REVIEW ARTICLE

Patient adherence to treatment: three decades of research. A comprehensive review

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SUMMARY

Low compliance to prescribed medical interventions is an ever present and complex problem, especially for patients with a chronic illness. With increasing numbers of medications shown to do more good than harm when taken as prescibed, low compliance is a major problem in health care. Relevant studies were retrieved through comprehensive searches of different database systems to enable a thorough assessment of the major issues in compliance to prescribed medical interventions. The term compliance is the main term used in this review because the majority of papers reviewed used this term.

Three decades have passed since the first workshop on compliance research. It is timely to pause and to reflect on the accumulated knowledge. The enormous amount of quantitative research undertaken is of variable methodological quality, with no gold standard for the measurement of compliance and it is often not clear which type of non-compliance is being studied. Many authors do not even feel the need to define adherence. Often absent in the research on compliance is the patient, although the concordance model points at the importance of the patient's agreement and harmony in the doctor–patient relationship.

The backbone of the concordance model is the patient as a decision maker and a cornerstone is professional empathy. Recently, some qualitative research has identified important issues such as the quality of the doctor–patient relationship and patient health beliefs in this context. Because non-compliance remains a major health problem, more high quality studies are needed to assess these aspects and systematic reviews/meta-analyses are required to study the effects of compliance in enhancing the effects of interventions.

INTRODUCTION

Low compliance to prescibed medical interventions is an ever present and complex problem, especially for patients with a chronic illness. With increasing numbers of medications shown to do more good than harm when taken as prescribed, low compliance is a growing concern, seriously undermining the benefits of current medical care (1, 2).

Medical non-compliance has been identified as a major public health problem that imposes a considerable financial burden upon modern health care systems (1, 3–5). This burden has been estimated to cost $100 billion each year in the USA (4), including 10% of hospital admissions and 23% of admissions to nursing homes (3, 5). Lack of compliance to medical advice is also a source of ongoing frustration to doctors (6).

Compliance to treatment is a key link between process and outcome in medical care (7). Rationally prescribed medications are a principle intervention in primary care and a major element when considering the economics of health care (7).

Poor compliance with a therapeutic regimen may have a major impact on clinical outcome (6). An estimated average compliance of 50%, rather than 100%, in a trial would increase the required sample size fivefold in order to maintain the same power (8).

One of the first studies on compliance, by Brian Haynes and David Sackett, explored factors

associated with non-compliance, focusing on the understanding, measurement and resolution of non-compliance (4). More than 200 variables have been studied since 1975, but none of them can be considered as consistently predicting compliance: neither socio-economic nor pathology-related factors (2, 4, 5, 9–11). Research into a phenomenon as complex as compliance is inevitably fragmented, but this is made worse by the absence of a model or theory to integrate the different studies.

METHOD

Comprehensive literature searches were undertaken through Medline, Psycinfo, Embase, Sociological abstracts, Dissertation abstracts and Eric from 1975 until 1999, and the analysis of the bibliographies of articles on compliance. The following keywords were used: patient compliance, adherence, health beliefs, doctor–patient relationship and patient expectations. The topics of interest in the field of patient compliance were: the extent of compliance or non-compliance, variables that influence compliance rates; compliance measurement methods and intervention strategies to improve patient compliance. Articles were selected when compliance was the main research topic of the study, when they gave an answer to at least one of the topics of interest, when they were review articles or when the articles reported on studies of good methodological quality.

RESULTS

Definition

Although this review is of articles found by searching on a number of terms, the different use of the terms is an important aspect of the research into this concept. The majority of articles take the term compliance for granted. Many authors do not even feel the need to define it (12). A comparative assessment of the compliance literature cannot be done across studies using different definitions of compliance (3).

Compliance

Compliance is a word with negative connotations. It suggests yielding, complaisance and submission. Compliant patients 'submit' to the prescriptions of doctors and take their medicine, or follow their advice, a phrase that also means accepting punishment (13). Non-compliance is failure or refusal to comply (14) and can imply disobedience.

In the context of health care, compliance has been defined as the extent to which the patient's actual history of drug administration corresponds to the prescribed regimen (7). This definition is probably only applicable to medical interventions. Some researchers have put this definition into operation by dividing their sample population into compliers and non-compliers based on statistical measures such as the median or mean levels of medicine taken (15). An alternative definition is that compliance is the extent to which a person's behaviour in terms of taking medication, following diets, or executing life-style changes coincides with medical or health advice (16). Inherent to all the definitions of compliance is the assumption that medical advice is good for the patient or that rational patient behaviour means following medical advice precisely (15).

Compliance can also be viewed in terms of the results of taking medication: the number of doses not taken or taken incorrectly that jeopardize the therapeutic outcome or the point below which the desired therapeutic result is unlikely to be achieved. These are process-orientated definitions. Outcome-orientated definitions differ from them because the emphasis is on the end-result or outcome of the actions taken. For example, in one study, 80% compliance to a medication regimen for hypertension was shown to lower the blood pressure to normal, whereas a 50% compliance was ineffective in lowering blood pressure (17). In this case compliance was defined only in terms of the outcome and not defined by the process used.

The process of seeking, receiving and following treatment and advice has many stages and many opportunities for non-compliance. Different types of non-compliance (18) include: delay in seeking care (population at risk), non-participation in health programmes (screening), breaking of appointments (follow-up), failure to follow doctors' instructions (treatment) (19). Further types can be distinguished: receiving a prescription, but not having it made up at a pharmacy (primary non-compliance), taking an incorrect dose, taking the medication at wrong times, forgetting one or more doses of the medication, stopping the treatment too

soon, either by ceasing to take the medication sooner than the doctor recommended or failing to obtain a repeat prescription (secondary non-compliance) (4). Furthermore, compliance may be intentional or unintentional. It is important that studies of non-compliance and recommendations to address issues raised should make clear which types of non-compliance are being studied.

Concordance

The members of a working party of the Royal Pharmaceutical Society of Great Britain on medicine taking, realized that the old ways of thinking about compliance were insufficient (18). Resistance to taking drugs is profound and pervasive. Moreover, there is something morally and psychologically flawed in the very concept of compliance. Perhaps non-compliance may be no more deviant than compliance (18). Non-compliance can be defined as a person's informed decision not to adhere to a therapeutic regimen (20). The Royal Pharmaceutical Society has now changed its terminology from compliance to concordance, which means agreement and harmony.

The backbone of the concordance model is the patient as a decision maker (18) and a cornerstone is professional empathy (21). This is a fundamental step away from the traditional compliance model (18). Compliance signifies the theoretical intention of prescription; concordance signifies the practical and ethical goal of treatment (18). Compliance is the extent to which an individual chooses a behaviour that coincides with a clinical prescription, whereas concordance is a patient's considered choice (17). Concordance indicates the extent to which what the patient thinks about what is asked from him matches what the health care-giver thinks the patient actually does (22).

Adherence

The term adherence has also been proposed as an alternative to compliance (20) and is growing in popularity (23). It is suggested that the term adherence reduces attribution of greater power to the doctor in the doctor–patient relationship which the term compliance brings (24).

We would prefer to use the term adherence to incorporate the broader notions of concordance, cooperation and partnership. However, as the majority of the papers reviewed here use the term compliance, we feel obliged to maintain its use when interpreting and synthesizing what is reported.

History of compliance research

David Sackett (24) became interested in compliance around 1972 when it dawned on him that in hypertension, unpredictable or disappointing responses to treatment were probably due to low compliance. A survey of the literature revealed few research articles. Between 1961 and 1974 only 245 articles were published on this issue. In 1974 the McMaster Workshop/Symposium on compliance with therapeutic regimens was held, resulting in a book on compliance and compliance research (6).

Many centuries ago, Hippocrates was aware of the fact that patients pretended to have taken their medication (16). Three physiologists drew attention to the compliance phenomenon at the end of the 1950s, when they studied outpatient therapy with a tuberculostatic agent (25). The growth in the number of effective medications forced attention on the problem of non-compliance. Long-term therapies seem to hold the most problems, as was recognized for the treatment of hypertension (25). By the end of the 1970s, it was clear that determinants of compliance were complex and poorly understood. Despite continuing research, few improvements or new insights have emerged since the 1980s (25).

Compliance research has focused on the extent and determinants of non-compliance, and strategies to improve compliance. One of the most striking reasons for the lack of progress in compliance research is the absence of a crucial factor: the patient's perspective (12). The lack of understanding of doctors' prescribing practice is another important gap.

The measurement of compliance

The question of how to measure compliance has vexed many researchers. The complexity of the problem has prevented the development of a gold standard method of measurement. The lack of a valid method for measuring non-compliance is by itself a major barrier to compliance research (3, 26).

There are a number of traditional measures of patients' compliance in taking medication,

including both direct and indirect measures. Direct measurements usually involve the detection of a chemical (metabolite or marker) in a body fluid (blood, urine). However, these are not available for all medications. Direct measures are considered to be the most accurate, but can be invasive and thus unacceptable. They may not account for the variability of pharmacokinetic factors of medications and individuals. In addition, they are often difficult to perform and are costly. Direct observation is practical only in single-dose therapy, intermittent administration and hospitalized patients (19).

Indirect measurements are more frequently reported in the literature than direct measures. They include process measures such as interviews, diaries, tablet counts, prescription filling dates and therapeutic and preventive outcome measures (19). Each of these has drawbacks. Patients can improve for reasons other than following the prescribed regimen and a person's condition can deteriorate or remain stable even when the medications are taken as prescribed. So outcome measurement may tell us nothing about compliance.

Interviews and all self-report methods are vulnerable to overestimates of compliance and underestimates of non-compliance. Interviews have been shown to identify 80% of the true non-compliance as assessed by pill count (sensitivity). However, interviews are not equally sensitive for all subgroups of patients (27).

The validity of prescription refill dates depends on the completeness of the pharmacy database, and counting tablets given to patients often overestimates compliance (26–29).

The development of microprocessor technology provides more accurate methods of measurement (30). The use of electronic devices, or MEMS (medication event monitoring system), enables both frequency and time of opening of the medication bottle to be measured (31, 32). This method has led to the discovery of 'drug holidays' and 'white-coat adherence', where the compliance is timed to meet the needs at consultation with the white-coated doctor (32). It has been suggested (32) that electronic medication dispensers may enhance compliance, although it is unlikely that noncompliant patients would make the effort to utilize an electronic dispenser in the expected manner on a daily basis if they do not intend to use the contents.

Although a variety of methods has been used, there are serious problems with each method for generating valid and reliable data to give an accurate estimate of extent of compliance.

The extent of poor compliance

Because of the difficulties in measuring compliance, no estimate of compliance or non-compliance can be generalized, but poor compliance is to be expected in 30–50% of all patients, irrespective of disease, prognosis or setting (3, 36–39).

Hypertension has served as a model for compliance research, and estimates of compliance are well documented: 50% of patients drop out of care, and two-thirds of patients remaining on treatment seem to consume sufficient medication to achieve blood pressure control (25). The consequences of such widespread poor compliance should be taken into account when prescribing and setting up trials of new medications. Often, little attention is paid to non-compliance in drug trials but it is difficult to contemplate the development of new drugs without taking compliance into account. The reliance on intention-to-treat analysis – whereby one ignores doses actually taken and analyses the results on the basis of the treatments to which patients were assigned – in drug trials has created a number of problems and biased estimates of drugs' effectiveness (33).

The medical and economic implications of compliance tend to go hand in hand, but are specific to the therapeutic field and drug concerned. Non-compliance with respect to a drug that is crucial to maintainance of vital physiological functions is more likely to have serious consequences than a medicine intended for symptomatic relief and whose use can be optional (33).

The causes of poor compliance

To date, none of the suggested explanations has accounted for more than a modest part of the observed variations in compliance (37). Almost 200 different doctor-, patient- and encounter-related variables have been studied but none of them is consistently related to compliance or fully predictive (18, 38). Although many correlations are weak, the possibility of a causal relationship is often suggested. The features of a disease, the referral

process, the clinical setting, and the therapeutic regimen do not seem to influence adherence (18). Demographic variables (age, sex, marital status, number of people in the household, social class) and disease factors are poor indicators of compliance. Although some associations have been found, the direction of these associations was inconsistent between studies. Other factors related to low compliance include psychiatric disorders (the more symptoms reported, the lower the compliance), and treatment factors, such as the duration of the treatment, the number of medications prescribed, the cost, and the frequency of dosing (3, 39). Generally, the higher the levels of these factors, the lower the compliance. Factors that have been found to relate to high compliance include the degree of disability, perhaps due to increased supervision, and parenteral medication administration (3, 39). Side-effects are, surprisingly, only mentioned by 5–10% as a reason for non-compliance. Most of the variables examined are inconsistently correlated with compliance and thus cannot be used to predict compliant behaviour adequately (3, 39). The prediction of medication non-compliance by doctors based on patient characteristics, or by researchers using multivariate models, has been shown to be inaccurate (40).

The complexity of the regimen and poor communication are often mentioned as common causes of non-compliance, especially in elderly patients with memory disorders, which make them unable to follow complex sets of instructions (38). The doctor–patient relationship seems to be an important variable in compliance, including the process of prescribing, but it is extremely difficult to assess the nature of this interaction and to measure its components (18).

Poor communication is traditionally measured in terms of patients' inability to recall doctors' instructions, with patients failing to recall between one-third and one-half of the statements given to them by doctors (41). However, the use of methods of measuring recall that rely on direct recall do not take account of the meaning imbued in statements. This may not incorporate patients' intentions, and may lead to false conclusions (38) and erroneous impressions (42).

Other factors contributing to non-compliance include patients' unresolved concerns, including the diagnosis, absence of symptoms, time between taking the drug and its effect, and the fear of adverse effects (42). The most salient influences on compliance are patients' beliefs about medications and about medicine in general (18). Their own knowledge, ideas and experiences, as well as those of family members and friends, have been shown to correlate with compliance (18, 43).

One application of the well-known Health Belief Model (44) has been to aid our understanding of compliance with treatments. Compliance is thought to be determined by the knowledge and attitudes of the patient. Patients must believe that they are vulnerable or susceptible to the disease or its consequences, that they actually have it, and that the consequences of the disease on their well-being could be serious. They must believe that by following a particular set of health recommendations the threat or severity of the condition will be abolished or reduced (39). However, these elements of the Health Belief Model, have only partly been studied experimentally.

Patients' own beliefs and the constraints of everyday life are important in determining compliance. The patient's perspective on health and illness has only recently begun to be taken into account in traditional compliance research (45, 46). It is important to know what sense individuals make of the advice given to them. When they arrive at the consultation, patients hold sets of beliefs and theories about health and illness. When confronted with a particular illness they will first try to deal with it and not yield control over their bodies to the medication regimen (46). Perhaps more and more patients want to take their own decisions as demanding consumers (41).

Social factors, such as a positive attitude by others in the community, improve compliance (41). Compliance seems to be related to the quality, duration and frequency of interaction between the patient and doctor. The doctor's attitude towards the patient and his ability to elicit and respect the patient's concerns, to provide appropriate information and demonstrate empathy are of the utmost importance (41). While a number of research articles emphasize the fact that patients make reasoned decisions about their treatment, others concentrate on the passive role that patients play in non-compliance (45, 46).

Patients are often confronted with conflicting information. Doctors are often not compliant with

diagnostic and therapeutic standards. There is considerable heterogeneity in prescribing, with doctors drawing upon their own knowledge and understanding when they decide upon a treatment regimen (47). It has been found that patients reduce their drug intake to diminish the risk of side-effects (46) or to discover the lowest drug dosage effective for them.

It is patients who should be the primary actors in medical decision making, and health professionals should adopt a supportive role. In essence, then, compliance is an elusive, flexible goal. Patients, especially those with chronic illness, make decisions about treatments that fit into their own beliefs and personal circumstances. Health professionals need to shift the emphasis away from attempting to encourage patients into taking the medication they prescribe, towards learning how they can contribute to the decisions that patients currently make about their medications (48).

One major obstacle to patient compliance is ignorance about important issues, such as the nature of the disease and the nature of the treatments and how effective these can be. Only a few studies have focused on provider behaviours that would enhance patient understanding and recall through the doctor's communication style and teaching strategies. Doctor responsiveness is associated with improved subsequent compliance (41), and doctor satisfaction was positively associated with actual patient behaviour.

Although many studies have investigated causal relationships between patient factors, doctor factors and compliance, no consistent story has yet emerged. It is possible that each condition, and each patient–doctor pair, involve different motivating factors which affect compliance. In the next section we investigate what interventions have been effective in improving compliance, although the underlying causes may still be unknown.

Enhancing compliance

Researchers designing clinical trials to evaluate a medical therapy may do so under two very different settings: (i) under ideal experimental circumstances with the treatments taken in the manner prescribed, or (ii) under the circumstances pertaining to usual medical practice. However, a true difference in efficacies may be diluted by differential compliance between treatment groups. Stratification of treatment and comparison groups by compliance may be useful for estimating its effect on outcomes. This type of analysis is complicated by the difficulty in measuring compliance accurately. Furthermore, compliance may vary over time and in a way that is dependent on other variables under study. It may therefore be preferable to study compliance as a dependent variable together with other outcome measures (6, 23).

The difficulty in measuring compliance hinders attempts to evaluate methods for enhancing compliance. Methods that have been investigated include short-term regimens, fewer doses per day, lower medication costs, easy-to-use packaging, reminders, tailoring, patient education, and patient satisfaction measurement. None of these is very beneficial, particularly in chronic and asymptomatic illnesses (41).

On the whole, research has shown that compliant patients generally have better outcomes, even if assigned to a placebo group in a controlled trial. It is possible that compliant patients may differ from noncompliant patients in other health behaviours or in baseline health status (3). Alternatively, side-effects may lead to lower compliance among those in the active medication group compared with those in the placebo group (40). Although compliance may vary over time and with type of treatment, it is important to assess the impact of side-effects of a treatment on compliance to that treatment.

Non-compliance with scheduled appointments creates problems for health care delivery and may also have important effects on health outcomes. Studies have identified potential predictors of appointment non-compliance and multiple associations have been found. Patient factors that have been investigated include patient characteristics as well as characteristics of the medical encounter and the medical care delivery system. Older age, higher educational levels, higher socioeconomic status, married status, retired status, patient and provider speaking the same language, continuity of care, patient-initiated appointments, patient satisfaction, shorter intervals between referral and appointment, shorter clinic waiting time, and prepayment/third-party payment have all been shown to improve compliance with appointments.

One of the most commonly advocated ways to improve compliance is the improvement of the doctor–patient relationship (48). Different aspects of this relationship have been suggested as being conducive to better compliance: doctors' friendliness and approachability, encouraging doctor–patient co-operation, the enhancement of patient-centredness, the improvement of doctors' teaching skills, the taking into account of spiritual and psychological dimensions which may be of primary importance to patients, and the accurate recognition of the patient's problem by the doctor (48).

Research has also addressed the way in which doctors present information. Making clear the link between the treatment and the illness could enhance the likelihood of a better compliance. Describing the effects of treatment could, on the other hand, significantly affect patients negatively. Better patient education, aimed at improving patients' understanding of their treatment and their doctor's instructions is suggested as compliance enhancing (48). Other possibilities lie in the types of medication prescribed and techniques that encourage patients to take the correct dosages. Simplifying prescribing, precribing fewer concurrent medications and the development of longer-acting preparations can lead to simplification of the therapeutic regimen, but may not necessarily improve compliance rates unless the complexity of the regimen is one of the patient's concerns.

Other practical compliance aids include organisers and reminders such as blister packs, calendars, dosage counters, special containers, dosage forms, controlled delivery and microprocessors. Adequate labelling and written information and oral information provided by pharmacists may also help (50). Collaboration between patients, consumer groups, pharmacists, doctors and other health-care providers may enhance shared decision-making, possibly leading to better adherence (3).

Many studies have led to partial and conflicting conclusions. A meta-analysis of adherence-aiding strategies concluded that combinations of strategies led to improved compliance (2). Educational strategies such as good verbal communication or one-to-one counselling have a positive effect, whereas written information increases knowledge and decreases medication utilization errors but has no effect on compliance. On the other hand, written information with verbal reinforcement enhances compliance more than written information alone. This leads to the conclusion that educational strategies alone may not significantly improve patient compliance. Combinations of educational and behavioural strategies have a better effect (2, 3). Eliciting patients' beliefs is important before providing information. Patients' perceptions may thus be corrected or reinforced. Recall can be aided by presenting treatment instructions in a clear and simple manner, the use of concrete and specific advice, by repeating and stressing the importance of the critical components of the advice, by checking understanding and by providing feedback (49).

Adherence-aiding strategies have been shown to be better when combined. Stategies could include: involvement of the patient in the negotiation of treatment goals, reduction of the complexity of the treatment regimen, tailoring the treatment to the patient's life-style, use of reminders, encouragement of family support, informing patients about side-effects, monitoring of adherence and provision of feedback to the patient (49–51). Thus, in order to enhance patient compliance the care-giver should have three goals in mind: improving patient comprehension, patient recall and patient motivation (52).

Up to now there is no evidence that any one method improves compliance better than another. A coaching and non-judgemental approach and an examination of what can be achieved by the patient seem to improve compliance (53). This suggests that a menu of compliance-enhancing strategies may be needed in order to select an appropriate strategy for an individual patient and treatment. It has been suggested that training patients, as well as doctors, in communication skills may be a cost-effective way to increase compliance and improve the overall health of patients (54). This could be a contributing factor in improving the skills of patients and health care professionals in selecting the most suitable strategy.

Doctor–patient relationship

As we move away from the paternalistic conception of the doctor–patient relationship, to a form of relationship where the patient's autonomy and fundamental right to self-determination is acknowledged, we should also abandon the

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present concept of compliance. If it is ultimately the patient who has to decide, after being duly informed and advised, then he cannot be non-compliant. He may be non-collaborative, obstructive, or foolish if he blatantly disregards the decisions to which he is a party, but this does not imply non-compliance, as he is complying with his own decision (55).

If patients are to be involved as equal partners in decisions concerning their health care, then doctors will have to adjust their role from being the sole decision-maker to being expert advisers. The term compliance should be replaced by 'co-operative behaviour' or 'adherence to treatment' (55). The literature contains sufficient evidence on the relationship between aspects of communication and the outcomes of patient satisfaction, recall and compliance for positive correlations to be made (56). A number of provider interactional skills, techniques to elicit and modify patients' health and treatment beliefs, and techniques to aid the recall of information are empirically related to patient adherence, making interaction skills a necessary and important part of clinical competence (49, 57).

Two major problems in the doctor–patient relationship are the patient's dissatisfaction with the communication aspect of the consultation and the patients not following advice given to them (57–59). Studies of the relationship between communication and outcome have shown that the quality of clinical communication is related to positive health outcomes. Concordance between doctor and patient in identifying the nature and seriousness of the clinical problem is related to improving and resolving the problem, and greater participation by the patient in the encounter improves satisfaction, compliance and outcome of treatment (58). This leads to the question of what are the most important things that could be done by doctors to improve clinical communication? One study (58) recommends encouraging patients to discuss their main concerns without interruption or premature closing. One should elicit patients' perceptions of the illness and associated feelings and expectations, learn methods of active listening and empathy, and give clear explanations, check the patient's understanding, negotiate a treatment plan and check the patient's attention to compliance. All these skills can be enhanced by training.

The majority of compliance research has been carried out by the health care providers and by the pharmaceutical industry. The focus has been on the extent and the possible determinants of non-compliance as a failure on the part of the patient (60), rather than on the shared responsibilities of doctor and patient.

Until now it has been the doctor's role to deliver the best care and to make all necessary decisions for the patient. This paternalism is no longer inappropriate. Respect for the patient's autonomy is now paramount and the patient's participation in the decision-making must be invited (61).

A patient-perception model of health is one framework for describing the complexity of illness experiences. Patients and doctors live in different conceptual worlds. Often they do not know how much their perceptions differ, nor why. The aspects of disease that lie outside the biomedical field have hitherto not been subjected to much medical research. However, recent developments in human science research may provide new conceptions and theories in this complex territory (62).

Patient perceptions

As discussed in the previous section, many theories about compliance locate the source of non-compliance in the doctor–patient relationship, patient knowledge or beliefs about treatment. An alternative perspective is to consider the patient's experience of illness, and the meaning of medication in people's everyday lives (63).

Patients define compliance in terms of apparent good health and seek treatment approaches that are manageable, tolerable and, in their view, effective. Although compliance may be a priority for health professionals, for the person, especially with a chronic health problem, concerns such as controlling symptoms, preventing medical crises, maintaining financial comfort or enjoying a quality lifestyle may take precedence. Patients do not view all recommended treatments as necessary for their best interests (43).

The patient has a right to non-compliance. Intelligent non-compliance is the clinical situation where a prescribed medication is intentionally not taken and the patient's reason for non-compliance appears ratonal when analysed dispassionately. Some examples are: misdiagnosis, inappropriate prescri-

bing, the patient experiences adverse reactions or side-effects, or the patient with a chronic condition becomes aware that the disease has changed (64).

Little attention has been paid to patients' ideas about medicines, and such ideas might well have relevance for understanding non-adherence to medication. Perceived properties of medicines and patients' general preference for taking or not taking medication are important themes. Patients have many fears and powerful negative images of medicines (64). If measures are to be taken to improve compliance, these should primarily be based on a closer understanding of the patients' experience of their illness and medication, rather than the perceptions and expectations of health care professionals.

Inadequacies of compliance research

Too many studies have been based on the assumption that patients should be passive, obedient and unquestioning recipients of medical instructions. The investigations therefore sought what was wrong with the patient to lead to non-compliance. Much compliance research is also based on the faulty assumptions that the medical regimen is the patient's sole treatment approach and that patients will improve their health if they adhere to treatment regimens prescribed for them (43). Between the 1960s and the 1980s, considerable attention was given to conceptualizing patient non-adherence as a problem in health-related decision-making, in which the individual's attitudes and beliefs may operate independently of levels of information, objective features of the condition or the treatment regimen (65).

The methodological quality of compliance studies ranges from poor to exceptionally high (3, 18, 66). Many show flaws and weaknesses in design and execution. For compliance research, particular attention should be paid to describing the illness, the therapeutic regimens, and the definition of compliance and to the method used for measuring compliance (66). Inadequate attention to these has led to very little consistent information, despite decades of research.

The absence of any theoretical framework for empirically testing compliance-enhancing methods (3, 18) and the lack of understanding of the compliance phenomenon (18) are common problems. In the 1970s, the first decade of compliance research, Sackett and his colleagues stressed the methodological issues and listed criteria for judging methodology (66, 67).

There is an immense need for sociological and psychological research models in order to study patients' attitudes and subjective perceptions such as the perceived efficacy of medicine, the balancing of risks and benefits, managing everyday life and the discrepancies between doctor's and patient's risk perception. Most of the published explanatory models are only partially satisfactory and hence have been seldom studied experimentally (18). Measurement methods failed to gather valid information on the extent of patient compliance. Qualitative methods, mainly questionnaires, used to gather subjective information, often failed to obtain the social and the historical context of medication use in peoples' own words (66). More attention should be paid to refining assessment approaches, to including multiple measures of outcome, and to establishing validity and reliability of any attitude scales used (67). Although patient factors have been examined extensively, this has rarely been done longitudinally (65).

DISCUSSION

Compliance is a very important issue in medical care for three main reasons. Medical non-compliance imposes a considerable financial burden upon health care systems. Compliance to treatment, to advice or to lifestyle changes is the key link between process and outcome in medical care. Lack of regard for levels of compliance may have a major impact on conclusions drawn from clinical research, especially drug trials.

It is clear that the term compliance can no longer be simply taken for granted. A paternalistic approach in this matter should be avoided because the doctor–patient relationship, communication and shared decision-making are important factors affecting compliance. Patients' health beliefs and the patient perspective should be incorporated in the doctor–patient encounter. It is preferable to use the term adherence instead of compliance to incorporate the broader notions of concordance, cooperation and partnership. However, as the majority of the papers reviewed here use the term compliance, we felt obliged to maintain its use when synthesizing the literature.

By the end of the 1970s, it was known that the determinants of compliance were complex. Despite much research in the 1980s and 1990s, few new insights arose. Almost no effort was made to use qualitative research methods in this endeavour.

However, research in the 1990s emphasized the importance of the changing doctor–patient relationship and the salient influence of the patient perspective on health beliefs in general and of their illness in particular. The key message is thus to abandon the paternalistic approach to the patient and to consider him as a partner, sharing decisions after being appropriately informed. Knowing each patient's health beliefs is the key feature of the new doctor–patient encounter. This may lead to a negotiated treatment plan to which both patient and doctor can adhere. Compliance research should now be focused on the reasons or motivations for the medication-taking behaviour. The social contexts that are involved in behaviour should not be ignored (3).

CONCLUSION

Three decades have passed since compliance research started. Despite continuing efforts, no substantial new insights have arisen from quantitative studies. Important issues such as the definition of compliance and the methods for measuring it remain inadequately addressed. Despite repeated recommendations, numerous studies continue to fail to meet the advocated standards and continue to produce contradictory and variable results. Some recent qualitative research has identified important issues such as the quality of the doctor–patient relationship and patient health beliefs. These results suggest that a shift from a paternalistic biomedical model to a model of shared decision-making is necessary.

Because non-compliance remains a major health care problem, high quality research studies are needed to assess these aspects and systematic reviews are required to investigate compliance-enhancing inteventions. Let us hope that the need will be met by 2031.

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