Starace, Fabrizio • Director • Consultation Psychiatry and Behavioural Epidemiology Service, Cotugno Hospital • Italy

With the active support of the WHO-HIV/AIDS care unit

Hypertension

Mendis, Shanti* • Coordinator • Cardiovascular diseases • WHO-HQ

Salas, Maribel • Senior Researcher • Caro Research Institute • USA

Smoking cessation

De Castro, Silvana • Technical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

Lam, Tai Hing • Professor • Head Department of Community Medicine and Behavioural Sciences, University of Hong Kong • China

Sabaté, Eduardo* • Medical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

Smirnoff, Margaret • Nurse Practitioner • Mount Sinai Center • USA

With the active support of the WHO-NMH/Tobacco Free Initiative department

Tuberculosis

Dick, Judy* • Senior Researcher • Medical Research Center of South Africa • South Africa

Jaramillo, Ernesto • Medical Officer • Stop TB, WHO • Switzerland

Maher, Dermot • Medical Officer • Stop TB, WHO • Switzerland

Volmink, Jimmy • Director of Research and Analysis • Global Health Council • USA

Special topics

Children and adolescents

Burkhart, Patricia • Assistant Professor and Nurse Researcher • University of Kentucky • USA

With the active support of the WHO-FCH/Child and adolescent health unit

Elderly patients

Di Pollina, Laura • Chief • Clinical Geriatrics, Geneva University Hospital • Switzerland

Health Economics

Kisa, Adnan • Associate Professor • Baskent University • Turkey

Nuño, Roberto • Health Economist • Spain

Sabaté, Eduardo* • Medical Officer • Adherence Project, Department of Management of Communicable Diseases, WHO • Switzerland

Patients' perception of illness

Horne, Rob • Director and Professor of Psychology in Health Care • Centre for Health Care Research, University of Brighton • England

Introduction

Objectives and target audience

This report is part of the work of the Adherence to Long-term Therapies Project, a global initiative launched in 2001 by the Noncommunicable Diseases and Mental Health Cluster of the World Health Organization.

The main target audience for this report are policy-makers and health managers who can have an impact on national and local policies in ways that will benefit patients, health systems and societies with better health outcomes and economic efficiency. This report will also be a useful reference for scientists and clinicians in their daily work.

The main objective of the project is to improve worldwide rates of adherence to therapies commonly used in treating chronic conditions.

The four objectives of this report are to:

- summarize the existing knowledge on adherence, which will then serve as the basis for further policy development;
- increase awareness among policy-makers and health managers about the problem of poor rates of adherence that exists worldwide, and its health and economic consequences;
- promote discussion of issues related to adherence; and
- provide the basis for policy guidance on adherence for use by individual
- articulating consistent, ethical and evidence-based policy and advocacy positions; and
- managing information by assessing trends and comparing performance, setting the agenda for, and stimulating, research and involvement.

How to read this report

As this report intends to reach a wide group of professionals, with varied disciplines and roles, the inclusion of various topics at different levels of complexity was unavoidable. Also, during the compilation of the report, contributions were received from eminent scientists in different fields, who used their own technical languages, classifications and *definitions* when discussing adherence.

For the sake of simplicity, a table has been included for each disease reviewed in section III, showing the factors and interventions cited in the text, classified according to the five dimensions proposed by the project group and explained later in this report:

- social- and economic-related factors/interventions;
- health system/health care team-related factors/interventions;
- therapy-related factors/interventions;
- condition-related factors/interventions; and
- patient-related factors/interventions.

The section entitled “Take-home messages” summarizes the main findings of this report and indicates how readers could make use of them.

Section I:

Setting the scene, discusses the main concepts leading to the definition of adherence and its relevance to epidemiology and economics.

Section II:

Improving adherence rates: guidance for countries, summarizes the lessons learned from the reviews studied for this report and puts into context the real impact of adherence on health and economics for those who can make a change.

Section III:

Disease-specific reviews, discusses nine chronic conditions that were reviewed in depth. Readers with clinical practice or disease-oriented programmes will find it useful to read the review related to their current work. Policy-makers and health managers may prefer to move on to the Annexes.

Annex I:

Behavioural mechanisms explaining adherence, provides an interesting summary of the existing models for explaining people's behaviour (adherence or nonadherence), and explores the behavioural interventions that have been tested for improving adherence rates.

Annex II:

Statements by stakeholders, looks at the role of the stakeholder in improving adherence as evaluated by the stakeholders themselves.

Annexes III and IV:

Table of reported factors by condition and dimension and Table of reported interventions by condition and dimension, provide a summary of all the factors and interventions discussed in this report. These tables may be used to look for commonalities among different conditions.

Annex V:

Global Adherence Interdisciplinary network (GAIN), lists the members of this network.

Take-home messages

Poor adherence to treatment of chronic diseases is a worldwide problem of striking magnitude

Adherence to long-term therapy for chronic illnesses in developed countries averages 50%. In developing countries, the rates are even lower. It is undeniable that many patients experience difficulty in following treatment recommendations.

The impact of poor adherence grows as the burden of chronic disease grows worldwide

Noncommunicable diseases and mental disorders, human immunodeficiency virus/acquired immunodeficiency syndrome and tuberculosis, together represented 54% of the burden of all diseases worldwide in 2001 and will exceed 65% worldwide in 2020. The poor are disproportionately affected.

The consequences of poor adherence to long-term therapies are poor health outcomes and increased health care costs

Poor adherence to long-term therapies severely compromises the effectiveness of treatment making this a critical issue in population health both from the perspective of quality of life and of health economics. Interventions aimed at improving adherence would provide a significant positive return on investment through primary prevention (of risk factors) and secondary prevention of adverse health outcomes.

Improving adherence also enhances patients' safety

Because most of the care needed for chronic conditions is based on patient self-management (usually requiring complex multi-therapies), use of medical technology for monitoring, and changes in the patient's lifestyle, patients face several potentially life-threatening risks if not appropriately supported by the health system.

Adherence is an important modifier of health system effectiveness

Health outcomes cannot be accurately assessed if they are measured predominantly by resource utilization indicators and efficacy of interventions. The population health outcomes predicted by treatment efficacy data cannot be achieved unless adherence rates are used to inform planning and project evaluation.

"Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments"¹

Studies consistently find significant cost-savings and increases in the effectiveness of health interventions that are attributable to low-cost interventions for improving adherence. Without a system that addresses the determinants of adherence, advances in biomedical technology will fail to realize their potential to reduce the burden of chronic illness. Access to medications is necessary but insufficient in itself for the successful treatment of disease.

Health systems must evolve to meet new challenges

In developed countries, the epidemiological shift in disease burden from acute to chronic diseases over the past 50 years has rendered acute care models of health service delivery inadequate to address the health needs of the population. In developing countries, this shift is occurring at a much faster rate.

¹Haynes RB. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database of Systematic Reviews*, 2001, Issue 1.

Patients need to be supported, not blamed

Despite evidence to the contrary, there continues to be a tendency to focus on patient-related factors as the causes of problems with adherence, to the relative neglect of provider and health system-related determinants. These latter factors, which make up the health care environment in which patients receive care, have a major effect on adherence.

Adherence is simultaneously influenced by several factors

The ability of patients to follow treatment plans in an optimal manner is frequently compromised by more than one barrier, usually related to different aspects of the problem. These include: the social and economic factors, the health care team/system, the characteristics of the disease, disease therapies and patient-related factors. Solving the problems related to each of these factors is necessary if patients' adherence to therapies is to be improved.

Patient-tailored interventions are required

There is no single intervention strategy, or package of strategies that has been shown to be effective across all patients, conditions and settings. Consequently, interventions that target adherence must be tailored to the particular illness-related demands experienced by the patient. To accomplish this, health systems and providers need to develop means of accurately assessing not only adherence, but also those factors that influence it.

Adherence is a dynamic process that needs to be followed up

Improving adherence requires a continuous and dynamic process. Recent research in the behavioural sciences has revealed that the patient population can be segmented according to level-of-readiness to follow health recommendations. The lack of a match between patient readiness and the practitioner's attempts at intervention means that treatments are frequently prescribed to patients who are not ready to follow them. Health care providers should be able to assess the patient's readiness to adhere, provide advice on how to do it, and follow up the patient's progress at every contact.

Health professionals need to be trained in adherence

Health providers can have a significant impact by assessing risk of nonadherence and delivering interventions to optimize adherence. To make this practice a reality, practitioners must have access to specific training in adherence management, and the systems in which they work must design and support delivery systems that respect this objective. For empowering health professionals an "adherence counselling toolkit" adaptable to different socioeconomic settings is urgently needed. Such training needs to simultaneously address three topics: knowledge (information on adherence), thinking (the clinical decision-making process) and action (behavioural tools for health professionals).

Family, community and patients' organizations: a key factor for success in improving adherence

For the effective provision of care for chronic conditions, it is necessary that the patient, the family and the community who support him or her all play an active role. Social support, i.e. informal or formal support received by patients from other members of their community, has been consistently reported as an important factor affecting health outcomes and behaviours. There is substantial evidence that peer support among patients can improve adherence to therapy while reducing the amount of time devoted by the health professionals to the care of chronic conditions.

A multidisciplinary approach towards adherence is needed

A stronger commitment to a multidisciplinary approach is needed to make progress in this area. This will require coordinated action from health professionals, researchers, health planners and policy-makers.

C O N T E N T S

Preface	V
Acknowledgement	VII
Scientific writers	VIII
Introduction	XI
Take-home messages	XIII
Section I – Setting the scene	1
Chapter I – Defining adherence	3
Chapter II – The magnitude of the problem of poor adherence	7
Chapter III – How does poor adherence affect policy makers and health managers?	11
Section II – Improving adherence rates: guidance for countries	17
Chapter IV – Lessons learned	19
Chapter V – Towards the solution	27
Chapter VI – How can improved adherence be translated into health and economics benefits?	39
Section III – Disease-specific reviews	45
Chapter VII – Asthma	47
Chapter VIII – Cancer (palliative care)	59
Chapter IX – Depression	65
Chapter X – Diabetes	71
Chapter XI – Epilepsy	87
Chapter XII – HIV/AIDS	95
Chapter XIII – Hypertension	107
Chapter XIV – Tobacco smoking cessation	115
Chapter XV – Tuberculosis	123
Annexes	133
Annex I – Behavioural mechanisms explaining adherence	135
Annex II – Statements by stakeholders	151
Annex III – Table of reported factors by condition and dimension	162
Annex IV – Table of reported interventions by condition and dimension	166
Annex V – Global adherence interdisciplinary network (GAIN)	171
Where to find a copy of this book	177
Official designated depositories libraries for WHO publications	179
Reference libraries for WHO publications	183
WHO official sales agents world wide	195
Selected WHO publications of related interest	197
A ready-to-use pamphlet for partners willing to promote this book	199

S E C T I O N I

Setting the scene

CHAPTER I

Defining adherence

1. What is adherence? 3
2. The state-of-the-art measurement 4
3. References 5

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 “bad” 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.

3. References

1. Sabate E. *WHO Adherence Meeting Report*. Geneva, World Health Organization, 2001.
2. Haynes RB. *Determinants of compliance: The disease and the mechanics of treatment*. Baltimore MD, Johns Hopkins University Press, 1979.
3. Rand CS. Measuring adherence with therapy for chronic diseases: implications for the treatment of heterozygous familial hypercholesterolemia. *American Journal of Cardiology*, 1993, 72:68D-74D.
4. *Dictionary of health services management*, 2nd ed. Owing Mills, MD, National Health Publishing, 1982.
5. Timmreck TC, Randolph JF. Smoking cessation: clinical steps to improve compliance. *Geriatrics*, 1993, 48:63-66.
6. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics*, 1999, 21:1074-1090.
7. DiMatteo MR, DiNicola DD. *Achieving patient compliance*. New York, Pergamon, 1982.
8. Norell SE. Accuracy of patient interviews and estimates by clinical staff in determining medication compliance. *Social Science & Medicine - Part E, Medical Psychology*, 1981, 15:57-61.
9. Cramer JA, Mattson RH. Monitoring compliance with antiepileptic drug therapy. In: Cramer JA, Spilker B, eds. *Patient compliance in medical practice and clinical trials*. New York, Raven Press, 1991:123-137.
10. Spector SL et al. Compliance of patients with asthma with an experimental aerosolized medication: implications for controlled clinical trials. *Journal of Allergy & Clinical Immunology*, 1986, 77:65-70.
11. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care*, 1986, 24:67-74.
12. Freudenheim JL. A review of study designs and methods of dietary assessment in nutritional epidemiology of chronic disease. *Journal of Nutrition*, 1993, 123:401-405.
13. Sumartojo E. When tuberculosis treatment fails. A social behavioral account of patient adherence. *American Review of Respiratory Disease*, 1993, 147:1311-1320.
14. Matsui D et al. Critical comparison of novel and existing methods of compliance assessment during a clinical trial of an oral iron chelator. *Journal of Clinical Pharmacology*, 1994, 34:944-949.
15. Vitolins MZ et al. Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials*, 2000, 21:188S-194S.
16. Nunnally JC, Bernstein IH. *Psychometric theory*, 3rd ed. New York, McGraw-Hill, 1994.