

Assessing patient adherence to chronic diseases treatment: differentiating between epidemiological and clinical approaches

Avaliação da adesão do paciente ao tratamento de doenças crônicas: diferenciando as abordagens epidemiológica e clínica

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Abstract

This review discusses the concepts and methods for assessing patient adherence to treatment, as applied to both epidemiological and clinical approaches within real health care practices. For the epidemiological approach, the assessment must be as accurate as possible. Self-reported questionnaires are the most feasible option in most circumstances, but most demonstrate low sensitivity combined with high specificity. We suggest that self-reported outcomes, where feasible, can increase the sensitivity for non-adherence of these questionnaires. In the clinical approach an accurate distinction between adherents and non-adherents is less useful. For the health provider, it is more important to be aware of the particular situation that each patient is currently experiencing with his/her treatment. Self-reported questionnaires applied in clinical settings can help the health provider to form an objective opinion. In any event, the patient-provider dialogue is still the best approach to assess patient adherence as well as to deliver good care.

Patient Compliance; Chronic Disease; Evaluation of Results of Therapeutic Interventions

Introduction

Good outcomes from chronic diseases largely depend on the degree of patient adherence to treatment. Many studies have shown that some degree of non-adherence occurs universally, in rich and poor countries alike, and is even seen in life-threatening diseases ^{1,2}.

Large variations have been reported in the extent of non-adherence in individual patients and populations. In addition, studies have presented different concepts of adherence as well as different measurements, without necessarily explaining how these criteria interplay.

This is a free review aiming to discuss concepts and methodological approaches for assessing adherence, applied at both epidemiological and clinical contexts within real health care practices. Our motivation to write it was based on discussions we have had in our research group on adherence which bring together epidemiologists and clinicians. We searched the PubMed and SciELO databases to select studies that discuss different concepts and methods for assessing adherence to chronic diseases. Most search results focused on reviews, but original papers were also included. Further references were selected from the bibliographies of cited papers.

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Measuring adherence: different definitions (but same methodology)

The concepts that are most commonly used are “compliance” and “adherence”. Compliance was defined as the extent to which a person’s behavior coincides with medical or health recommendations³.

This definition became popular in the late 1970s, and was considered to be less judgmental compared with other terms that classified patients as “recalcitrant”, “careless” or “irresponsible”. The concept led to patients that were not following treatment being considered as a scientific problem which could be potentially studied and addressed⁴. However, many studies have criticized this concept, both for its coercive connotation as well as the fact that it reduces the issue to a matter of patient obedience^{5,6,7}.

Adherence was defined as the extent to which a person’s behavior corresponds with agreed recommendations from a health care provider⁸.

The notion of adherence proposes an alliance relationship, whereby therapeutic guidance should be agreed upon between patient and health professional, thus recognizing partial autonomy of the patient with regard to how treatment is followed⁸.

Many studies have discussed both notions. This includes some who consider compliance as a dimension of adherence⁹, those who “advocate” one concept or another^{10,11}, those who use the terms interchangeably¹², and those who propose new notions attempting to overcome the limitations attributable to both compliance and adherence¹³.

This debate, however, does not seem to have significantly affected empirical studies. Indeed these have frequently employed both terms, irrespective of the methodology used¹⁴. This “theoretical indifference” appears not to have occurred by chance. Studies measuring adherence are essentially epidemiological studies, in other words, aimed at population contexts. In these settings it is of little importance whether the adherent groups are “obedient” or “autonomous”. The key focus is on accurately measuring the number of adherents. After all, the end goal is to understand the problem from an epidemiological point of view, in so far as determining the adherence rate in the group under study. In this context, the title by Baril¹⁵ (p. 13) seems quite fitting: “*Observance, adherence, compliance... different words for better therapeutic results*”.

This discussion takes on a different meaning in a clinical context, as will be discussed. Indeed, we shall seek to discuss some methodological issues involved in getting highest accuracy and

greatest explanatory value from studies assessing adherence in epidemiological contexts.

Addressing adherence in epidemiological contexts: seeking better accuracy

The majority of studies have used an acceptable rate of doses taken/prescribed or even general behavioral patterns of patients in relation to the medication as carelessness/forgetfulness.

Methods that quantify medication taken over a period of time allow for several continuous measurements as well as mean values. However, the majority of studies establish a cut-off point that represents an acceptable limit of non-adherence. The cut-off point is generally based on prior studies which have compared other methods and takes into account the acceptable clinical response for each disease. Thus for hypertension, “adherents” are considered as those that take at least 80% of prescribed medicines¹⁶, while for AIDS treatment most studies have adopted 95% or more¹⁷.

Different cut-off points obviously lead to different quantitative values of adherence. For example, a study in hypertension which defines adherent patients as those who take at least 80% of their medication and detect some 70% of adherence, will report a lower percentage of adherent individuals upon adopting a stricter stance, accepting only those taking 95% of the prescribed dose¹⁸.

Questionnaires seeking to estimate patterns of adherence behavior need to establish arbitrary cut-off points in defining non-adherent subjects¹⁹. Depending on the response to one or more questions, an individual shall be categorized as non-adherent, thereby establishing the frequency of non-adherent individuals in a given group.

Patient self-reports through structured interviews are the most used options in observational studies due to their ease of application and low cost. Self-report measures should be assessed on the basis of their validity and electronic monitoring can be used as a reference standard. Pill counting, which is easy to apply and low cost, can also be used as standard although it presents more accuracy problems than electronic monitoring²⁰.

An important criticism concerning questionnaires used in epidemiological studies regards the conditions under which they are applied. Firstly, there is the issue of why questionnaires focus on undesirable behavior and why patients do not feel at ease answering these within the care facility they attend. Nevertheless, it should

be recognized that some measures traditionally viewed as more objective, such as manual pill counting or electronic monitoring may also not guarantee reliable results: pills may be discarded and even electronic chips on bottles can be tampered ^{1,21,22}. Therefore a self-report conducted through a well designed questionnaire in a confidential interview has been considered a useful measure of adherence ^{23,24}.

Moreover many self-reported questionnaires have provided reliable adherence measurements. This has been observed in studies on AIDS ^{25,26,27}, hypertension ^{28,29} and immunosuppressant therapy ³⁰.

In addition to obtaining different adherence rates, the correlation amongst the various measures of adherence has frequently been low ^{31,32,33}. The key differences obtained for each of the adherence measures has led to recommendations for simultaneous use of more than one method in a bid to improve the performance of the final measurement ^{8,34,35}.

Combined measurements should however aim to ascertain simultaneously the several dimensions of adherence, and not solely the percentage of doses taken. In any event, if we accept that adherence is composed of the act, process and effect of adherence, we require measurements which can reflect as accurately as possible these different analytical facets.

A composite adherence score that uses electronic monitoring, pill counts, and patient self-reports ^{36,37} can assess all these facets but may be not feasible in many settings. For most settings, questionnaires still are the cheapest and most feasible option. Non-threatening and non-judgmental questions are capable of detecting both the act of adhering (through taken/missed doses) and the process (through regular/erratic timing of medication).

The effect of adherence, which is evidently a favorable clinical outcome, warrants further discussion.

Although clinical measures are widely used as indicators of adherence by physicians in clinical contexts ³⁸, few authors used clinical control as part of the "deciding rule" to consider the individual as adherent in epidemiological study. The classical definitions of adherence used in most studies do not consider clinical outcomes as a component of adherence. In such studies, the clinical outcome is commonly used to establish correlations between levels of adherence and outcome, and to validate the adherence measurement or even establish cut-off points between adherents and non-adherents ^{16,39}.

The use of clinical outcomes as an indirect measurement of adherence is evidently limited

by the fact that clinical improvement depends not only on correctly taking medication, but on several other factors. Among them, the most important is the non-response whose distinction from non-adherence is a crucial matter to the clinical approach. From an epidemiological point of view, this distinction is also very important in clinical trials assessing the efficacy of medicines.

However, the chronic disease treatments that are carried out in most health care services establish their average efficacy beforehand. Therefore, from an epidemiological point of view the measure of ratios and means of adherence does not always need to take into account rates of non-response. The association between adherence and mortality rates independently of the response has already been well established for many chronic conditions ⁴⁰. Another important focus of epidemiological studies on adherence is the association between adherence rates and the level of quality of health care services ^{41,42}.

The most important methodological requirement to measures of adherence in epidemiological studies is their accuracy. Some self reported indicators of outcomes can be useful to improve the accuracy of adherence measures.

Blood pressure reading, a simple and easily applied measure, was used in an early study on adherence to treatment in hypertension. Considering non-adherents as those reporting non-adherence and presenting uncontrolled blood pressure, the rate of non-adherence increased from 67.6% to 79.6% ²⁸.

We have recently developed a self-reported questionnaire to measure adherence to hypertension treatment. The questionnaire contains three questions which sought to assess the three dimensions discussed above. The final non-adherence rate is composed of self reported missed doses (act of adhering), timing of pill consumption (process of adhering) and the presentation of uncontrolled blood pressure (effect of adhering). The rate of non-adherence increased from 17.4% (for missed doses) to 28.3% (for timing) and to 30.7% (for report of uncontrolled arterial pressure). The combined measurement was 47.73%. Using also a combined measurement as a gold standard comprised of pill counting (the act), the Morisky et al. ¹⁹ questionnaire (process) and blood pressure measurement (effect), sensitivity was 63% and the predictive positive value was 91% ⁴³.

Self reported clinical outcome, when feasible, is able to increase sensitivity for non-adherence, i.e. the detection of true non-adherents of the questionnaires used in the epidemiological studies in the usual health care settings. This is an advantage in view of the fact that the major-

ity of self-reported cases achieve low sensitivity coupled with high specificity (since patients who state they are non-adherent almost always are but not the opposite i.e. patients who state they are adherent may not be in many cases).

On the other hand, improving sensitivity can increase the proportion of false positives, i.e. erroneously considering those who adhere as non-adherents. This can be, however, an additional advantage, since the choice of method should, as well as its validity and reliability, be based on its usefulness in light of the researcher's goals. If, for instance, we intend to use adherence ratios as indicators of the quality of care in health services (or the effectiveness of an intervention), overestimating the number of non-adherents (through false-positive individuals) seems appropriate. In any event, the main aim in this situation is to identify the greatest number of non-adherents possible for subsequent targeting by the health care team.

The studies on adherence within the epidemiological contexts contribute towards the devising of policies and achieving more effective managerial and clinical practices. The quality of this contribution depends on the quality of methodological approaches. However, this also depends on the correct interpretation and incorporation of findings into practice.

Studies of adherence to AIDS antiretroviral treatment in Brazil, for instance, have shown that low schooling and missed follow-up are associated with greater odds of non-adherence^{42,43}. The results led to strong recommendations to AIDS related health services for the organization of delivering care which prioritizes those groups, providing for instance, swift medical care to those missing appointments, or special activities (such as groups, home visits and so forth) for those with low schooling.

It should be noted, however, that the associations found refer to groups with greater odds of non-adherence, not necessarily implying that individuals belonging to these groups are necessarily non-adherents. Creating special flowcharts for these groups cannot be a substitute for individual care and, most importantly, should not imply discriminatory attitudes to those erroneously called "high risk for non-adherence", as has unfortunately been seen in some contexts^{44,45}. In contrast, this entails offering special care to those who are most vulnerable, precisely in a bid to actively foster equity. This discussion is however more relevant for the clinical context.

Addressing adherence in the clinical context: seeking better care

Whereas epidemiological studies seek to differentiate accurately between adherent and non-adherent groups, this division is meaningless in the realm of individual care. In this context clinical control is the most often used "measure" of adherence employed by physicians^{46,47}.

Indeed, if the patient is doing well, all is well. Thus, for instance, in a strategy of "intelligent non-adherence" patients rightly conclude they may achieve the same therapeutic success while reducing the medication prescribed, a fact long acknowledged amongst people with hypertension^{48,49}. Even recent AIDS treatment studies have shown that for some antiretroviral regimens there is no need for "almost perfect" adherence as early studies had suggested⁵⁰.

For health professionals, chiefly the physician, it is important to assess patient adherence when clinical outcome is not as expected. In this case, the professional's impression based on questioning the patient is widely used. However, the physician's opinion as a method of measuring adherence is classically criticized. Many studies have shown high values of disagreement amongst adherence rates assessed by professional and those self-reported by patients and by electronic monitoring^{51,52}. These studies however, refer to differences amongst adherence ratios of groups. For this reason, studies measuring adherence in the epidemiological context rarely use clinicians' opinions as a method of measurement. When used, it is only considered as part of composed scales of adherence (once it is recognized that the clinicians' assessments of their patients' adherence are strongly based on the clinical and laboratorial results)^{49,50}.

Individual care, on the other hand, clearly cannot override medical opinion, for risk of undermining the technical basis of medical work, grounded in the autonomy of reaching judgments and taking decisions also based on the individual meeting with the patient⁵³. In other words, it is impossible for the physician not to base their decision on the impression they acquire from contact with the patient.

Obviously, the inherent subjectivity of the medical decision can be balanced through additional instruments. This highlights when it is necessary to differentiate between not-enough adherence and non-response.

The usual "objective" adherence measures (such as manual or electronic pill count) may be used in some clinical settings. However all of them have well-known limits of reliability and feasibility. Most importantly they can be counter-

productive since the patients may perceive them as intrusive and suggestive of a lack of trust from the provider^{12,54,55}.

In the clinical context of adherence measures must be practical, inexpensive and suitable in the context of the patient-provider relationship. Therefore questionnaires (whose reliability and validity had been tested in epidemiological studies) can be helpful in increasing the objectivity of the physician's decisions^{56,57}.

However, these questionnaires should be viewed as auxiliary instruments and be used carefully. To repeatedly measure a patient's adherence may have some undesirable effects on the patient-provider relationship as well as reinforce the "white coat adherence" effect.

In spite of these limits, it is essential for the physician to be aware of patient adherence. Together with the clinical parameters, adherence is important to enable therapeutic modifications. The exact dose of medication needed to achieve the desired clinical outcome has only been well established for a few diseases. In the majority of cases, the dose required must be adjusted for each patient. Therefore in most cases the physician has to know the patient's adherence, and not "to figure out" whether he/she is "adherent" or "non-adherent" but rather to be aware of the particular situation each patient is currently experiencing with the prescribed treatment. It is also very important to counsel patients in establishing routines of use, particularly important for chronic diseases.

However no adherence "measure" is able to render spoken patient reports objective to the point of making them totally transparent to the physician. This is only possible if the patient-health team relationship is based on mutual trust and truthful dialogue.

It is this very issue that represents the greatest promise for discussion on the ideas of compliance and adherence. The notion of adherence has attempted to bring into focus the patient's point of view with regard to treatment plans. However, while for advocates of "adherence" the notion represented an evolution in the meaning of considering the autonomy of the patient, more radical propositions argue that there is little difference between adherence and compliance.

Several proposals have already criticized the notions of compliance and adherence, proposing their replacement by ideas which better reflect the need to value the autonomy of the patient in relation to the treatment. Examples include notions of collaboration⁵⁸, autonomy motivation⁵⁹ and empowerment⁶⁰.

By the same token, the Royal Pharmaceutical Society of Great Britain⁶¹ suggested substituting

both terms for the notion of concordance which attempts to express the process of prescribing/taking medicines as a therapeutic partnership between physician and patient.

The notion of concordance has become frequently used in studies from the United Kingdom. Its definition has changed over time from one which focused on the consultation process, to a broader notion which ranges from prescribing communication to patient support in medicine taking⁶². Recent studies have pointed out that concordance is synonymous with neither compliance nor adherence. For them, the notion does not refer to patient's medicine-taking behavior, but rather the provider-patient interaction⁶³.

With regard to different theoretical origins, all of these new conceptual approaches and particularly the notion of concordance have been sought to acknowledge actively the presence of another party – the patient – in the health care arena. Therefore they highlight the crucial role of communication in the clinical context.

Concerning this point a fruitful proposition has been disseminated in Brazil. Based on the philosophical concept of Care, it proposes that health providers revisit their attitudes and conceptions, that are oriented in a strictly biomedical sense^{64,65,66,67,68}. It argues that those patients' needs beyond those strictly related to clinical control are not effectively incorporated into health care process, and continue as barriers to adherence⁶⁹. Addressing the issue Ayres⁶⁷ (p. 72-3) argues: "*In a consultation, in attentive listening, yet oriented in a purely technical sense, elements may arise from patients which are deemed as the non-comprehension of instructions (...), or disregard for health. In listening (...) which does not have technical success as a strict goal of the dialogue, the same elements may appear as a conflict of values in adopting guidance (...), practical obstacles to observance of the prescription (...) or simply a mismatch between what [the patient] is looking for [in the health service] and what is being offered*".

This notion of care understands that those "nontechnical" dimensions have to be actively considered by the health care provider (and not be only informally responded to by means of providers' personal initiatives and compassionate feelings). It argues that that the technical success of the treatment depends on a "practical success" i.e. the capacity of the health care in focusing, beyond the clinical outcome, on the aspirations of the patients relating to health, but also and especially to life more broadly. In this sense, it proposes that care must include a negotiation of the best possible outcome given

the patient's project of life and well-being at the time^{65,67,68}.

It is almost intuitive to realize that the good health provider-patient dialogue is a basic underlying condition for both "concordance" and "care" notions. The notion of care however seems more useful in helping to understand the issue of adherence to treatment in the clinical context through criticizing the understanding of treatment as being restricted to an instrumental relationship between that which holds the best technique (the physician) and that which is the object of this technique (the "patient").

It seems however, that the best potential of this notion of care lies in the recuperation of the human side of health work, without diminishing the weight of its technical dimension. Evidently, work in health shall always have a technical goal: we work towards ensuring patients follow treatment and improve their health. However, this

aim cannot be artificially separated from the human relationship established in a bid to achieve this, nor can the price at which this is achieved be ignored.

Epidemiological research on taking medicines can work with different definitions of the issue. The usefulness of their contributions predominately lies in their methodological coherence and accuracy. In the clinical context, recognizing adherence as a dynamic phenomenon⁷⁰ and accepting that all chronic disease patients have their moments of non-adherence⁷¹ appears to be the best approach to care. Moreover, accepting patient behavior in our relationships with patients is also needed. As Bernardini⁷² (p. 227) says "*Would it help to adopt Fred Rogers' theme, 'I like you just the way you are', to improve relationships with patients who would then be more likely to comply?*".

Resumo

Esta revisão discute conceitos e métodos de avaliação da adesão do paciente ao tratamento de saúde, aplicáveis para a abordagem epidemiológica e para a abordagem clínica. Na abordagem epidemiológica, a avaliação deve ter a melhor acurácia possível. Os questionários de auto-relato são a opção mais viável na maioria dos contextos. Entretanto, a maior parte dos questionários apresenta baixa sensibilidade aliada a alta especificidade. Sugere-se que o desfecho clínico auto-relatado, quando factível, é capaz de aumentar a sensibilidade desses questionários. Para a abordagem clínica, uma acurada discriminação entre aderentes e não aderentes é pouco útil. Para o profissional de saúde, é mais importante conhecer a situação particular pela qual o paciente está, no momento, passando com seu tratamento. Questionários de auto-relato aplicados no contexto clínico podem auxiliar a melhorar a objetividade da opinião do profissional. Em qualquer caso, contudo, o diálogo paciente-profissional é ainda a melhor abordagem para avaliar a adesão, assim como para prover um bom cuidado.

Cooperação do Paciente; Doença Crônica; Avaliação de Resultado de Intervenções Terapêuticas

Contributors

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