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Regimen Difficulty and Medication Non-Adherence and the Interaction Effects of Gender and Age

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ABSTRACT

Medication non-adherence is a global health issue. Numerous factors predict it. This study is aimed to identify the association between regimen difficulty and medication non-adherence among patients with chronic conditions and testing the interaction effects of gender and age on the same. It was a cross-sectional study conducted among 479 outpatients from India. Convenience sampling method was used. Multiple regression analyses were performed to find the predictors of non-adherence and to test interaction effects. Regimen difficulty predicted medication non-adherence. The patient's gender and age have interaction effects on the relationship between regimen difficulty and medication non-adherence.

KEYWORDS
Regimen difficulty; medication non-adherence; interaction effects; gender; age

Medication non-adherence is a serious health issue affecting all the stakeholders of the healthcare industry. Medication non-adherence increases the health care cost (Kennedy-Martin, Boye and Peng 2017). Worldwide, despite many efforts made, non-adherence still prevails among patients with chronic conditions. Non-clarity of instructions on a prescription, misunderstanding, and communication gap between the health care provider and the patient may lead to medication non-adherence. This study aims to take a different approach to study non-adherent behavior of patients with chronic conditions by identifying the association between regimen difficulty and medication non-adherence and testing the interaction effects of gender and age on the same. There is an extensive literature focusing on non-adherence to medication across chronic diseases. The available evidence, points out that during the last decade 2004 to 2014 reported rates of chronic disease medication non-adherence were varying from 15% to 84% across studies and were explained by various predictors. A large body of literature on non-adherence research is mainly focused on medication non-adherence and most of the data is collected through control group trials.

In the present study medication non-adherence is referred to as all degrees of patient discontinuation of the treatment, not filling the prescription, non-conformity to medication as prescribed by the doctor and not doing diagnostic tests as instructed by the doctor. Regimen difficulty is referred to as the inability to understand and follow up of the treatment regimen as prescribed by the doctor.

In past four decades 1974 to 2014, various theoretical models have been used to predict non-adherent behavior. The theoretical models such as; Necessity-concern framework; Health Belief Model; Theory of Reasoned Action; Theory of Planned Behavior; and Trans-theoretical Model have been demonstrated effective in evaluating health behavior. The constructs and variables studied have changed over the years. In present study health care team related factor is considered to predict medication non-adherence. Further the patient demographics are also tested for additional variance if any explained in medication non-adherence.

Regimen difficulty as a predictor of non-adherence

Clarity of instructions on a prescription is a prerequisite for the successful follow up of the regimen. A prescription survey conducted in Goa, India found that the prescriptions were incomplete (Patel, et al.

2005). Past research has reported that a complex treatment regimen (Robert 2009), duration of the therapy (Bhattacharya, et al. 2012), confusion about medication (Banerjee and Varma, 2013; George, et al. 2005), lack of clear instructions (Banerjee and Varma 2013), poor understanding of the treatment regimen (Hinchagery, et al. 2012), and patient's unwillingness to medication (Furthauer, Maria and Andreas 2013) impacted on non-adherence. Christensen and Johnson (2002), found that the rate of non-adherence vary with symptoms and the type of treatment regimen. Redzuan, Lee and Shah (2014), in their study found that the number of medications did not significantly affect adherence and persistence, whereas Stack, et al. (2010); Turner, et al. (2012); Sabbatini, et al. (2014) and Nirojini, Bollu and Nadendla (2014), found that varying number of medicines impact non-adherent behavior. Physicians failure to communicate medication use while initiating new medications, may lead to non-adherence (Tarn, et al. 2006). Illiteracy, linguistic problems, and complex treatment regimen may confuse the patients to follow regimen independently. Chronic illnesses require long term treatment and self- management. Regimen difficulty may limit treatment adherence in patients, in spite of their willingness to adhere. Non-adherence to treatment regimen can be a major cause of treatment failure.

Gender as a predictor of non-adherence

Research has shown with or without interaction effect, the correlation between gender, age and adherence/non-adherence. One of the reason for tuberculosis treatment default was due to work related problems and the group vulnerable to treatment default was male (Jaggarajamma et al. 2007). Among adult hypertensive patients, adherence was significantly higher in female than male (Iloh Gabriel, et al. 2014). In Ireland, and Nigeria men were non-adherent to medication (Al-Lawati 2014; Adisa, et al. 2009). Women were more non-adherent to psychiatry (Banerjee and Varma, 2013) and diabetes (Ujjinappa, et al. 2013) treatments than men. Adherence to medication in Greece among young chronically ill patient was high (Plakas, et al. 2016). In a longitudinal study among Human Immunodeficiency Virus positive adults in South Africa, gender by time and gender by age were found to interact significantly with adherence

to Highly Active Antiretroviral Therapy (HAART) (Dikokole, et al. 2011).

Age as a predictor of non-adherence

Research in Ireland has shown that people with different age groups show different coping styles to adherence/non-adherence (Al-Lawati 2014). With older adults, non-adherence increases with complex regimen (Syed and Lynn 2009). Age was associated with non-adherence to medication among diabetes patients in Malaysia (Ahmad, et al. 2013). In a longitudinal study among HIV positive adults in South Africa, age by gender and age by education were found to interact significantly with adherence to HAART (Dikokole, et al. 2011).

Interaction effects

An interaction implies that the magnitude of the relation between one predictor and the criterion varies as a function of at least one other predictor (Preacher, et al. 2006). The interaction effects make us understand the conditions under which the relation between the variables changes in strength and direction (Aguinis and Gottfredson 2010). As suggested by Baron and Kenny (1986), the interaction terms were introduced as the researcher expected inconsistent relation between the predictor and the criterion variable across the subgroups. It was predicted from theory as well as noticed during data screening of the study that the relationships between regimen difficulty and medication non-adherence may vary with patients' demographics. The interaction terms may reduce the unexplained variance in medication non-adherence and expand the understanding of the specific factor or the blend of multiple factors that contribute most to non-adherence. To explore these possibilities, the interaction terms were introduced in multiple regression analyses.

Interaction terms formed were: gender by regimen difficulty and age by regimen difficulty. The dependent variable was medication non-adherence.

Methods

It was a cross-sectional study. Prior permissions to conduct the survey among patients were sought
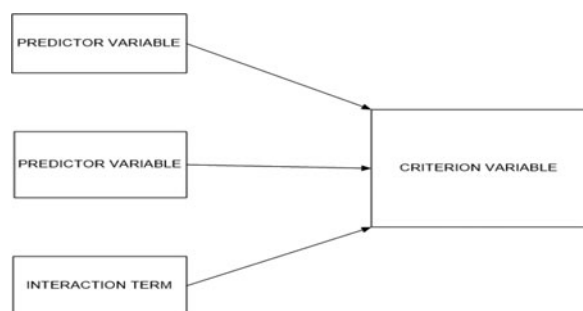
Figure 1. Basic Model for Testing Two-Way Interaction Effect.

from the hospital authorities. With prior informed consent, 479 respondents willing to participate in survey were recruited from the health care facilities from Goa and Karnataka, India. The self-reported, structured questionnaires developed by the researchers were administered to the respondents. Convenience sampling method was used. The respondents were contacted in the waiting areas in various hospitals/clinics. The time required for filling a questionnaire was 15 to 20 minutes.

Analysis and results

SPSS version 18.0 was used for data analysis. Multiple regression analysis was performed to find the predictor of non-adherence. The statistical outputs and the interaction graphs were achieved with the help of Interaction Version 1.7.2211 by Daniel Soper. The basic model for testing interaction effects is given in Figure 1.

Patients' characteristics

A total of 479 outpatients completed the questionnaires. The sample comprised of 42.6% female. The average age of the respondents was 52.52 Years and standard deviation 13.68. 18.2% of the respondents were illiterate. 4% were staying alone. 33.8% were employed. 10.6%, 14.2%, 16.5%, 32.4%, 5.4%, 7.3%, 5.7% and 7.9% of the respondents were taking treatment for Cancer, Chronic Obstructive Pulmonary Diseases, Arthritis and chronic back pain, Diabetes, Cardiac problems, Chronic renal failure, HIV/AIDS, and other chronic illnesses (epilepsy, depression bipolar disorder) respectively.

Regression

The t- test for significance of the independent variable indicates that at the significance level of 1% (confidence

Table 1. Research Model for Testing Gender by Regimen Difficulty Interaction on Medication Non- Adherence.

Model Summary	R Square: 0.046 R Square contribution of the interaction term: 0.011
Model Analysis of Variance	F(df 3,475) = 7.7074, P value < 0.05
Model Coefficients	Interaction term b = 0.219, t = 2.412, P value < 0.05
Effect Size	0.048

level of 99%), regimen difficulty and medication non-adherence is positively correlated.

Interaction effects

The research model and the interaction graph for testing gender by regimen difficulty interaction on medication non- adherence are given in Table 1 and interaction graph 1 respectively.

The R^2 0.046, indicates 4.6% variance in medication non-adherence, which is explained by regimen difficulty, gender and gender by regimen difficulty. The R^2 contribution of the interaction term 0.011 indicates 1.1% of the variance which is explained exclusively by the interaction term. The research model is statistically significant at F (df 3,475) = 7.707 and P value < .05. For the interaction term, the unstandardized regression slope is b = 0.219, t = 2.412, p < .05. The coefficient for the interaction term is statistically significant, this implies that the slope that predicts the relationship between regimen difficulty and medication non-adherence differs significantly between the male and female groups. The effect size of 0.048, indicates, small magnitude of the combined impact of gender and regimen difficulty on medication non-adherence.

The interaction graph shows, that the slopes are positive for both the levels of moderating variables indicating a positive relation between regimen difficulty and medication non-adherence. However the impact of regimen difficulty on medication non-adherence is greater for females than males.

The research model and interaction graph for testing age by regimen difficulty interaction on medication non- adherence are given in Table 2 and interaction graph 2 respectively.

The R^2 0.102 indicates 10.2% variance in medication non-adherence, which is explained by age, regimen difficulty, and age by regimen difficulty. The R^2 contribution of the interaction term 0.013 indicates 1.3% of the variance exclusively explained by the interaction term. The research model is statistically significant

at F (df 3,475) = 11.288 and P value < 0.05. For the interaction term, the unstandardized regression slope is b = 0.008, t = 2.654, p < .01. The coefficient for the interaction term is statistically significant, this implies that the slope that predicts the relationship between regimen difficulty and medication non-adherence differs significantly between the patients' age groups. The effect size of 0.114, indicates, large magnitude of the combined impact of the age and regimen difficulty on medication non-adherence.

The interaction graph indicates that the slopes at −1 and +1 standard deviation levels of age are positive, the relationship between regimen difficulty and medication non-adherence are positive. This shows for the patients both young and old, higher the regimen difficulty, the higher is the medication non-adherence. However, the impact of regimen difficulty on medication non-adherence was higher among old patients than young patients.

Discussions

Regimen difficulty is a predictor of medication non-adherence. This finding is at par with other studies by Sewith, et al. (2004); Tarn, et al. (2006); Doggrell (2010); Mbuagbaw, et al. (2012); Hinchageri, et al. (2012) and Ujjinappa, et al. (2013) among patients with chronic conditions.

Patient's gender has an interaction effect on the relationship between regimen difficulty and medication non-adherence. The study results show that females with higher regimen difficulty have greater medication non-adherence than males. This may be due to illiteracy, linguistic and patient-physician communication problems. It was observed that patients in migrated population have difficulties in communicating with health care professionals. Also in countries like India females do a lot of housekeeping work, looking after kids and even employed too. Many a times females

Table 2. Research Model for Testing Age by Regimen Difficulty Interaction on Medication Non- Adherence.

Model Summary	R Square: 0.102 R Square contribution of the interaction term: 0.013
Model Analysis of Variance	F(df 3,475) = 11.288, P value < 0.05
Model Coefficients P value < 0.01	Interaction term b = 0.008, t = 2.654
Effect Size	0.114

assume a more sacrificing role in the family in male dominated societies like India.

Although researchers Koulayev, Skipper, and Simeonova (2013) and Talam, et al. (2008), have found gender impacting on non-adherence, its interaction effect has not been examined. The only study which examined interaction effect was by Dikokole, et al. (2011), and they found that gender had interacted significantly with adherence to Highly Active Antiretroviral Therapy (HAART). Hence, as suggested by Banerjee and Varma (2013), there is a need for gender sensitive research studies.

Patient's age has an interaction effect on the relationship between regimen difficulty and medication non-adherence. It was observed that younger patients wished to keep the sickness and treatment a secret. Patients of all ages with greater regimen difficulty had higher medication non-adherence. However, the impact of regimen difficulty on medication non-adherence was higher among old patients than young patients. The reason for age to accentuate the relationship between regimen difficulty and medication non-adherence may be that the loss of memory among elderly patients. Most of the time illiterate and poor elderly patients require facilitation from others for adherence to medication regimen. Females and old age patients did not continue the treatment, fill the prescription, take medicines as prescribed, follow scheduled visits to the doctor, and do diagnostic tests as instructed by the doctor due to regimen difficulty than men and young patients. As suggested by Syed and Lynn (2009), streamlining the regimen for ease and discussing the same with the patient may improve adherence. The positive effect of social support is likely to reduce regimen difficulty. Koulayev, Skipper, and Simeonova (2013) and Levesque, Li and Pahal (2012), found that older patients were more likely to adhere to medication and lifestyle change than younger patients. Horne (1997) has stated that young chronic patients were less adherent than the old patients. Although researchers Al-Lawati (2014); Sharma, et al. (2012); Mandal, et al. (2012); and Mumu, et al. (2014), have found age impacting on non-adherence, but its interaction effects have not been examined.

Conclusions

The study results demonstrated that medication non-adherence is higher when regimen difficulty is higher

among patients with chronic conditions. The demographic factors like gender and age have explained additional variances in medication non-adherence beyond what was explained by regimen difficulty. Differences in non-adherence across the demographic groups were found. The impact of regimen difficulty on medication non-adherence is greater for females than males and was higher among old patients than young patients. This study has enumerated health system and patient's personal characteristics related issues which are neglected but are impacting non-adherence. Medication non-adherence is not viewed as an important element of public health policy. It is argued that patient alone should not be blamed for non-adherence. Medication non-adherence due to regimen difficulty is flexible and is amenable to being shaped by the health care system work culture. A shift in health care provider's attitude towards consultation and patient wellbeing is essential. The study findings also emphasize the need to sensitize the patients about adherence. The recent research and predictions are emphasizing on the use of technological interventions to improve adherence (Regan 2016; Seung 2017; Deloitte Centre for Health Solutions). Overall the health care systems should be reoriented to address the challenges posed by the prevalence of medication non-adherence due to regimen difficulty. It should also aim at fulfilling the patients' needs, wants and expectations by focusing the difficulty level of each patient to understand and follow the regimen.

Limitations and future research

Data collected was self-reported, hence it may be biased. Only two-way interaction effects of interaction terms were tested.

Further longitudinal studies are required to study three-way interaction effects of patient personal characteristics on the associations between regimen difficulty and medication non-adherence.

Ethical considerations

Prior permissions to conduct the survey among patients with chronic conditions were secured from the health care facilities from Goa and Karnataka, India. The informed consents from the patients to participate in the survey were secured.

Disclosure

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Appendix

INTERACTION GRAPH 1: Gender by Regimen Difficulty Interaction on Medication Non- Adherence
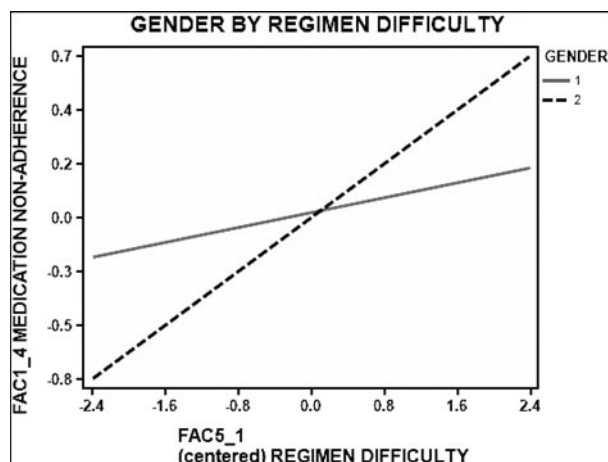
Gender 1= Male, 2= Female

INTERACTION GRAPH 2: Age by Regimen Difficulty Interaction on Medication Non- Adherence