

# Effectiveness of public health interventions on improving prescription redemptions and medication adherence among Type 2 Diabetes mellitus patients: Systematic Review and meta-analysis of Randomized Controlled Trials

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## *Abstract*

**Background:** Despite an inadequate filling of prescriptions among chronic care patients has been a problem, little is known about the intervention effect on it.

**Objective:** The aim of this systematic review and meta-analysis (SRMA) was to investigate the effectiveness of various public health interventions on primary and secondary medication adherence among T2DM patients.

**Methods:** Searching was done from the major databases; Cochrane Library, Medline/PubMed, EBSCOhost, and SCOPUS. Hand search was made to find grey literatures. Articles focused on interventions to enhance primary and secondary medication among type 2 diabetes mellitus patients were included. After screening and checking eligibility, the methodological quality was assessed. Secondary medication adherence was synthesized descriptively due to measurement and definition variations across studies. Finally, meta-analysis was made using the fixed effects model for primary medication adherence.

**Results:** 3,992 studies were screened for both primary and secondary medication adherences. Among these, 24 studies were included in the analysis for primary (5) and secondary (19) medication adherences. Pooled relative medication redemption difference was RD=8% (95% CI: 6-11%) among the intervention groups. Age, intervention, provider setting, and IDF region were determinant factors of primary medication adherence. About two-thirds of the studies revealed that interventions were effective in improving secondary medication adherence.

**Conclusion:** Both primary and secondary medications were enhanced by a variety of public health interventions for patients worldwide. However, there is a scarcity of studies on primary medication adherence globally, and in resource-limited settings for type of adherences.

**Key words-** T2DM, medication adherence, intervention, meta-analysis, RCT

## I.

### INTRODUCTION

Medication adherence has not been the only interest of the patient to purchase or take the prescribed medications, but numerous factors have been affecting it among chronic and comprehensive care patients [1,2]. Medication cost, patient-physician communication, disease, medication and patient-related characters, and health care system are all affect both primary and secondary medication adherences among chronic ill patients including type 2 diabetes mellitus (T2DM) patients [3–6]. On the other hand, diabetes pandemically has been affecting around half a billion (463 million) people across the globe. T2DM constitutes 90-95% of all kinds of diabetes. If this pandemic is left uncontrolled, this number is expected to reach 0.7 billion in 2045 [7].

When patients are well adhered to, both their medications, increase the probability of prognosis and quality of life [8–10], lower hospitalization rate [11,12], balance blood glucose level [13,14], reduce both direct and indirect healthcare costs [15–18], diabetes related morbidities and mortality [19,20] among patients. However, the issue of primary medication adherence (PMA) has been a shallowly explored theme in healthcare and did not receive the required attention until the recent years [2,21,22]. Additionally, vast differences has been existing in the definition and measurement of secondary medication adherence among diabetic patients across the globe [23]. One of the recent SRMA on PMA reported that antidiabetic medication redemption was the lowest among other chronic diseases nearly 10% [24].

Nevertheless, through the active involvement of society, public health interventions are essential for promoting health, preventing disease, and prolonging life of the population. These interventions involve various approaches and require well-planned, organized, and integrated efforts of society alongside with healthcare professionals to achieve goals and targets [25,26].

Therefore, we aimed to investigate the overall effectiveness of public health interventions on improving redemption and medication adherence among T2DM patients.

### II. METHODS

Preferred reporting Items for systematic review and Meta-analysis (PRISMA) was used [27].

#### *A. Eligibility criteria*

##### *Inclusion and exclusion criteria*

The study was carried out based on the framework of PICOS (Population, Intervention, Control, Outcome, and Study design) for achieving easy, clear and vigorous stages [28] to achieve the objectives among study participants. (TABLE I) below

##### *B. Search strategy, data sources, extraction, bias assessment, and synthesis*

Cochrane Library, MEDLINE (EBSCOhost), MEDLINE/PubMed, and SCOPUS databases were used to quest for relevant articles. STATA 14 version was used to analyze the data. Secondary adherence was analyzed manually. Risk of bias was assessed using JBI tool. Pooled relative redemption difference was calculated for the effectiveness of public health intervention on PMA among T2DM patients (dichotomous data) along with a 95% confidence interval.

### III. RESULTS}

A total of 3,992 studies were found from databases and other sources. After removal of the duplicates, 2,790 were screened for eligibility. After thorough screening, 158 full texts were found eligible for further inclusion. After checking for inclusion, 24 studies met the criteria. Among twenty-four, twenty (1 primary and 19 for secondary adherence) studies were included in the qualitative synthesis and 4 PMA in the meta-analysis. (Figure 1)

Three studies from USA [29–31], and one each from Denmark [32] and Hungary [33]. All of them evaluated the impact or effectiveness of their respective public health interventions on PMA. Studies are only available

from Europe [32,33] and North American and Caribbean [29–31] IDF regions, and high-income countries as well.

#### *Overall effect size of public health interventions on Primary Medication Adherence*

The pooled effectiveness of public health interventions on PMA was significant with relative redemption of prescription among IG than control group with RD=8% (95% CI: 6-11%) with  $I^2=93.9%$ ,  $p<0.001$  with the fixed effects assumption (Figure 2). This effect shows a considerable variation across the studies. Thus, after considering the variation across the studies by applying random effects assumption, the pooled effectiveness was RD=7% (95% CI: -5-18%) with  $I^2=93.9%$ ,  $p<0.001$ . However, following a small number of studies, we ignored the heterogeneity. Thus, with the aim of improving a clinical relevance among patients, we continued our interpretation with the fixed effects assumption. **(Figure 2) below**

#### *Subgroup analysis*

Subgroup analysis was conducted using intervention type, provider, period, IDF region, WB economic classification, age group, adherence measurement (patient/prescription), continent, and study settings. However, all studies were from a single category of WB.

Intervention setting period, IDF region, and service providers come as potential contributors of heterogeneity and showed a significant effect on the outcome variables. (TABLE II) below.

#### **A. Types of public health intervention**

Multiple types of public health interventions were delivered to patients with various approaches. Interventions were provided mainly in three categories. Behavioral counselling includes direct face to face and internet supported, educational information aided materials like pictorial, simulation, leaflets and thirdly mobile phone services such as phone call, sending the reminder via SMS were mentioned.

#### *Sensitivity analysis and publication bias*

One by one omission of each study has no significant influence on the pooled outcome. However, O'Connor and colleagues' study has a marginally higher value than others on the overall effect size.

Statistically findings showed no existence of publication bias. Harbord's test with Galbraith plot fitted the regression [34] line that there is no publication bias, with the estimated intercept is 1.664 and standard error of 1.397,  $p=0.66$ . A unit increase of 1.664 log relative ratio for each unit increase will increase in the standard error of the log relative ratio. Thus, we could not decide that the publication bias was assessed since there were small numbers of included trials to accurately evaluate a funnel plot or more advanced regression-based calculations [35].

#### **B. Secondary medication adherence**

The medication adherence definitions and measurements used by the studies were not consistent. This was a hurdle to carry out the quantitative (meta-analysis) on the effectiveness of public health interventions on secondary medication adherence. About 73.7% of studies reported that the interventions were effective in enhancing secondary medication adherence among T2DM patients. This is quite in line with the previous finding [36]. Additionally, it strengthens the conclusion that multicomponent interventions provided to enhance secondary medication adherence were found be effective [23].

## **IV. CONCLUSION**

Overall effect size claimed that public health interventions for T2DM patients were found effective in enhancing prescription redemption. In a qualitative synthesis, behavioral changing, educational materials provided, and electronic or health information technology guided intervention were effective. Despite the inconsistency of measurements and the variety of interventions existing among studies for evaluating secondary medication adherence, by considering cost-effectiveness and suitability of the intervention type, it is better to scale up interventions to resource limited settings. Thus, we suggest pragmatic, vigorous, and clear randomized trials should be done to assess the effect of PMA among T2DM patients regardless of geopolitical and economic circumstances.

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TABLE I

ELIGIBILITY CRITERIA		Inclusion criteria	Exclusion criteria
Framework			
Population		Adult patients (greater than 18 years and above), all ethnicity, both sex, who had been on antidiabetic drugs at the baseline	T1DM, gestational DM and other forms of diabetes
Intervention		Any type of public health intervention (behavioral change through information education and communication, provision of medical supplies and drugs, upgrading or capacity building of skill and competencies, human resource acquisition, short message services, applications, health promotion, psychological care) either locally adapted approach or HIT guided	Those interventions deviate from the listed ones
Comparator		T2DM patients on placebo, usual/standard care or no care at all	If there is reported information contamination or intervention that equates with intervention groups
Outcome		Redemption, refilling or adherence to antidiabetic and related medication prescriptions	Other biomarker outcomes as primary interest of outcome
Study design		Randomized Controlled Trials, quasi-experimental	Other study designs
Study setting		Global	NA
Language		All languages	NA
Publication year		Not time bounded	NA
HIT- Health information technology, HIT- diabetes mellitus	NA- Not applicable	T1DM- type 1	diabetes mellitus, T2DM- type 2

TABLE II

SUBGROUP ANALYSIS OF PRIMARY MEDICATION ADHERENCE								
Subgroups	Categories	Number of studies	Sample size (IG vs CG)	Relative redemption difference (%)	95% CI	I <sup>2</sup> (%)	p-value	
Type of provider of intervention	Pharmacist	1	221 vs 199	8	2-14	NA	NA	
	GP	1	521 vs 493	21	16-26	NA	NA	
	Nurses	1	148 vs 142	-2	-6-3	NA	NA	
	Healthcare team	1	481 vs 458	-2	-12-8	NA	NA	
Intervention setting	Institutional	2	629 vs 600	-2	-2-6	0	0.998	
	Community	2	742 vs 692	17	13-21	91.1	0.001	
Intervention period in months	Less than six	2	369 vs 341	4	-1-9	65.2	0.009	
	Greater than six	2	1002 vs 951	10	7-13	97.8	<0.001	
IDF region	Europe	1	521 vs 493	21	16-26	NA	NA	
	NAC	3	850 vs 799	1	-1-3	70.7	0.033	

CG- control group, IG-intervention group, NA-Not applicable, NAC- North America and Caribbean

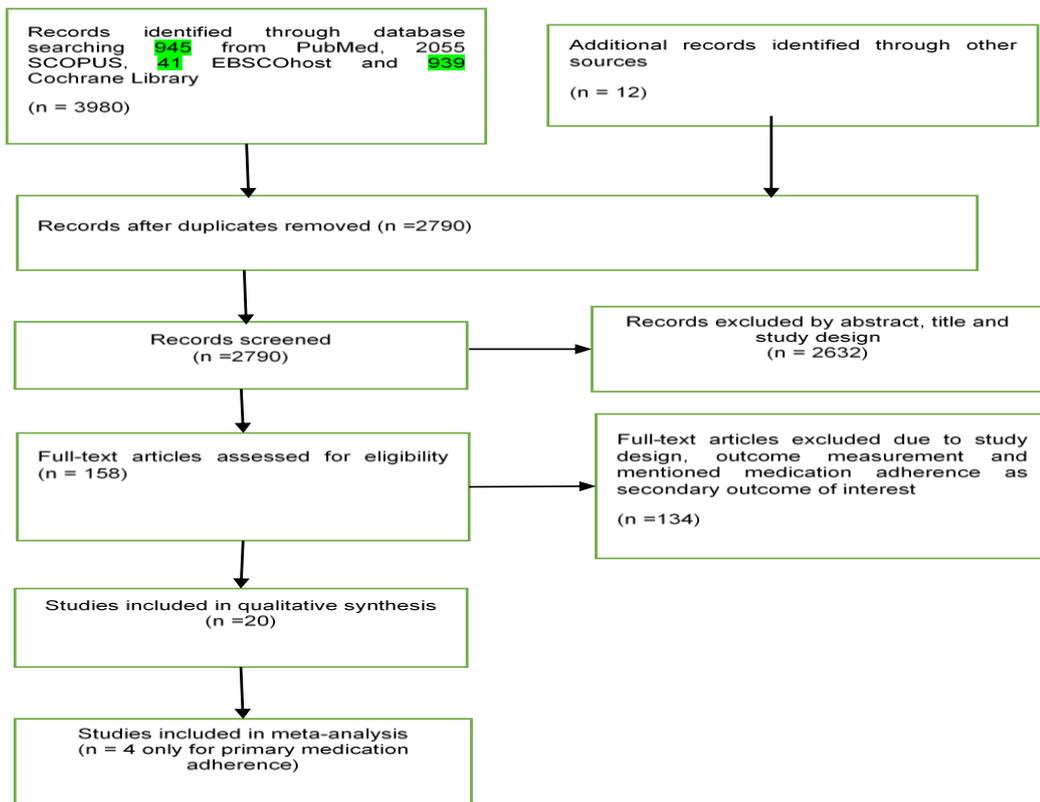


Figure 1 Study characteristics of primary Medication adherence among T2DM

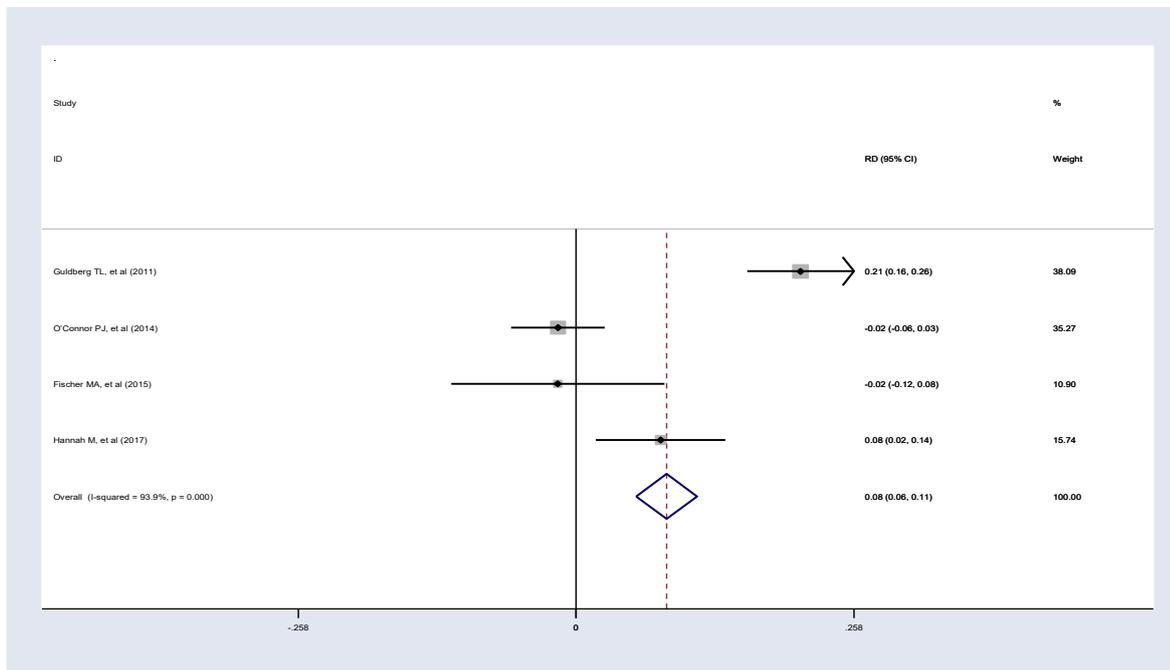


Figure 2 Forest plot for the overall effectiveness of public health interventions on primary medication adherence of included trials