

DEMATEL Analysis of Medication Non-Adherence Behavior of Patients: A Study Based on the Perspective of Physicians

Saibal Kumar Saha, Sikkim Manipal Institute of Technology, Sikkim Manipal University, India*

 <https://orcid.org/0000-0002-7842-698X>

Anindita Adhikary, Sikkim Manipal Institute of Technology, Sikkim Manipal University, India

Ajeya Jha, Sikkim Manipal Institute of Technology, Sikkim Manipal University, India

 <https://orcid.org/0000-0003-0491-5008>

Vijay K. Mehta, Sikkim Manipal Institute of Medical Sciences, Sikkim Manipal University

ABSTRACT

Physicians are directly responsible for the treatment of patients. They affect patient behaviour and beliefs. Their point of view with respect to medication adherence behaviour of patients is crucial for getting insights into the cause-and-effect relationship of factors of medication non-adherence. This paper tries to find the cause-and-effect relationship of seven factors based on the physician perspective. With the help of paired comparison method, the expert beliefs of 30 physicians were captured using a structured questionnaire. DEMATEL analysis was done to find the cause-and-effect relationship between different factors. ‘Belief that medication adherence is not important’ emerged as the most important factor for medication non-adherence. If patients’ beliefs can be modified through intervention, their behaviour may be altered, improving medication adherence rates.

KEYWORDS

Communication, Dose Complexity, Medication Adherence, Medication Regime, Patient Belief, Physicians, Side Effect, Symptom

INTRODUCTION

Physicians play an important role in educating patients regarding their illness, side effects of drugs and the importance of adherence to the regime (Hugtenburg et al., 2013). Apart from the treatment of disease (Beverly et al., 2012), they also play a significant role in influencing patient beliefs (Hong, 2019). Non-adherence of prescribed regime leads to complications (Banuelos Mota et al., 2019) and deterioration of patient’s health condition (Alfian et al., 2019), leading to the increased cost of care (Lam & Fresco, 2015) and patient-physician frustration (Stavropoulou, 2011). It also increases the chance of disease advancement (Kleinsinger, 2018) and causes higher mortality rates (Arbuckle et al., 2019; Matsui, 2013) among patients with long term chronic diseases. A study based on physicians’ perspective on medication non-adherence behaviour of patients can reveal new insights on the

DOI: 10.4018/IJRQEH.295081

*Corresponding Author

This article published as an Open Access Article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and production in any medium, provided the author of the original work and original publication source are properly credited.

cause and effect relationship of non-adherence factors. Furthermore, their perspective can reveal improvement in techniques for enhancing medication adherence among patients (DiMatteo et al., 2000).

Medication adherence is the term given to a “type of health behaviour in which patients follow a particular medication regime prescribed by a professionally qualified healthcare provider to control health conditions” (Sabaté et al., 2003). The regime could be concerning time, quantity or the frequency of taking medications or all of them. The process of adherence commences with the filling of medication prescription at a pharmacy and ends when taking medicine becomes a habit (Cramer et al., 2008). In certain disease, if medication is taken incorrectly, it can deteriorate patients’ condition.

Medication non-adherence is a complex set of behaviours. Both unintentional and intentional causes are associated with it (Chan et al., 2020). It is a major barrier to attaining ideal effects in chronic diseases (Sabaté et al., 2003). Unintentional non-adherence happens when the patient is interested in adhering to the regime but cannot do it due to incapability or lack of resources. The patient may not understand the instruction or forget to take medication (Oñatibia-Astibia et al., 2020). The term intentional non-adherence is associated with the behaviour when the patient does not want to follow the medication. It may be due to perceptual factors like beliefs and preferences, which play a role in motivation to start and continue the medication (Hamrahian, 2020).

From the literature, it is found that most studies are based on patient surveys. Views of physicians, an important stakeholder, have not been given much attention. This is a serious gap as poor adherence results in poor healthcare outcomes, physicians’ poor reputation, and their legal accountability. Physicians associated with World Health Organization (WHO) have declared poor adherence as an epidemic (Park et al., 2019). Furthermore, most of the studies are based on clinical trials and are under controlled conditions. Therefore, the macro view of the factors associated with non-adherence has not been analysed.

This study aims to find the cause and effect relationship of various factors related to medication non-adherence behaviour of patients based on the perception of physicians. The work of Saha et al., (2021) identified 95 different factors associated with the medication non-adherence behaviour of patients. With the help of a pilot survey with few physicians, seven prominent factors common among patients in Sikkim were identified for this study. However, due to the limitations of the complexity of paired comparison questionnaire method to be used in “Decision-Making Trial and Evaluation Laboratory” (DEMATEL) analysis, the number of factors was limited to seven.

BACKGROUND

For this study, seven factors have been identified based on the literature review, which affects the medication non-adherence behaviour of patients. A summary of the factors is shown in table 1.

F1: Belief that Medication Adherence Is Not Important

Many patients believe that following the prescribed medication regime is not important (Olowookere et al., 2015). For example, a study reports that 19% of tuberculosis patients believed that the medication regime is unnecessary for treating disease (Rehman et al., 2017). “Belief that medication adherence is not important” leads to non-adherence (Kressin et al., 2007; Hill-Briggs et al., 2005; Perez-Stable & Salazar, 2004). However, positive belief on the importance of medication has an important role in the success of recovery (Chapman, 2004). Therefore, a different approach for behavioural compliance may be required (Cushing et al., 2014).

F2: Belief That Disease Is Not Critical

The absence of knowledge about sickness procedure and its criticality is an essential factor that can prompt non-adherence (Senzaki, 2015). Patients or their family members might be new to their medicine’s postponed remedial impacts or be befuddled by undesirable symptoms. It may lead to non-adherence (Bugni et al., 2012; Pelajo et al., 2012). Studies conducted on asthma patients revealed

Table 1. Summary of factors and citation

Sl.No.	Factors	Variable	Citation
1	Belief that medication adherence is not important	F1	Cushing et al., 2014; Chapman, 2004; Rehman et al., 2017; Olowookere et al., 2015; Kressin et al., 2007; Mann et al., 2009; Hill-Briggs et al., 2005; Mochari et al., 2007; Perez-Stable & Salazar, 2004
2	Belief that disease is not critical	F2	Senzaki, 2015; Bugni et al., 2012; Le et al., 2008; Gatti et al., 2009; Pelajo et al., 2012
3	There are no symptoms	F3	Chen et al., 2009; Tedla & Bautista, 2016; Vik et al., 2004; Subotnik et al., 2014
4	Dose is complex	F4	San et al., 2008; Olowookere et al., 2015; Osterberg & Blaschke, 2005; Donohoe et al., 2001; Wright et al., 2008; Zanardi et al., 2013
5	Benefits about medication adherence are not communicated	F5	Okuyan et al., 2013; Reidel et al., 2008; Friedman et al., 1996; Egede et al., 2011; Osterberg & Blaschke, 2005; Tsai et al., 2018
6	Adverse side effects	F6	Olowookere et al., 2015; Rehman et al., 2017; Tsai et al., 2018; Vlasnik et al., 2005; Col et al., 1990; Chao et al., 2007; Kaplan et al., 2004; Brown et al., 2005; Vik et al., 2004; Zhou et al., 2018
7	Patient forgets to take medication	F7	Olowookere et al., 2015; Senzaki, 2015; Patel et al., 2018; Zhang et al., 2019; Woodham et al., 2018 Osterberg & Blaschke, 2005; Vik et al., 2004; Shah et al., 2018

a negative association of adherence with the belief that disease is not critical (Gatti et al., 2009; Le et al., 2008).

F3: There Are No Symptoms

Many diseases do not show early symptoms. Patients often fail to understand the symptoms and do not take the disease seriously. Adherence to medication regime has a close relationship with the symptoms of the disease. Patients adhere to a medication regime when they get symptoms of the disease (S. L. Chen et al., 2009). However, at the onset of side effect symptoms, patients stop adhering to the medication regime (Tedla & Bautista, 2016). Greater medication adherence is achieved for lower levels of negative symptoms (Subotnik et al., 2014).

F4: Dose is Complex

The complexity of medicine dose influences adherence (San et al., 2008; Olowookere et al., 2015). Patients with confounded medication timetables and polypharmacy have more issues. When patients are treated with higher than prescribed portions of the dose, they may have the danger of rising antagonistic occasion (Osterberg & Blaschke, 2005; Donohoe et al., 2001). The complexity of dose is often related to non-adherence. Literature reveals that the increase in dose complexity is directly proportional to non-adherence (Zanardi et al., 2013; Wright et al., 2008).

F5: Benefits About Medication Adherence Not Communicated

Patients and their family should be educated regarding the benefits of adherence, which rests on physicians and pharmacists. The study by Okuyan et al. (2013) found that 64.5% of the test units had optimal medication knowledge. Studies confirm an increase in adherence rate when benefits were communicated to patients (Reidel et al., 2008; Friedman et al., 1996). Egede et al. (2011), in their study, found that despite knowing the benefits of medication adherence, adherence rates varied between 36

and 93%. However, the study of Tsai et al. (2018) in Taiwan found that the absence of information related to medication and treatment of the disease were the real reasons behind poor adherence.

F6: Adverse Side Effects

Side effects of drugs are associated with medication non-adherence (Olowookere et al., 2015). As side effects increase, patients do not adhere to their medication regime in their desire to counter the side effect(s) (Tsai et al., 2018). Vlasnik et al. (2005) cited side effect, cost and complexity of dose as the major factors for non-adherence. The study conducted by Col et al. (1990) reported that 35% of the test subjects cited side effects to be the main reason for medication non-adherence.

F7: Patient Forgets To Take Medication

Forgetting to take medication has been reported as one of the major factors of medication non-adherence (Olowookere et al., 2015). Forgetfulness is a common factor for school going children (Senzaki, 2015). Patel et al. (2018) attribute “patient forgets to take medication” as the most common reasons for non-adherence. Zhang et al. (2019) reported that more than 75% of their test subjects forget to take medication. Woodham et al. (2018) reported that all their test subjects forgot to take medication at some point in time. The study conducted by Shah et al. (2018) in India reported that 41.2% of the test subjects attributed forgetfulness to medication non-adherence.

MATERIALS AND METHODS

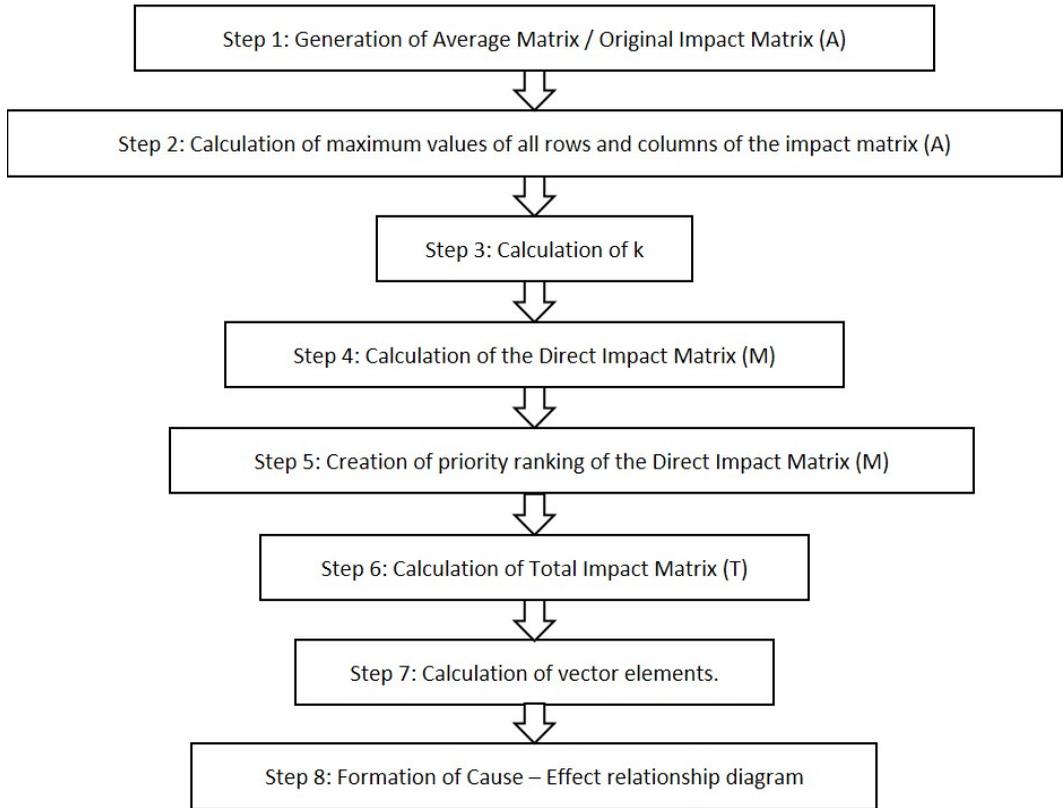
Using paired comparison method (as per the requirement of DEMATEL), questions regarding the effect of one factor on another was formed, e.g. what is the impact of (F1) ‘belief that medication regime is not important’ on (F2) ‘belief that disease is not critical’? The factors which did not affect the other was given a score of ‘0’. The questionnaire was validated (face validity) by five experts, and based on their comments, the design was simplified, keeping the essence intact. Pilot testing was done with five samples to check the data consistency and respondents’ understanding of the questionnaire. Based on a structured questionnaire, the expert opinion of 30 physicians from three prominent hospitals in Sikkim has been taken. As Sikkim is a small place, the three hospitals cater to nearly 70% of the Sikkim’s population. Since expert opinion from physicians was taken for this study, the sample size was limited to 30 which is adequate for DEMATEL analysis (X. Zhang & Su, 2019; Mahmoudi et al., 2019). The survey was conducted with general physicians who possessed a minimum qualification of Bachelor of Medicine and Bachelor of Surgery (MBBS) and had at least five years of experience. The judgemental sampling method was used for selecting the physicians for the survey. 43% of the physicians were female, while 57% were male. The age of the physicians ranged from 35 to 58 years. Respondents were asked to evaluate the dependence of one factor on the other by a score between ‘0’ to ‘4’. ‘0’ meant the belief that there is no effect of the factor on another factor. Score ‘1’ was assigned when the factor had a low effect on another factor. Score ‘2’ was assigned when the factor had a medium effect on another factor. Score ‘3’ was assigned when the effect was high and score ‘4’ was assigned to the factor when it had extreme effect on another factor (Chen et al., 2011).

Microsoft Excel 2016 was used for the analysis and generation of the cause and effect relationship diagram.

Ethics

Ethical clearance for the research was obtained from the Ethical Committee of Sikkim Manipal Institute of Medical Sciences, Sikkim (Ethical Application Ref: SMIMS/IEC/2018-064). The physicians explained the research objectives, and their signatures were taken in a written consent form.

Figure 1. Flowchart of steps for calculation of DEMATEL



DEMATEL

Evolved from Graph Theory, DEMATEL is a standard tool used to explain multifaceted problems that can corroborate interdependence among variables (Tzeng et al., 2007; Lin & Tzeng, 2009). The process of DEMATEL has been used in several studies: business strategy (Acuña-Carvajal et al., 2019), manufacturing planning (Bathrinath et al., 2019), height accidents in construction projects (Gholamnia et al., 2019), healthcare supply chain (Almutairi et al., 2019), risk of adverse events in hospitals (Ortiz-Barrios et al., 2018) etc. to find the cause and effect relationship between different factors (Yang et al., 2008). For this study, the cause and effect relationship between the factors of medication non-adherence based on physicians' perspective has been found with DEMATEL analysis.

The following steps, as shown in Fig 1, were used for DEMATEL analysis (Gupta et al., 2020; Altuntas & Gok, 2021):

RESULTS

DEMATEL Calculations and Analysis

Step No. 1: The data obtained from 30 physicians in the survey for each pairwise comparison was averaged and put in the matrix to obtain the Original Impact Matrix, as shown in table 2.

Table 2. Original Impact Matrix / Average Matrix (A)

A	F1	F2	F3	F4	F5	F6	F7	Σa_{ij}
F1	0.0000	2.4667	0.0000	1.9333	0.0000	0.0000	2.0333	6.4333
F2	2.2667	0.0000	0.0000	0.0000	0.0000	0.0000	1.6333	3.9000
F3	2.8667	3.0333	0.0000	0.0000	0.0000	0.0000	1.9667	7.8667
F4	2.3667	1.9000	1.5000	0.0000	2.3667	2.2667	1.9667	12.3667
F5	3.1000	2.6000	0.0000	0.0000	0.0000	0.0000	2.4000	8.1000
F6	1.7333	1.6000	0.0000	1.9000	2.1333	0.0000	1.9000	9.2667
F7	2.7000	2.6667	0.0000	0.0000	2.6333	0.0000	0.0000	8.0000
Σa_{ji}	15.0333	14.2667	1.5000	3.8333	7.1333	2.2667	11.9000	

Interpretation of Original Impact Matrix:

1. 'Belief that medication adherence is not important' (F1) highly impacts the factor 'belief that disease is not critical' (F2) (2.4667)
2. 'Belief that disease is not critical' (F2) highly impacts the factor 'belief that medication adherence is not important' (F1) (2.2667)
3. Impact of the factor 'no symptoms of illness' (F3) is high on 'belief that disease is not critical' (F2) (3.0333)
4. Impact of the factor 'complexity of dose' (F4) is high on both the factors 'belief that medication adherence is not important' (F1) and 'benefits about medication adherence are not communicated' (F5) (2.3667)
5. The factor 'benefits about medication adherence are not communicated' (F5) has a high impact on 'belief that medication adherence is not important' (F1) (3.1)
6. 'Adverse side effects' (F6) highly impacts the factor 'benefits about medication adherence are not communicated' (F5) (2.1333)
7. 'Patient forgets to take medication' (F7) has a high degree of impact on 'belief that medication adherence is not important' (F1) (2.7)

Step No. 2: From the impact matrix (A), maximum values of all columns and rows are calculated

Max of $\Sigma a_{ij} = 12.3667$ and max of $\Sigma a_{ji} = 15.0333$

Step No. 3: Finding the value of 'k'.

$$k = \text{Min} \left(\frac{1}{\max_{1 \leq i \leq n} \sum_{j=1}^n |a_{ij}|}, \frac{1}{\max_{1 \leq j \leq n} \sum_{i=1}^n |a_{ji}|} \right)$$

Where $i, j = 1, 2, 3, \dots, n$

$$k = \text{Min} \left(\frac{1}{12.3667}, \frac{1}{15.0333} \right)$$

$$k = \text{Min} (0.0809, 0.06652)$$

Hence, $k = 0.06652$

Step No. 4: Direct Impact Matrix (M) as shown in table 3.

Table 3. Direct Impact Matrix (M)

M=K*A	F1	F2	F3	F4	F5	F6	F7	Σa_{ij}
F1	0.0000	0.1641	0.0000	0.1286	0.0000	0.0000	0.1353	0.4279
F2	0.1508	0.0000	0.0000	0.0000	0.0000	0.0000	0.1086	0.2594
F3	0.1907	0.2018	0.0000	0.0000	0.0000	0.0000	0.1308	0.5233
F4	0.1574	0.1264	0.0998	0.0000	0.1574	0.1508	0.1308	0.8226
F5	0.2062	0.1729	0.0000	0.0000	0.0000	0.0000	0.1596	0.5388
F6	0.1153	0.1064	0.0000	0.1264	0.1419	0.0000	0.1264	0.6164
F7	0.1796	0.1774	0.0000	0.0000	0.1752	0.0000	0.0000	0.5322
Σa_{ji}	1.0000	0.9490	0.0998	0.2550	0.4745	0.1508	0.7916	

Step No. 5: Priority ranking as shown in table 4.

Table 4. Priority Table

Factors	Σa_{ij}	Σa_{ji}	Row sum + column sum	Priority
F1	0.4279	1.0000	1.4279	1
F2	0.2594	0.9490	1.2084	3
F3	0.5233	0.0998	0.6231	7
F4	0.8226	0.2550	1.0776	4
F5	0.5388	0.4745	1.0133	5
F6	0.6164	0.1508	0.7672	6
F7	0.5322	0.7916	1.3237	2

From the priority table, it is found that the highest impact priority is obtained by the factor ‘belief that medication adherence is not important’. The second highest priority is the factor ‘patient forgets to take medication’ and the third by the factor ‘belief that disease is not critical’. ‘Complexity of dose’ has the 4th impact priority. Finally, ‘Benefits about medication adherence are not communicated’, ‘adverse side effects’ and ‘no symptoms of illness’ have the lowest impact priority.

Step No. 6: Total Impact Matrix (T) (Sharma et al., 2020).

$$T = M (I-M)^{-1}$$

Table 5. (I – M) matrix

I - M	F1	F2	F3	F4	F5	F6	F7
F1	1.0000	-0.1641	0.0000	-0.1286	0.0000	0.0000	-0.1353
F2	-0.1508	1.0000	0.0000	0.0000	0.0000	0.0000	-0.1086
F3	-0.1907	-0.2018	1.0000	0.0000	0.0000	0.0000	-0.1308
F4	-0.1574	-0.1264	-0.0998	1.0000	-0.1574	-0.1508	-0.1308
F5	-0.2062	-0.1729	0.0000	0.0000	1.0000	0.0000	-0.1596
F6	-0.1153	-0.1064	0.0000	-0.1264	-0.1419	1.0000	-0.1264
F7	-0.1796	-0.1774	0.0000	0.0000	-0.1752	0.0000	1.0000

In the above formula, “I” represents the Identity matrix. table 5 shows the (I – M) matrix, and table 6 represents the (I – M) inverse matrix.

Table 6. (I – M) inverse matrix

(I - M) inverse	F1	F2	F3	F4	F5	F6	F7
F1	1.1184	0.2561	0.0146	0.1466	0.0636	0.0221	0.2131
F2	0.2002	1.0696	0.0026	0.0263	0.0314	0.0040	0.1526
F3	0.2917	0.3020	1.0038	0.0382	0.0448	0.0058	0.2165
F4	0.3594	0.3269	0.1064	1.0665	0.2427	0.1608	0.2966
F5	0.3117	0.2834	0.0041	0.0409	1.0506	0.0062	0.2473
F6	0.2767	0.2610	0.0165	0.1651	0.2158	1.0249	0.2535
F7	0.2910	0.2854	0.0038	0.0381	0.2010	0.0058	1.1087

$$T = M (I-M)^{-1}$$

In the above matrix, as shown in table 7, highlighted cells represent values that are greater than the threshold value ($\alpha = 0.21$). Although the average of the matrix elements is 0.1403, the value of threshold α has been set at 0.21 to eliminate a large number of minor effects and focus on the major factors (Kaushik, 2015).

Step No. 7: Vector elements calculation (Jha et al., 2020).

From the Total Impact Matrix (T), column sum vector (C) and row sum vector (R) was obtained. These vector elements were used to find the mutual effects of factors. For greater values of (R + C) (row and column sum vector), the mutual effects of factors are considered to be greater (Seyed-Hosseini et al., 2006). For example, table 8 represents that (R + C) is greater for ‘belief that medication adherence is not important’ (2.6838), which indicates that the mutual effect of ‘belief that medication adherence is not important’ is the highest. The net impact of the Total Impact Matrix is given by (R - C) (row and column difference vector). If the value of (R - C) is greater than zero, it signifies that the factor’s impact on other factors is higher. Therefore, it is named ‘cause’. If the value of (R - C)

Table 7. Total Impact Matrix (T).

T	F1	F2	F3	F4	F5	F6	F7	R
F1	0.1184	0.2561	0.0146	0.1466	0.0636	0.0221	0.2131	0.8346
F2	0.2002	0.0696	0.0026	0.0263	0.0314	0.0040	0.1526	0.4867
F3	0.2917	0.3020	0.0038	0.0382	0.0448	0.0058	0.2165	0.9028
F4	0.3594	0.3269	0.1064	0.0665	0.2427	0.1608	0.2966	1.5594
F5	0.3117	0.2834	0.0041	0.0409	0.0506	0.0062	0.2473	0.9442
F6	0.2767	0.2610	0.0165	0.1651	0.2158	0.0249	0.2535	1.2135
F7	0.2910	0.2854	0.0038	0.0381	0.2010	0.0058	0.1087	0.9338
C	1.8492	1.7844	0.1518	0.5218	0.8499	0.2295	1.4884	

Table 8. Cause-Effect Relationship Table

Factors	R	C	R+C	R-C	
F1	0.8346	1.8492	2.6838	-1.0145	Effect
F2	0.4867	1.7844	2.2711	-1.2977	Effect
F3	0.9028	0.1518	1.0546	0.7510	Cause
F4	1.5594	0.5218	2.0812	1.0376	Cause
F5	0.9442	0.8499	1.7941	0.0942	Cause
F6	1.2135	0.2295	1.4430	0.9841	Cause
F7	0.9338	1.4884	2.4221	-0.5546	Effect

is less than zero, the factor's impact on other factors is small. Therefore, it is called an effect. The Cause-Effect Relationship is shown in table 8.

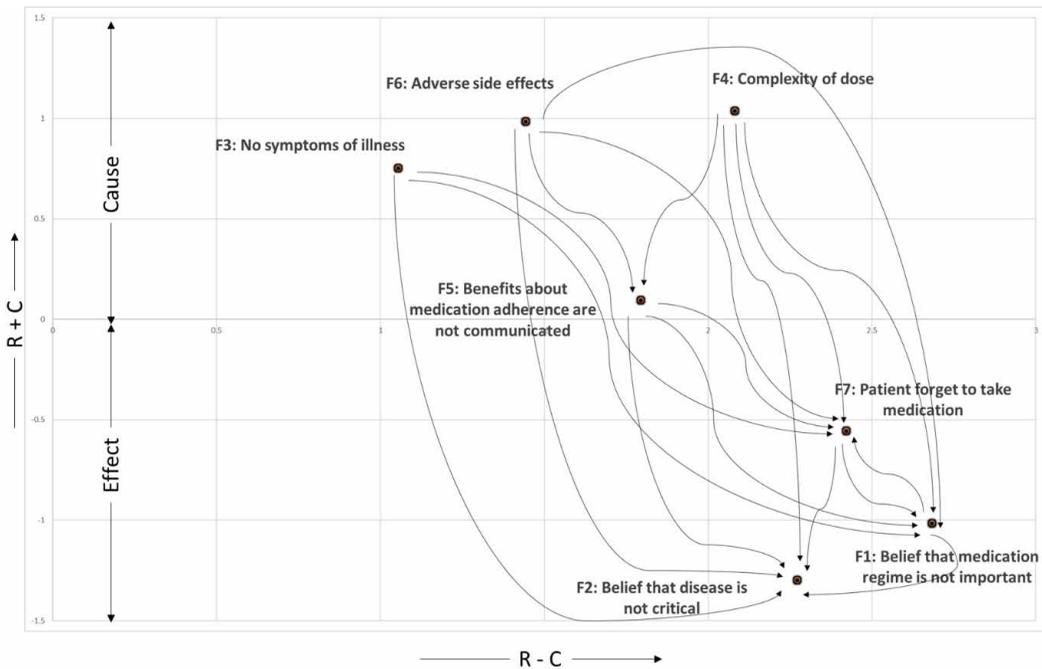
Step No. 8: Formation of Cause-Effect relationship diagram

As shown in figure 2, the cause-effect relationship diagram is created using the values of 'row and column difference vector' and 'row and column sum vector'. The diagram is divided into two quadrants. The factors with positive values of (R+C) were identified as the cause, and negative values were identified as the effect. From the total impact matrix table, the relationship between the different factors was established. For validation of results, respondent physicians were again approached to confirm if the resultant outcomes are consistent with their understanding. Mostly they agreed and provided the following reasons for the same. This found resonance in the literature review also.

DISCUSSION

F6 → F5: When medicine appears to be worse than disease or equally as bad as the disease, there is a discouragement to take medicine (Atkins & Fallowfield, 2006; Colom et al., 2005). If adverse effects of the drug are very pronounced, patients may believe that symptoms are very pronounced, and therefore, medicines are not taken. But if they are aware that despite the adverse side effects, the benefit that the medicine will provide is higher, then patients may continue to take medication. For example, a physician pointed out that he prescribed Amaryl 2 mg for his diabetic patient. The

Figure 2. Cause-Effect relationship diagram



patient stopped taking it as the weakness induced by falling sugar levels and weight gain were worse than the disease for him.

F4 → F5: when the dose is complex and multiple medicines are taken with varied frequencies followed by too many instructions, the human mind gets confused and looks for simple regulations (Menditto et al., 2020). Patients make their own simple rules and begin to falter the medication regime. This happens when they are not sure about the benefits of a medication regime. Suppose the benefits of medication adherence are communicated to patients and shown that the benefits are immense (Ramsey & Holbein, 2020). In that case, they will make greater efforts to accept dose complexity and adhere to the regime. A physician had prescribed a complicated dosage regime for his patient suffering from Hemorrhoid. The patient failed to comply with the regime because of the confusion it caused. Most physicians pointed out that a large number of patients are from rural background and illiterates or poorly literate and hence even simple instructions are not understood properly resulting in poor adherence.

F3 → F7: when there is no pronounced symptom, there is a greater tendency to forget medication intake, thus increasing non-adherence. F4 → F7: when the drug regime is complex, there is a greater tendency to forget the medication (Piña et al., 2020). When there are too many instructions to be maintained, like medication before the meal or after the meal, complexity in the frequency of dose tends to forget (Ibrahim et al., 2020). Physicians opined that patients respond more to symptoms and less to the disease. Antibiotics, in particular, are consumed only till infections have pronounced symptoms and patients forget to take them after normalcy is resumed. This leads to a large number of cases where infections relapse.

F5 → F7: when patients are not very sure about the benefits of their medication, they do not pay much attention to it. The theory of attention (Treisman & Gelade, 1980) indicates that people forget those they do not believe are important, useful, or beneficial. A physician referred to an extreme case

where a diabetic-hypertensive patient did not believe that diseases are severe, and he preferred to take recourse to naturopathy. Within two years, he suffered a cardiac arrest and died.

F6 → F7: when the adverse effects are very pronounced, the patient is scared (Bellack et al., 2009) to take the medication. In addition, subconscious attention plays a role (Sansbury et al., 2014) and patients tend to forget or delay their medication, leading to non-adherence.

F1 → F7: many patients believe for various reasons that the medication regime is not important (Pona et al., 2020). When patients believe that something is not important, the tendency to forget it is very high (Han et al., 2020). Responding physicians opined that lack of trust in medication is a significant challenge to them. Patients will not consume medicines as is needed if it is not important for them.

F6 → F1: when the side effects are very pronounced, the patient gets a feeling that the medicine is worse than the disease, and therefore they begin to believe that the disease is bearable and the belief that medication regime is not important sets in (Fekadu et al., 2020; Buchman-Wildbaum et al., 2020). For example, a physician pointed out that anti-allergic prescribed to individuals whose livelihood required frequent driving wouldn't take medicine as it caused heavy drowsiness and was contra-indicated for driving.

F4 → F1: when the dose is complex, patients make a mistake in adhering to their medication regime (Murdoch et al., 2020). As a result, they start believing that the medication regime is not important and do not have to be particular about it (Qiao et al., 2020).

F7 → F1: the relationship between forgetfulness and “belief that the medication regime is not important” is directly proportional to each other (Demoz et al., 2020). As physicians pointed out, asymptomatic diseases such as diabetes and rare diseases such as epilepsy are associated with poor adherence as often patients forget to take medications.

F5 → F1: There is a direct relationship between “benefits about medication adherence not communicated” and “belief that the medication regime is not important” (Thuy et al., 2020). Medicines are taken when there is a dire need for them. Hence, to increase the adherence rate, benefits must be communicated to patients; otherwise, they will start believing that the regime is not important (Rauscher et al., 2020). A physician mentioned that special effort is made to explain the consequences of poor adherence for diabetic patients, which helps them stick to healthy adherence.

F3 → F1: when there are no symptoms of illness, medication adherence is adversely affected (Campos et al., 2010). Patients believe that disease is not critical (F3 → F2), and therefore medication may not be important. They tend to forget because the remembrance of medicines is directly related to the severity of the symptoms (Ulrik et al., 2006).

F6 → F2: Adverse side effects will be accepted because patients believe that medication is needed. When patients believe that adverse side effects are too pronounced, the feeling that disease is not critical sets in (Piette et al., 2011). Informing the possibility of adverse effects in advance and precautions to be taken has been important to discourage patients from poor adherence.

F6 → F2: If the perception of dose complexity sets in the minds of patients and is ranked higher than the disease itself, then it leads to the belief that disease is not so critical (Murphy, 2010; Golin et al., 2002; Kane, 2006). According to a physician, it is a human tendency to act on simplified rules. In complicated regimes, mind devices simplify practices, resulting in poor adherence, particularly when disease does not appear to be serious.

Summary of DEMATEL Analysis

1. The factor F1 is affected by the factors F4, F5, F3, F7 and F6. F1, in turn, affects the factors F2 and F7.
2. F2 is affected by the factors F4, F3, F7, F5, F6 and F1.
3. The factor F3 is not affected by any of the factors. It, however, affects the factors F2, F1 and F7.

4. Factor F4 is not affected by any of the factors. However, it was found to affect the factors F1, F2, F7 and F5.
5. Factor F5 is affected by two factors F4 and F6. It further affects the factors F1, F2 and F7.
6. Factor F6 is not affected by any factor. However, It affects the factors F1, F2, F7 and F5.
7. Factor F7 is affected by the factors F4, F6, F5, F3 and F1. In addition, it affects the factors F1 and F2.

‘Belief that medication adherence is not important’ has emerged as the most important factor for medication non-adherence. It is affected by F4, F5, F3, F7, which means that several factors change the belief that medication adherence is not important (Wisnivesky et al., 2019). ‘Patient forgets to take medication’ is the second most important factor. In a study conducted in Thailand, 30.3% of the test subjects discontinued the medication when feeling well, and 12.1% skipped medication due to the costs incurred (Shah et al., 2018). Only if patients are informed about medication adherence benefits may they realise its importance, improving adherence rates. Calendars and journaling have proved to improve medication adherence (Senzaki, 2015). The factor ‘belief that disease is not critical’ is fundamental. When patients start believing that their disease is not critical, they begin to neglect their health and stop following physician instructions and medication regime. The factor ‘benefits of medication adherence are not communicated’ may be neglected by physicians and pharmacists. Suppose the benefits of the regime are conveyed to the patient and their family. It may affect the factor ‘belief that medication adherence is not important’ and help increase the adherence level. Adverse side effects have been reported to be a major factor of medication non-adherence by many researchers. There are mixed reports on the correlation between side effects and medication adherence based on literature. The work of Rehman et al. (2017) on tuberculosis treatment reveals that more than 80% of his test subjects did not know the side effect of drugs. The study of Tsai et al. (2018) on the influence of side effects on medication adherence in Taiwanese patients with chronic myeloid leukaemia reveals that patients adhered to their regime despite side effects. The work of Zhou et al. (2018) also reveals that there is no noteworthy association between side effects and adherence.

NOVELTY/SIGNIFICANCE OF THE WORK

- The paper presents cause and effect relationships between seven factors related to medication non-adherence behaviour of patients.
- The technique of DEMATEL has been used for determining the cause and effect relationships.
- Priority of the factors related to non-adherence has been found based on the perspective of physicians.
- A macro view of factors related to non-adherence has been presented in this study.

FUTURE RESEARCH DIRECTIONS

- The cause and effect relationships identified in the study could serve as a basis for further studies.
- Future studies are possible with healthcare costs, patient-physician relationships, social groups, locus of control, and type of disease.
- Factors could also be taken to find their cause and effect relationships.

LIMITATIONS

- The research is confined to a small state of Sikkim in India.
- The study is limited to a sample size of 30.

RECOMMENDATIONS

- With more extensive sample sizes, subgroup analysis based on demographic factors of physicians can be done to get more insights into the cause and effect relationship between the factors of medication non-adherence.
- Advanced analytical tools like regression and structured equation modelling can be done with large sample sizes.

CONCLUSION

The study aimed to find the cause and effect relationship of various factors related to the non-adherence behaviour of patients based on the perception of physicians. The cause and effect relationship diagram obtained from the analysis shows that patients' beliefs are greatly affected by other factors that have been taken in the study. If patients' beliefs can be modified through intervention, their behaviour may be altered, improving medication adherence rates. By explaining the importance of medication and the seriousness of the disease, even if the disease is asymptomatic, a chain of modified perceptions may be initiated, leading to better outcomes in terms of medication adherence, quick and complete recovery, and increased faith in the healthcare system. The practical implications of the study are enormous. It has been brought out that physicians consider poor adherence as a major challenge, to the extent of calling it an epidemic. Their understanding of factors leading to poor adherence has also been captured. To address poor adherence, it is important to communicate to the patients that diseases, even if asymptomatic, have severe consequences if adherence is not observed. Proper addressing of side-effects and medication's value as the central pillar of treatment need constant and consistent communication. Forgetfulness may result from many factors, but mechanisms need to be provided to overcome this forgetfulness and resulting non-adherence. This study has used numbers to make it conclusive. But it throws up many questions specifically related to the explanations of the identified relationships. This requires a qualitative research approach to explore and identify underlying reasoning for such a relationship. Future studies may focus on the same.

FUNDING

This research was funded by the All India Council for Technical Education (AICTE), India, under Research Promotion Scheme for North Eastern Region (RPS-NER) for the grant entitled "Impact of Active Reminders on Medication Adherence" as per letter No 8-104/RIFD/RPS-NER/Policy-1/2019-19 dated 14 March 2019.

REFERENCES

- Acuña-Carvajal, F., Pinto-Tarazona, L., López-Ospina, H., Barros-Castro, R., Quezada, L., & Palacio, K. (2019). An integrated method to plan, structure and validate a business strategy using fuzzy DEMATEL and the balanced scorecard. *Expert Systems with Applications*, *122*, 351–368. doi:10.1016/j.eswa.2019.01.030
- Alfian, S. D., Pradipta, I. S., Hak, E., & Denig, P. (2019). A systematic review finds inconsistency in the measures used to estimate adherence and persistence to multiple cardiometabolic medications. *Journal of Clinical Epidemiology*, *108*, 44–53.
- Almutairi, A. M., Saloniitis, K., & Al-Ashaab, A. (2019). Assessing the leanness of a supply chain using multi-grade fuzzy logic: A healthcare case study. *International Journal of Lean Six Sigma*, *10*(1), 81–105. doi:10.1108/IJLSS-03-2018-0027
- Altuntas, F., & Gok, M. S. (2021). The effect of COVID-19 pandemic on domestic tourism: A DEMATEL method analysis on quarantine decisions. *International Journal of Hospitality Management*, *92*, 102719. doi:10.1016/j.ijhm.2020.102719 PMID:33519015
- Arbuckle, C., Tomaszewski, D., Brown, L., Schommer, J., Morisky, D., Parlett-Pelleriti, C., & Linstead, E. (2019). Exploring the relationship of digital information sources and medication adherence. *Computers in Biology and Medicine*, *109*, 303–310. doi:10.1016/j.combiomed.2019.04.023 PMID:31100583
- Atkins, L., & Fallowfield, L. (2006). Intentional and non-intentional nonadherence to medication amongst breast cancer patients. *European Journal of Cancer*, *42*(14), 2271–2276. doi:10.1016/j.ejca.2006.03.004 PMID:16644208
- Bathrinath, S., Charan, V. S., Ponnambalam, S. G., & Saravanasankar, S. (2019). Identification and Evaluation of Criteria of Agile Manufacturing Using DEMATEL: A Case from an Indian Metal Fabrication Industry. *Journal of Modern Manufacturing Systems and Technology*, *2*, 61–74.
- Bellack, A. S., Bowden, C. L., Bowie, C. R., Byerly, M. J., Carpenter, W. T., Copeland, L. A., Dassori, A. M., Davis, J. M., Depp, C. A., Diaz, E., Dixon, L. B., Docherty, J. P., Elbogen, E. B., Ghaemi, S. N., Keck, P. E., Keith, S. J., Kikkert, M. J., Lauriello, J., Lebotz, B. D., & Zeber, J. E. et al. (2009). The expert consensus guideline series: Adherence problems in patients with serious and persistent mental illness. *The Journal of Clinical Psychiatry*, *70*(Suppl. 4), 1–48. doi:10.4088/JCP.7090su1cj PMID:19686636
- Beverly, E. A., Ritholz, M. D., Brooks, K. M., Hultgren, B. A., Lee, Y., Abrahamson, M. J., & Weinger, K. (2012). A qualitative study of perceived responsibility and self-blame in type 2 diabetes: Reflections of physicians and patients. *Journal of General Internal Medicine*, *27*(9), 1180–1187. doi:10.1007/s11606-012-2070-0 PMID:22549299
- Brown, C., Battista, D. R., Bruehlman, R., Sereika, S. S., Thase, M. E., & Dunbar-Jacob, J. (2005). Beliefs about antidepressant medications in primary care patients: Relationship to self-reported adherence. *Medical Care*, *43*(12), 1203–1207. doi:10.1097/01.mlr.0000185733.30697.f6 PMID:16299431
- Buchman-Wildbaum, T., Váradi, E., Schmelowszky, Á., Griffiths, M. D., Demetrovics, Z., & Urbán, R. (2020). Targeting the problem of treatment nonadherence among mentally ill patients: The impact of loss, grief and stigma. *Psychiatry Research*, *290*, 113140. doi:10.1016/j.psychres.2020.113140 PMID:32512354
- Bugni, V. M., Ozaki, L. S., Okamoto, K. Y. K., Barbosa, C. M. P. L., Hilário, M. O. E., Len, C. A., & Terreri, M. T. (2012). Factors associated with adherence to treatment in children and adolescents with chronic rheumatic diseases. *Jornal de Pediatria*, *88*(6), 483–488. doi:10.2223/JPED.2227 PMID:23269234
- Campos, L. N., Guimarães, M. D. C., & Remien, R. H. (2010). Anxiety and depression symptoms as risk factors for nonadherence to antiretroviral therapy in Brazil. *AIDS and Behavior*, *14*(2), 289–299. doi:10.1007/s10461-008-9435-8 PMID:18648925
- Chan, A. H. Y., Horne, R., Hankins, M., & Chisari, C. (2020). The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. *British Journal of Clinical Pharmacology*, *86*(7), 1281–1288. doi:10.1111/bcp.14193 PMID:31823381
- Chao, J., Nau, D. P., & Aikens, J. E. (2007). Patient-reported perceptions of side effects of antihyperglycemic medication and adherence to medication regimens in persons with diabetes mellitus. *Clinical Therapeutics*, *29*(1), 177–180. doi:10.1016/j.clinthera.2007.01.014 PMID:17379058

- Chapman, J. R. (2004). Compliance: The patient, the doctor, and the medication? *Transplantation*, *77*(5), 782–786. doi:10.1097/01.TP.0000110411.23547.D4 PMID:15021849
- Chen, F. H., Hsu, T. S., & Tzeng, G. H. (2011). A balanced scorecard approach to establish a performance evaluation and relationship model for hot spring hotels based on a hybrid MCDM model combining DEMATEL and ANP. *International Journal of Hospitality Management*, *30*(4), 908–932. doi:10.1016/j.ijhm.2011.02.001
- Chen, S. L., Tsai, J. C., & Lee, W. L. (2009). The impact of illness perception on adherence to therapeutic regimens of patients with hypertension in Taiwan. *Journal of Clinical Nursing*, *18*(15), 2234–2244. doi:10.1111/j.1365-2702.2008.02706.x PMID:19583655
- Col, N., Fanale, J. E., & Kronholm, P. (1990). The role of medication noncompliance and adverse drug reactions in hospitalisations of the elderly. *Archives of Internal Medicine*, *150*(4), 841–845. doi:10.1001/archinte.1990.00390160093019 PMID:2327844
- Colom, F., Vieta, E., Tacchi, M. J., Sánchez-Moreno, J., & Scott, J. (2005). Identifying and improving non-adherence in bipolar disorders. *Bipolar Disorders*, *7*(s5), 24–31. doi:10.1111/j.1399-5618.2005.00248.x PMID:16225557
- Cramer, J. A., Roy, A., Burrell, A., Fairchild, C. J., Fuldeore, M. J., Ollendorf, D. A., & Wong, P. K. (2008). Medication compliance and persistence: Terminology and definitions. *Value in Health*, *11*(1), 44–47. doi:10.1111/j.1524-4733.2007.00213.x PMID:18237359
- Cushing, C. C., Walters, R. W., & Hoffman, L. (2014). Aggregated N-of-1 randomised controlled trials: Modern data analytics applied to a clinically valid method of intervention effectiveness. *Journal of Pediatric Psychology*, *39*(2), 138–150. doi:10.1093/jpepsy/jst083 PMID:24284134
- Demoz, G. T., Wahdey, S., Bahrey, D., Kahsay, H., Woldu, G., Niriayo, Y. L., & Collier, A. (2020). Predictors of poor adherence to antidiabetic therapy in patients with type 2 diabetes: A cross-sectional study insight from Ethiopia. *Diabetology & Metabolic Syndrome*, *12*(1), 1–8. doi:10.1186/s13098-020-00567-7 PMID:32695232
- DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, *160*(14), 2101–2107. doi:10.1001/archinte.160.14.2101 PMID:10904452
- Donohoe, G., Owens, N., O'Donnell, C., Burke, T., Moore, L., Tobin, A., & O'Callaghan, E. (2001). Predictors of compliance with neuroleptic medication among inpatients with schizophrenia: A discriminant function analysis. *European Psychiatry*, *16*(5), 293–298. doi:10.1016/S0924-9338(01)00581-8 PMID:11514132
- Egede, L. E., Gebregziabher, M., Hunt, K. J., Axon, R. N., Echols, C., Gilbert, G. E., & Mauldin, P. D. (2011). Regional, geographic, and ethnic differences in medication adherence among adults with type 2 diabetes. *The Annals of Pharmacotherapy*, *45*(2), 169–178. doi:10.1345/aph.1P442 PMID:21304026
- Fekadu, G., Bekele, F., Bekele, K., Girma, T., Mosisa, G., Gebre, M., Alemu, T., Tekle, T., Gamachu, B., & Diriba, A. (2020). Adherence to anti-tuberculosis treatment among pediatric patients at nekemte specialised hospital, Western Ethiopia. *Patient Preference and Adherence*, *14*, 1259–1265. doi:10.2147/PPA.S258292 PMID:32801656
- Friedman, R. H., Kazis, L. E., Jette, A., Smith, M. B., Stollerman, J., Torgerson, J., & Carey, K. (1996). A telecommunications system for monitoring and counseling patients with hypertension impact on medication adherence and blood pressure control. *American Journal of Hypertension*, *9*(4), 285–292. doi:10.1016/0895-7061(95)00353-3
- Gatti, M. E., Jacobson, K. L., Gazmararian, J. A., Schmotzer, B., & Kripalani, S. (2009). Relationships between beliefs about medications and adherence. *American Journal of Health-System Pharmacy*, *66*(7), 657–664. doi:10.2146/ajhp080064 PMID:19299373
- Gholamnia, R., Ebrahimiyan, M., Gendeshmin, S. B., Saeedi, R., & Firooznia, S. (2019). Effective Factors on the Occurrence of Falling from Height Accidents in Construction Projects by Using DEMATEL Method. *Advances in Intelligent Systems and Computing*, *819*, 293–305. doi:10.1007/978-3-319-96089-0_32
- Golin, C. E., Liu, H., Hays, R. D., Miller, L. G., Beck, C. K., Ickovics, J., Kaplan, A. H., & Wenger, N. S. (2002). A prospective study of predictors of adherence to combination antiretroviral medication. *Journal of General Internal Medicine*, *17*(10), 756–765. doi:10.1046/j.1525-1497.2002.11214.x PMID:12390551

- Gupta, A., Sharma, N. D., Saha, S. K., & Jha, A. (2020). Inter-relational dynamics of identified motivational challenges: Study of skill development courses in Sikkim. *Journal of Critical Reviews*, 7(17), 3173–3180.
- Hamrahian, S. M. (2020). Medication Nonadherence: A Major Cause of Resistant Hypertension. *Current Cardiology Reports*, 22(11), 1–7. doi:10.1007/s11886-020-01400-3 PMID:32910342
- Han, Z., Yang, Y., Zhang, Q., & Mo, L. (2020). Can you voluntarily forget what you are planning to forget? Behavioral evidence for the underlying truth of the cost–benefit principle. *Psychological Research*, 1–16. doi:10.1007/s00426-020-01339-8 PMID:32318802
- Hill-Briggs, F., Gary, T. L., Bone, L. R., Hill, M. N., Levine, D. M., & Brancati, F. L. (2005). Medication adherence and diabetes control in urban African Americans with type 2 diabetes. *Health Psychology*, 24(4), 349–357. doi:10.1037/0278-6133.24.4.349 PMID:16045370
- Hong, S. H. (2019). Potential for physician communication to build favorable medication beliefs among older adults with hypertension: A cross-sectional survey. *PLoS One*, 14(1), e0210169. Advance online publication. doi:10.1371/journal.pone.0210169 PMID:30615656
- Hugtenburg, J. G., Timmers, L., Elders, P. J. M., Vervloet, M., & van Dijk, L. (2013). Definitions, variants, and causes of nonadherence with medication: A challenge for tailored interventions. In *Patient Preference and Adherence* (Vol. 7, pp. 675–682). doi:10.2147/PPA.S29549
- Ibrahim, N., Edis, Z., & Al-Owais, K. (2020). Adherence of geriatric patients and their beliefs toward their medicines in the United Arab Emirates. *Journal of Pharmacy & Bioallied Sciences*, 12(1), 22. doi:10.4103/jpbs.JPBS_93_19 PMID:32801597
- Jha, A., Dheer, A., Mehta, V. K., & Saha, S. K. (2020). Inter-Relational Dynamics of Various HR Aspects in High Altitude Illness Attrition. In *Innovative Management and Business Practices in Asia* (pp. 114–132). IGI Global. doi:10.4018/978-1-7998-1566-2.ch006
- Kane, S. V. (2006). Systematic review: Adherence issues in the treatment of ulcerative colitis. *Alimentary Pharmacology & Therapeutics*, 23(5), 577–585. doi:10.1111/j.1365-2036.2006.02809.x PMID:16480396
- Kaplan, R. C., Bhalodkar, N. C., Brown, E. J. Jr, White, J., Brown, D. L., Brown, E. J., White, J., & Brown, D. L. (2004). Race, ethnicity, and sociocultural characteristics predict noncompliance with lipid-lowering medications. *Preventive Medicine*, 39(6), 1249–1255. doi:10.1016/j.ypmed.2004.04.041 PMID:15539064
- Kaushik, S. (2015). DEMATEL: A Methodology for Research in Library and Information Science. *International Journal of Librarianship and Administration*, 6(2), 179–185.
- Kleinsinger, F. (2018). The Unmet Challenge of Medication Nonadherence. *The Permanente Journal*, 22. Advance online publication. doi:10.7812/TPP/18-033 PMID:30005722
- Kressin, N. R., Wang, F., Long, J., Bokhour, B. G., Orner, M. B., Rothendler, J., Clark, C., Reddy, S., Kozak, W., Kroupa, L. P., & Berlowitz, D. R. (2007). Hypertensive patients' race, health beliefs, process of care, and medication adherence. *Journal of General Internal Medicine*, 22(6), 768–774. doi:10.1007/s11606-007-0165-9 PMID:17364243
- Lam, W. Y., & Fresco, P. (2015). Medication Adherence Measures: An Overview. In *BioMed Research International* (Vol. 2015). Hindawi Publishing Corporation. doi:10.1155/2015/217047
- Le, T. T., Bilderback, A., Bender, B., Wamboldt, F. S., Turner, C. F., Rand, C. S., & Bartlett, S. J. (2008). Do asthma medication beliefs mediate the relationship between minority status and adherence to therapy? *The Journal of Asthma*, 45(1), 33–37. doi:10.1080/02770900701815552 PMID:18259993
- Lin, C. L., & Tzeng, G. H. (2009). A value-created system of science (technology) park by using DEMATEL. *Expert Systems with Applications*, 36(6), 9683–9697. doi:10.1016/j.eswa.2008.11.040
- Mahmoudi, S., Jalali, A., Ahmadi, M., Abasi, P., & Salari, N. (2019). Identifying critical success factors in Heart Failure Self-Care using fuzzy DEMATEL method. *Applied Soft Computing*, 84, 105729. doi:10.1016/j.asoc.2019.105729
- Mann, D. M., Ponieman, D., Leventhal, H., & Halm, E. A. (2009). Predictors of adherence to diabetes medications: The role of disease and medication beliefs. *Journal of Behavioral Medicine*, 32(3), 278–284. doi:10.1007/s10865-009-9202-y PMID:19184390

- Matsui, D. (2013). Medication adherence issues in patients: Focus on cost. *Clinical Audit, 5*, 33. doi:10.2147/CA.S30125
- Menditto, E., Orlando, V., De Rosa, G., Minghetti, P., Musazzi, U. M., Cahir, C., Kurczewska-Michalak, M., Kardas, P., Costa, E., Sousa Lobo, J., & Almeida, I. F. (2020). Patient centric pharmaceutical drug product design—The impact on medication adherence. *Pharmaceutics, 12*(1), 44. doi:10.3390/pharmaceutics12010044 PMID:31947888
- Mochari, H., Ferris, A., Adigopula, S., Henry, G., & Mosca, L. (2007). Cardiovascular disease knowledge, medication adherence, and barriers to preventive action in a minority population. *Preventive Cardiology, 10*(4), 190–195. doi:10.1111/j.1520-037X.2007.06619.x PMID:17917515
- Mota, A. B., Sala, E. E. F., Perdomo, J. M., Solis, J. A., Solorzano, W. M., Hochman, M., & Reilly, J. M. (2020). Assessing barriers to medication adherence among Latinos with diabetes: A cross-sectional study. *Journal of General Internal Medicine, 35*(2), 603–605. doi:10.1007/s11606-019-05041-3 PMID:31161564
- Murdoch, I., Nyakundi, D., Baker, H., Dulku, S., & Kiage, D. (2020). Adherence with medical therapy for primary open-angle glaucoma in Kenya – a pilot study. *Patient Preference and Adherence, 14*, 221–225. doi:10.2147/PPA.S236468 PMID:32103906
- Murphy, K. R. (2010). Adherence to inhaled corticosteroids: Comparison of available therapies. *Pulmonary Pharmacology & Therapeutics, 23*(5), 384–388. doi:10.1016/j.pupt.2010.06.001 PMID:20542129
- Okuyan, B., Sancar, M., & Izzettin, F. V. (2013). Assessment of medication knowledge and adherence among patients under oral chronic medication treatment in community pharmacy settings. *Pharmacoepidemiology and Drug Safety, 22*(2), 209–214. doi:10.1002/pds.3275 PMID:22514147
- Olowookere, A. J., Olowookere, S. A., Talabi, A. O., Etoneyaku, A., Adeleke, O. E., & Akinboboye, O. O. (2015). Perceived family support and factors influencing medication adherence among hypertensive patients attending a Nigerian tertiary hospital. *Annals of Tropical Medicine and Public Health, 8*(6), 241–245. doi:10.4103/1755-6783.162668
- Oñatibia-Astibia, A., Malet-Larrea, A., Gastelurrutia, M. Á., Calvo, B., Ramírez, D., Cantero, I., & Goyenechea, E. (2020). Effect of health professional intervention on adherence to statin use according to the cause of patient non-adherence. *International Journal of Clinical Pharmacy, 42*(2), 331–335. doi:10.1007/s11096-020-01024-1 PMID:32301066
- Ortiz-Barrios, M. A., Herrera-Fontalvo, Z., Rúa-Muñoz, J., Ojeda-Gutiérrez, S., De Felice, F., & Petrillo, A. (2018). An integrated approach to evaluate the risk of adverse events in hospital sector: From theory to practice. *Management Decision, 56*(10), 2187–2224. doi:10.1108/MD-09-2017-0917
- Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *The New England Journal of Medicine, 353*(5), 487–497. doi:10.1056/NEJMra050100 PMID:16079372
- Park, J. Y. E., Li, J., Howren, A., Tsao, N. W., & De Vera, M. (2019). Mobile phone apps targeting medication adherence: Quality assessment and content analysis of user reviews. *JMIR mHealth and uHealth, 7*(1), e11919. doi:10.2196/11919 PMID:30702435
- Patel, P. D., Patel, S. R., & Patel, K. P. (2018). *Medication Adherence in Patients With Type 2 Diabetes Mellitus : a Study At Tertiary Care Teaching Hospital*. 10.20959/wjpps20186-11826
- Pelajo, C. F., Sgarlat, C. M., Lopez-Benitez, J. M., Oliveira, S. K. F., Rodrigues, M. C. F., Sztajnbok, F. R., Diniz, C. C., & Miller, L. C. (2012). Adherence to methotrexate in juvenile idiopathic arthritis. *Rheumatology International, 32*(2), 497–500. doi:10.1007/s00296-010-1774-x PMID:21246362
- Perez-Stable, E. J., & Salazar, R. (2004). Issues in achieving compliance with antihypertensive treatment in the Latino population. *Clinical Cornerstone, 6*(3), 49–64. 10.1016/S1098-3597(04)80064-4
- Piette, J. D., Beard, A., Rosland, A. M., & McHorney, C. A. (2011). Beliefs that influence cost-related medication nonadherence among the “haves” and “have nots” with chronic diseases. *Patient Preference and Adherence, 5*, 389–396. doi:10.2147/PPA.S23111 PMID:21949602
- Piña, I. L., Di Palo, K. E., Brown, M. T., Choudhry, N. K., Cvengros, J., Whalen, D., Whitsel, L. P., & Johnson, J. (2020). Medication adherence: Importance, issues and policy: A policy statement from the American Heart Association. In *Progress in Cardiovascular Diseases*. W.B. Saunders. doi:10.1016/j.pcad.2020.08.003

- Pona, A., Cline, A., & Feldman, S. R. (2020). *Reasons for nonadherence*. Springer. doi:10.1007/978-3-030-27809-0_1
- Qiao, X., Tian, X., Liu, N., Dong, L., Jin, Y., Si, H., Liu, X., & Wang, C. (2020). The association between frailty and medication adherence among community-dwelling older adults with chronic diseases: Medication beliefs acting as mediators. *Patient Education and Counseling*, *103*(12), 2548–2554. Advance online publication. doi:10.1016/j.pec.2020.05.013 PMID:32461040
- Ramsey, R. R., & Holbein, C. E. (2020). *Treatment Adherence Within Consultation-Liaison Services*. Springer. doi:10.1007/978-3-030-35598-2_32
- Rauscher, E. A., Hesse, C., & Campbell-Salome, G. (2020). Applying Family Communication Patterns to Patient-provider Communication: Examining Perceptions of Patient Involvement, Satisfaction, and Medical Adherence. *Journal of Health Communication*, *25*(2), 180–189. doi:10.1080/10810730.2020.1728596 PMID:32116144
- Rehman, F., Ravindra, N., Rao, S., Hasan, A., & Raoof, M. A. (2017). Patient's Perception on Adverse Drug Reaction of Tuberculosis Treatment in a Teaching Hospital. *International Journal of Applied Pharmaceutical Sciences and Research*, *2*(2), 36–40. Advance online publication. doi:10.21477/ijapsr.v2i2.8158
- Reidel, K., Tamblyn, R., Patel, V., & Huang, A. (2008). Pilot study of an interactive voice response system to improve medication refill compliance. *BMC Medical Informatics and Decision Making*, *8*(1), 46. Advance online publication. doi:10.1186/1472-6947-8-46 PMID:18845004
- Sabaté, E., & Sabaté, E. et al. (2003). *Adherence to long-term therapies: evidence for action*. World Health Organization.
- Saha, S. K., Adhikary, A., Jha, A., & Mehta, V. K. (2021). Use of Interventions to Overcome Medication Nonadherence. *International Journal of Asian Business and Information Management*, *12*(3), 289–318. doi:10.4018/IJABIM.20210701.0a18
- San, L., Casillas, M., Ciudad, A., & Gilaberte, I. (2008). Olanzapine orally disintegrating tablet: A review of efficacy and compliance. *CNS Neuroscience & Therapeutics*, *14*(3), 203–214. doi:10.1111/j.1755-5949.2008.00053.x PMID:18801113
- Sansbury, B., Dasgupta, A., Guthrie, L., & Ward, M. (2014). Time perspective and medication adherence among individuals with hypertension or diabetes mellitus. *Patient Education and Counseling*, *95*(1), 104–110. doi:10.1016/j.pec.2013.12.016 PMID:24480361
- Senzaki, S. V. (2015). *Identifying factors in medication nonadherence in teens diagnosed with juvenile arthritis: A pilot study*. Academic Press.
- Seyed-Hosseini, S. M., Safaei, N., & Asgharpour, M. J. (2006). Reprioritization of failures in a system failure mode and effects analysis by decision making trial and evaluation laboratory technique. *Reliability Engineering & System Safety*, *91*(8), 872–881. doi:10.1016/j.ress.2005.09.005
- Shah, A. J., Singh, V., Patil, S. P., Gadkari, M. R., Ramchandani, V., & Doshi, K. J. (2018). Factors affecting compliance to antihypertensive treatment among adults in a tertiary care hospital in Mumbai. *Indian Journal of Community Medicine*, *43*(1), 53–55. doi:10.4103/ijcm.IJCM_40_17 PMID:29531441
- Sharma, B., Saha, S. K., & Jha, A. (2020). Understanding Inter-Relational Dynamics of Different Factors Impacting the Cymbidium Orchids-Based Economy in Sikkim, India Using DEMATAL. In *Handbook of Research on Managerial Practices and Disruptive Innovation in Asia* (pp. 282–299). IGI Global. doi:10.4018/978-1-7998-0357-7.ch016
- Stavropoulou, C. (2011). Nonadherence to medication and doctor-patient relationship: Evidence from a European survey. *Patient Education and Counseling*, *83*(1), 7–13. doi:10.1016/j.pec.2010.04.039 PMID:20541884
- Subotnik, K. L., Ventura, J., Gretchen-Doorly, D., Hellemann, G. S., Agee, E. R., Casaus, L. R., Luo, J. S., Villa, K. F., & Nuechterlein, K. H. (2014). The impact of second-generation antipsychotic adherence on positive and negative symptoms in recent-onset schizophrenia. *Schizophrenia Research*, *159*(1), 95–100. doi:10.1016/j.schres.2014.07.008 PMID:25108771
- Tedla, Y. G., & Bautista, L. E. (2016). Drug Side Effect Symptoms and Adherence to Antihypertensive Medication. *American Journal of Hypertension*, *29*(6), 772–779. doi:10.1093/ajh/hpv185 PMID:26643686

- Thuy, L. T., Monkong, S., Pookboonmee, R., Leelacharas, S., & Viwatwongkasem, C. (2020). Factors Explaining Medication Adherence of Older Adults with Hypertension: A Cross-sectional Study. *Pacific Rim International Journal of Nursing Research*, 24(3), 306–320.
- Treisman, A. M., & Gelade, G. (1980). A feature-integration theory of attention. *Cognitive Psychology*, 12(1), 97–136. doi:10.1016/0010-0285(80)90005-5 PMID:7351125
- Tsai, Y. F., Huang, W. C., Cho, S. F., Hsiao, H. H., Liu, Y. C., Lin, S. F., Liu, T. C., & Chang, C. S. (2018). Side effects and medication adherence of tyrosine kinase inhibitors for patients with chronic myeloid leukemia in Taiwan. *Medicine (United States)*, 97(26), e11322. Advance online publication. doi:10.1097/MD.0000000000011322 PMID:29953021
- Tzeng, G. H., Chiang, C. H., & Li, C. W. (2007). Evaluating intertwined effects in e-learning programs: A novel hybrid MCDM model based on factor analysis and DEMATEL. *Expert Systems with Applications*, 32(4), 1028–1044. doi:10.1016/j.eswa.2006.02.004
- Ulrik, C. S., Backer, V., Søres-Petersen, U., Lange, P., Harving, H., & Plaschke, P. P. (2006). The patient's perspective: Adherence or nonadherence to asthma controller therapy? *The Journal of Asthma*, 43(9), 701–704. doi:10.1080/02770900600925569 PMID:17092852
- Vik, S. A., Maxwell, C. J., & Hogan, D. B. (2004). Measurement, correlates, and health outcomes of medication adherence among seniors. *The Annals of Pharmacotherapy*, 38(2), 303–312. doi:10.1345/aph.1D252 PMID:14742770
- Vlasnik, J. J., Aliotta, S. L., & DeLor, B. (2005). Medication adherence: Factors influencing compliance with prescribed medication plans. *The Case Manager*, 16(2), 47–51. doi:10.1016/j.casemgr.2005.01.009 PMID:15818344
- Wisnivesky, J. P., Agarwal, P., Lin, J., Muellers, K., O'Connor, R., Wolf, M. S., & Federman, A. (2019). *Mediational Effect of Medication Beliefs on the Relationship Between Health Literacy and Medication Adherence Among Patients with Chronic Obstructive Pulmonary Disease: A Structural Equation Modeling Approach*. 10.1164/ajrccm-conference.2019.199.1_MeetingAbstracts.A5566
- Woodham, N. S., Taneepanichskul, S., Somrngthong, R., & Auamkul, N. (2018). Self-care management among elderly patients with hypertension and poor adherence to treatment, living in rural thailand: A qualitative study. *Pakistan Journal of Public Health*, 8(2), 84–89. doi:10.32413/pjph.v8i2.131
- Wright, J. W., Mizutani, S., & Harding, J. W. (2008). Pathways involved in the transition from hypertension to hypertrophy to heart failure. Treatment strategies. *Heart Failure Reviews*, 13(3), 367–375. doi:10.1007/s10741-007-9060-z PMID:17987382
- Yang, Y.-P. O., Shieh, H.-M., Leu, J.-D., & Tzeng, G.-H. (2008). A novel hybrid MCDM model combined with DEMATEL and ANP with applications. *International Journal of Operations Research*, 5(3), 160–168.
- Zanardi, R., Colombo, L., Marcheggiani, E., Rossini, D., Delmonte, D., Fulgosi, M. C., Gavinelli, C., & Colombo, C. (2013). Paroxetine drops versus paroxetine tablets: Evaluation of compliance in a six-month study. *Rivista di Psichiatria*, 48(3), 261–267. doi:10.1708/1292.14294 PMID:23752809
- Zhang, M., Zhang, D., Peng, S., Fu, L., Tan, J., Ye, M., Huang, Q., Luo, L., Liu, X., & Wu, Y. (2019). Chronic Kidney Disease Medication Adherence and its Influencing Factors: An Observation and Analysis. *Proceedings - 2018 IEEE International Conference on Bioinformatics and Biomedicine, BIBM 2018*, 1959–1966. doi:10.1109/BIBM.2018.8621113
- Zhang, X., & Su, J. (2019). A combined fuzzy DEMATEL and TOPSIS approach for estimating participants in knowledge-intensive crowdsourcing. *Computers & Industrial Engineering*, 137, 106085. doi:10.1016/j.cie.2019.106085
- Zhou, G., Li, X., Qiao, S., Shen, Z., & Zhou, Y. (2018). Influence of Side Effects on ART Adherence Among PLWH in China: The Moderator Role of ART-Related Knowledge. *AIDS and Behavior*, 22(3), 961–970. doi:10.1007/s10461-017-1791-9 PMID:28509998

APPENDIX A

Ethical Committee Certificate of Sikkim Manipal Institute of Medical Sciences, Sikkim (Ref: SMIMS/IEC/2018-064)

URL of Ethical Committee Certificate:

<https://smu.edu.in/content/dam/manipal/smu/smit/documents/research/ActiveReminders/Ethical%20Committee%20Clearance%20Certificate.jpg>

Questionnaire:

Qualification: _____ Experience (in years): _____

Age: _____ Gender: _____

Please rate the effect of following on a scale of 0 to 4 (Box 1):

0 – No effect 1 – Low effect 2 – Medium effect 3 – High effect 4 – Extreme effect

Box 1.

1. What is the effect of patient belief that medication regime is not important on:	patient belief that disease is not critical	
	complexity of dose	
	patient forget to take medication	
2. What is the effect of patient belief that disease is not critical on:	patient belief that medication regime is not important	
	patient forget to take medication	
3. What is the effect of no symptoms of illness on:	patient belief that medication regime is not important	
	patient belief that disease is not critical	
	patient forget to take medication	
4. What is the effect of complexity of dose on:	patient belief that medication regime is not important	
	patient belief that disease is not critical	
	no symptoms of illness	
	benefits about medication adherence are not told to patients	
	adverse side effects	
	patient forget to take medication	
5. What is the effect of benefits about medication adherence not being told to patients on:	patient belief that medication regime is not important	
	patient belief that disease is not critical	
	no symptoms of illness	
	complexity of dose	
	adverse side effects	
	patient forget to take medication	
6. What is the effect of adverse side effects on:	patient belief that medication regime is not important	
	patient belief that disease is not critical	
	no symptoms of illness	
	benefits about medication adherence are not told to patients	
	patient forget to take medication	
7. What is the effect of patient forgetting to take medication on:	patient belief that medication regime is not important	
	patient belief that disease is not critical	
	no symptoms of illness	
	complexity of dose	
	benefits about medication adherence are not told to patients	
	adverse side effects	

Saibal Kumar Saha (UGC NET Qualified) holds a first class Master's degree in MBA and a first class Bachelor's Degree in Electronics and Communication Engineering. He has 10+ years of experience and has worked in MNCs like Cognizant Technology Solutions and Tata Aig Life. He has served National Institute of Technology - Silchar, Jyotirmoy School of Business – Kolkata, University of Technology and Management - Shillong and is presently working as Assistant Professor at Sikkim Manipal Institute of Technology - Majitar, India.

Anindita Adhikary is currently a Professor in Management, Sikkim Manipal University, India. A commerce graduate from Gauhati University, India, she happens to be an MBA from Tezpur Central University, India and was awarded Doctorate by Gauhati University in 2009. Dr. Adhikary has 21 years of professional experience in academics and corporate sector. She has 68+ research publications (select papers in Scopus) to her credit and has been abroad a number of times in order to have an enriched exposure at international level. Dr. Adhikary had participated in 30 professional workshops and delivered talks as Guest Speaker at different Orientation Programmes initiated through National Productivity Council, MSME, Govt. of India and Department of Commerce. Govt. of Sikkim. Her domain of interest includes Finance and International Trade.

Vijay Kumar Mehta, MBBS, MD, PGDCA, is currently working as the Dean of Sikkim Manipal Institute of Medical Sciences. After retiring from Indian Armed Forces as Brigadier on 30th Sept. 2013 joined Sikkim Manipal Institute of Medical Sciences, Gangtok on 21st Oct. 2013 as Professor in the department of Community Medicine. Subsequently, took over as Professor and Head department of Community Medicine at Sikkim Manipal Institute of Medical Sciences, Gangtok on 1st Feb. 2014. Have more than 22 years of teaching experiences including twelve and half years as Professor and 5 years as Professor and HOD Community Medicine in SMIMS, Gangtok.