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Adherence to Long-Term Therapy – A Model of Assessment into Primary Care

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1. Introduction

Adherence to long-term therapy is a challenge for patients worldwide. In developing countries the focus is placed on adherence to antiretroviral treatment for HIV and antibacterial treatment for TB, while patients and health care providers in developed countries grapple with adherence to treatment of chronic lifestyle diseases such as diabetes. Adherence is a crucial element of successful treatment – some say it is the backbone of any medical treatment. It is therefore of utmost importance for health care providers to assess how adherent their patients are. However, this is often overlooked in routine patient assessments in primary care.

This chapter describes the challenges of adherence with long-term treatments by using the example of antiretroviral treatment for HIV. It introduces the most common adherence measures and describes the experiences of integrating adherence assessment in primary health care settings in Cape Town, South Africa. Even though it focuses on adherence in pediatric patients, the observations and conclusions drawn from this chapter are highly relevant to any age group.

2. Adherence - “Drugs don't work in patients who don't take them”¹

Chronically ill patients need to take medication for the rest of their life. This requires a lot of discipline and commitment from the patients' part, as well as good education and communication from the health care providers' side. In the past, the term “compliance” was used to characterize the patients' following of health care providers' instructions. As models of patient-physician relationship have changed, so has the definition of “compliance”. The new definition challenges the often paternalistic model of decision-making and emphasizes a more equal cooperation between patient and health care provider. The term “compliance” has been replaced with “adherence”, to acknowledge the patient's more active participation in the decision-making process and seeing medication-taking behaviour from the patient's perspective: “Adherence is the engaged and accurate participation of an informed patient in

¹ Quote by C. EVERETT KOOP, Professor of Pediatrics and Paediatric Surgery, University of Pennsylvania; Surgeon General of the United States 1982 - 1989, quoted in: OSTERBERG and BLASCHKE (2005; p. 487)

a plan of care. It is a broader term than compliance – the extent to which patients follow the instructions of their healthcare providers – and implies understanding, consent, and partnership. Adherence includes entering into and continuing in a program or care plan, attending appointments and tests as scheduled, taking medications as prescribed, modifying lifestyle as needed, and avoiding risk behaviours. It includes adherence to care and adherence to medication, but is usually regarded as more than the sum of its parts.”². Osterberg and Blaschke (2005) further elaborate on the difference between compliance and adherence: “The word “adherence” is preferred by many health care providers, because “compliance” suggests that the patient is passively following the doctor’s orders and that the treatment plan is not based on a therapeutic alliance or contract established between the patient and the physician.” The World Health Organization suggests broadening the definition of the term adherence to “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” (WHO 2003; p. 3), according to Berg and Arnsten (2006; p. 579), this behaviour is “individual, complex and dynamic”. Table 1 illustrates the various dimensions of adherence, and each dimension’s correlate in the patient’s behaviour.

Adherence Behaviour	Behavioural Task
Medication-refill adherence	Patient picks up a prescription refill
Medication-interval adherence	Patient takes a medication at the right time of the day
Medication-quantity adherence	Patient takes the right number of pills
Medication-diet adherence	Patient takes medication in accordance with dietary requirements (if specified)

Table 1. Dimensions of adherence

Contrary to this concept, clinical practice often limits the term adherence to the intake of medication and disregards the broader implications of its definition. Adherence is usually reported as the percentage of the prescribed doses actually taken by the patient over a specified period of time, and thus reduced to recommendations that instruct the patient on tablet intake. For these instructions, adherence can vary along a continuum from 0 to 100 percent, sometimes over 100 percent if patients take more than the prescribed amount of medication. Adherence can also be reported as a dichotomous variable, classifying patients into the categories adherent or non-adherent. Since there is no consensual standard for what constitutes adequate adherence, the cut-off value for these categories depends on the patient’s condition, the characteristics of the regimen prescribed, on pharmacokinetics of the prescribed medication and on individual research protocols. For HIV infection, an adherence rate greater than 95 percent is considered adequate and necessary for treatment success (Chesney 2003; Paterson et al. 2000). However, common to all these definitions of adherence is the fact that they solely focus on the intake of medication and do not allow for an inclusion of dietary instructions, lifestyle changes or general health behaviour of patients.

In the industrialised world, adherence has been in the focus for medication of chronic diseases such as diabetes and hypertension, or for patients taking immunosuppressants after organ transplantation. In developing countries, HIV infection emerged as a relatively

² Quote from RABKIN et al. (2005; p. 11)

new chronic illness and the introduction of Highly Active Antiretroviral Therapy (HAART) placed a new emphasis on assessing adherence to HAART. Adherence has a significant impact on all outcome parameters of antiretroviral treatment: on plasma HIV RNA levels, on CD4+ lymphocyte count as well as on survival rates. Bangsberg et al. (2000) demonstrated a strong linear relationship between adherence to HAART and plasma HIV RNA levels, with a 10% decrease in adherence leading to a doubling of HIV RNA plasma levels. Among patients with undetectable HIV RNA load, adherence predicts the time that viral load is kept at undetectable levels (Raboud et al. 2002). Adherence was found to be significantly associated with successful virological outcome (Paterson et al. 2000) and an increase in CD4+ lymphocyte count (Singh et al. 1999). To the same extent that adequate adherence is linked to positive treatment outcomes, non-adherence can result in an increased viral load, emerging drug resistance that limits further treatment options, and, ultimately, in more rapid progression to clinical AIDS and increased mortality (Knobel et al. 2001).

There have been great concerns over whether the infrastructural, socio-economic and political difficulties in the countries of the developing world will allow for demanding and complicated treatment programs resulting in treatment success (Harries et al. 2001). The World Health Organization (WHO) advises that treatment principles in resource-limited settings be the same as for the developed world (WHO 2004); recent initiatives such as the Global Fund To Fight AIDS, Tuberculosis and Malaria (GFATM) and the Presidential Emergency Plan for AIDS Relief (PEPFAR) have provided funding to ensure availability and sustainability of antiretroviral treatment for these countries. Since the number of patients in developing countries is by far greater than in the developed world (UNAIDS 2008), these countries follow a public health approach in providing HAART for adults and children. The choice of antiretroviral drugs is limited, and fixed drug combinations are provided in so-called first- and second-line regimens. The term first-line regimen describes the initial antiretroviral drug combination that a patient starts with. Upon the development of resistance to one or more of the drugs a switch to the second-line regimen, which includes different drugs, is possible. These fixed combinations do not allow the possibility for patient-individualized, "tailor-made" regimens as available in the developed world (WHO 2005). In this way, the cost of antiretroviral drugs is reduced and treatment programs are more affordable and can allow for large amounts of patients. Given this limited choice of treatment options, the imperative of good adherence is of even greater importance in these settings. However, it has been contested whether or not good adherence would be possible.

In a public statement made in 2001, the then chief of the U.S. Agency for International Development (USAID), Andrew Natsios, was quoted to have said that Africans "don't know what Western time is" and thus could not take antiretroviral treatment on the proper schedule. Additionally he reportedly stated that when Africans were asked to take their drugs at a certain time of the day, they "do not know what you are talking about"³. This statement, implying that the culture and the general attitude of people living in African countries would render them unable to adhere to antiretroviral treatment, has been strongly condemned by patients, physicians and patients worldwide. In the following years,

³ See ATTARAN et al.: "Dead wrong on AIDS". Published on 15th July 2001 in The Washington Post, United States.

numerous studies from resource-limited settings with HIV-infected adults and children taking HAART have highlighted that adherence is, in fact, rather good (Byakika-Tusiime et al. 2005; Nachega et al. 2004, Vreeman et al. 2008). In the first of two South African studies, Orrell et al. (2003) from Cape Town found that of 278 adults followed over 48 weeks, the median adherence was 94%, and concluded that low socio-economic status was not a barrier to achieving good adherence to antiretroviral triple therapy. In the other South African study Nachega et al. (2004) could show that 97% of HIV-infected adults receiving antiretroviral treatment at a public hospital in Johannesburg had adherence levels of greater than 90 percent. These findings are consistent with a meta-analysis comparing the adherence to antiretroviral treatment in patients from the United States to the adherence in patients from Sub-Saharan Africa, which found that the latter patient group showed higher pooled rates of adherence, and underlined the ability of African patients to adhere to their treatment (Mills et al. 2006).

As lined out above, adherence in resource-limited settings is of even greater importance, yet may also be more difficult to achieve (Gill et al. 2005). In order not to jeopardize the limited options of treatment, virological suppression should be sustained for as long as possible. Emerging studies from various settings in resource-limited countries underline the findings by Mills et al. (2006) and show adherence rates that are as high or even higher than in the developed world (Byakika-Tusiime et al. 2005; Oyugi et al. 2004). In the context of these countries, structural and social inequalities have an unmistakable impact on the health status of patients. A recent report by the WHO Commission on Social Determinants of Health (CSDH 2008) indicates that the quality of urban and rural living conditions such as housing, sanitation and access to clean water are vital contributors to health. This should be borne in mind when comparing the outcomes of antiretroviral treatment in developing countries to outcomes from Europe and North America; it should also be borne in mind that the risk of treatment failure is higher when poorer health statuses exist, regardless of adherence. Since primary care health workers (physicians, nurses, pharmacists and community care workers) are at the forefront of the health care system, they often encounter the patient within her social and economic space. Primary care needs to take the social determinants of health into account, and the same applies to the social determinants of adherence. In order to do this, primary care providers need to know how to assess adherence in their patients.

3. Assessing adherence in primary care

Accurately measuring levels of adherence to medication has importance in clinical trials as well as in clinical practice. For clinical trials, the knowledge of patients actually taking the medication studied is imperative to allow examination of dose-response relationships and treatment efficacy. In clinical practice, the failure of a therapy to provide the desired clinical outcome can be due to either drug failure or poor adherence, and health care providers need information on adherence to make the adequate clinical decision. Most often, it is primary care providers who discuss the importance of adherence with their patients, and on whom it falls to assess whether patients adhere to their treatment plans or not. As with other chronic illnesses, in the case of HAART it is known that adherence levels decrease over time (Howard et al. 2002). The reasons for this are manifold and not difficult to imagine: treatment fatigue, forgetfulness, patients running out of medication, unforeseen

circumstances in which medication is not readily available, and, in less resourced countries, medication stock-outs at the point of distribution. Adherence monitoring is necessary to identify patients in need of adherence-improvement interventions before the clinical effects of non-adherence start to show. Measures in clinical settings should be effective, practical and inexpensive, with the aim of identifying poorly adherent patients. This is of even greater importance in resource-limited settings where limited treatment options often do not accommodate for drug changes that become necessary after the development of resistant viral strains due to poor adherence (Gill et al. 2005). Among the variety of available adherence measures, one can differentiate between direct and indirect measures (Farmer 1999). Direct measures of adherence provide proof that the drug has been taken by the patient. There are two ways to achieve this: either by monitoring the drug (or its metabolites) in the patient's body, or by actually supervising the patient taking the drug. The former is called therapeutic drug monitoring, and drug metabolites are usually monitored in blood or urine, although often they can also be traced in other bodily fluids and even hair. This method requires knowledge of the pharmacokinetics of the studied drug and is an invasive procedure. Based on the drug plasma concentration the patient is classified as adherent or non-adherent. Therapeutic drug monitoring is often reserved for clinical trials, where the scientific interest justifies the invasive procedure to obtain the blood/ urine sample. Evidently, it requires a multitude of clinical resources (staff to take the sample and process it in an adequately equipped lab), and the results are not available immediately. On the other hand, directly-observed therapy (DOTS) – the monitoring of the actual intake of the drug by the patient – is relatively inexpensive and requires little to no resources. It is the basis of many successful tuberculosis treatment programs in the developing world. Often, it is carried out in the home of the patients – here, community care workers play a crucial role. While it requires a good infrastructure and availability of care workers (or even relatives) to supervise the patient taking her medication, the resources required from the health care system are minimal.

Indirect measures of adherence can be categorized into subjective (self-reporting by the patient) and objective methods (medication measurement by pill count or estimation of liquid drug formulations, use of electronic monitoring devices and pharmacy prescription record review). These are the most common methods used in primary care settings and will be discussed in detail further on in this chapter.

Each method has advantages and disadvantages that need to be weighed against each other. In general, the accuracy of measures is determined by calculating the sensitivity and specificity of the method with a standard of reference (Ransohoff and Feinstein 1978). For adherence measures, sensitivity denotes the proportion of adherent patients that are correctly identified as adherent. Specificity denotes the proportion of non-adherent patients rightly picked out as non-adherent; high specificity means that as few non-adherent patients as possible should be wrongly identified as adherent. The overall accuracy of the method is calculated by incorporating the proportion of patients that are correctly identified as adherent or non-adherent. However accurate one single measure of adherence may be, it is recommended to use a combination of measures to adjust for possible bias of each single method: “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.” (WHO 2003). A further way of validating adherence measures is by determining their

correlation with a surrogate marker of adherence. For HIV infection, undetectable HIV RNA plasma levels, indicating that HAART effectively works against the HI virus, serve as surrogate markers for adherence to HAART (Arnsten et al. 2001).

3.1 Patient self-report

Self report is an inexpensive and quick tool to assess adherence at a health care facility or at home. It can be administered by doctors or nurses, counsellors, social workers, clinical psychologists or community care workers. Depending on the relationship of the patient to the interviewer or the administering physician, results can vary in truth and reliability. Self report measures can be structured questionnaires asking about doses that were missed during a specified time before the clinic visit and thus quantifying non-adherence. These questionnaires can be handed out to the patients to be filled out anonymously. For patients with poor literacy or eye-sight, they can be read by the interviewer to assure that the information given is correct. Information on missed doses is used to classify patients or caregivers into adherent and non-adherent groups. Visual Analogue Scales (VAS, see Figure 1) require patients to self-rate their adherence in percent and measure adherence as a continuous variable (Byrne et al. 2002; Giordano et al. 2004). Open interviews can highlight problems around adherence but make it more difficult to quantify adherence rates. A recent meta-analysis of various self-report measures in adult patients with HIV showed that in 85% of all studies reviewed, self-reported adherence was significantly associated with virological outcome (Simoni et al. 2006). There are numerous questionnaires that assess self-reported adherence. Visual Analogue Scales are among the most widely used self-reporting tools. Often abbreviated VAS, they combine the recollection memory with a visual component – patients are asked to rate their adherence on a scale. The scale, ranging from zero to one hundred percent, allows patients to estimate their adherence without forcing them to recollect specific drug intake moments. The visual component makes it suitable for patients who are less literate.

While Visual Analogue Scales ask about drug doses that a patient has actually taken, questionnaires inquire about doses that a patient missed or forgot to take. Different formats of questionnaires span different recollection time intervals. It is common to ask for drug doses that were missed in the previous day, the previous three days, the previous week and the previous month. It is important to note that patients' memories become less accurate the longer the recollection time span is – a very understandable phenomenon, since who would remember forgetting to take medication 3 weeks ago? With the data gained from missed drug dose questionnaires, adherence rates can be calculated. This step might not necessarily be required in clinical practice, but is routinely used to standardise adherence rates in research. Questionnaires that are routinely used in HIV treatment adherence research are the ACTG and PACTG (for adult and paediatric missed drug dose recollection, respectively), developed by the AIDS Clinical Trial Group. These questionnaires are widely available and can serve as a blueprint for tailor-made self-report measures.

An important limitation that needs to be noted for self-reported adherence measures is the inability to objectively confirm the information obtained from the patient. Self-report adherence measures are prone to over-reporting of adherence because patients often feel compelled to answer what they think the health care worker wants to hear. This social desirability (Simoni et al. 2007) can be caused by a lack of faith in the health care worker –

Visual Analogue Scale (VAS)

Most people with HIV have many medicines to take at different times during the day. Many people find it hard to always remember to take medicines. For example:

- Some people get busy and forget to carry the drugs with them.*
- Some people find it hard to take the medicine according to all the instructions, such as “with food” or “on an empty stomach,” “every 8 hours,” or “with plenty of fluids.”*
- Some people decide to skip giving medicine to avoid side effects or to just not give medicine that day.*

We need to understand what people with HIV are really doing with their medicines. Please tell us what you are actually doing. Don't worry about telling us you don't take all your medicine. We need to know what is really happening, not what you think we “want to hear”. The results of this survey will not influence your treatment at the clinic.

INSTRUCTIONS: Please put an “X” on the line at the point showing your best guess about how much medicine you have given in the last four weeks. We would be surprised if this was 100% for most people.

For example, 0% means you have taken no medicine
50% means you have taken half of the medicine
100% means you have taken every single dose of the medicine



Fig. 1. A Visual Analogue Scale to assess HIV treatment adherence.

patients fear that they would receive inferior treatment for not adhering well enough, or might feel ashamed at their 'failure' (Safren et al. 2006). This is an important issues especially in resource-limited settings where access to health care is limited, patients are less empowered and often depend on the only health care provider in the area. A trustful patient-provider relationship is key to ensuring that patients feel that they can be honest about their adherence behaviour, and it is imperative that health care providers remain non-judgemental and keep encouraging patients to adhere rather than judge or penalise them for not adhering.

3.2 Pill count

For pill count adherence measurement, patients are asked to return their unused medication at each clinic visit. A health care provider or researcher then calculates the percentage of prescribed pills that are absent from the medication container, thus enabling a measurement of adherence as a continuous variable (Steele et al. 2001). Pill count is a relatively quick and easy assessment of adherence, and once a patient has established the routine of returning unused medication, can be completed within a few seconds. For children who receive their medication in liquid form, the pill count concept is also applicable, although slightly more complicated. Upon return of the unused medication syrups, health care workers can measure the amount of liquid returned and calculate an adherence rate based on the amount of liquid the child had initially received. The accuracy of pill count assessment methods depends on the patient's cooperation in returning their unused medication.

3.3 Electronic Monitoring Devices

Electronic Monitoring Devices, also called EMDs are seen as the objective way to measure adherence. They are a relatively new assessment method that uses pressure-sensitive microchips, such as the Medication Event Monitoring System (MEMS), which is implanted in the caps of medication containers (Figure 2). The microchip records time and date of all bottle opening events as presumptive doses taken by the patient; the data is stored in the chip until downloaded onto a computer. MEMS caps allow the examination of patterns of adherence and detailed aspects of medication-taking, such as dose interval adherence, correct timing of dose-taking and prospective adherence assessment over time (Figure 3 shows a sample analysis of data from a MEMS device). In HIV adherence research, MEMS caps are often used as a “gold standard” for adherence assessment in adults, because of a closer correlation with undetectable HIV RNA plasma levels than other single measures (Arnsten et al. 2001). Recently, MEMS caps have also been used to measure the adherence of children who take liquid medication (Müller et al. 2008).



Fig. 2. MEMS container with cap and MEMS terminal to read the microchip

Electronic Monitoring Devices have several advantages over more traditional adherence measures. Most outstanding is their ability to record not only adherence rates, but veritable



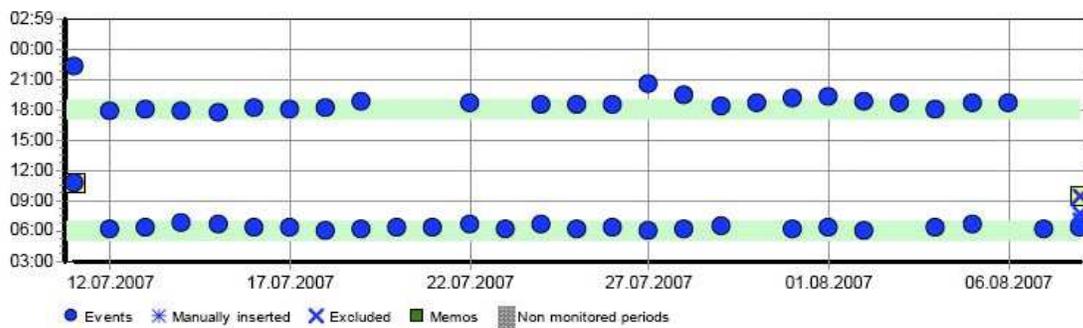
PowerView

Compliance Report

Patient number:	000011	Monitor number:	223589
Drug name:	Lamivudine	Regimen:	Twice a day
Results: 11.07.2007 08:00 to 08.08.2007 12:00 (1)			
Number of monitored days:	29	% Prescribed number of doses taken:	87.7%
Number of prescribed doses:	57	% Days correct nbr of doses taken:	75.9%
Number of doses taken:	50	% Prescribed doses taken on schedule:	3.6%



Chronology



Missing doses

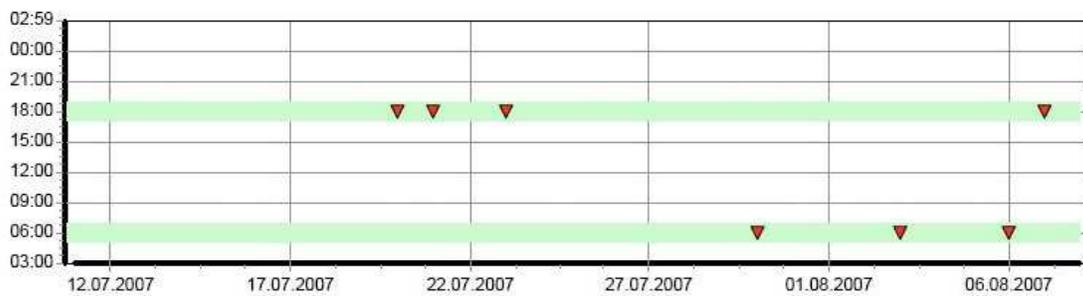


Fig. 3. A report by MEMS, an electronic monitoring device. The report is created with software and shows a) overall adherence statistics, b) drug doses taken by day, c) the chronology (timing) of doses taken and d) missed doses by day

adherence patterns. The microchip records the date and time of every container opening, and health care providers can trace each drug dose in detail. Hence, it is the only adherence measure that can record the exact time of drug dose taking – this is particularly important for drug regimen that depend on constant drug plasma levels, like antiretrovirals against HIV. The detailed report allows the health care worker to analyse together with the patient what the challenges to adherence are – for example if patients struggle more to keep medication times on weekends, or on certain days during the week. Often, these analyses reveal adherence challenges that patients were not aware of before. In this way, adherence assessment with Electronic Monitoring Devices also supports patients to adhere to their drug regimen. Newer electronic devices have evolved even more, and come with build-in timers and alarm clocks that serve as reminders to take drug doses. Another advantage of electronic devices is that they provide the most objective data of all indirect adherence measures. Similar to pill count, health care workers don't rely on information obtained from the patient, but can actually access adherence information directly from the microchip. Unlike pill count, the microchip is also more difficult to tamper with – because it measures medication-taking behaviour over the whole time in-between health facility visits, it cannot be changed or manipulated should patients try to do so before returning it to their health care worker.

3.4 Pharmacy data

Another way of assessing adherence is to record and analyse patient's patterns of obtaining refills and new prescriptions of their medication from pharmacies. Provided that patients either use the same pharmacy, or their records are stored in a central database – or that patients visit a pharmacy affiliated to the primary care facility – records on when patients pick up their renewed prescriptions gives an indication on how much of their previous medication they have taken. The presumption here is that patients who are adherent to their medication will use up all their stock in time for a new prescription (i.e. monthly prescriptions for HIV medication) and failure to adhere will lead to a surplus in medication that is reflected in late pharmacy pick ups. Another assumption is that a patient's adherence to scheduled pharmacy pick-ups is a surrogate marker for her medication adherence.

An adherence rate is calculated in comparing the amount of doses prescribed and the amount of doses obtained from the pharmacy over a specified time period. This method is more applicable for large population-based studies where individual adherence rates are of less importance (Steiner and Prochazka 1997), but it can also be used to get an overview of individual patient's adherences. For HIV treatment adherence, it has been found to be correlated with virological outcome in adults (Grossberg et al. 2004; Low-Beer et al. 2000).

4. Cost comparison of adherence measures - experience from South Africa

In a recent study, a research team from the Desmond Tutu HIV Centre at the University of Cape Town set out to evaluate the cost-effectiveness and feasibility of a range of adherence measures at a paediatric primary care facility (Müller et al. 2010). In a cross-sectional study design, 53 paediatric patients were enrolled to have their adherence monitored by electronic monitoring devices, self-report by Visual Analogue Scale and missed-dose recall, by pharmacy refill data and by pill count (for most children this meant measurement of

returned syrups). The feasibility of each measure in a primary care setting was explored by its month-long use through primary care providers, and additionally a cost comparison of all measures was performed. The results highlighted crucial issues in the use of adherence assessment in primary care settings.

The cost comparison of the adherence measures used an ingredients-based methodology in order to most accurately assess the cost of the measures (Drummond et al. 2005). This means measuring the utilization of staff time and measures (the ingredients) required to perform the task, and the cost of each measure. For each adherence measure all tasks performed by staff members over and above standard practice in the absence of adherence measurement were determined. For each task, a research assistant observed the clinic staff using the adherence measures, recording the time taken to perform the task and all consumables and other resources used. The costs of staff time were based on the annual cost of employment of the staff grade performing the task. The costs of other resources were based on their commercial prices with the costs of durable items being depreciated across their expected lifetime. Table 2 shows the costing of each adherence measure. It is quite clear that MEMS, the electronic monitoring device, was considerably more expensive than any of the other measures. This was primarily due to the high initial purchasing cost (\$120 per cap; additionally the battery life limits the length of use to 3 years) but also due to high additional expected input from the pharmacist (annual wage \$37,341) and pharmacist assistant (annual wage \$8,487) in managing the adherence measurement process. All other measures were considerably cheaper, mostly because of the low cost of the required resources, but also because they could easily be carried out by lower qualified health care workers like health counsellors.

Adherence monitoring method	Resources	Annual cost per patient
1. Electronic Monitoring Device	MEMS equipment	\$ 46.30
	Staff time	\$ 11.53
	Total cost	\$ 57.83
2. Pharmacy Refill Data	Staff time	\$ 2.58
3. Visual Analogue Scale	Staff time	\$ 0.19
4. Missed dose questionnaire	Staff time	\$ 0.39

Table 2. Cost comparison of adherence measures

5. Conclusion

Continuous adherence to medication is crucial for therapeutic success for every medical condition. Adherence is always challenging, but even more so for chronic conditions that require patients to take their medication for long periods of time, or even life-long. In the recent 15 years, HIV treatment adherence has become one of the main adherence research areas, and it has added a new perspective on adherence issues, particularly in developing countries with limited resources to spend on health and patient support. Adherence assessment can occur at all levels of the health care system, but most often it is carried out by health care workers in primary care. This is not accidental – it is primary care workers that are most likely to know the patient and her social surroundings, and carry for

chronically ill patients in continuous care. Adherence is a team effort and requires constant commitment from patients – but also constant encouragement and support from health care workers. In order to recognise adherence challenges and potential adherence failures, health care workers need to monitor adherence systematically. This chapter has introduced the most common adherence measures in primary care, and highlighted their advantages and disadvantages. Clearly, every patient and every situation requires an individual assessment, and often the best adherence assessment is a combination of more than one measure. Perhaps more than anything else, issues around adherence speak to the challenges of leading a 'normal' life with a chronic illness, and highlight how patients integrate their illness (through their medication) into their daily lives. The implications of poor adherence or even non-adherence are often dire, and health care workers need to support patients by recognising early signs of poor adherence. Often this can be assessed in conversations with patients, but adherence measures provide a crucial tool to quantify and compare adherence in a more structured way.

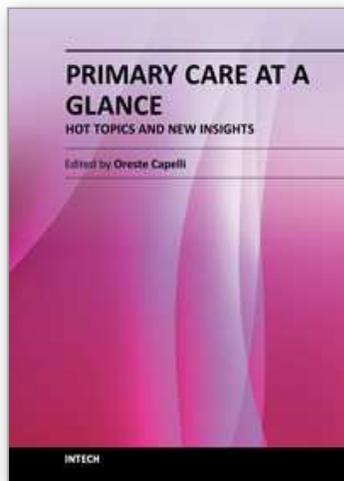
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"Both among scientists and clinical practitioners, some find it easier to rely upon trivial explanations, while others never stop looking for answers". With these surprising words, Augusto Murri, an Italian master in clinical medicine, reminds us that medical practice should be a continuous journey towards knowledge and the quality of care. The book brings together contributions by over 50 authors from many countries, all around the world, from Europe to Africa, from Asia to Australia, from North to South America. Different cultures are presented together, from those with advanced technologies to those of intangible spirituality, but they are all connected by five professional attributes, that in the 1978 the Institute of Medicine (IOM)¹ stated as essentials of practicing good Primary Care: accessibility, comprehensiveness, coordination, continuity and accountability. The content of the book is organized according to these 5 attributes, to give the reader an international overview of hot topics and new insights in Primary Care, all around the world.

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