

## Meta-Analysis: Effect of Acupuncture Therapy on HbA1c Levels in Type II Diabetes Mellitus

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### ABSTRACT

**Background:** Diabetes mellitus is a chronic condition that occurs when there is an increase in glucose levels in a person's blood because the body cannot produce enough of the insulin hormone, or cannot use the insulin it produces effectively. This study aims to estimate the effect of acupuncture therapy on changes in HbA1c in people with type II diabetes mellitus.

**Subjects and Method:** This research is a systematic review and meta-analysis carried out using the PRISMA flow diagram and PICO model including Population = Type II diabetes patients; Intervention = Acupuncture Therapy; Comparison= No acupuncture therapy or sham acupuncture; Outcome= Change in HbA1c and quality of life. Article searches through journal databases include: PubMed, Science Direct, Google Scholar, Springer Link, BMC and Hindawi. Search keywords: acupuncture, AND "type 2 diabetes mellitus", "acupuncture for diabetes mellitus type 2" AND HbA1c OR "quality of life" AND "randomized controlled trial". Inclusion criteria are full paper articles, Randomized Controlled Trial (RCT) research. The measure of relationship used is Mean SD. Eligible articles were analyzed using the Revman 5.3 application.

**Results:** Randomized Controlled Trial (RCT) from China, England, Iran, Egypt and Taiwan. Acupuncture therapy can reduce HbA1c in type II diabetes mellitus patients by 0.57 units higher than in controls (SMD -0.57; 95% CI= -1.15 to 0.02; p=0.060). Acupuncture therapy improved the quality of life in type II diabetes mellitus patients by 0.87 units compared to controls (SMD 0.87; 95% CI= 0.00 to 1.74; p=0.050).

**Conclusion:** Acupuncture therapy is effective in reducing HbA1c levels and improving quality of life in patients with type II diabetes mellitus.

**Keywords:** Acupuncture, Diabetes Mellitus, HbA1c, Quality of Life, Meta-Analysis.

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### BACKGROUND

Diabetes is one of the most serious chronic diseases that affects human health throughout the world (Sun et al., 2022). Diabetes mellitus (DM) is a metabolic disease charac-

terized by high levels of sugar in the blood (hyperglycemia) as a result of insufficient insulin secretion, impaired insulin activity, or both (Damayanti, 2017). This disease often occurs in people who are less active,

too lazy to exercise, genetic factors, obesity, and the most common occurrence is consuming foods that contain high fat or have a lot of sweetness from sugar (IDF, 2019).

According to the International Diabetic Federation (IDF) reports in 2019, as many as 463 million people suffered from diabetes worldwide, with 80% from low and middle-income countries (Saeedi et al., 2019). More than 70% of global deaths are caused by non-communicable diseases, infectious diseases, including diabetes, cardiovascular disease, cancer, and respiratory diseases. On average, diabetes reduces life expectancy in people aged 40-60 years by 4-10 years and independently increases the risk of death. Diabetes is one of the leading causes of non-traumatic lower extremity amputations and blindness, especially in people of working age. The co-occurrence of these morbidities severely impairs quality of life, reduces productivity, and causes great suffering (Chan et al., 2020).

According to Arsana et al., (2019) stated that there are various ways to control blood sugar levels, including pharmacological therapy and non-pharmacological therapy. Pharmacological therapy is carried out by consuming antidiabetic and non-pharmacological drugs, one of which is acupuncture therapy. Acupuncture is a stimulation therapy performed on certain acupuncture points to achieve therapeutic goals. Various acupuncture techniques currently available include electroacupuncture (EA), acupressure, moxibustion, warm acupuncture, and transcutaneous electrical stimulation of acupuncture points, and these techniques are usually applied to acupuncture points on the body and earlobes (Feng et al., 2018).

Several studies focused on the hypoglycemic effects of acupuncture, including finding a significant decrease in fasting

blood glucose (FBG) and hemoglobin A1c (HbA1c) (Liang et al., 2016). Based on existing literature, summary statistics are needed to calculate estimates of the effect of acupuncture therapy on changes in HbA1c in people with type II diabetes mellitus. This study aims to analyze previous primary studies in assessing the effect of acupuncture therapy on changes in HbA1c in people with type II diabetes mellitus.

## SUBJECTS AND METHOD

### 1. Study Design

This research uses a systematic review and meta-analysis method, namely a way of analyzing data originating from primary studies from a database based on the PRISMA diagram. The search for articles in this research used electronic databases such as PubMed, Science Direct, Google Scholar, Springer Link, BMC and Hindawi. The keywords used in the database search were acupuncture, AND "type 2 diabetes mellitus", "acupuncture for diabetes mellitus type 2" AND HbA1c OR "quality of life" AND "randomized controlled trial".

### 2. Steps of Meta-analysis

- 1) Formulate research questions using the PICO model including P= Type II Diabetes Mellitus Patients; I= acupuncture therapy; C= No acupuncture therapy or sham acupuncture; O= Change in HbA1c and Quality of life
- 2) Search for primary study articles from electronic databases such as PubMed, Science Direct, Google Scholar, Springer Link, BMC and Hindawi.
- 3) Conduct screening and carry out critical appraisal of primary studies.
- 4) Extract data and enter the mean and standard deviation (SD) from each primary study into the RevMan 5.3 application. The results of the article analysis are presented in the form of an overall SMD, using the 95% Confidence

Interval (CI) model effect and data heterogeneity (I<sup>2</sup>)

- 5) Interpret the results and draw conclusions.

### 3. Inclusion Criteria

The inclusion criteria for this study were primary research articles, full paper articles with the Randomized Controlled Trial (RCT) research method, measuring the relationship used with the Mean SD, the intervention provided was acupuncture, the research subjects were type II diabetes sufferers.

### 4. Exclusion Criteria

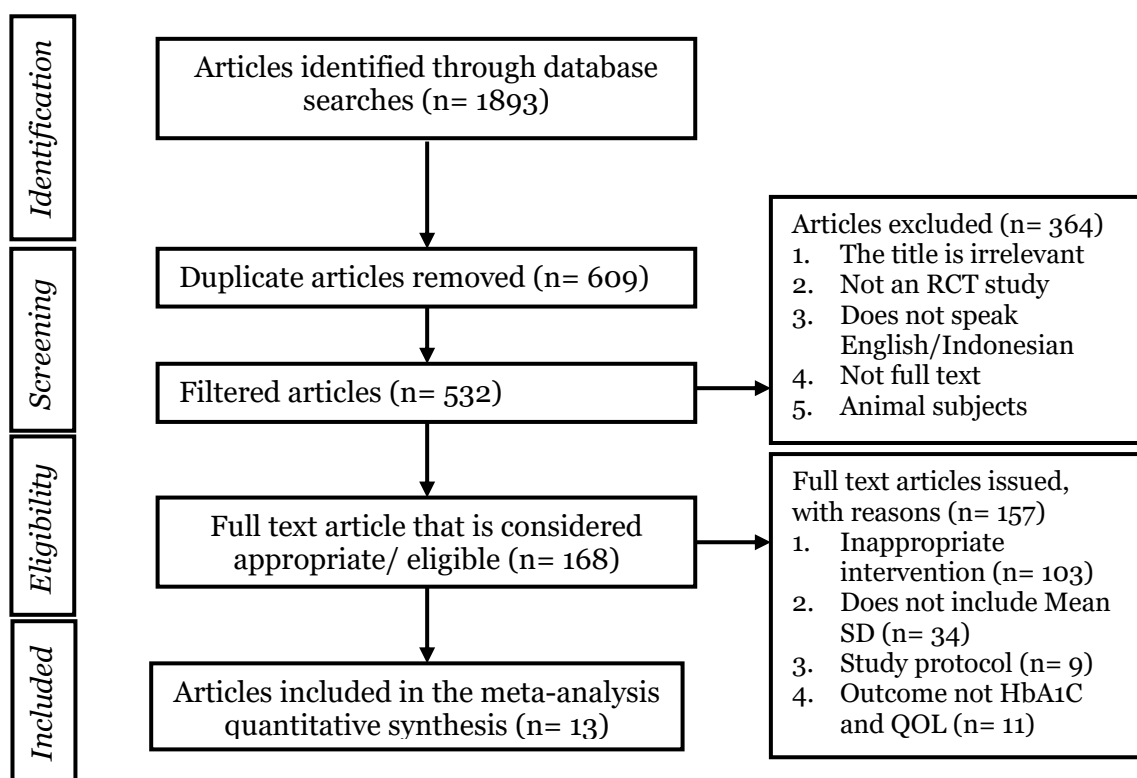
Research articles published before 2010, research articles published in other than English and Indonesian, non-Randomized Controlled Trial (RCT) study design.

### 5. Definisi Operasional

**Acupuncture therapy** is a treatment method by inserting needles into acupuncture points on the body to treat disease. Using certain acupuncture needles (filiform needles).

**HbA1c** is a substance formed from the reaction between glucose and hemoglobin or the part of red blood cells which is responsible for transporting oxygen to all parts of the body.

**Quality of Life** is a multi-dimensional concept that can fully reflect a person's overall health situation by measuring physical health, physiological health, social health and mental health.



**Figure 1. PRISMA Flow Diagram of Effect of Acupuncture Therapy on HbA1c Levels in Type II Diabetes Mellitus**

**RESULTS**

The process of searching for articles in this meta-analysis involves searching through journal databases, namely PubMed, Science Direct, Google Scholar, Springer Link, BMC and Hindawi with a time span between 2010-2023. Keywords used in database searches include acupuncture, AND "type 2 diabetes mellitus", "acupuncture for diabetes mellitus type 2" AND HbA1c OR "quality of life" AND "randomized controlled trial". The article search process accor-

ding to the PRISMA flow diagram can be seen as follows.

Figure 1 shows the initial search process which displays a total of 1,893 articles. After the process of deleting articles that were duplicated in more than one journal, 609 articles were obtained with 168 of them meeting the requirements for further full text review. Then there were 13 articles that met the requirements for full text review.



**Figure 2. Regional division of articles**

Figure 2 shows a general overview of the research areas used in this meta-analysis which are spread across 3 continents, namely Asia, Africa and Europe. There were

13 articles at the end of the review process that met quantitative requirements. All articles use Randomized Controlled Trial studies.

**Table 1. Critical Appraisal of Randomized Controlled Trial Study on the Effect of Acupuncture Therapy on Changes in HbA1c and Quality of Life in Type II Diabetes Mellitus Patients**

Primary Study	Criteria of Questions														Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Chuang <i>et al.</i> (2019)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Garrow <i>et al.</i> (2014)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25

Guirguis <i>et al.</i> (2016)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Hui <i>et al.</i> (2016)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Mood <i>et al.</i> (2021)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Najafi <i>et al.</i> (2020)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Qi <i>et al.</i> (2018)	2	2	2	2	2	2	1	1	0	2	2	2	2	2	24
Tong <i>et al.</i> (2010)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Wang <i>et al.</i> (2014)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Wang <i>et al.</i> (2019)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Wang <i>et al.</i> (2023)	2	2	2	2	2	2	1	1	0	2	2	2	2	2	24
Wu <i>et al.</i> (2022)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25
Xie <i>et al.</i> (2022)	2	2	2	2	2	2	2	1	0	2	2	2	2	2	25

**Description of the question criteria:**

- 1 = Is the population in the primary study the same as the population in the PICO meta-analysis?
- 2 = Is the operational definition of intervention in the primary study the same as the definition intended in the meta-analysis?
- 3 = Is the operational definition of the comparison used in the primary study the same as the scheme planned in the meta-analysis?
- 4 = Is the operational definition of the outcome variable examined in the primary study the same as that planned in the meta-analysis?
- 5 = Is the sample selected from the population so that the sample represents the population?
- 6 = Was the allocation of subjects into experimental and control groups carried out by randomization?
- 7 = Are the interventions and outcome variables measured using the same instruments (measuring tools) in all primary studies?
- 8 = If the variable is measured on a categorical scale, are the cutoffs or categories used the same across primary studies?

- 9 = Was double-blinding carried out, that is, the research subjects and research assistants who helped measure the outcome variables did not know the intervention status of the research subjects?
- 10 = Is there no possibility of “Loss-to-Follow-up Bias”?
- 11 = Have primary study researchers made efforts to prevent or overcome such bias?
- 12 = Are outcome data comparable between the experimental group and the control group after the intervention?
- 13 = Are all data analyzed according to randomization results?
- 14 = Is there no possibility of a conflict of interest with the research sponsor, which could cause bias in concluding the research results?

**Description of the answer score:**

- 0 = No
- 1 = Hesitant
- 2 = Yes

**Table 2. Summary of primary randomized controlled trial (RCT) study articles on the Effect of Acupuncture Therapy on Changes in HbA1c in Type II Diabetes Mellitus Patients with each PICO (N=454)**

Author	Country	Sample Size	(P) Population	(I) Intervention	(C) Comparison	(O) Outcome
Chuang <i>et al.</i> , (2019)	Taiwan	28	T2DM patients with diabetic neuropathy (AND)	Acupressure <45 days at SP 6 point	Sham acupressure	HbA1c
Guirguis <i>et al.</i> , (2016)	Mesir	40	T2DM female patient	Acupressure at SP 6 point	Hypoglycemic drugs	HbA1c
Hui <i>et al.</i> , (2016)	China	44	T2DM Patients	Laser acupoint points LI 4, LI 11, ST 36, SP 6	Drug treatment	HbA1c
Mood <i>et al.</i> , (2021)	Iran	60	T2DM patients	Acupressure points LV 2, LI 4	Sham acupressure	HbA1c
Najafi <i>et al.</i> , (2020)	Iran	63	T2DM patients	ST 36 point acupressure and medication	Pharmacological treatment	HbA1c
Tong <i>et al.</i> , (2010)	China	63	DM patients with diabetic peripheral neuropathy (DPN)	Acupuncture points LI 4, ST 40, LI 11, ST 36, SP 6	Sham acupuncture	HbA1c
Wu <i>et al.</i> , (2022)	China	120	Elderly Diabetes Patients	Management of Traditional Chinese Medicine	Routine treatment and management of diabetes	HbA1c
Xie <i>et al.</i> , (2022)	China	36	T2DM patients	Abdominal Massage points RN 10, RN 12, RN 13, ST 21, ST 29	Health education, guidance on healthy eating habits, and exercise	HbA1c

There are 13 articles with randomized controlled trial studies regarding the effect of acupuncture therapy on changes in HbA1c in people with type II diabetes

mellitus with a total sample of 454. This research was conducted in five countries including China, Iran, Egypt and Taiwan.

**Table 3. Summary of primary randomized controlled trial (RCT) study articles on the Effect of Acupuncture Therapy on the Quality of Life of Type II Diabetes Mellitus Sufferers with each PICO (N=449)**

Author	Country	Sample Size	(P) Population	(I) Intervention	(C) Comparison	(O) Outcome
Garrow <i>et al.</i> , (2014)	Inggris	45	DM patients with diabetic peripheral neuropathy (DPN)	Acupuncture points LV 3, KI 3, SP 6, SP 10, ST 36	Sham acupuncture	General health QOL

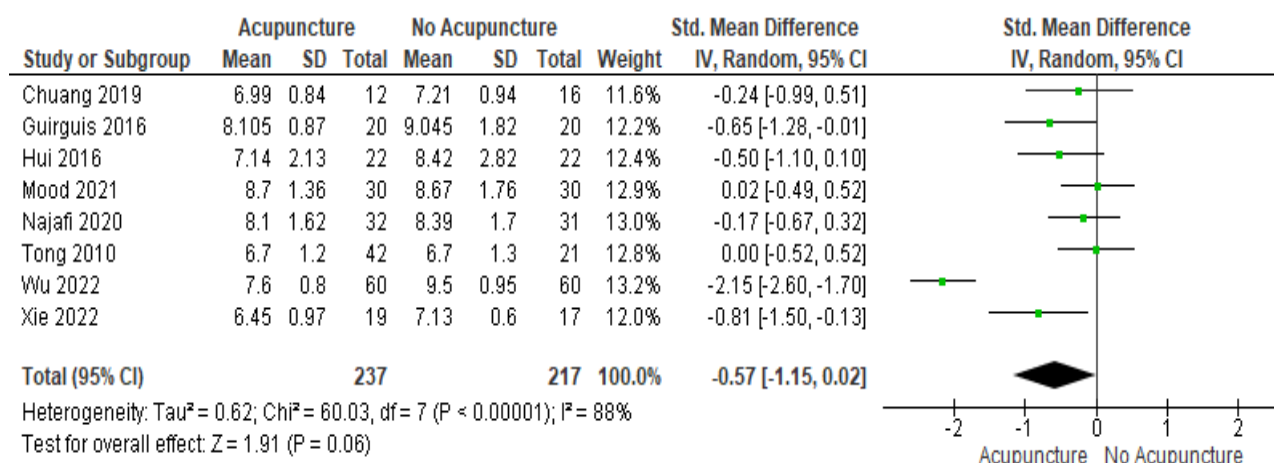
Author	Country	Sample Size	(P) Population	(I) Intervention	(C) Comparison	(O) Outcome
Qi <i>et al.</i> , (2018)	China	126	T2DM patients with lower-extremity arterial disease (LEAD)	Acupuncture points ST 36, SP3, SP 6, ST 40, KI 3, GB 34, LI 4, LI 11, ST 42, SP 9, EX-LE 10, EX-LE 5 and hydrotherapy	Without treatment	Health-related QOL
Wang <i>et al.</i> , (2014)	China	62	T2DM patients with chronic kidney disease (CKD)	Auricular acupressure of shenmen, kidney, spleen, heart points and conventional treatment	Conventional medicine	QOL
Wang <i>et al.</i> , (2019)	China	96	DM patients with diabetic peripheral neuropathy (DPN)	Acupuncture points BL 21, BL 13, BL 23, LI 4, LI 11, PC 6, TE 4, ST 36, LV 3, GB 34, SP 6	Routine treatment	QOL
Wang <i>et al.</i> , (2023)	China	120	DM patients with diabetic peripheral neuropathy (DPN)	TCM foot soak and light moxibustion points BL 13, BL 20, BL 23, ST 36 combination of conventional treatment	Conventional medicine	QOL

There are 5 articles with randomized controlled trial studies regarding the effect of acupuncture therapy on quality of life in people with type II diabetes mellitus with a

total sample of 449. This research was conducted in five countries including China and England.

**Table 4. Estimated effects of all primary studies included in the meta-analysis of acupuncture to reduce HbA1c**

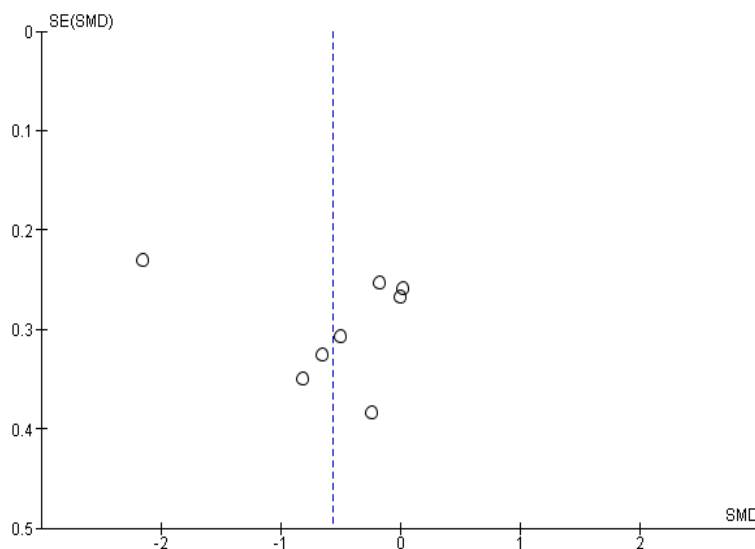
Author (Year)	Akupunctur		Non Acupuncture	
	Mean	SD	Mean	SD
Chuang <i>et al.</i> (2019)	6.99	0.84	7.21	0.94
Guirguis <i>et al.</i> (2016)	8.11	0.87	9.05	1.82
Hui <i>et al.</i> (2016)	7.14	2.13	8.42	2.82
Mood <i>et al.</i> (2021)	8.7	1.36	8.67	1.76
Najafi <i>et al.</i> (2020)	8.1	1.62	8.39	1.7
Tong <i>et al.</i> (2010)	6.7	1.2	6.7	1.3
Wu <i>et al.</i> (2022)	7.6	0.8	9.5	0.95
Xie <i>et al.</i> (2022)	6.45	0.97	7.13	0.6



**Figure 3. Forest Plot of acupuncture to reduce HbA1c**

The forest plot in Figure 3 shows that acupuncture therapy can reduce HbA1c in cases of type II diabetes mellitus compared to other interventions or no intervention and this effect is not statistically significant. Diabetes patients who experienced a decrease in HbA1c had an average score of 0.57 units compared to those with other

interventions or no intervention (SMD - 0.57; 95% CI= -1.15 to 0.02; p=0.060). The forest plot shows high heterogeneity of effect estimates between primary studies I<sup>2</sup> = 88%; p<0.001. Thus, the calculation of the average estimated effect is carried out using the Random Effect Model approach.



**Figure 4. Funnel plot of acupuncture to reduce HbA1c**

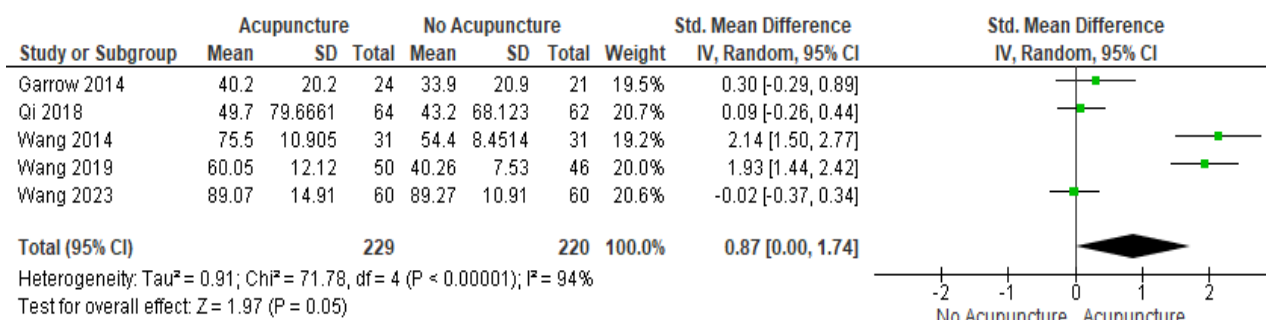
The funnel plot in Figure 4 shows that the distribution of estimates between studies is asymmetric, namely the distribution or distribution of effect estimates to

the right of the vertical line, the average estimated effect is relatively larger than to the left (overestimate). Thus, this funnel plot indicates that there is publication bias.



**Table 5. Effect estimates from all primary studies included in the meta-analysis of acupuncture for improving quality of life**

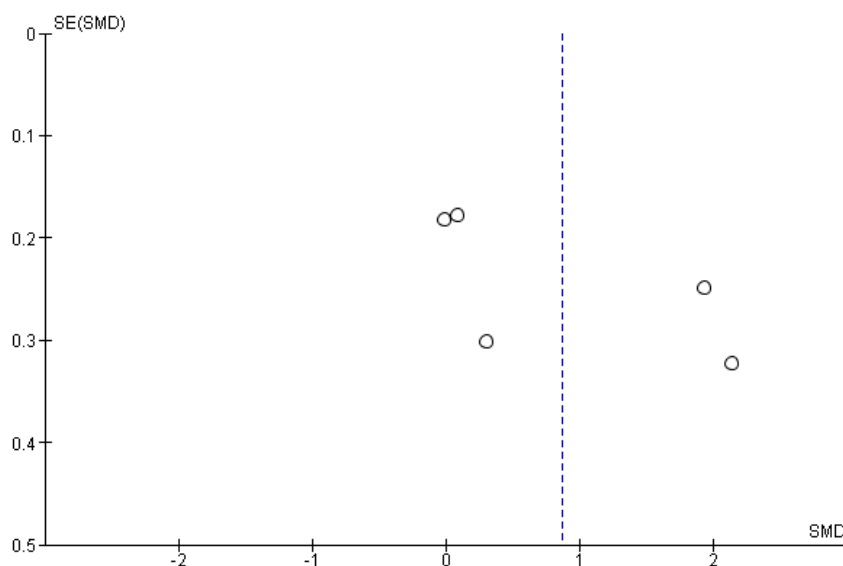
Author (Year)	Akupunktur		Non Acupuncture	
	Mean	SD	Mean	SD
Garrow <i>et al.</i> (2014)	40.2	20.2	33.9	20.9
Qi <i>et al.</i> (2018)	49.7	79.67	43.2	68.123
Wang <i>et al.</i> (2014)	75.5	10.905	54.4	8.451
Wang <i>et al.</i> (2019)	60.05	12.12	40.26	7.53
Wang <i>et al.</i> (2023)	89.07	14.91	89.27	10.91



**Figure 5. Forest plot Acupuncture to improve quality of lifep**

The forest plot in Figure 5 shows that acupuncture therapy can improve the quality of life in cases of type II diabetes mellitus compared to other interventions or no intervention and this effect is not statistically significant. Diabetes patients who experienced an improvement in quality of life had an average score of 0.87 units

higher than those with other interventions or no intervention (SMD 0.87; 95% CI= 0.00 to 1.74; p=0.050). The forest plot shows high heterogeneity of effect estimates between primary studies I<sup>2</sup> = 94%; p<0.001. Thus, the calculation of the average estimated effect is carried out using the Random Effect Model approach.



**Figure 6. Funnel plot of acupuncture to reduce HbA1c**

The funnel plot in Figure 6 shows that the distribution of estimated effects is mostly located to the left rather than the right of the average vertical line. Thus, there is no publication bias in the meta-analysis research on the effect of acupuncture therapy on improving quality of life.

## DISCUSSION

Increased blood glucose levels in the body are caused by disorders of the pancreas in producing insulin or the ability of insulin receptors on body cells to be insensitive. Glucose that cannot be carried to the body's cells by insulin will have an impact on cell performance, so that they cannot produce energy according to the individual's needs. A person who experiences diabetes mellitus usually shows various typical symptoms such as feeling hungry/eating a lot (polyphagia), getting thirsty/drinking a lot (polydipsia), frequent urination (polyuria), blurred vision and weight loss (WHO, 2019)

Around 25%-57% of diabetes sufferers use complementary or alternative medicine to treat their disease. Complementary and alternative treatment methods for diabetes include herbs, yoga and acupuncture (Grossman et al., 2018). The systematic review and meta-analysis research in this study raised the theme of the effect of acupuncture therapy on changes in HbA1c in people with type II diabetes mellitus. The intervention in this study was acupuncture therapy.

### **a. Acupuncture to reduce HbA1C**

Glycosylated hemoglobin or HbA1c reflects the average glucose exposure integrated over the half-life of hemoglobin in red blood cells, which is approximately 120 days. Stimulation of acupuncture points can reduce blood glucose levels by regulating the function of the viscera by utilizing the homeostatic mechanism of

the autonomic system through the sympathetic and parasympathetic nerves by stimulating the vagus nerve and stimulating the production of insulin release (Cho et al., 2001) as well as affecting the internal organs of the innervation segments. the same through the dermatome area, involving the central nervous system in the hypothalamus which can repair endocrine disorders and restore pancreatic beta cells (Tian et al., 2018).

The endocrine system and nervous system regulate metabolic activities in the body and both influence each other significantly. Increasing insulin secretion activity can reduce blood glucose levels thereby reducing HbA1c.

In another study by Najafi et al., (2020) which was conducted to determine the effect of acupressure points on fasting blood glucose and glycosylation levels in diabetes patients for 12 weeks, it showed that there was no significant difference between the average blood glucose levels of the three groups before and after the intervention.

There are 8 research articles with a randomized controlled trial design from Taiwan, Iran, Egypt and China as a source of meta-analysis of the effect of acupuncture therapy on reducing HbA1c levels in sufferers of type II diabetes mellitus. The results of research on the forest plot show that acupuncture therapy has a score of reducing HbA1c levels -0.57 units higher compared to other interventions or no intervention, but it is not statistically significant (SMD -0.57; 95% CI= -1.15 to 0.02; p= 0.060).

### **b. Acupuncture to improve quality of life**

Diabetic peripheral neuropathy (DPN) is the most common complication of type 2 diabetes mellitus (Abbott et al in Garrow, 2014). The causes of this condition are not

fully understood, but age, duration of diabetes, and diabetes control have all been shown to be associated with DPN (Abbott et al in Garrow, 2014)

Typical symptoms include burning or shooting pain at night in the legs and feet, indicating interference or damage to small nerve fibers. Symptoms often persist for years, they can decrease sensory nerve conduction velocity (SNCV) and impair sensation or movement and are associated with decreased physical activity, increased fatigue, and sleep problems, which negatively impact quality of life (Zelman et al in Garrow, 2014).

The role of acupuncture in this case is anti-inflammatory by inhibiting the activation of spinal microglia and the release of inflammatory factors TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 to improve peripheral nerve dysfunction (Tang et al, 2020).

Chao et al., (2019) explained that their research aimed to assess the effect of acupuncture on diabetic neuropathic pain. The results showed that acupuncture could significantly reduce the average, worst, and least pain intensity compared with the control group when measured at weeks 6 and 12. However, the quality of life, physical function, and neuropathic symptoms between the acupuncture and control groups did not significantly differ.

There are 5 research articles with a randomized controlled trial study design from England and China as a source of meta-analysis of the effect of acupuncture therapy on improving the quality of life in people with type II diabetes mellitus. The results of research on forest plots show that acupuncture therapy can improve the quality of life in type II diabetes mellitus sufferers by 0.87 units compared to other interventions or no intervention, but this is not statistically significant (SMD 0.87; 95% CI= 0.00 to 1.74; p =0.050).

#### **AUTHOR CONTRIBUTION**

Fatimah Wahyu as the main researcher who chose this topic, carried out searches to collect data in this research.

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The researcher would like to thank all parties who have helped in preparing this article and also thank the database providers PubMed, Science Direct, Google Scholar, Springer Link, BMC and Hindawi.

#### **CONFLICT OF INTEREST**

There is no conflict of interest in this study.

#### **FUNDING AND SPONSORSHIP**

This study is self-funded.

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