

## The Effect of High Knowledge on Diabetes Type 2 and Strong Belief in Medicine with Non-Adherence of Anti Diabetic Medication: A Meta-Analysis

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### ABSTRACT

**Background:** By 2045, the number of people with diabetes mellitus (DM) was expected to increase from 424.9 million in 2017. Healthcare professionals have had a difficult time managing diabetes because of nonadherence to therapy. Additionally, the efforts made to clarify and enhance patient adherence to their medication are not always successful. This study investigated the factors such as high knowledge on diabetes type 2 and strong belief in medicine that lead to medication non-adherence in adults.

**Subjects and Method:** This article was a systematic review and meta-analysis study conducted by searching for articles from online databases such as EBSCO, ProQuest, and PubMed. Populations: adults with diabetes mellitus; Intervention: a strong belief in anti-diabetic medication and high knowledge of diabetes mellitus; Comparison: a weak belief or none in anti-diabetic medication and little knowledge of diabetes mellitus; Outcome: non-adherence of anti-diabetic medication. The independent variables is strong belief and high knowledge, the dependent variable is non-adherence to anti-diabetic medication. The inclusion criteria for this study were full articles using a cross-sectional study, with the publication year until 2022. We conduct the analysis using RevMan 5.3 software.

**Results:** A total of 6 articles reviewed in the meta-analysis (consisted 4 articles in each variables), from countries: Ethiopia, Australia, Uganda, Iran, Palestine and China, showed that respondents with strong belief in anti-diabetic medicines (aOR= 0.66; 95% CI= 0.48 to 0.90; p= 0.008) and high knowledge of diabetes mellitus (aOR= 0.85; 95% CI= 0.79 to 0.93; p= 0.0005) had lower level of non-adherence to anti-diabetic medication.

**Conclusion:** A strong belief in anti-diabetic medicines and high knowledge of diabetes mellitus can lower non-adherence to anti-diabetic medication.

**Keywords:** diabetes mellitus type 2, medication adherence, predictors

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### BACKGROUND

By 2045, the number of people with diabetes mellitus (DM) was expected to increase from 424.9 million in 2017 (Jeannette et al., 2017;

WHO, 2016). As the condition progressed, the intensity of the treatment also increased. Diabetes treatment plans sometimes involve

numerous medicines, varying dosages, and frequent delivery (Alexopoulos et al., 2021).

Healthcare professionals have had a difficult time managing diabetes because of nonadherence to therapy. Additionally, the efforts made to clarify and enhance patient adherence to their medication are not always successful (Hugtenburg et al., 2013). A crucial and significant factor in preventing serious unwanted consequences and lowering the use of healthcare resources is patient's compliance with their anti-diabetic drug regimens (Elsous et al., 2017).

Poor adherence to therapies is common, especially when comorbidities exist (Kardas, 2005), and is believed to be influenced by several factors divided into five categories: patient-centered factors, therapy-related factors, health care system factors, social and economic factors, and disease-related factors (Hutchins et al., 2011; Rwegerera, 2014; Wong et al., 2011). With different outcomes, a number of studies have examined medication adherence to anti-diabetic drugs. Financial issues, forgetfulness, youth, education level, pre-existing diabetes complications, and challenges with taking the pills alone are some characteristics that have been linked to non-adherence to antidiabetic medication (Arifulla et al., 2014; Huber and Reich, 2016; Rwegerera, 2014; Tiv et al., 2012).

This study investigated the factors such as high knowledge on diabetes type 2 and strong belief in medicine that lead to medication non-adherence in adults with DM in light of the significance of medication adherence as previously mentioned, the potential for early disease control in patients with DM, and the need to prioritize scarce health care resources in light of the growing DM epidemic.

## SUBJECTS AND METHOD

### 1. Study Design

This study uses a systematic review and meta-analysis study design. The Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) standards were followed for conducting this systematic review and meta-analysis (Hutton et al., 2015). Only English language-based literature was used in an electronic search of EBSCO, ProQuest, and PubMed/Medline, Direct from their establishment to April 30, 2022. The search term used was (medication adherence OR non-adherence) AND (predictors OR variables) (diabetes mellitus OR diabetes type 2). Additionally, to find any pertinent studies, we manually examined the referenced articles of earlier cohort studies, meta-analyses, and review papers.

### 2. Inclusion Criteria

All studies were included if they met the following eligibility criteria: (a) articles on anti-diabetic medication adherence or non-adherence; (b) independent variables influencing medication adherence or non-adherence was a belief in anti-diabetic medication and knowledge about diabetes; (c) associations measured by an adjusted odds ratio; and (d) respondents were general adults with diabetes mellitus. (e) observational studies published in English only.

### 3. Exclusion Criteria

Case series, case reports, human-based randomized controlled trials, literature reviews, editorials, and studies not meeting the inclusion criteria were excluded.

### 4. Study Variables

variabel dependen medical non adherence, Independent strong knowledge of diabetes and weak belief in medication.

### 5. Operational definition of variables

The strategy for research was PICO: 1) P (population): adults with diabetes mellitus; 2) I (Intervention): a strong belief in anti-diabetic medication and high knowledge of

diabetes mellitus; 3) C (control): a weak belief or none in anti-diabetic medication and little knowledge of diabetes mellitus; 4) O (outcome): non-adherence of anti-diabetic medication.

**High knowledge of diabetes and weak belief in medication:** The level of knowledge is everything that the patient knows about the meaning, signs, symptoms, risk factors, complications and their management regarding diabetes mellitus.

**Medical non adherence:** defined behavior of an individual or care worker who fails to adhere to a health promotion plan or treatment plan agreed upon by the individual (or family, or community) and health professional resulting in a clinically ineffective outcome.

## 6. Study Instruments

The electronic databases were searched independently by two reviewers. Duplicate studies were checked for and eliminated using the EndNote Reference Library software version 20.0.1 (Clarivate Analytics). Two reviewers concurrently and independently extracted data and evaluated the quality of the included studies. The effectiveness of the cross-sectional studies was evaluated using the Newcastle-Ottawa Scale (NOS). A NOS score of 1 to 5 was seen as having a high risk of bias, a score of 6-7 as being moderate, and a score of >7 as having a low risk of bias (details of scoring are provided in Table 1).

## 7. Statistical Analysis

All statistical evaluations were conducted using Review Manager Version 5.3. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014). A random-effects model was used to combine the data from the various investigations. The adjusted odds ratio (aOR) and associated 95 percent confidence intervals were used to

analyze the results (CI). The scale for heterogeneity, according to Higgins et al., was as follows:  $I^2 = 25-60\%$  moderate,  $50-90\%$  substantial,  $75-100\%$  considerable, and  $p < 0.01$  significant heterogeneity (Higgins et al., 2003). All analyses required a significance level of  $p < 0.05$  or above.

## RESULTS

### A. Articles Search Result

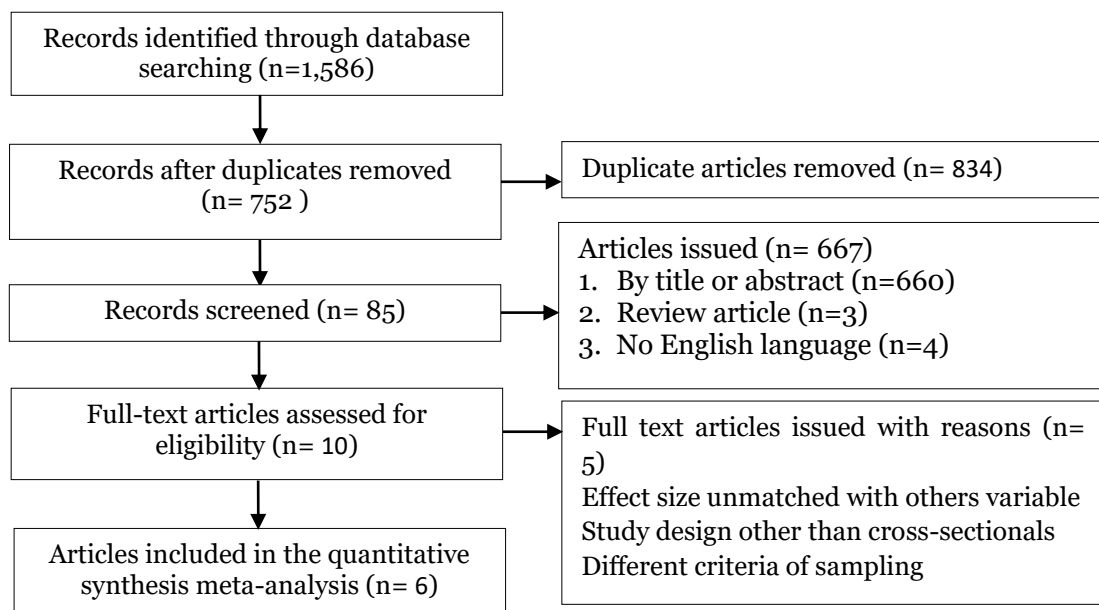
One thousand and five hundred eighty six suitable researchs were found after a preliminary search of the three electronic databases. The entire texts of 85 studies were evaluated for potential inclusion after exclusions based on titles and abstracts. There were still six studies available for quantitative analysis. The findings of our literature search are summarized in Figure 1.

### B. Study characteristics

The fundamental attributes of the selected research are presented in Table 1. Six published studies were analyzed in this study (Ali et al., 2017; Dhippayom & Krass, 2015; Kalyango et al., 2008; Pirdehghan & Poortalebi, 2016; Sweileh et al., 2014; Xu et al., 2020). Each study was cross-sectional. This analysis included 1796 respondents with DM in total. Each of Uganda, Ethiopia, Australia, Iran, China, and Palestine contributed one study. There were three research looking at the relationship between strong knowledge of diabetes mellitus and medication non-adherence, and five studies looking at the relationship between medication belief and non-adherence.

### C. Quality assessment

Detailed score has described in table 1, was evaluated using the Newcastle-Ottawa Scale (NOS).



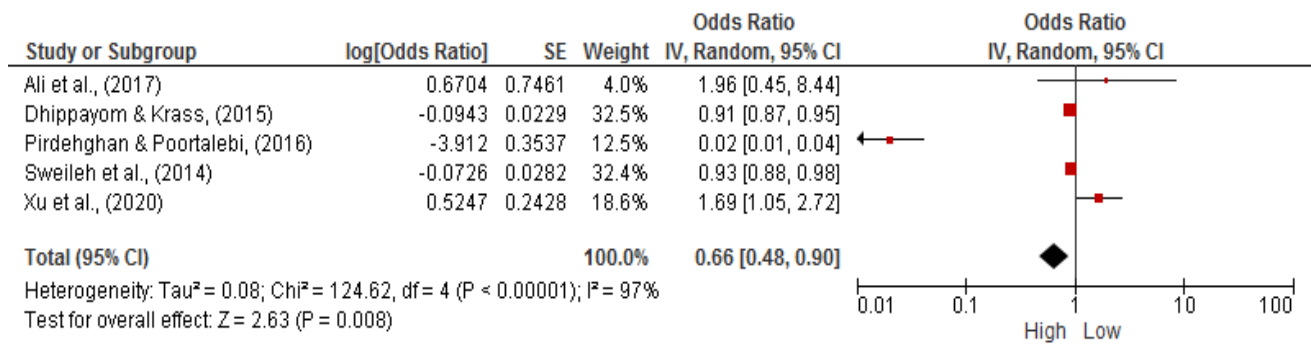
**Figure 1. PRISMA flow diagram**

**Table 1. Quality assessment of cross-sectional studies using the Newcastle–Ottawa scale**

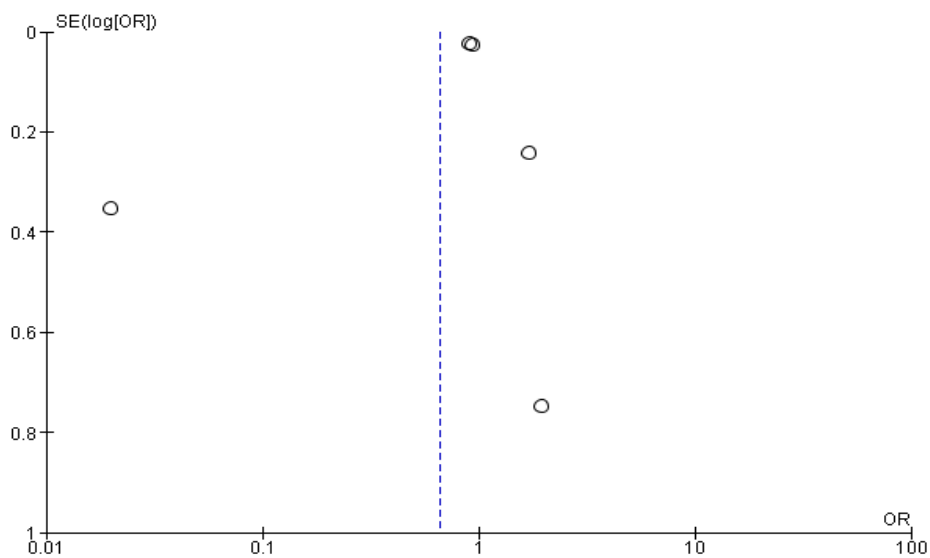
Variable	Ali et al., (2017)	Dhippayom & Krass, (2015)	Kalyango et al., (2008)	Pirdehghan & Poortalebi, (2016)	Sweileh et al., (2014)	Xu et al., (2020)
<b>Selection</b>						
Representativeness of the sample	0	0	0	1	0	0
Sample size	1	1	1	1	1	1
Ascertainment of exposure	2	2	1	2	2	2
Non-respondents	1	1	1	1	1	1
<b>Comparability</b>						
The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.	2	2	2	2	2	2
<b>Outcome</b>						
Assessment of outcome	1	1	1	1	1	1
Statistical Test	1	1	1	1	1	1
<b>Total Score</b>	<b>8</b>	<b>8</b>	<b>7</b>	<b>9</b>	<b>8</b>	<b>8</b>

**Table 2. Basic characteristics of selected studies**

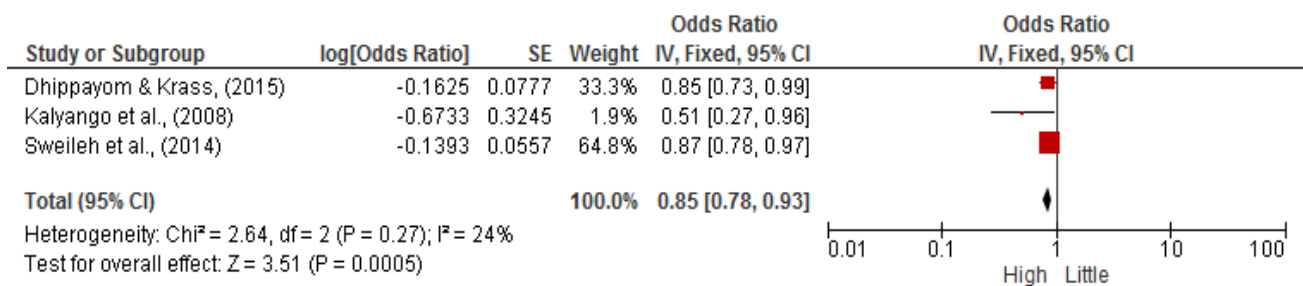
Study (year)	Country	Study Design	Total Sample	Age (years)		Exposure	Control	aOR (95% CI)
				Mean	SD			
Ali et al., (2017)	Ethiopia	Cross-sectional	146	46.5	14.7	Strong belief in medicines	Weak belief in medicines	1.96 (0.45–8.44)
Dhippayom and Krass, (2015)	Australia	Cross-sectional	543	63.0	10.6	Strong belief in medicines; High knowledge of DM	Weak belief in medicines; Little knowledge of DM	0.91 (0.87–0.96); 0.85 (0.73–0.99)
Kalyango et al., (2008)	Uganda	Cross-sectional	402	50.0	13.8	High knowledge of DM	Little knowledge of DM	0.51 (0.27–0.95)
Pirdehghan and Poortalebi, (2016)	Iran	Cross-sectional	300	55.84	10.39	Strong belief in medicines	Weak belief in medicines	0.02 (0.01–0.07)
Sweileh et al., (2014)	Palestine	Cross-sectional	405	58.3	10.4	High knowledge of DM; Weak belief in medicines	Little knowledge of DM; Weak belief in medicines	0.87 (0.78–0.97); 0.93 (0.88–0.99)
Xu et al., (2020)	China	Cross-sectional	1,002	Undescribed	Undescribed	Strong belief in medicines	Weak belief in medicines	1.69 (1.05–2.74)



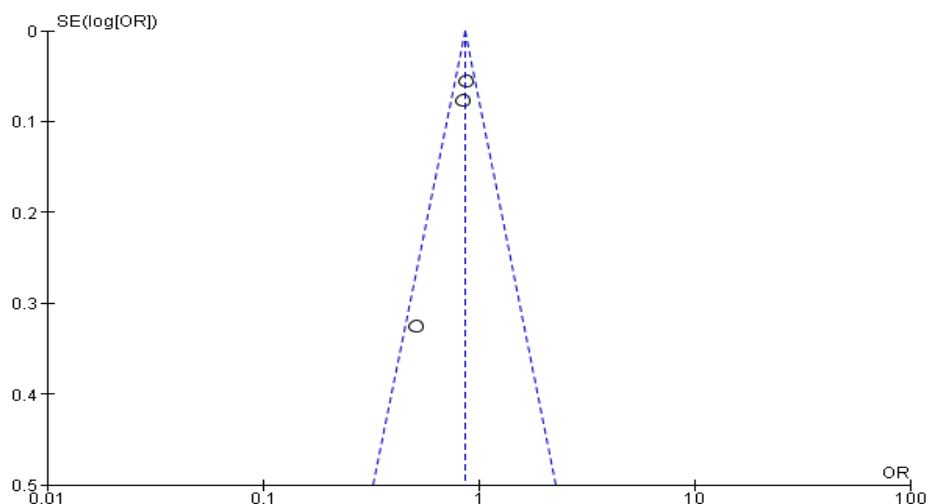
**Figure 2. Forest plot showing association between beliefs in medicines with medication non-adherence to anti-diabetic medicine**



**Figure 3. Funnel plot of association between beliefs in medicines with medication non-adherence to anti-diabetic medicines**



**Figure 4. Forest plot showing association between knowledge of diabetes mellitus with medication non-adherence to anti-diabetic medicines**



**Figure 5. Funnel plot of association between knowledge of diabetes mellitus with medication non-adherence to anti-diabetic medicines**

**a. Forest plot**

A detailed forest plot (Figure 2), outlining the association between belief in medicines with medication non-adherence of anti-diabetic. Five studies were used to conduct the analysis. The random analysis of pooled AOR suggests there is a strong association between strong belief in medicines with lower medication non-adherence of anti-diabetic medicines compared to weak belief in medicines and it was statistically significant (aOR= 0.66; 95% CI= 0.48 to 0.90; p= 0.008).

The heterogeneity ( $I^2$ ) showed a substantial category with a value of 97% and it was significant  $p < 0.001$ . The fixed analysis of pooled aOR from 3 studies suggests there is a moderate association between high knowledge of diabetes mellitus with lower medication non-adherence to anti-diabetic medicines compared to little knowledge of diabetes mellitus and it was statistically significant (aOR= 0.85; 95% CI= 0.79 to 0.93; p= 0.005). The heterogeneity ( $I^2$ ) showed a moderate category with a value of 24% and it was not significant  $p = 0.27$  (Figure 3).

**b. Funnel plot**

Based on the funnel plot described at figure 4 and 5, the researchers reported that it showed evidences that both of the results might affected by publication bias. The result of association between belief in medicine with medication non-adherence to anti-diabetic medicines might overestimates because one of the bullet represent of article was leaning towards right side. Meanwhile, the result of association between knowledge of diabetes mellitus with medication non-adherence to anti-diabetic medicines might underestimates because one of the bullet represent of article was leaning towards left side.

**DISCUSSION**

Around 537 million persons worldwide will have diabetes in 2021. More than 90% of all cases of diabetes globally are of the kind called diabetes mellitus (Webber, 2013). DM has a strong influence on the quality and length of patient’s lives, and puts a significant financial burden on them (Gebremedhin et al., 2019; Moucheraud et al., 2019). Diabetes is a chronic disorder with numerous complications, therefore managing it would require adequate levels of awareness,



self-care practices, and medication adherence (ADA, 2013; DACA., 2010). A high level in drug compliance helps to lower morbidity, mortality, and healthcare expenses. Healthcare systems incur enormous costs as a result of patient non-adherence to medication (Conn and Ruppap, 2017; Cutler et al., 2018).

The findings of this study imply that great faith in anti-diabetic medications will reduce anti-diabetic drug non-adherence. We contrasted the group that had a high or strong believe in anti-diabetic medications with the group that had a low or weak belief. This result was similar to study by Schoenthaler et al., (2012). It was stated that patient beliefs about the need for their medications were associated with better adherence to oral hypoglycemic medications (Schoenthaler et al., 2012). Study by Alatawi et al., (2016) also supported with their conclusion that suggest perceived medication benefits were significant predictors for medication adherence (Alatawi et al., 2016).

Although there is currently no treatment for diabetes, proper self-management helps to slow or stop its growth (Habebo et al., 2020). Patients must have sufficient level of understanding about diabetes related self-care in order to have effective treatment and good glucose control, a concept that can encourage adherence to prescriptions (Gautam et al., 2015; Saleh et al., 2012). It would be crucial to improve affordable access to regular follow-ups including promotion of healthy behaviors through health education and control of diabetes mellitus-related complications (Nonogaki et al., 2019).

According to our research, those with more understanding about diabetes mellitus than those with less information have lower rates of anti-diabetic drug non-adherence. It was supported by Bagonza et al., (2015). They stated that adherence was associated

with having received diabetic health education (Bagonza et al., 2015). An ethnic minority population's glycemic control was found to be significantly improved by community health workers' intervention as opposed to written instructional materials, according to research by The Mexican American Trial of Community Health Workers (MATCH) (Rothschild et al., 2014).

This study has a few limitations, this meta-analysis still only included a small number of primary research. The included researches were only in the English language and the literature search was limited to three databases, which may have left out pertinent data. Additionally, due to the little data from the primary studies, we did not perform the subgroup analysis. Future research should permit the use of more primary studies and subgroup analysis. The results of the meta-analysis suggested that a strong belief in anti-diabetic medications and a high knowledge of diabetes mellitus can lower non-adherence to anti-diabetic medication. This study brought to light the variables we must take into account when creating health promotion initiatives. Additionally, it is necessary to construct health literacy, counseling, and education programs in both clinical and community settings.

#### **AUTHOR CONTRIBUTION**

Artha and Aris participated in data collection, analyzed the data and drafted the manuscript. Santi and Ayu contributed to the interpretation of the results and revised the manuscript. Artha also conceived the idea. Joko and Asruria. participated in data collection, reviewed the manuscript and provided valuable comments. All authors have read and agreed to the published version of the manuscript.

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### CONFLICT OF INTEREST

There is no conflict of interest in this study.

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