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Patient Compliance: Fact or Fiction?

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Abstract

The word ‘compliance' comes from the Latin word complire, meaning to fill up and hence to complete an action, transaction, or process and to fulfil a promise. In the Oxford English Dictionary, the relevant definition is ‘The acting in accordance with, or the yielding to a desire, request, condition, direction, etc.; a consenting to act in conformity with; an acceding to; practical assent”. Compliance with therapy is simply patients understanding of medication, motivation toward having this medication is a prescribed manner with the belief that the prescriber and prescribed medicine will be beneficial for his well-being. Although this is often the case, in a number of situations, the physician and pharmacist have not provided the patient with adequate instructions or have not presented the instructions in such a manner that the patient understands them. Nothing should be taken for granted regarding the patient's understanding of how to use medication, and appropriate steps must be taken to provide patients with the information and counseling necessary to use their medications as effectively and as safely as possible. 20% to 30% of new prescriptions are never filled at the pharmacy. Medication is not taken as prescribed 50% of the time. For patients prescribed medications for chronic diseases, after six months, the majority take less medication than prescribed or stop the medication altogether. There are both federal and state laws that make using or sharing prescription drugs illegal. If someone take a pill that was prescribed to someone else or give that pill to another person, not only is it against the law, it's extremely dangerous.

Keywords: Adherence, Drug Therapy, Non-compliance, Patient, Medication

Introduction

According to the WHO, lack of adherence to medical treatment regimen gives rise to major clinical problems in patients, mostly with chronic illness. Rates of nonadherence with any medication treatment varies from 15% to 93%, with an average estimated rate of 50% worldwide. “Drugs don't work if people don't take them.” This observation made by former Surgeon General C Everett Koop in his keynote address at a symposium on Improving Medication Compliance, provides a clear statement of one of the consequences of noncompliance. In many cases noncompliance results in underuse of a drug, thereby depriving the patient of the anticipated therapeutic benefits and possibly resulting in a progressive Medication nonadherence for patients with chronic diseases is extremely common, affecting as many as 40% to 50% of patients who are prescribed medications for management of chronic conditions such as diabetes or hypertension. This nonadherence to prescribed treatment is thought to cause at least 100,000 preventable deaths and $100 billion in preventable medical costs per year. Despite this, the medical profession largely ignores medication nonadherence or sees it as a patient problem and not a physician or health system problem. A recent BMJ study shows annual costings of medication nonadherence range from USD 100 to USD 290 billion in USA, €1.25 billion in Europe and approximately $A7 billion in Australia. Along with staggering economic losses, patient compliance also presents a major hurdle to patient health. For instance, compliance rates below 90% for HIV patients can cause viral replication and disease progression while for diabetics, proper compliance is essential in preventing hypertension and myocardial infarction. Adherence consists of three essential factors:

A. Patient: Takes treatment decision process by their own, based on individual literacy and feedback from others, mostly non-professionals.
B. Provider: Prescribe drug/non-drug treatments and face communication barriers
C. Healthcare system: Access to care, time allotted for technical support

1.1. Types of patients:

Based on the acceptance of diagnosis and treatment initiation, patients are categorized into four types:

- **Non-compliers:** Those who do not accept both diagnosis and need treatment.
- **Partial compliers:** Those who accept diagnosis and treatment but fulfill the recommended actions partially, occasionally and sometimes never.
- **Over compliers:** These patients are rare.
- **Adequate compliers:** Those who follow treatment advise adequately to improve or control their disorder (Manmohan et.al., 2012)

1.2. Types of Medication Taking Behavior

a. Compliance: Understanding providers instructions consciously and behavior coincides with medical & health advice, also applicable for other situations such as medical device use, self-care, self-directed exercises, or therapy sessions. Given a specific prescription, compliance can be further classified with respect to the potential ways a patient can deviate from a

provider's instructions. Primary compliance is defined as a patient's fidelity of filling and refilling prescriptions. Secondary compliance refers to whether a patient actually consumes their medication.

b. Adherence: WHO defines adherence as “The extent to which a person's behavior, corresponds with agreed recommendations from a health care professional”. Adherence is broadly related to instructions concerning medicine intake, use of medical device, diet, exercise, life style changes, rest and return for scheduled appointments.
c. Concordance: Consultative and consensual therapy partnership between the consumer and their doctor. Concordance is when a patient and clinician make decisions together about treatment.
d. Persistence: A person's ability to continue medical advice that may range from few days to life-long (Fraser, 2010 and Klobusicky et.al, 2017).

1.3. Dimensions of Patient Medication Adherence

Adherence is a multidimensional phenomenon determined by the interaction of five sets of factors-- termed "dimensions" by the WHO. These dimensions are:

- **Social/economic:** It is a social support from acquaintance or caregivers to assist with medication regimens have better adherence to treatment. People with poor healthcare access, unstable living, financial lack, high medication costs are of decreased adherence rates.
- **Provider-patient/health care system:** A good provider patient relationship, reinforce and motivates patients to adhere treatment regimens. Conversely, Poor or lack of communication contributes nonadherence, especially in older adults with cognitive dysfunction.
- **Condition-related:** In chronic illness, where drug administration is lengthy, adherence significantly declines over time, its human nature. Mostly happens when symptoms are not prominent, diminished or absent.
- **Therapy-related:** The complexity of the medication regimen, numbers of medications and their daily doses, long-term therapy recommended that interferes patient's lifestyle or the untoward effects that discomfort patients results non-adherence.
- **Patient factors:** Physical impairments and cognitive dysfunctions may increase the risk for nonadherence in older adults. Poor knowledge about the disease and the reasons why medication is needed, lack of motivation, low self-efficacy, and substance abuse are associated with poor medication adherence (Fatima et.al, 2018, Wu et.al, 2008, Sabate, 2003).

1.4. Medication Non-adherence: An Eccentric East West Analogy

Medication nonadherence remains a substantial public health problem. Causes of medication non-adherence are complex and include psychosocial (e.g., alcohol use, depression, stigma), structural (eg, distance from clinics, medication costs), therapyrelated (e.g., toxicities) and health system–related barriers (e.g., lack of counselling, poor user-experience with the health system) (Subbaraman et.al, 2018). Studies have found that patients' beliefs about medicines and their perception of their illness contribute towards poor adherence (Kumar et.al, 2016). Worldwide, between 25% and 50% of patients do not take their medications as recommended. In the USA, suboptimal adherence has been associated with 125,000 deaths, 10% of hospital-

izations, and costs 300 billion USD annually (Zullig et.al, 2018). The economic impact was also in PubMed and Scopus in September 2017, which shows an increase in total healthcare cost (>80%), pharmacy costs (70%), inpatient and outpatient costs (50%), emergency department visit and medication costs (<30%), and hospitalization costs (<20%) (Cutler et.al, 2018). Nearly 70% of all medication-related hospital admissions are due to medication non-adherence alone (Kuo et.al, 2016). Across South Asia, overall hypertension prevalence is estimated to be 27%. Prospective Urban Rural Epidemiology study has shown more than 50% are unaware of it and up to 80% of hypertensive patients have low adherence to medication (Naheed et.al, 2018). Uncontrolled BP was found more than 50% in Bangladesh, 70% in Pakistan and almost 60% in Sri Lanka (Jafar et.al, 2018). American Diabetes Association and the European Association for the Study of Diabetes guidelines in 10 developing countries from Africa (Egypt, South Africa), Middle East (Israel, Saudi Arabia, United Arab Emirates, Iran and Lebanon) and South Asia (Bangladesh, India and Pakistan) shows more than 25% and around 70% patients did not have any follow-up visit by a diabetologist or a GP, respectively. More than 35% patients did not receive any diabetes education (AlMansari et.al, 2018). In a study conducted among people with diabetes, only 30% were compliant with drug regimens and the non-compliance was higher among the lower socioeconomic groups (Shrivastava et.al, 2013).

1.5. Non-patient Factors associated with Non-adherence

- The nature of patient illness
- Therapeutic regime
- Treatment duration
- Frequency of drug administration
- Adverse events
- Taste of medication

2. Patient Non-Compliance

Non-compliance with drug treatment is widespread. When patients are given medication by their doctors, nearly half do not take the drug or do not take it as prescribed, and most will stop the treatment as soon as they are feeling better. A major problem in identifying the non-compliant patient is the unreliability of many of the measures used for assessing compliance. There are few social and demographic characteristics associated with non-compliance. The type of disease, also, generally has little influence on the level of compliance. Psychological factors such as the patients' levels of anxiety, motivation to recover, attitudes towards their illness, the drug and the doctor, as well as the attitudes and beliefs of significant others in their environment do influence the patients' levels of compliance (Evans et.al., 1983). One of the more compelling rationales offered for expanding drug coverage is that affordability problems have clinical as well as economic consequences; that is, patients who have difficulty paying for medications are less likely to take them and can suffer adverse health effects as a result of noncompliance (Kennedy et.al., 2002).

2.1. Types of Non-compliance

The situations most commonly associated with noncompliance with drug therapy include following situations:

a. Some patients for whom medication has been prescribed do not even take their prescriptions to a pharmacy, and some others who do take their prescriptions to a pharmacy fail to pick them up when they are completed.
b. The omission of doses is one of the most common types of noncompliance and occurs when a medication is to be administered at frequent intervals and/or for an extended period of time.
c. *Errors of dosage* include situations when incorrect amount of an individual dose or frequency of administration occurs d) Examples of the *incorrect administration of medication* include not using the proper technique in using metereddose inhalers and, in some cases, giving medication by the wrong route of administration.
d. *Errors in the time of administration* of the drug may include situations in which medication is administered in an inappropriate relationship to meals. Certain drugs—e.g., tetracycline, alendronate (Fosamax)—should be administered apart from meals to achieve optimal absorption. The time of day at which a drug is administered also may be important in the use of some medications; e.g., diuretics are best administered in the morning.
e. *The premature discontinuation of treatment* occurs commonly with the use of antibiotics as well as medications used in the treatment of chronic disorders such as hypertension (Hussar, 2006).

2.2. Reasons of Non-compliance in elderly patients

Currently the aging population is rapidly increasing, particularly in developing regions of the world, due to longer expectancy of life, better healthcare facilities and greater awareness about healthy lifestyle. Today, in developed countries, more than 75% die after the age of 75 years (Lunenfeld et.al, 2013). Because of the progressively increasing geriatric population requiring special care, there is a growing global concern to improve the health care delivery systems, particularly against chronic and recurrent illnesses that occur more commonly during later life such as: diabetes mellitus, hypertension, IHD, arthritic disorders, neurodegenerative disorders, psychiatric illnesses, gastrointestinal disorders, ocular disorders, genitourinary disorders, respiratory disorders etc., which may require chronic medication with multiple drugs. Because of the chronic nature of the disease, the need for multiple drug therapy with complex medication regime, increasing cost of therapy, adverse effects, drug interactions, forgetfulness, lack of familial and social support and care, elderly patients may not be fully compliant to long term medications. In general, only 50% of general population has been estimated to adhere to their medications, and this may range from 47 to 100% in elderly. Poor compliance among older persons is a public health concern, as it accounts for adverse outcomes, medication wastage with increased cost of healthcare, and substantial worsening of the disease with increased disability or death (Shruthi et.al, 2016). However, Notable Reasons behind elderly non-compliance issues are:

- Adverse effects
- Increased, or decreased sensitivity to drugs
- Frequent change of prescriptions (prescription cascade)
- Living alone
- Lack of social support system
- Difficulty in opening the medication container that has flip off type of lid
- Going to pharmacist/chemist due to physical problems like (osteoarthritis)
- Cognitive impairment

- Impaired mobility or dexterity
- Swallowing problems
- Financial issues like, Low income and high cost of medications
- Everyday inconvenience in carrying and taking of medicines (Jin et.al., 2016)

2.3. Consequences of Non-compliance

Physicians frequently do not effectively communicate to their patients about the basic information of treatment plans. Patients may be left with concerns about adverse effects and with lack of comprehension of disease and treatment that adversely affect their adherence. Framing the problem of poor adherence on patients' fear of side effects or lack of understanding does not clearly emphasize the physician's responsibility to appropriately address these concerns. The same hurdle can be reformulated as a problem of physicians' inadequate, ineffective communication to patients of critical information. This reformulation demonstrates that physicians have a responsibility to minimize barriers to non-compliance by changing that which physicians have control over patients' own behavior (Devine et.al, 2018). Notable non-compliance results are:

a. *Underuse* of a drug, deprives the patient of the anticipated therapeutic benefits and possibly resulting in a progressive worsening or other complications of the condition being treated e.g. underutilization and nonadherence of warfarin among nonvalvular AF patients is both prevalent and costly (Casciano et.al., 2013). The statins significantly reduce morbidity and mortality in patients with CHD and in patients with hyperlipidemia, when they are used on a continuing basis (Rosuvastatin, up to 55% reduction in LDL, up to 20% lowering in triglycerides, and up to 10% increase in HDL) (Lardizabal et.al., 2010). Underuse of antihypertensive medications may be associated with hospitalization that could have been prevented if patients had complied with their treatment regimens.
b. *Overuse* of a drug, mostly increases risk of ADR e.g. MOH reported with antimigraine drugs (ergots and triptans) including nausea, dizziness and coronary vasoconstriction (González-Hernández et.al, 2018). AIM survey noted that 25% of patients rely on SABA monotherapy to manage their persistent asthma, many of whom use albuterol daily. MEPS noted that 15% of patients with asthma use more than 1 canister of albuterol per month. These patients had twice the risk of an asthma-related emergency department visit or hospitalization as compared to those who filled albuterol less frequently (Gerald et.al., 2015)

3. Factors Associated with Non-compliance

3.1. Disease:

Antipsychotic medication reduces the severity of serious mental illness (SMI), nonadherence to the treatment of SMI increases the risk of relapse and hospitalization. Poor insight was identified as a reason for nonadherence in more than 50% of studies, followed by a negative attitude toward medication in 30% and cognitive impairments in nearly 15% (Velligan et.al, 2017). Patients with chronic disorders, particularly conditions such as hypertension (45% in Bengaluru, 50% in Pakistan and 60% in Mumbai) (Shah et.al., 2018) and hypercholesterolemia (60% in Kuwait) (Al-Foraih et.al, 2016), which often are not associated with symptoms are also more likely to be noncompliers. Patients understandably tend to become discouraged with extended therapeutic programs that do not produce cures of the conditions.

3.2. Therapeutic Regimen

a. **Multiple Drug Therapy**: Even when specific dosage instructions for the medications are provided, problems still can occur with multiple drugs. The similarity of appearance (e.g., size, color, or shape) of certain drugs may contribute to the confusion that can exist in the use of multiple drugs. The prevalence of non-adherence in elderly patients receiving polypharmacy ranged from 6% to 55%. Medication adherence was negatively associated with large caregiver burden, impaired hearing, poor cognition and greater number of drugs in elderly patients (Zelko et.al, 2016).
b. **Frequency of Administration**: Patients with chronic diseases appear to be more adherent with once-daily compared with more frequently scheduled medication regimens (Coleman et.al, 2012). ATSP was shown to be an effective strategy to improve medication adherence in cardiovascular patients (Jung et.al., 2017 and Shroufi et.al., 2010)
c. **Duration of Therapy**: The potential for noncompliance is greater when the treatment period is long. In a free retroviral therapy by CDC in China with HIV patients (duration 17.7 month) revealed non-adherence with progression of time. Therefore, high priority must be given to the assessment of adherence behavior as well as any necessary intervention for non-adherence during the early stages of treatment (Yu et.al., 2018)
d. **Adverse Events**: Side effects can be a problem with blood pressure medications. Some people find that the treatment may make them feel worse than the disease, which usually has no symptoms (WebMD, 2017). The adverse events (e.g., nausea, vomiting, hair loss) associated with the use of many antineoplastic drugs are sufficiently distressing to a number of patients with cancer that they do not take their medication in the manner intended. The ability of certain drugs to cause sexual dysfunction is a reason for noncompliance by some patients, with the antipsychotic agents, antidepressants (TCAs 30%, MAO inhibitors 40%, SSRIs 60%–70%, venlafaxine 70% and duloxetine 46% in Western populations) (Lahon et.al., 2011) and antihypertensive agents (thiazide-class diuretics, β-blockers, and centrally acting sympathoplegics reported) being implicated most frequently (Al-Khaja et.al., 2016).
e. **Patients may be asymptomatic or Symptoms subside:** Situations frequently occur in which patients do not complete a full course of antibiotic therapy once they feel that the infection has been controlled. Many studies have shown that two-thirds of hypertensive patients do not achieve control. Poor adherence is probably more common in chronic conditions that are relatively asymptomatic for example hypertension (Chia, 2008).
f. **Cost of Medication:** The financial burden of medications may lead individuals to adopt various rationing or restrictive behaviors, such as CRNA to medications. The prevalence of CRNA varies between 4% and 36% in Canada (Gupta et.al, 2018). Estimated prevalence of CRNA among all older adults varied from <3% in the France, Norway, Sweden, Switzerland and the UK to 16.8% in the USA. Older adults in the USA were approximately six times more likely to report CRNA than older adults in the UK (Morgan et.al, 2017).
g. **Administration of Medication:** Close to 6,800 prescription medications and countless over-the-counter drugs are available in the United States. Each year, in the United States alone, 7,000 to 9,000 people die as a result of a medication error. The total cost of looking after patients with medication-associated errors exceeds $40 billion each year. Typical errors include the healthcare provider writing the wrong medication, wrong route or dose, or the wrong frequency. These ordering errors account for almost 50% of medication errors. It is obvious that medication errors are a pervasive problem, which is preventable. Data show that nurses and pharmacists identify anywhere from 30% to 70% of medication-ordering errors (Bhimji et.al., 2018)

h. **Complexity of treatment:** The complexity of treatment regimens is another frequently cited barrier that can be reframed as "the physicians prescribed too complex a treatment regimen." Adherence is best in patients who were prescribed 1 medication rather than multiple medications. Higher frequency of dosing also reduces adherence. While there may be reasons to avoid prescribing combination products (e.g., if they are costly), the potential to improve adherence and outcomes by reducing the number of medications and frequency of dosing should not be ignored (Devine et.al, 2018 and Kleinsinger et.al, 2018).
i. Taste of Medication: Approximately 4% of 4 billion medications dispensed in the United States are flavored liquid medications. This means that approximately 160 million liquid prescriptions per year are candidates for custom medication flavoring. About 85% of the interviewed subjects in the intercept survey said that the taste of liquid medicine is v very or somewhat important to them and to their child. Overall, 79% of children complained about bad tasting medication or taste that is "too yucky" to take. Seven out of t end (70%) mothers surveyed filled 4 or more prescriptions per year – with the average respondent filing 4.3 prescriptions per year for their children (Wertheimer AI and Wilson JM, 2014)

3.3. Patient-Provider Interaction

These observations are equally important with respect to the interaction between the pharmacist and the patient. The following factors are among those that could influence compliance adversely if inadequate attention is given to the scope and quality of the interaction with the patient.

a. **Failure to Comprehend Importance of Therapy**: Patients have fewer idea and least interest about illness, therapy indicated and its benefit and impact of non-compliance. A cross-sectional study (2014-2015) in South Indian tertiary hospital reveals 17% were illiterates, 65% of them had lack of information about prescribed medications 45% patients were not aware of the side effects of the prescribed medication, more than 70% patients were not aware of what happens on missing medications regularly, nearly 65% and 60% of patients were not performing exercise and not following advice on diet respectively (Divya et.al., 2015).
b. **Poor Understanding of the Instruction:** To help combat poor health literacy and its negative effect on medication adherence, a "shame-free" environment must be created. Possible solutions to poor patient literacy include providing the patient with pictorial and audiovisual educational material instead of written instructions (Brown et.al., 2011)

- In some cases, confusion arises and mistakenly medications are given in wrong rout (e.g., swallowing suppositories, installing eardrops for otitis media to mouth, IV given to IM).
- A patient being prepared for Nitroglycerin patch or Pilocarpine Ocusert. Although he had understood the instructions to apply, no instruction had been provided regarding their removal.

4. Non-compliance Detection

Current detection methods include *indirect measures*, such as self-report, interview, therapeutic outcome, pill count, change in the weight of metered-dose inhaler canisters, medication-refill rate, insurance prescription claims databases, and computerized compliance monitors, and di-

rect measures, such as biological markers, tracer compounds, and assay of body fluids. In general, *the direct methods of detection* have a higher sensitivity and specificity than the indirect methods. However, all of these methods have their limitations. To help overcome limitations of the assessment methods and to provide corroborative information, it is recommended that at least two different detection methods be used to measure compliance.

4.1. Indirect Methods:

Self-reports and interviews with patients are the most common and simplest methods of attempting to determine compliance with therapy. Pill counts are another detection method used to measure compliance and frequently are used in clinical drug studies. A patient's compliance with a medication regimen can be assessed by the difference between the number of dosage units initially dispensed and the number remaining in the container on a return visit or during an unscheduled home visit. However, *pill dumping* (i.e., attempts by patients to misrepresent their compliance by discarding medication) is common, and several studies have shown that return counts grossly overestimate actual compliance rate.

4.2. Direct Methods:

Biological markers and tracer compounds indicate patient compliance over an extended period. For example, measurement of glycosylated hemoglobin in patients with diabetes mellitus gives an objective assessment of metabolic control during the preceding 3month period. Tracer compounds—small amounts of agents with long half-lives such as phenobarbital—have been added to drugs in some studies and measured in biological fluids as pharmacological indicators of compliance (Hussar, 2006; Bond et.al., 1991; Liu et.al., 2010)

5. Improving Compliance

Pharmacists have a particularly valuable opportunity to encourage compliance since their advice accompanies the actual dispensing of the medication, and they usually are the last health professional to see the patient prior to the time the medication is to be used.

a. **Identification of Risk Factors--**These factors should be considered in planning the patient's therapy so that the simplest regimen that is, to the extent possible, compatible with the patient's normal activities can be developed.
b. **Development of Treatment Plan--**The more complex the treatment regimen, the greater is the risk of noncompliance, and this must be recognized in the development of the treatment plan. Respecting each patient's autonomy, drawing out ambivalence about change, evoking change talk, and allowing the patient to develop and/or own the treatment plan greatly improve the odds of achieving positive clinical outcomes (Butterworth, 2008)
c. **Patient Education**--One of the findings of the report of the Office of the Inspector General is “education is the best way to improve compliance.” Complex terms and unnecessary jargon are never appreciated by any patient. Patient should repeat the instructions for their better understanding and memorization and also should be encouraged to ask questions. Further, communication that ascertains patients' needs, perspectives and values is also considered effective, as it a key feature of patient-centered care (Braaf et.al, 2018).

d. **Oral communication/counseling**—Oral communication is the most effective patient education tool. It is most effective when privacy assured and free of distraction.
e. **Written communication**—Many pharmacists provide patients with medication instruction PPIs. The provision of supplementary PPIs appears to be most effective in improving compliance with short-term therapeutic regimens (e.g., antibiotic therapy). For drugs used on a long-term basis, written information as plays an important role for patient compliance (Bosworth et.al., 2011 and Mazzullo, 1978)
f. **Audio-visual materials**— The use of audio-visual aids may be particularly valuable in certain situations because patients may get a better picture of the illness or how their medication acts or is to be administered (e.g., the administration of insulin, the use of a metered-dose inhaler). The introduction of a video can reduce failure of adherence to safety-critical tasks and contribute to patient safety (Pratt et.al., 2017 and Kandler et.al., 2016)
g. **Controlled therapy**—It has been proposed that hospitalized patients be given the responsibility for self- medication prior to discharge. Usually, patients go from a complete dependence on others for the administration of their medication while hospitalized to a situation in which they are given the full responsibility when discharged, often with the assumption that they know about their drugs because they were taking them in the hospital. The suggested arrangement would permit patients to start using the medications on their own before discharge, so that health-care professionals can more directly identify problems or situations that might undermine compliance, and answer patient questions (Waring et.al, 2014 and Reinhard et.al, 2008).
h. **Patient Motivation**-- Motivation is the driving force underlying the wish to change behavior. HCPs reported that EMMA supported patient-centered consultations in adults with type 2 diabetes by facilitating dialogue, reflection, and patient activity. The use of tools elicited patients' perspectives and facilitated patient participation and shared decision-making. After 2 months, nearly 60% participants stated that they followed the goal and plan to a high or very high extent (Varming et.al, 2015).

6. Compliance Aids

6.1. Labeling:

The importance of the accuracy and specificity of the information on the label of the prescription container has been noted. Auxiliary labels that provide additional information regarding the use, precautions, and/or storage of the medication also will contribute to the attainment of compliance. The inclusion of pictograms in labeling and patient information leaflets has been demonstrated to have a positive effect in the acquisition and understanding of information regarding medications prescribed for patients with limited literacy skills.

6.2. Special Medication Calendars and Drug Reminder Charts:

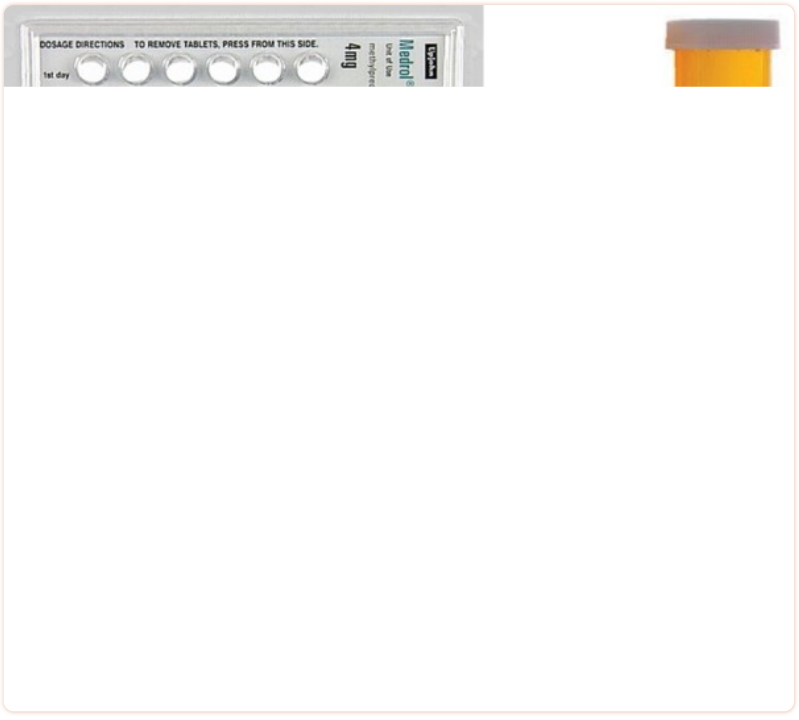
Various forms, such as medication calendars, have been developed and are designed to assist patients in selfadministering drugs. In addition to their use in helping patients understand which medication to take and when to take it, the forms on which patients are to check the appropriate area for each dose of medication they take, can be evaluated by the pharmacist or

physician when the patients return for more medication or have their next appointment. An automatically generated reminder chart is a practical and cost- effective aid to compliance (Boeni et.al., 2014 and Saghaeiannejad-Isfahani et.al., 2017)

6.3. Special Medication Containers, Caps and Systems:

Specially designed caps for prescription containers also have been developed to facilitate compliance, and include features such as a digital timepiece that displays the time and day on which the last dose of medication was taken, and an alarm and flashing light when it is time to take the otherwise have difficulty reading information on next dose. Containers/caps that contain all or some of prescription labels, products such as Talking Rx these features include The Prescript Time Cap, The Pill (MaxiAIDS.com), Scrip Talk (En-Vision America®, 2011), and Timer, and Remind Cap Closures. The use of Aloud Talking Prescription Labels have been developed to microelectronic medication monitors, MEMS in the caps of play a prerecorded message when activated. Instructions prescription containers found to be increase adherence for using the medication are recorded in a small electronic 94% in patients taking anti-hypertensives (Checchi et.al, unit or microchip that is attached to the bottom of the 2014). For patients with vision impairment or who container or embedded in a label.

Figure:



(1) Medrol Dosepak (2) Talking Rx (3) Medicine-On-Time

6.4. Compliance Packaging:

A compliance package is a prepackaged unit that provides one treatment cycle of the medication to the patient in a ready-to-use package, and a comprehensive review of the use of such packaging as a patient education tool has been published.

- This type of packaging usually is based on blister packaging using unit-of-use dosing and is designed to serve as a patient-education tool for health professionals and to make it easier for patients to understand and remember to take their medications correctly at home. Specially designed packaging for oral contraceptives was one of the first initiatives of this type and has been valuable in increasing patient understanding of how these agents are to be taken.
- Special packages of certain corticosteroids (eg. *Medrol Dosepak*) also have been designed to facilitate the use of steroids in dosage regimens that may be difficult to understand or remember (Baptist Health, 2018)
- The Medicine-On-Time system is an example of a packaging system that provides unit-of-use dosing with specific labeling in a plastic card that is set up like a calendar. In addition to simplifying the use of medications for patients who self-administer their medications, these systems also have been very useful in the distribution and administration of medications in assisted living and other patient-care facilities (Bouvier, 2012).
- A possible negative effect of drug packaging on patient compliance is seen with the use of the childresistant containers. Some patients, particularly the elderly and those with conditions like arthritis, asthma and Parkinsonism, have difficulty opening some of these containers and may not persist in their efforts to do so. There also may be difficulty opening some foil-packed drugs. Pharmacists should be alert to problems of this type and, when appropriate, suggest use of standard containers or caps (Ozturk et.al., 2016; National Research Council, 2010; New medical devices 2014)

6.5. Dosage Forms:

New dosage forms of certain drugs also have been developed, in large part in recognition of problems of noncompliance. For example, the development of longer- acting, controlled-release dosage forms of numerous medications (egg, calcium channel blocking agents) has permitted less frequent administration of these agents, which facilitates compliance. The use of transdermal delivery systems permits less-frequent administration of the drugs (egg, nitroglycerin, fentanyl) given by this route (Hussar, 2006).

6.6. Monitoring Therapy

a. **Self-Monitoring:** Patients should be apprised of the importance of monitoring their own treatment regimen and, in some situations, the response parameters.
b. **Pharmacist Monitoring:** Since pharmacists and pharmacy staff frequently interact with their patients and establish strong pharmacist-to-patient relationships, they are uniquely positioned to address their patient's medication concerns and help improve adherence (Taitel et.al, 2017). The pharmacist's role in minimizing noncompliance does not end when the prescription is dispensed. Pharmacist follow-up with telephoned or mailed refill reminders has been found to increase compliance. One approach in which both health professionals and patients have collaborated effectively in reviewing/monitoring the use of medication has been the *brown bag* program (Willeboordse et.al, 2014 and Köberlein-Neu

et.al, 2016). The Administration on Aging and NCPIE have encouraged older consumers to put all their medicines in a bag and take them to their health professional for a personalized medicine review (Mohiuddin, 2018).

c. **DOT:** A method of drug administration in which a health care professional watches as a person takes each dose of a medication. Directly observed therapy (DOT) is used to ensure the person receives and takes all medications as prescribed and to monitor response to treatment. With DOT, a patient meets with a health care worker every day or several times a week. The health care worker also asks the patient about any problems or side effects with the medication. DOT should be done at a time and place that is convenient for the patient. DOT is widely used to manage tuberculosis (TB) disease. In HIV treatment, DOT is sometimes called directly administered antiretroviral therapy (DAART) (Lucas et.al, 2002; Garvie et al, 1008; Hart et.al, 2010; Write et al, 2015; Moonan et.al, 2011).

> *"No single strategy or programmatic focus showed any clear advantage compared with another. Comprehensive interventions combining cognitive, behavioral, and affective components were more effective than single-focus interventions." (Roter et.al., 1998; Sabate, 2003; Agabna, 2014)*

7. Role of Pharmacist in Patient Compliance

Pharmacists' involvement in health management is very crucial. They can

- Suggest medical staff on proper selection of drugs.
- Plan, monitor and evaluate drug programs to improve health and reduce health inequalities.
- Ensure that medicines are managed safely and effectively so that they are appropriate for the age, sex, body weight and clinical status of the patient
- Not only dispense medications but also counsels' patients regarding general health topics such as diet, exercise, stress management, OTC medications etc.
- Provide specialized services to help patients with diabetes, asthma, smoking cessation, drug addiction, and patients with high blood pressure.
- Can prevent drug interaction, counsel patient regarding the disease and medication e.g. providing information, advice and assistance about medication and therapy due to their access of interpersonal communication.
- Clarify and verify instruction during patient counseling
- Establish protocols, set order, monitor medication profile, support and facilitate patient/drug entry during prescribing
- Organize drug storage and shelving, use of clinical information and clear instruction to nurse patients during dispensing
- Follow up diagnosis, screening and daily review of drug profiles (Usherwood et.al., 2017; Amir et.al., 2018; Jimmy et.al., 2011; Lemay et.al., 2018; Erku et.al., 2017; Ensing et.al., 2018; Fisher et.al., 1992)

8. Benefits of patient compliance

When patients experience chronic or acute episodes, many treatment options require patients to partake in lifestyle changes in order to address the root cause of their illness. The improvement of compliance will result in a situation in which all parties benefit. Most importantly, pa-

tients benefit from the enhancement of the efficacy and safety of their drug therapy. Pharmacists benefit because there is an increased recognition and respect for the value of the advice and service that they provide. Pharmaceutical manufacturers benefit from the favorable recognition that accompanies the effective and safe use of their drugs as well as from the increased sales resulting from the larger number of prescriptions being dispensed. Finally, society and the health care system benefit as a result of fewer problems associated with noncompliance. Although an increase in compliance will result in more prescriptions being dispensed and a higher level of expenditures for prescription medications, this increase in costs will be more than offset by a reduction in costs (eg, physician visits, hospitalizations) attributable to problems due to noncompliance (Suri et.al., 2017; Stefanacci et.al., 2013; Mardon, 2018; Foster et al. 2010)

Conclusion

After decades of compliance research, very little consistent information is available, except that people do not take their medications as prescribed. Many have argued that much of the existing compliance literature also lacks conceptual rigor. Although we know that people do not take their medications consistently, we do not know specifically why they have done so. One reason for this lack of understanding is that compliance research has been dominated by the perspective of the health professional. Efforts toward improving patient compliance in medication focus on either identifying trends in patient features or studying changes through an intervention. Numerous factors may influence compliance among which patient's characteristics, disease peculiarities, drug treatment modalities, physician's attitudes and health system organization. The consequences of non-compliance to drug therapy may not only be harmful for patient's health, but could also negatively impact the financial cost of public health services. Thus, all efforts should be focused to improve drug compliance, if possible, by targeting all causes responsible for poor adherence to medications.

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Glossary

Abbreviations:

(AF)	Atrial Fibrillation
(ATSP)	Administration Timing Simplification Protocol
(AIM)	Asthma Insight and Management
(BMJ)	British Medical Journal
(CHD)	Coronary Heart Disease
(CRNA)	Cost-Related Nonadherence
(DOT)	Directly Observed Treatment
(EMMA)	Empowerment, motivation, and medical adherence
(MEPS)	Medical Expenditure Panel Survey
(HCP)	Health care professional
(MOH)	Medication Overuse Headache
(MAO)	Monoamine Oxidase
(MEMS)	Medication Event Monitoring System
(SABAs)	Short Acting Beta Agonists
(PPIs)	Patient package inserts
(SMI)	Serious Mental Illness
(SSRIs)	Selective Serotonin Reuptake Inhibitors

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