

**Medication adherence: the critical step towards better patient outcome****Anish Desai<sup>1\*</sup>, Nilesh Mahajan<sup>1</sup>, Sandeep Sewlikar<sup>2</sup>, Reshmi Pillai<sup>3</sup>**<sup>1</sup>Medical Affairs & Clinical Operations, Johnson & Johnson Medical, India,<sup>2</sup>Clinical Affairs, Johnson & Johnson Medical, India,<sup>3</sup>Medical Affairs, Johnson & Johnson Medical, India**Received:** 08 July 2014**Revised :** 16 July 2014**Accepted:** 25 July 2014**\*Correspondence to:**Dr. Anish Desai,  
Email: adesai8@its.jnj.com**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.**ABSTRACT**

Medication adherence is defined as patient's adherence to take their medications as prescribed and continue to take the prescribed medication for stipulated time frame. Medication non-adherence is a growing concern to physicians, healthcare systems, and other stakeholders (e.g., payers) and there is an increasing evidence of its prevalence and is associated with adverse clinical outcomes eventually resulting into higher costs of care. The cost of non-adherence has been estimated at \$100 billion to \$300 billion annually, including costs from avoidable hospitalizations, nursing home admissions, and premature deaths. Improving adherence to medication is critical to improve the quality of health care, to encourage better chronic care management, and promote better health outcomes. Reasons for non-adherence are multiple and complex. Studies have reported that poor adherence to drug dosage is due to patient perception that the disease is non-significant, adverse drug effects, lack of treatment effectiveness, and the patient's poor or incomplete knowledge of the disease and (cost). A multifactorial approach is required to tackle this complex problem as a single approach will be ineffective for all patients. The most effective intervention is to use a combination of approaches and address literacy, behavior, and organizational issues. There are challenges as well as opportunities in addressing the public health issue of medication adherence. Changing healthcare reforms, advances in digital health media, social media and modern technologies can now provide alternatives to tackle this issue.

**Keywords:** Patient, Adherence, Medication, Cost, Health care system**INTRODUCTION**

Over the past few decades, advances in drug discovery has led to improved management of many chronic, that need medication, including diabetes, hypertension, high cholesterol, tuberculosis, rheumatoid arthritis and human immunodeficiency virus (HIV). If untreated or undertreated, these conditions often lead to serious complications (e.g., heart attacks, stroke, kidney failure, immune compromise, severe disability) that adversely influence patient's quality of life and increase their risk of mortality and morbidity.<sup>1</sup>

It has been proven beyond doubt that medical management can have a positive and favorable impact on health of the individual. Optimal management and control of an illness, however, requires that the prescribed medication regimen be well followed by the patient.

Drug adherence is defined as the extent to which a patient takes his or her medication as prescribed. The importance of drug adherence can be seen in the unnecessary costs that are often incurred, when treatments/therapy are not taken for their full prescribed course. Evidence suggests that improved medication adherence, i.e., getting people to take medicines prescribed to them by their physicians, is associated with greatly reduced total health care use and costs. Patients who adhere to their medication regimens have better health outcomes and make less use of emergency care and hospital services, compared with patients with similar medical conditions who are non-adherent.<sup>2-4</sup>

This is relevant to chronic conditions that are highly prevalent, expensive to treat, or both. These include asthma, congestive heart failure, depression, diabetes, epilepsy, gastrointestinal disorders, hypertension, osteoporosis, schizophrenia, and dyslipidemia.

Poor adherence to treatment is a worldwide problem of striking magnitude. Several voluntary health organizations – the World Health Organization (WHO), the National Institutes of Health and the National Council on Patient Information and Education – have identified poor adherence as a significant public health issue.<sup>5</sup>

In recent years, the WHO has reported that, in developed countries, adherence among patients suffering from chronic diseases averages only 50% and is much lower in developing countries.<sup>5</sup>

Poor adherence leads to poor health outcomes and increased healthcare costs for healthcare systems. Research conducted by the New England Healthcare Institute in 2009 estimated that, in the US, the overall cost of poor adherence, measured in otherwise avoidable medical spending, is close to \$310 billion annually, representing approximately 14% of total healthcare expenditures.<sup>6</sup>

The objective of this article is to look at the economic impact of non-adherence, evaluate factors affecting adherence, influencers of adherence/reasons for non-adherence and review commonly adopted adherence interventions and look at some newer methodologies and technology to tackle the issue of adherence.

***Causes of medication non-adherence and factors affecting adherence barriers to medication adherence***

More than 100 factors have been observed to be associated with medication non-adherence,<sup>7,8</sup> thus making the

importance of tailoring management to individuals’ needs and using a multifaceted approach very apparent.<sup>9</sup> Previous studies have reported that poor adherence to too many drugs is due to patient perception that the disease is not significant, adverse drug effects, lack of treatment effectiveness, and the patient’s poor or incomplete knowledge of the disease.<sup>10</sup>

There are several barriers to the ability of the patient to adhere to treatment plans in an optimal manner (Table 1).<sup>11</sup>

Healthcare stakeholders need to address each factor to improve patient adherence to therapies. Multifactorial nature of the issue and interdependencies within them makes it more complex to address. Furthermore, at any given point in time multiple factors can influence patient attitudes and behaviors toward treatment, which can also change in their level of importance over the length of treatment.<sup>11</sup>

***Economic impact of non-adherence***

Non-adherence to medication is being recognized as a significant burden on the healthcare system. Data from studies estimate that the costs of non-adherence to the US healthcare system are close to \$300 billion per annum in direct and indirect costs.<sup>12</sup>

Economic outcomes calculated as the cost of hospitalization<sup>13,14</sup> or hospital costs; these exclude medical costs incurred outside the hospital, such as ambulatory and nursing care.<sup>9</sup> This can result in an underestimation of the actual cost of non-adherence and its impact on healthcare financing. To evaluate the complete impact of non-adherence

**Table 1: Barriers to medication adherence**

Patient-level factors related to medication non adherence	<ul style="list-style-type: none"> <li>• Lacks Knowledge to understand and act on health</li> <li>• Information of disease and treatment</li> <li>• Beliefs related to diagnosis and complications related to the disease and treatment</li> <li>• Lack of understanding of drug/dosage instructions</li> <li>• Lack of follow-up visits</li> <li>• Forgetfulness and patient attitude</li> <li>• Emotional status of the patient</li> <li>• Socio-economic status</li> </ul>
Physician-level and healthcare system related factors for medication non adherence	<ul style="list-style-type: none"> <li>• Ability of physicians to recognize non adherence is poor and training to alleviate this issues lacking</li> <li>• Barriers to adherence are also related to poor interactions and/or communication between patients, healthcare providers, and the healthcare system.</li> <li>• Cost of Therapy/medication and insurance/Access</li> <li>• Non availability of the medication</li> </ul>
Treatment/Medication-related factors	<ul style="list-style-type: none"> <li>• Efficacy and side effects of medications</li> <li>• Route, frequency and timings of administration</li> <li>• Failure to understand complex treatment regimen</li> <li>• Past treatment failures</li> <li>• Multiple treatment regimens</li> </ul>
Disease related factors	<ul style="list-style-type: none"> <li>• Acute or chronic disease</li> <li>• Disability of disease</li> <li>• Severity and progression of the disease</li> <li>• Prognosis of the disease</li> </ul>

and the benefits of adherence to medication, estimation of the full cost of non-adherence is necessary. This may include in Table 2.

The estimate of indirect costs of non-adherence is not addressed in the literature. It needs to be studied to assess the true impact of non-adherence and design the necessary intervention. These costs can be measured in financial terms<sup>9</sup> or utility terms, such as the quality-adjusted life years gained.<sup>15</sup>

Published literature on non-adherence focuses on a number of chronic medical conditions.<sup>10</sup> These chronic illnesses include hypertension, diabetes, hyperlipidemia, asthma, HIV, and mental health. These are high prevalence, chronic diseases with rising and recurring costs. These diseases have unique characteristics, and no uniform intervention can be designed to target them.<sup>11</sup> Therefore, any assessment of the impact of non-adherence and the effectiveness of the interventions should be spread across diseases.

Among patients with Type 2 diabetes mellitus, adherence to prescribed medications has been reported to be as low as 60%, meaning that many patients may not be following the treatment plan that has been prescribed for them. The importance of treatment adherence is intuitive: better adherence would promote better outcomes. Data show this to be the case: for every 25% increase in medication adherence, a patient's glycated hemoglobin (HbA1c) is reduced by 0.34%. Unfortunately, only a little more than half of patients with diabetes achieve an HbA1c target below 7%. Poor therapeutic adherence affects diabetes-related costs. Patients who are non-adherent are far more likely to require hospitalization and to incur significantly higher healthcare costs.<sup>18</sup>

Non-adherence in high-risk cardiovascular patients leads to hospitalizations and avoidable additional required medical care. A lack of adherence to central venous (CV) medication is strongly associated with adverse cardiac events such as

coronary heart disease, myocardial infarction (MI), and stroke among patients with coronary artery disease (CAD)<sup>3</sup>. Non-adherence to statins in the year after hospitalization for MI was associated with 12-25% increased relative hazard for mortality. For the chronic CAD patient, non-adherence to medications ( $\beta$ -blockers, statins, and/or angiotensin-converting enzyme) was associated with 10-40% relative increased in risk of CV hospitalizations and 50-80% relative increase in risk of mortality<sup>3</sup>. Adherence to antihypertensive medications is associated with significantly lower total annual healthcare costs, \$7,182 for those with medication possession ratio (MPR) >80% compared with \$7,995 with MPR <60%, 11% increase.<sup>19,20</sup>

Finally, another economic concern that needs to be evaluated is whether interventions are cost-effective. Surely, many interventions improve adherence. However, the benefits of improved adherence need to be sufficiently quantified to generate cost-efficacy or cost-efficiency estimates.

Non-adherence to medical treatment programs has significant impacts for patients and the economy. For patients, these impacts include increased morbidity, reduced quality-of-life and mortality. For the economy, these impacts affect hospitalization and treatment (medication) costs.

**Influencers of adherence**

Multiple stakeholders influence patient behavior during the course of their interactions at various time points of treatment.

Physicians are the most important influencers that have confidence of patients, who expect strong guidance from them. However, due to lack of time, physicians are less able to stress the importance of adherence to patients, and restrict their conversation to medical regimen.

Other influencers include peers (other patients), family, and

**Table 2: Cost evaluation of non-adherence**

Direct costs	Hospital costs: Health care and medicine costs that occurred due to increased morbidity and hospital visits as a result of non-adherence to medical instructions and recommendations <sup>15</sup> Hospital related costs: Costs outside the hospital setting that are caused by non-adherence, such as ambulatory care & nursing care costs, laboratory tests costs, etc., <sup>16</sup>
Indirect costs	Productivity costs: The costs incurred by the patient and society because of lost or impaired ability to work due to morbidity and lost economic productivity due to early death <sup>17</sup> Social welfare costs: Costs to the social welfare system (e.g., Invalid's Benefit) given an individual's inability to work Personal costs: Costs to the patient due to loss of health and subsequent loss of income as a result of non-adherence <sup>18</sup> Costs to the patient's family and friends: Costs to family members and other associates, such as time associated with caring for the patient Other associated costs: All other negative impacts not covered above. For example, non-adherence with infectious diseases treatment may cause public health problems if other patients are infected, development of resistance <sup>19</sup>

media providing healthcare information. Nurse/pharmacist policymakers, payers, providers and pharmaceutical companies also have a role to play.<sup>11</sup>

Given the many factors contributing to poor adherence to medication, a multifactorial approach is required, since a single approach will not be effective for all patients.<sup>11</sup>

### ***Interventions Adopted for Adherence***

No single intervention strategy has been shown to be equally effective across patients, disease conditions and settings. Interventions that target adherence must be customized to particular disease related needs of the patient. Thus, the most effective interventions use a combination of approaches and address literacy, behavior, and organizational issues. System or administrative factors are derived from a patient's inability to afford or difficulty in affording their medication and may include, for example, lack of adequate healthcare coverage, unemployment, retirement, and indigence.

Improving medication adherence in the context of chronic diseases can be addressed in three steps. The first step is initiation, followed by adjustment, and then maintenance. Medication adherence management starts with instructing the patient at the initiation of treatment and providing careful monitoring and support during the early treatment stage.<sup>21,22</sup> An ideal system for improving adherence would not only engage the patient themselves, but also leverage their selected healthcare providers, caregivers, and community support network (Table 3).<sup>11</sup>

### ***Medication adherence in India***

Medication adherence in India is associated with certain unique issues compared to US, UK and other developed countries. There are few controlled studies evaluating medication adherence in India.<sup>23</sup> The major factors which can influence adherence to medication regimens in India is good family support.<sup>24</sup> The joint family system prevalent in India can impact adherence positively as family caregivers administer medication to members of the family.

**Table 3: Methods adopted for improving adherence.**

<b>Innovation</b>	<ul style="list-style-type: none"> <li>• Formulation development</li> <li>• New Delivery systems</li> <li>• Innovative packaging</li> <li>• Newer drugs/dosage</li> <li>• Combination pill</li> </ul>
<b>Patient Literacy</b>	<ul style="list-style-type: none"> <li>• Specifying the problem in concrete terms.</li> <li>• Identifying possible solutions.</li> <li>• Developing a plan for implementing the solutions.</li> <li>• Trying out the solutions.</li> <li>• Evaluating the results.</li> </ul>
<b>Patient advocacy and Reminders</b>	<ul style="list-style-type: none"> <li>• Telephones/Alarms</li> <li>• SMS/Apps</li> <li>• E-reminders</li> <li>• Disease educators and Patient forums</li> <li>• Behavioral changes/reinforcement</li> </ul>
<b>Financial Method</b>	<ul style="list-style-type: none"> <li>• Financial assistance schemes for payment</li> <li>• Patient Incentives for Adherence</li> </ul>

Additionally, paid domestic caregivers trained in matters of basic healthcare are employed by families. These domestic nurses are of great benefit for adherence to medication and treatment regimens.

Doctor-patient relationship<sup>23</sup> in India is a critical factor; the concept of a family doctor who is managing medical problems within the local area is quite common. Patients and families have long-term bonds with these doctors, and this relationship has a positive impact on medication adherence.

However, a large section of population living in rural areas does not have access to basic medical care. In addition the doctor - patient ratio in India is very low,<sup>25</sup> and hence, doctors spend inadequate time with the patients to acquaint them with the nature of the disorder and its implications and the nature of their treatment. This leads to patients underestimating the impact of the disease, leading to medication non-adherence in several cases.

Illiteracy of the patients leading to poor understanding of their disease condition, poor socio-economic status, and lack of the pharmacist support to prescribed medication have seriously undermined efforts made by health care professionals to ensure medication adherence.<sup>21</sup>

In a country where a large population lives close to or below the poverty line affordability has a major impact on healthcare delivery and medication adherence.

### ***The way forward future trends***

There are both challenges and opportunities in addressing the public health issue of medication adherence. One important aspect is that the multifactorial basis for non-adherence needs a multifaceted solution involving multiple stakeholders. The initial step is a common understanding of some of the key issues among stakeholders and the need to routinely measure and track adherence in standard practice. To improve patient adherence, increased collaboration between healthcare stakeholders is vital. Bringing health care to the doorstep of the rural population will be an important change and increase the success quotient for Government campaign like DOTS. Partnership of health care partners, healthcare organizations and various non-governmental organizations will help increase disease and disease management awareness. Changing healthcare reforms, advances in digital health media, social media and modern technologies now provide the change to happen. Physicians and providers will remain the critical stakeholders; influencing adherence through direct face-to-face patient contact, their influence is declining. Payers are expected to influence the scenario, along with pharmacies/nurse disease educators.<sup>11</sup>

Globally, policy makers are moving toward patient empowerment and incentives for better health outcomes

to reduce burden on healthcare while maintaining or improving quality. Policy makers are focusing on patient adherence to improve healthcare systems' effectiveness and efficiency.

Electronic medical records will influence the adherence issue. Stakeholders will be able to identify the exact points of non-adherence in a patient care pathway, identify reasons for such treatment gaps, and create programs to address them with the required tools and incentives to improve an individual's health outcomes.<sup>26</sup>

Timely and unobtrusive interventions, to influence patients to take their medication as prescribed will enhance patient adherence. Technological and digital advances allow smart interaction with patients, depending upon the desired level of involvement. This range from formulation development and pill calendars to new technologies and digital approaches via apps on smart phones Table 4.<sup>11,21</sup>

Several studies have confirmed that these adherence measures lead to better clinical outcomes. For example, statin medication adherence is associated with reductions in subsequent total health care costs and cardiovascular disease-related hospitalizations.<sup>27</sup> Adherence to blood pressure medications is linked to significantly lower total health care costs, odds of cardiovascular-related hospitalizations and emergency department visits.<sup>20</sup> Medication adherence by patients with at least one of four chronic vascular diseases (congestive heart failure, hypertension, diabetes, and/or dyslipidemia) leads to substantial medical savings due to reductions in hospitalization and emergency department use.<sup>26</sup>

Compared with the use of 2 or more separate medications, fixed-dose combination therapies have been found to reduce patient non-adherence by 26%.<sup>28</sup> Studies have also reported that a fixed-dose combination of two diabetes medicines increased adherence by almost 13% compared with taking

two separate medicines and that almost 80% of hypertensive patients taking a fixed-dose combination adhered to therapy, compared with <70 % of patients taking two separate medicines.<sup>29,30</sup> Thus, a rational fixed dose combination may also lead to better medication adherence.

Further, Adherence of medication is also becoming relevant to oncology as chemotherapy used to treat various cancers is increasingly available in oral form, resulting in greater patient convenience. Patients can self-administer these drugs in the comfort of their own homes instead of visiting their physician's clinic for infusion therapy. The ability to self-administer chemotherapy has even more benefit as the course of some therapies has moved from intense short therapies to ones that cover several months to years. As cancer becomes more chronic in nature, this convenience cannot be underestimated for patients living and working while undergoing treatment. A common assumption around cancer treatment is that the patient, given the choice of self-administered chemotherapy doses, will be 100% compliant. Evidence suggests otherwise and points to patients administering these drugs inconsistently and irregularly. Adherence rates in some studies are as low as 20%. Medication adherence management programs are designed to help patients follow the prescribed drug regimen, and better manage the expected side-effects of the chemotherapy, allowing patients to stay more compliant with the prescribed regimen and reduce costs associated with side-effects. In addition to optimizing the oncology drug's impact and patient quality of care, there is also a direct cost impact. The result can be lower overall drug costs due to reduced therapy holiday and re-started regimens, reductions in avoidable medical costs such as emergency room visits and hospitalizations due to side-effect progression to adverse drug event status.<sup>31</sup>

This steady increase in the use of oral anticancer drugs in modern oncology has created a paradigm shift, challenging

**Table 4: New web based technologies aids adherence.**

<p>Social Network/online forums/Web Search Engines</p>		<ul style="list-style-type: none"> <li><input type="checkbox"/> Articles on health, diseases, treatments are available on Health wiki</li> <li><input type="checkbox"/> Open access medical information for medical fraternity enabling information, knowledge and experience sharing</li> <li><input type="checkbox"/> Patients support and advocacy group for disease like obesity, diabetes etc.</li> </ul>
<p>Blogs / micro blogs</p>		<ul style="list-style-type: none"> <li><input type="checkbox"/> Health care professionals offering personal perspectives, experiences on weblogs</li> <li><input type="checkbox"/> Tweets on micro-blogging service</li> </ul>
<p>Video-sharing / podcasts</p>		<ul style="list-style-type: none"> <li><input type="checkbox"/> Video sharing on websites on various health topics</li> <li><input type="checkbox"/> NIH Podcasts provides information research findings, campaigns etc</li> </ul>

traditional attitudes toward cancer care and requiring new concepts of organization of oncology services.

## CONCLUSION

Non-adherence to prescribed medical interventions is a persistent and complex problem, especially for patients with a chronic illness. Considering multiple factors of medication adherence, “one size fits all” intervention strategy will not succeed. Technology use will increase and is likely help many patients and influence outcomes, but further development of technology needs continued input from all stakeholders, especially the patients and physicians on how to incorporate these advances into clinical practice. We need to examine alternative methods of implementing interventions. Reimbursement models for medication adherence are additional ideas that are needed to be further explored.

An ideal system for improving adherence would not only to engage the patient themselves, but also to leverage their selected Physician/healthcare providers, caregivers, and community support network.

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