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Use of Interventions to Overcome Medication Non-Adherence

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ABSTRACT

Medication non-adherence is a global problem and has existed for centuries. Patients have paid a very high price for their behaviour of non-adherence in the form of impaired cost, prolonged diseases, a burden to family, or even by their lives. In the era of science and technology where there is a solution for every odd problem, the issue of medication non-adherence can also find a remedy. This paper tries to highlight the factors of non-adherence and looks for solutions through various forms of technology. The review of different published literature highlights the findings of researchers and tries to assimilate a solution for addressing the prolonged problem of medication non-adherence.

KEYWORDS

Drug Regime, eHealth, Medication Adherence, Medication Compliance, Medication Schedule, mHealth, Non-Adherence, Non-Adherence Factors

INTRODUCTION

Medication non-adherence is a global health care problem which has persisted over the years (De Geest et al., 2019). It is complex and costly, contributing to deprived treatment results and erosion of health care resources (Arbuckle et al., 2019). Proper adherence to medications is very important for assuaging symptoms and curing disease (Yap et al., 2016). According to Kravitz & Melnikow, (2004) effects of non-adherence on health care costs and adverse events differ due to type of disease, degree of non-adherence and treatment. Approximately 33% to 69% of medication-related hospitalizations are due to poor adherence. Annual costings of medication non-adherence range from nearly US$100 billion to U$290 billion in the USA (Osterberg & Blaschke, 2005), €1.25 billion in Europe and approximately $A7 billion in Australia (Cutler et al., 2018). Patient's health is adversely affected by medication non-adherence (Ruddy et al., 2009). It can negatively impact a patient's relationship with the physician or health care provider (Waterhouse et al., 1993). To produce desired therapeutic effect,

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enough medication needs to be taken by patients. Hence, intake of ≥80% of prescribed medications is referred to as adequate adherence. Although, according to Vik et al., (2004) this threshold is arbitrary.

The paper is broadly divided into six sections. In the first section, a brief about medication adherence and non-adherence behaviour of patients are addressed. In the second section, different factors associated with non-adherence is reckoned and tabulated. The third section highlights the measurement techniques of non-adherence. In the fourth section, different techniques used for addressing the problem of medication non-adherence is addressed. This section is further divided into six subsections each emphasizing the studies that have been done on a technique for increasing adherence viz: traditional reminders, active reminders, phone call, short message service (SMS), mobile applications and tailored reminders. The fifth section gives a brief about the benefits of medication adherence while the sixth section enumerates the behavioural models used to encompass medication non-adherence behaviour of patients.

MEDICATION ADHERENCE

According to Cramer et al., (2008) adherence is "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen." One of the causal factors of preventable adverse events is proper medication adherence. According to Doggrell, (2010) and George et al., (2008) the rate of medication adherence varies from 30% to 100% which are influenced by patient characteristics and diversity of socio-medical constructs. Studies showed adherence rates of 30-70% for patients with asthma, 5-90% for patients with hypertension and 20-90% for patients with schizophrenic. Ho et al., (2006) worked on diabetic patients and reported that all-cause hospitalization was 23.2% for non-adherent patients compared to 19.2% for adherent. Sokol et al., (2005) classified medication adherence rates into 5 subsets: 0-20%, 21-40%, 41-60%, 61-80%, and > 80%. The study was conducted for congestive heart failure (CHF), diabetes, hypercholesterolemia and hypertension patients below the age group of 65 years. It was found that hospitalization risk and healthcare costs was inversely correlated with each of the levels of medication adherence. The reports highlighted that hospitalization risk for diabetes was 13% for adherent and 24% for non-adherent, CHF (57% vs. 63%), hypercholesterolemia (12% vs. 14%) and hypertension (19% vs. 23%). Sullivan, (1990) attributed 2.9% to 19.5% of hospital admissions to medication non-adherence. The work of Lau & Nau, (2004) on type 2 diabetes reveal that non-adherent patients were hospitalized more frequently than adherent (≥80%) patients. Hospitalization rate for 100% adherent patients was 4.1%, which increased to 14.8% when adherence dropped below 40%. Based on Medicare and Medicaid pharmacy claims data, Esposito et al., (2009) performed a cohort study on heart failure patients' and found that adherent patients were 13% less likely to have hospital admissions and medical costs were 15% less. Zed et al., (2008) also conducted a study in Canadian tertiary care hospital and found that 3% of Emergency Department (ED) visits were due to non-adherence.

Non-Adherence

Non-adherence can be broadly classified into two categories: intentional or unintentional (Nair et al., 2011) and it varies among patients. Unintentional non-adherence patients plan to take their medication as instructed but are unable to do so due to forgetfulness, carelessness or some other reason. Unintentional non-adherence is swayed by characteristics of patients, patient–provider issues and treatment factors (Wroe, 2002). Intentional non-adherence patients make coherent decision of not taking medication as per instruction due to beliefs, feelings or perceptions. These patients weigh the benefits of treatment against any adverse effects of the treatment (Daleboudt et al., 2011) and choose not to follow the medication regime. In order to mitigate the problems of non-adherence different interventions are required (Garfield et al., 2011) (Xie et al., 2019). Clinical complications due to non-adherence may depend on severity and condition of the disease (DiMatteo et al., 2012). For example, if a patient misses' numerous doses of hypertension medications may not add to extra

health care service use or result in deleterious consequences, but over dose or under dose of insulin in type 1 diabetes, blood thinners (Warfarin) or anti-infectives for AIDS and TB may end up in austere impediments and extra health care costs.

Factors for Non-Adherence

The work of Vik et al., (2004) attributes 16% (range 10.6% to 58%) of medication non adherence to forgetfulness, 47%-95% to adverse effects, 15%-52% to belief that medication is not required in the nonexistence of symptoms. Nair et al., (2011) worked on hypertensive patients and cited the reasons for non-adherence as: forgetfulness (62%), side effects (<1%), too busy (3%), medicare copay barrier (5%) and other (22%). However, the study of Doggrell, (2010) reported cost (27.6%) to be the most common cause of non-adherence and forgetfulness (21.3%) as the second. The study of Col et al., (1990) reports that out of 315 elderly patients admitted to hospital, 11% was due to medication non-adherence. Out of these 11%, 25% of non-adherence was due to forgetfulness, 15% was because of confusion, and 35% was due to side effects. The other factors identified for non-adherence were: "unnecessary meds" (10%), cost (15%), inadequate instruction (10%), "more is better" (10%) and "dislikes taking meds" (5%). The study of Malhotra et al., (2001) in a tertiary care hospital in India attributes 7.6% of the ED visits to non-adherence and less than 1% of all ED visits to forgetfulness. In another study, cases of non-adherence leading to hospital admissions cited "inadequate instruction" (25.4%) as the most common reason. In the study conducted by Faught et al., (2009) non-adherence was associated with higher inpatient days and admission rates. The rate of non-adherence patients was high among uninsured low-income patients generally suffering from chronic disease (Fernandez-Lazaro et al., 2019). Following table lists the different factors for medication non-adherence for various diseases.

Measurement of Non-Adherence

Non-adherence is difficult to measure precisely and most of the interventions used to reduce it has been mostly unsuccessful (Dayer et al., 2013). Some of the common methods used to measure adherence are patient self-reports, biological monitoring, pill counts, electronic monitoring and refill rates. All these methods have been reported to have limitations and are regarded as proxy measures (Claxton et al., 2001) (Cramer et al., 1989). As patient self-reports depend on memory, they may not always be accurate and are prone to recall bias (Weingart et al., 2008). Pill counts are not reliable as patients may not return the bottles or scrap medicines former to the count (Osterberg & Blaschke, 2005). Electronic monitoring and refill rates cannot confirm whether patients have actually taken the medication. Biological monitoring (for example sampling urine, blood) is either not feasible and intrusive as for accurate measurement by this method, dose and time administered before sampling are required to be verified. Studies also report that the process of cap removal may not reflect dose ingestion. To calculate adherence rates for dose taking and dose timing, electronic monitoring system is regarded as the best method to measure adherence (Paterson et al., 2002) (Spilker & Cramer, 1991) (Urquhart, 1997). The work of Browne et al., (2018) highlights the use of edible ingestion sensor to remotely monitor detailed dosing history of medicine intake behaviour of patients. Adherence checking should be done regularly to confirm therapeutic effectiveness, redundant dose and regimen changes should be avoided. Costs related to health care should be controlled and any cases of resistance to therapy should be prevented from emerging (Weingart et al., 2008).

ADDRESSING THE PROBLEM OF MEDICATION NON-ADHERENCE

In order to improve the medication adherence behaviour of patients most methods aim to alter the behaviour of patients (Conn et al., 2016). Some of the common methods include: education of patients, counselling, using reminders, dosage simplification, reinforcement or amalgamation of these methods (Haynes et al., 1996). Interventions for mitigating the problems of medication non-adherence are

Table 1. Factors for medication adherence, non-adherence

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
1	Belief about medication	Depression	(Aikens et al., 2005)				
		Asthma	(Apter et al., 2003) (Le et al., 2008) (Wells et al., 2008)				
			(Gatti et al., 2009)				
		Hypertension					(Wang et al., 2002)
2	Fear about long-term effects of medicine	Diabetes		(Aikens & Piette, 2009)			
		Hypertension		(Aikens & Piette, 2009)			
				(Brown et al., 2005)			
		Coronary heart disease		(Khanderia et al., 2008)			
3	Perception of having side effect	Diabetes		(Chao et al, 2007)	(Mann et al., 2009)		
				(Mann et al., 2007) (Kaplan et al., 2004) (Vlasnik et al., 2005)			
4	Beliefs about necessity of medication to maintain health	Diabetes					(Aikens et al., 2005)
		Hypertension					(Aikens et al., 2005)
5	Patient satisfaction with health care provider	Diabetes	(Albright et al., 2001)				(Trevino et al., 2005)
		Hypertension					(Trevino et al., 2005) (Kim et al., 2007)
		Hyperlipidemia					(Sung et al., 1998)
6	Personal stress level	Diabetes					(Albright et al., 2001)
		Hypertension					(Thorpe et al., 2009) (Wang et al., 2002)

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
7	Social support	Diabetes	(Albright et al., 2001)				(Gazmararian et al., 2006)
		Asthma					(Apter et al., 2003)
		Heart transplant or lung transplant	(Dew et al., 2008)				
		Hypertension					(Gazmararian et al., 2006) (Kim et al., 2007) (Li & Froelicher, 2007) (Wang et al., 2002) (Thorpe et al., 2009)
		Coronary heart disease	(Mondesir et al., 2018)				
		Depression	(Voils et al.,, 2005)				
8	Social support at home	Heart failure	(J.-R. Wu et al., 2008)				
9	Communication	Asthma					(Apter et al., 2003)
10	Poor patient-clinician communication	Asthma			(Apter et al., 1998)		
11	Better provider communication		(Ogedegbe et al., 2008)				
12	Pharmacy interactions	Hyperlipidemia					(Sung et al., 1998)
13	Knowledge	Asthma	(Wells et al., 2008)				(Apter et al., 2003)
		Hypertension					(Thorpe et al., 2009) (Wang et al., 2002)
14	Negative knowledge	Diabetes		(Mann et al., 2009)			(Trevino et al., 2005)
15	Lower knowledge	Hypertension			(Kim et al., 2007)		(Trevino et al., 2005) (Hyre et al., 2007)
16	Health literacy						(Gatti et al., 2009)
		Hypertension					(Thorpe et al., 2009)

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
17	Depression	Asthma			(Smith et al., 2006)		(Apter et al., 2003) (Janson et al., 2008)
		Overactive bladder					(Balkrishnan et al., 2006)
		Diabetes		(Chao et al., 2007) (Kilbourne et al., 2005) (Jeffrey S Gonzalez et al., 2007) (Nau et al., 2007) (J Safren Gonzalez et al., 2008)	(Lin et al., 2004)		(Balkrishnan et al., 2003) (Gazmararian et al., 2006)
				(Brown et al., 2005) (Gatti et al., 2009) (Kaplan et al., 2004) (Ogedegbe et al., 2008)			(Insel et al., 2006)
		Hypertension		(Siegel et al., 2007) (Wang et al., 2002)	(Ogedegbe et al., 2008)		(Chapman et al., 2005) (Gazmararian et al., 2006) (Kim et al., 2007)
		Coronary heart disease			(Gehi et al., 2005)		
		Kidney transplant hemodialysis		(Cukor et al., 2009)			
		Anticoagulation therapy					(Platt et al., 2008)
		Heart failure					(J.-R. Wu et al., 2008)
18	Poor patient-clinician communication	Asthma		(Apter et al., 1998)			
19	Perceived health status	Overactive bladder	(Balkrishnan et al., 2006)				(Janson et al., 2008)
		Diabetes					(Balkrishnan et al., 2003)
		Anticoagulation therapy					(Platt et al., 2008)
20	Lower perceived health status				(Wroth & Pathman, 2006)		

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
21	More number of prescribed medicines	Overactive bladder					(Balkrishnan et al., 2006)
		Diabetes	(Trevino et al., 2005)				
		Hypertension	(Trevino et al., 2005) (Siegel et al., 2007)	(Chapman et al., 2005)			(Patel & Taylor, 2002)
		Heart failure					(J.-R. Wu et al., 2008)
				(Stoehr et al., 2008)	(Phatak & Thomas III, 2006)		(Williams et al., 1998)
22	Smoking	Overactive bladder					(Balkrishnan et al., 2006)
		Diabetes					(Balkrishnan et al., 2003)
		Hypertension		(Bautista, 2008)			(Hyre et al., 2007)
		Coronary heart disease			(Gehi et al., 2005)		
		Anticoagulation therapy					(Platt et al., 2008)
23	Physical activity	Overactive bladder					(Balkrishnan et al., 2006)
		Diabetes					(Balkrishnan et al., 2003)
24	Alcohol consumption	Overactive bladder					(Balkrishnan et al., 2006)
		Diabetes					(Balkrishnan et al., 2003)
		Hypertension		(Bautista, 2008)			
		Coronary heart disease			(Gehi et al., 2005)		
25	Hospitalization	Diabetes					(Balkrishnan et al., 2003)
26	Lesser number of medical visits	Hypertension		(Bautista, 2008)			(Schectman et al., 2002)
		Diabetes					(Schectman et al., 2002)
		Hyperlipidemia					(Schectman et al., 2002)
27	Increased number of clinic visits	Hypertension	(Vawter et al., 2008)				

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
28	Frequency of concurrent prescriptions		(Billups et al., 2000)				
		Diabetes	(Schectman et al., 2002)				
		Hyperlipidemia	(Schectman et al., 2002)				
		Hypertension	(Schectman et al., 2002)				
29	Number of days supplied per prescription	Diabetes	(Schectman et al., 2002)				
		Hyperlipidemia	(Schectman et al., 2002)				
		Hypertension	(Schectman et al., 2002)				
30	Number of chronic conditions		(Billups et al., 2000)				
31	Mental health index						(Billups et al., 2000)
32	Mental-health status	hypertension					(Thorpe et al., 2009)
33	General health perception						(Billups et al., 2000)
34	Physical functioning index						(Billups et al., 2000)
35	More confidence to take medicines	Diabetes	(Trevino et al., 2005)				
		Hypertension	(Trevino et al., 2005)				
36	Took the disease seriously	Asthma	(Chambers et al., 1999)				
37	More active in making decisions with a physician	Asthma	(Chambers et al., 1999)				
38	Motivation to maintain health	Asthma					(Chambers et al., 1999)
39	Frustration with adhering to therapy	Asthma					(Chambers et al., 1999)
40	Perceived uncontrollable barriers to adhering	Asthma					(Chambers et al., 1999)

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
41	Fewer perceived barriers		(G. C. Williams et al., 1998)				
42	Benefits of medication adherence	Asthma					(Chambers et al., 1999)
43	Therapies initiated closer together in time	Hypertension	(Chapman et al., 2005)				
44	Self-efficacy	Coronary heart disease	(Clark & Dodge, 1999)				
			(Gatti et al., 2009) (Náfrádi et al., 2017)				
		Diabetes	(Shiyanbola et al., 2018)				
		Hypertension				(Ogedegbe et al., 2008)	(Kim et al., 2007)
45	Loci of control like internal, powerful others, and chance	Kidney transplant hemodialysis					(Cukor et al., 2009)
46	Avoidance of disease triggers	Asthma	(De Smet et al., 2006)				
47	Years since diagnosis	Asthma	(De Smet et al., 2006)				
48	Perceived benefits of medication	Asthma	(De Smet et al., 2006)				
49	More persons providing instructions	Asthma	(De Smet et al., 2006)				
50	Higher self-rated severity of illness	Depression			(Sirey et al., 2001)		
51	Self-reported health status	Glaucoma	(Friedman et al., 2009)				
52	Perceived health outcome	Glaucoma	(Friedman et al., 2009)				

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
53	Drug regime complexity	Coronary heart disease		(Gazmararian et al., 2006)			
		Diabetes		(Gazmararian et al., 2006) (Capoccia et al., 2016)			
		Hypertension		(Gazmararian et al., 2006)			
		Parkinson's disease		(Kulkarni et al., 2008)			
				(Vlasnik et al., 2005)			
54	Patients being comfortable asking questions to doctor	Hypertension	(Hyre et al., 2007)				
55	Spending more time with doctor	Hypertension		(Hyre et al., 2007)			
56	Memory composite score						(Insel et al., 2006)
57	Perceived disease severity	Asthma	(De Smet et al., 2006)		(Janson et al., 2008)		
		Hypertension	(Li et al., 2006)				(Li & Froelicher, 2007)
					(Mann et al., 2007)		
58	Overuse of medicines	Coronary heart disease		(Khanderia et al., 2008)			
59	Belief about disease	Hypertension					(Kim et al., 2007)
60	Perceived outcome	Hypertension					(Li & Froelicher, 2007)
61	Negative perceived outcome	Diabetes			(Mann et al., 2009)		
62	Expected treatment duration				(Mann et al., 2007)		
63	Medicine characteristics	Diabetes			(Mann et al., 2009)		
64	Living alone	Coronary heart disease			(Gehi et al., 2005)		

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
65	Symptom severity	Diabetes		(Gonzalez et al., 2007) (Gonzalez et al., 2008)			
66	Lower beliefs in drug effectiveness	Osteoporosis			(McHorney et al.,2007)		
67	Lower drug-safety beliefs	Osteoporosis			(McHorney et al., 2007)		
68	Beliefs about medicines	Hypertension			(Mochari et al., 2007)		
					(Phatak & Thomas III, 2006)		
69	Patient-physician trust	Inflammatory bowel disease	(Nguyen et al., 2009)				
70	Lower patient-provider trust				(Wroth & Pathman, 2006)		
71	Patient provider relationship	Heart failure					(J.-R. Wu et al., 2008)
72	Perceived control over disease	Hypertension		(Patel & Taylor, 2002)			(Thorpe et al., 2009)
73	Higher dose	Hyperlipidemia		(Pedan et al., 2007)			
							(Stoehr et al., 2008)
74	Higher volume of patients per physician	Hyperlipidemia		(Pedan et al., 2007)			
75	Higher co-payments	Hyperlipidemia		(Pedan et al., 2007)			
76	Number of prescribed refills	Hyperlipidemia	(Pedan et al., 2007)				
77	Lower mental function	Anticoagulation therapy			(Platt et al., 2008)		
78	Lower cognitive function	Anticoagulation therapy		(Turner et al., 2012)	(Platt et al., 2008)		
79	Travel distance to a pharmacy	Diabetes					(Schectman et al., 2002)
		Hyperlipidemia					(Schectman et al., 2002)
		Hypertension					(Schectman et al., 2002)

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
80	Once-daily dosing	Diabetes					(Schectman et al., 2002)
		Hyperlipidemia					(Schectman et al., 2002)
		Hypertension					(Schectman et al., 2002)
81	Higher perceived stigma	Depression			(Sirey et al., 2001)		
82	Composite score for perceived barriers to medication	Hypertension		(Thorpe et al., 2009)			
83	Emotional well-being	Hypertension	(Trivedi et al., 2008)				
84	Internal locus of control	Depression		(Voils et al., 2005)			
			(Náfrádi et al., 2017)				
85	External locus of control	Hypertension					(Wang et al., 2002)
				(Náfrádi et al., 2017)			
86	Locus of control						(Williams et al., 1998)
87	Difficulty in affording medicines	Asthma		(Wells et al., 2008)			
88	Inability to get an appointment	Asthma		(Wells et al., 2008)			
89	More perceived physician support		(G. C. Williams et al., 1998)				
90	More patient autonomy for improving health		(G. C. Williams et al., 1998)				
91	Medicine frequency	Heart failure					(J.-R. Wu et al., 2008)
		Kidney failure		(Oh et al., 2019)			
92	Cost			(Vlasnik et al., 2005) (Polonsky & Henry, 2016) (Holt et al., 2013)			

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Table 1. Continued

Sl.No	Factors	Disease	Citation for:				
			Adherence		Non adherence		No association
			Positive association	Negative association	Positive association	Negative association	
93	Substance abuse			(Vlasnik et al., 2005)			
94	Pill burden			(Vlasnik et al., 2005)			
95	Quality of life	Heart failure	(Silavanich et al., 2019)				

categorized based on education, behaviour and organization. Attempts to improve the adherence rates is done by lifting barriers allied with medication complication, giving more information, altering patient's environment or incentives and improving communication with care providers (Graves et al., 2009). Vrijens, (2019) proposed a Six Sigma framework consisting of "DMAIC (Define, Measure, Analyse, Improve and Control)" approach to reduce medication non-adherence. Stirratt et al., (2018) identified three stages of adherence: initiation, implementation and persistence and investigated the barriers, facilitators and determinants of each stage. Interventions should be designed considering the specific stage and strategies to target them should be designed accordingly. Following are some of the interventions used for enhancing adherence rates.

Traditional Reminders

Pill reminder systems include unit-of-use packaging, packaged calendars or weekly pill boxes. For unintentional non-adherence these aids prove to be helpful (Harbig et al., 2012) (Rolnick et al., 2011). In the traditional reminder systems, patients of self-medication are not given access to their adherence data. Any sort of educational information is also not provided to them. The tested method of pill reminder systems has proved to be useful across different medications. However, these systems are cumbersome for complex schedules. These systems only act as passive reminders for medication intake (Mahtani et al., 2011) (Zedler et al., 2011).

Active Reminders

With the advancement of technology, electronic reminder system (pager, telephone, and audio-visual devices) are being used to proactively deliver reminders. Behaviour of patients can be influenced by mobile phones due to its ease of use, worldwide acceptance and instant information transmitting capabilities (Maddison et al., 2018). These systems if united with alternate behavioural strategies could solve the problems of non-adherence largely. The study of Frick et al., (2001) in Mombasa, Kenya, reveals that use of alarm devices expressively improved non-ART medication adherence rates. According to Fenerty et al., (2012) electronic reminder systems may not be realistic for widespread use.

Phone Call

By integrating cellular phone and internet based education system, an attempt was made to check the association of blood glucose levels of diabetic patients with the frequency of accessing eMOD (electronic Management of Diabetes) system. The results revealed that the relationship was positive (Noh et al., 2010). Statistics reveal that in developed countries the strategy used for improving adherence for ART in chronic disease by mobile phone is promising (Lester & Karanja, 2008) (Chang et al., 2008) (Fjeldsoe et al., 2009). For adolescents and young adults interventions by cell phone calls can improve adherence (Sayegh et al., 2018).

Short Message Service (SMS)

Teenager patients suffering from asthma gave high ratings for the parameters: usefulness, acceptability and ease of use when they were sent personalized reminders in the form of text messages (Britto et al., 2012). In a study, it was seen that weekly reminders showed significant improvement in adherence, but daily reminders did not. It was presumed that daily messages could have been deliberated as invasive (Pop-Eleches et al., 2011). The study of Thakkar et al., (2016) reports increase in adherence for middle-aged patients with chronic disease. The work of Adler et al., (2017) reveals that use of SMS as intervention to improve medication adherence is useful for patients suffering from cardiovascular disease. According to Oyugi et al., (2007) weekly reminders proved effective in reducing the occurrence of treatment interruptions. While sending messages as reminders one should keep in mind that patients may be using shared mobile phones and their phone or number may change (Shet et al., 2010). However as per Simoni et al., (2006) there is no consensus as to which is the finest approach to improve adherence.

Mobile Applications

Along with improving the medication adherence rate, smartphone apps can reduce costs of traditional adherence interventions. By using traditional means of telecommunication (SMS) behaviour of patients can be changed and adherence levels can be measured for short term studies (Vervloet et al., 2012). Sending photographs of medication capsules in the phone of patients before ingestion help to acquire precise time measures of adherence (Galloway et al., 2011). Although studies on use of smartphones for improving adherence has been done in clinical settings but studies on empirically testing them are missing (Wu et al., 2011). According to Henny et al., (2018) there is lack of theoretical premise including behavioural theories behind the use of eHealth interventions.

The study conducted by Dayer et al., (2013) reports that the apps present in the market lacks interconnection with other information providing systems. The study lacks to find an app, which is totally assimilated with patient record systems (medical records and community pharmacy prescription databases). An interfacing adherence app with interconnection with pharmacy prescription records could be used by pharmacists to send drug regime reminders to patients in their apps. These interconnected apps may help to solve adherence problems in challenging cases by collective collaboration efforts of patients and pharmacists (Capoccia et al., 2016).

The possibility of connecting medical records with smartphone apps and with other devices can enhance adherence competencies to a great extent (Ahmed et al., 2018). "Proteus Digital Health Feedback System" is an advanced system where solid oral dosage of patient is united with ingestible sensors. The sensors record physiologic parameters post eating and send information to a patch or dermal sensor, which can transmit data to a smartphone. With the help of this system, authentic ingestion of doses can be precisely recorded. An app integrated with such a system can send tailored reminders to patients whenever they miss a dose. Numerous apps and technologies for diabetes self and programmed monitoring have been developed. Studies have reported improvement in diabetes (Cafazzo et al., 2012) (O'grady et al., 2012) and blood pressure control (Morawski et al., 2018) medication adherence. As reminders predominantly focus on unintentional non-adherence, adherence apps require infusion of a well-developed scale for assessing unintentional non-adherence with multimodal strategy to result in unremitting enhancements in adherence (Gadkari & McHorney, 2012) (Santo et al., 2016).

Tailored Reminders

The present generation smartphones can perform multi discipline functions and can be used effectively to mitigate the problems of medication non-adherence (Mrosek et al., 2015) (Badawy et al., 2019). These smartphones allow constant access to communication and allow multiple functions to address non-adherence. These apps are available at very low to no cost. Some of the features offered by these

apps include education of patients, timely reminder for medication and refill, offers a storehouse for patient and medication specific information. The data logs can be used to generate reports, which can be used by patients, caregivers or physicians. With smart engines inbuilt in the apps, disease specific information can be consolidated to provide refined well-targeted behaviour changing messages and information to the patients. Apps can handle complex medication regimens for patients, family members or care givers and help to increase the adherence rates. Some of the apps are also integrated with pharmacies to provide drug related information, pharmacy care contacts or discount coupons (Dayer et al., 2013).

Efforts are being made to integrate health-monitoring devices with smartphones. Several researchers reported that empirical analyses of smartphone apps usage for addressing medication non-adherence is lacking (Wohlers et al., 2009) (Gamble, 2009) (Sposaro & Tyson, 2009) (Lee et al., 2011) (Delpier et al., 2013) (Kharrazi et al., 2012). The work of Vervloet et al., (2012) reveals an integrated system of electronic pill boxes that monitor box opening events and transmit signals to server. Whenever a patient miss opening a box, SMS text message is sent as a reminder. This system has been reported to improve adherence. "Trans theoretical model stages of change" or "motivational interviewing" models of behavioural change could be used to improve customized messages for improving unintentional and intentional non-adherence (Ogedegbe et al., 2008) (Ficke & Farris, 2005). Several studies have been done using tailored interventions with smartphones to improve dietary intake of vegetables and fruits (Kerr et al., 2012).

BENEFITS OF ADHERENCE

Based on data of employer-sponsored insurance beneficiaries, Roebuck et al., (2011) conducted a retrospective review of pharmacy and medical claim records. The study compared the effects of adherence rates for patients with dyslipidemia, diabetes, hypertension and heart failure. It was seen that adherent patients had reduced average annual medical expenditures and lesser inpatient hospital days. In the study of Hepke et al., (2004) cost of ED visits and inpatient hospital admissions for diabetic patients decreased with increase in medication adherence rates.

For prevention and treatment of Human Immunodeficiency Virus (HIV), medication adherence is important for Pre-Exposure Prophylaxis (PrEP) and Antiretroviral Therapy (ART). Baker, (2018) studied the relationship between the different dynamics of social support and physical environment which can affect PrEP and ART adherence across populations. The study also focused on physical settings like home security and privacy. The study reports that PrEP can diminish the risk of HIV, but the medication works well when it is taken regularly (Marrazzo et al., 2015) (Anderson et al., 2012) (Corneli et al., 2014). Association of alcohol and drug use with HIV medication adherence, have been studied extensively over the years. The factors like physical environment settings, social support, partnership types and dynamics have not been studied extensively (Arnsten et al., 2002) (Cook et al., 2001) (Samet et al., 2004) (Hinkin et al., 2004) (Azar et al., 2010) (Chander et al., 2006). According to DiMatteo, (2004) and Protopopescu et al., (2009) partners may offer social support which could encourage positive medication adherence behaviours for improving PrEP or ART adherence.

Based on cause of non-adherence, interventions can be designed to overcome the relevant barrier. Mobile Device Management System (MDMs) are used to address the barriers of mild cognitive deficits forgetfulness, physical impairment (e.g., dexterity, impaired vision), low health literacy and confusion. Based on the complexity of medical regime (dosing frequency and number of prescribed medications) (Hajjar et al., 2007) and factors like food-dosing restrictions (George et al., 2008), MDMs can be used to address non-adherence. MDMs are unlikely to remove the barriers of health beliefs, number of dispensing pharmacies used, negative side effects and cost are not addressed by MDMs.

BEHAVIOURAL MODELS OF ADHERENCE

Based on several social cognition models, several models for medication adherence have been made which include health theory of planned behaviour (Ajzen, 1991), social cognitive theory (Bandura, 1986) and belief model (Rosenstock et al., 1988). These models are developed based on the belief of individuals, information interpretation along with their experiences. All these ultimately influence their behaviour (Petrie & Weinman, 1997). According to Lehane & McCarthy, (2007) health behaviour of patients is based on rational decisions developed from available information. The dosing behaviour is affected by individual beliefs, culture perspectives, anticipated outcomes, social experiences and different worldviews (Amico et al., 2018). It is a big challenge to improve medication adherence among patients with chronic diseases (Banuelos Mota et al., 2019). Hence, multifaceted interventions are required to improve adherence for long-term treatment (Holloway & Van Dijk, 2011). Conn & Ruppar, (2017) suggests that behavioural strategies should be framed for targeting habit-based interventions, to change knowledge and beliefs of patients.

CONCLUSION

Due to lack of standardized medication adherence metrics it is tough to make conclusions for consequences of medication non-adherence, barriers of adherence and rates (Gellad et al., 2011). Differences in terminology, study designs, definitions, and inclusion criteria have also been attributed to ineffectiveness of estimating adherence rates. Due to these, even the interventions that are used for improving adherence rates are not being able to get standardized (Conn et al., 2009). Techniques of data collection like pharmacy claims and 'use refill' may either overrate or underrate adherence based on inclusiveness of records. The method of pill counts may overrate non-adherence as patient may refill before the existing stock is finished. Vik et al., (2004) also presumes that those who report non-adherence are truly non-adherent while some patients who report adherence may not be. To capture the actual adherence rates one should use more than one measure of adherence.

Most studies confirm involvement of behavioural interventions to improve adherence (Conn et al., 2009) (Bain-Brickley et al., 2011). However, lost cost reminder devices do not improve adherence (Choudhry et al., 2017) (Kessler et al., 2018). The study of Spaan et al., (2018) found psychosocial interventions enhancing adherence among HIV patients. Data suggest that for improving adherence of patients who are under medication of more than six types of drugs, education is one of the best methods. Customized interventions like patient self-monitoring, patient education and stimuli to take medications could be developed on the basis of patient characteristics and type of non-adherence for effective adherence improvement (Haynes et al., 2008) (Conn et al., 2009) (Williams et al., 2008). Linn et al., (2011) conducted a systematic review of Internet-based adherence interventions and found results to be promising.

Non-adherence does not necessarily deteriorate patient health or cause surplus health care consumption (Alemagno et al., 2004) (Osterberg & Blaschke, 2005). Certain studies report that if the treatment is inappropriate, flawless adherence to prescribed treatment can be harmful. The study of Launer et al., (2011) reports that "intensive glucose control increased mortality and did not prevent cardiovascular events in type 2 diabetes". It is difficult to measure adherence rates due to various types of biases (Hughes, 2007). Studies based on self-reports of non-adherence using survey method, may have different adherence rates due to the problems of patient recall bias and social desirability bias (Col et al., 1990).

Haynes et al., (2008) preformed a Cochrane review of randomized trials of adherence interventions. The results revealed that less than 50% showed improvement in both clinical outcomes and long-term adherence. It was found that effective interventions were the ones, which had complex blends of numerous strategies. Individualized adherence tools have proved to be effective for adherence (Ostrop & Gill, 2000) (Safren et al., 2003) (Nelson et al., 2018) (Vrijens et al., 2017). The study of T. S.

Nguyen et al., (2019) reports that quality of life and medication adherence rate improved in patients after implementation of pharmaceutical care programme. The work of Jangi et al., (2018) reports that reminders sent for vaccines proved to be very effective. Calling intervention was cited as the most effective way of reminder system in the study. The use of pill bottle strip with toggles, digital timer cap and standard pillbox were cited as not effective. The study suggests sending targeted reminders and reminders in the form of videos and picture messages to enhance the medication adherence rates.

From the study conducted, it is clear that medication non-adherence is a common problem. It is necessary that patient, physician, service provider and family take adequate measures to ensure timely intake of medicines to expedite recovery and ensure full effect of medicine. Researchers believe that intervention of technology can help improve adherence rates but it must be used strategically so that the behaviour of patients can be targeted for improvement of adherence rates. Future research can be done to find out the effect of interventions specially targeting the behavioural models for addressing problems of non-adherence. There is lack of published literature for adherence of diet and exercise. This is a wide field of research, which can be explored for increasing the adherence of diet and exercise regimen.

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