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The Prevalence of Depression among Type 2 Diabetic Patients in Malaysia: A Systematic Review and Meta-Analysis

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ABSTRACT

Aims : This review aimed to determine the prevalence of depression among type 2 diabetes mellitus (T2DM) and to compare prevalence estimates obtained using various diagnostic tools and in different regions of Malaysia**.**

Methods: We used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to design the data extraction using the Web of Science, Google Scholar, PubMed, and EBSCO databases. All statistical analysis was conducted with R version 4.1.4. The Egger regression test was used to assess the risk of publication bias, and the pooled prevalence was determined using a forest plot**.**

Results: There were 18 studies included in this meta-analysis, with a total of 7669 participants, and the overall pooled prevalence was 17% (95%CI; 13-23). Depression was most common in Perak and Kedah states, with 36.8% (95%CI; 29.5–44.2) and 28.3% (95%CI; 6.95–66.66), respectively, and DASS-21 was used as a diagnostic tool for depression by eight studies, yielding an overall pooled prevalence of 12.51% (95%CI; 7.15–20.98).

Conclusion: Malaysian diabetic patients have a high prevalence of depression, indicating that T2DM patients are at a risk of depression disorder. As a result, additional research and health education are required.

Keywords: Prevalence, Depression, T2DM, Malaysia

Introduction

Diabetes is defined as a metabolic disease characterized by an increase in the blood sugar level resulting from abnormalities in insulin secretion and insulin action, or a combination of these. It is a chronic medical condition which can affect a person's physical , physiological and mental health [1].Approximately 463 million people worldwide have diabetes, ranging in age from 20 to 79 years old, and this prevalence is expected to increase in the future up to 200 million by 2040, according to the International Diabetes Federation (IDF) [2]. In Asia, particularly the East region, the prevalence of DM was about 36% [3]. Diabetes complications and comorbidities are serious consequences. DM is frequently associated with a variety of complications, such as dyslipidemia, hypertension and cardiovascular disease [4]. Uncontrolled diabetes can lead to microvascular problems like nephropathy, neuropathy, and retinopathy [5] as well as to macrovascular sequelae [6]. People who have diabetes can become depressed and anxious because of the emotional strain that comes from being diagnosed with diabetes and the possible complications and comorbidities that come with it [7, 8].

It is estimated that depression and anxiety in 2015 occurred at rates of 4,4% and 3,6%, respectively, according to the World Health Organization . In 2021, the prevalence of depression disorder in Malaysia was nearly 26% [9]. It was reported that diabetic patients are 10% to 15% more likely to suffer from depression compared to the non-diabetic individuals [10]. Patients who are diabetic are more likely to suffer from anxiety and depression, which can negatively affect their quality of life, as well as have higher medical costs and more complications [11]. As a result, numerous studies have found a link between diabetes and depression disorder. Firstly, in the progression of either disease, as the presence of one may lead in the development of the other, and secondly, in the exacerbation of symptoms. Additionally, co-existence of both diseases has been shown to result in non-adherence to treatment plans [12,13]. Additionally, the literature demonstrates that treating depression improves long-term diabetes management significantly [14].

Several previous studies examined the association between depression and T2DM patients in a numerous of countries e.g Iran by Khaledi, M et al., [15] , Romania by Bădescu, S. V et al, [16], Spain by Salinero-Fort, M. A et al [17] , China by Zhang, Y et al., [18] and Malaysia by Lee, K.W et al , [19]. A recent review article included studies published in the USA and China reported that depression plays a significant role to predict the prognosis of chronic diseases [20]. The prevalence of depression predictors was examined by Shuhaida, M.H.N et al. [21] in T2DM patients attending primary healthcare centers in Kuala Lumpur, Malaysia, and reported a high rate of depression among diabetic patients.

According to one Meta-analysis which included 33 articles and concluded that 41% of depressed patients develop mellitus type I and 32% were at high risk to develop type 2 diabetes [22]. As reported by Radzi, A.M. and colleagues in [23], a cross-sectional study conducted in Kedah, Malaysia found

that 32.1% of diabetic patients suffer from depression. Another research of diabetic patients at a Tertiary Hospital in Kuala Lumpur, Malaysia discovered that more than one fifth (n=60/300) of patients with T2DM experience depression [24].Another study was done in Pulau Penang and Melaka, Malaysia, and found that 26.6%, 40%, and 19.4% of people there had depression, anxiety, and stress [25].

Despite the existence of indicators supporting the prevalence of depression in diabetic patients as well as an accurate estimation of the overall prevalence in Malaysia remains a challenge. The aim of this meta-analysis to identify literature gaps and to establish a solid foundation for future research on the subject by estimating the prevalence of depression among T2DM patients in numerous regions of Malaysia and comparing the differences between various diagnostic tools.

Methodology

Study design

A meta-analysis and a systematic review

Search duration

Data extracted from 1 October 2021 to 15 December 2021 and covered all studies carried out in various Malaysian regions between 2005 and 2022.

Search strategy

This meta-analysis was conducted using all studies published in Malaysia to determine the prevalence of depression in patients with T2DM. The systematic review was carried out by two reviewers (X, and Z) working independently to screen and review all the articles according to the inclusion criteria. Disagreements were resolved through consultation with a third independent reviewer (Y). The search strategy of our structured literature, data extraction , and data selection, all followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26]. The published literature on depression in patients with T2DM was compiled using Medical Subject Headings (MeSH terms) and keywords related to “depression or depressive disorders”, “diabetes, T2DM or diabetic patients” and “Malaysia”, which were combined through the Boolean operator “AND” and “OR. Electronic searches were conducted in the following databases: PubMed, Google Scholar, Scopus, and EBSCO. In PubMed search; (("Depression" [Mesh]) AND "Diabetes Mellitus" [Mesh]) AND "Malaysia / Kuala Lumpur / prevalence" [Mesh]. In EBSCO search; (DE "MENTAL depression") AND (DE "DIABETES" OR "DIABETES 2" DE "ACETONEMIA" OR DE "ALLOXAN" OR DE "ALLOXAN diabetes" OR DE "DIABETES in elderly" OR DE "DIABETES in child" OR DE "DIABETIC foot" OR DE "EXPERIMENTAL diabetes" OR DE "FELINE diabetes" OR DE "GESTATIONAL diabetes" OR DE "GLYCOSURIA" OR DE "INSULIN shock" OR DE "PREDIABETIC state" OR DE "PREGNANCY in diabetic women" OR DE "TYPE 1 diabetes" OR DE "TYPE 2 diabetes" AND DE "TYPE 2 diabetes" AND DE "TYPE 1 diabetes") AND "Malaysia".

Inclusion and exclusion criteria

The title and abstract screening for eligibility was carried out independently by the authors. Following that, the full-text screening was carried out based on the inclusion and exclusion criteria listed below.

Inclusion criteria

The search for literature was limited to: aadult patients over the age of 18 , studies in which patients with type 2 diabetes were diagnosed, English-language articles, research into the association between the prevalence of depression and diabetes mellitus, and only Malaysian studies were conducted.

Exclusion criteria

Patients under the age of 18, studies involving patients with T1DM and gestational diabetes, randomized controlled trials.

Data extraction, Synthesis and Quality Assessment

The primary data extraction form included the study title, ID number, and population type. To begin, studies were identified and imported into Rayyan QCRI, a systematic review web app citation manager [27], and the software Endnote was used to remove the duplicate studies. Each study article was thoroughly reviewed, and the following information was recorded: the title of the study, the first author, the article ID number, the time frame, the study design, the population type, and the characteristics of the patients (age mean, age range, and gender), medical condition, region, depression prevalence, and diagnostic tool

Statistical analysis

The pooled proportions and 95% confidence intervals were calculated using R version 4.1.4. We used random-effects models to reflect the differences shown across studies, and the Q and I2 statistics to assess heterogeneity.between studies. The combined prevalence is expressed as an event rate (i.e 0.60) but interpreted as prevalence (i.e 60.0%).The inter-study heterogeneity was estimated using the Cochrane's Q test [28] and the Higgins I^2 statistic [29] ($I2 > 50\%$ was considered statistically significant). For meta-regression analysis, all the outcomes are considered significant at $p < 0.05$ to detect the effect of sample size and publication year. The Egger's regression and visual inspection of funnel plots were used to assess publication bias [30].

Quality Assessment [NOS 32]

For coding cross-sectional studies, the Newcastle-Ottawa Scale [31] was used to assess the risk of bias in all studies. It is divided into three sections (Selection, Comparability, and Outcome), and each section has seven questions with a total of ten stars. Finally, a critical evaluation was performed on the systematic reviews that met the inclusion criteria. The sum of the disagreements has been chosen and resolved to assent.

Results

Search Results

Figure 1 depicts the study selection and identification process. From the systematic search, a total of 229 studies were identified. In 229 of these studies, 11 duplicate data were found and removed. Following a review of the titles and abstracts, 107 irrelevant studies (non-English articles, abstracts, and age <18), were eliminated. An additional 75 articles were excluded due to review articles after an examination of the full texts of the remaining studies, clinical trials, incorrect outcomes, and lack of article access. After that, a total of 18 studies were deemed eligible for inclusion in the final analysis.

Table 1 shows the characteristics of the included studies. This review included 18 studies with a total of 7869 patients. Among 18 studies, five of them [19, 32, 33,34,35] were conducted in Selangor, four studies [9, 24,11,36] were in KL, two studies were in Kedah [23, 37 two studies [38, 39] werein Pahang, one study [40] was in Sabah, one study [41] was in Perak, one study 25 was in Melaka, one study [42] was in Negeri Sembilan, and one study 43 was in Penang. All of the studies were cross-sectional in nature and were carried out in a hospital setting. The studies with the largest and smallest sample sizes were conducted in Klang Valley [35] and Kuantan collectively [38] respectively. Eight articles used the DASS-21 as a diagnostic tool of depression, four articles used the HADS, two articles used the PHQ-9, another two articles used the BDI-II, only one article used the CES-S, and only one article used the DSM-IV.

Depression among T2DM patients in Malaysia

The total pooled prevalence of depression was calculated using the random-effects model and revealed substantial heterogeneity among the articles. As a result, the analyses were conducted using a random-effects model. The pooled prevalence of depression among patients with type 2 diabetes reported by 18 studies was 17% (95%CI; 13- 23), with significant inter-study heterogeneity (I^2=97%, P < 0.001) (Figure 2).

Subgroup analyses

Region

To assess the possibility of heterogeneity among studies, subgroups analysis by study region was performed. Perak had the highest estimated prevalence of depression at 36.8% (95 % CI: 29.5-44.2), followed by Kedah at 28.3% (95 % CI: 6.95-66.66), while the lowest prevalence of depression was found in Hulu Selangor 4.3% (95%CI; 26.6- 69.2) , and in Sabah 4.5 % (95%CI; 27.5- 73.8) (Figure 3).

Diagnostic Tools

DASS-21 and HADS-D were the most commonly used diagnostic tools to diagnose depression, with an overall prevalence of 12.51 % (95%CI; 7.15-20.98), and 25.23% (95%CI; 12.74-43.83), respectively, followed by BDI-II, which had a total prevalence of 20.49% (95%CI; 5.16-54.95). Furthermore, the CES-D-10 was the least frequently used diagnostic tool, with only one study reporting a prevalence of 16.25% (95%CI; 12.6- 20.71) (Figure 4).

Publication bias

Due to the lack of asymmetry, visual inspection of the funnel plot (Figure 5) revealed no publication bias. The presence of publication bias was investigated using funnel plots and the Egger's test, which revealed no evidence of publication bias. The funnel plot shows that each point represents a separate article and has an asymmetrical distribution that indicates the presence or absence of publication bias [30].

The effect size of each study was plotted against the standard error, and a visual inspection of the funnel plot revealed no asymmetry, with five studies on the left side of the line, six studies on the right side, and

the rest distributed across the plot representing the pooled prevalence (Figure 5). Egger's test was also used to look into publication bias. The test revealed that there was no evidence of publication bias (P=0.32).

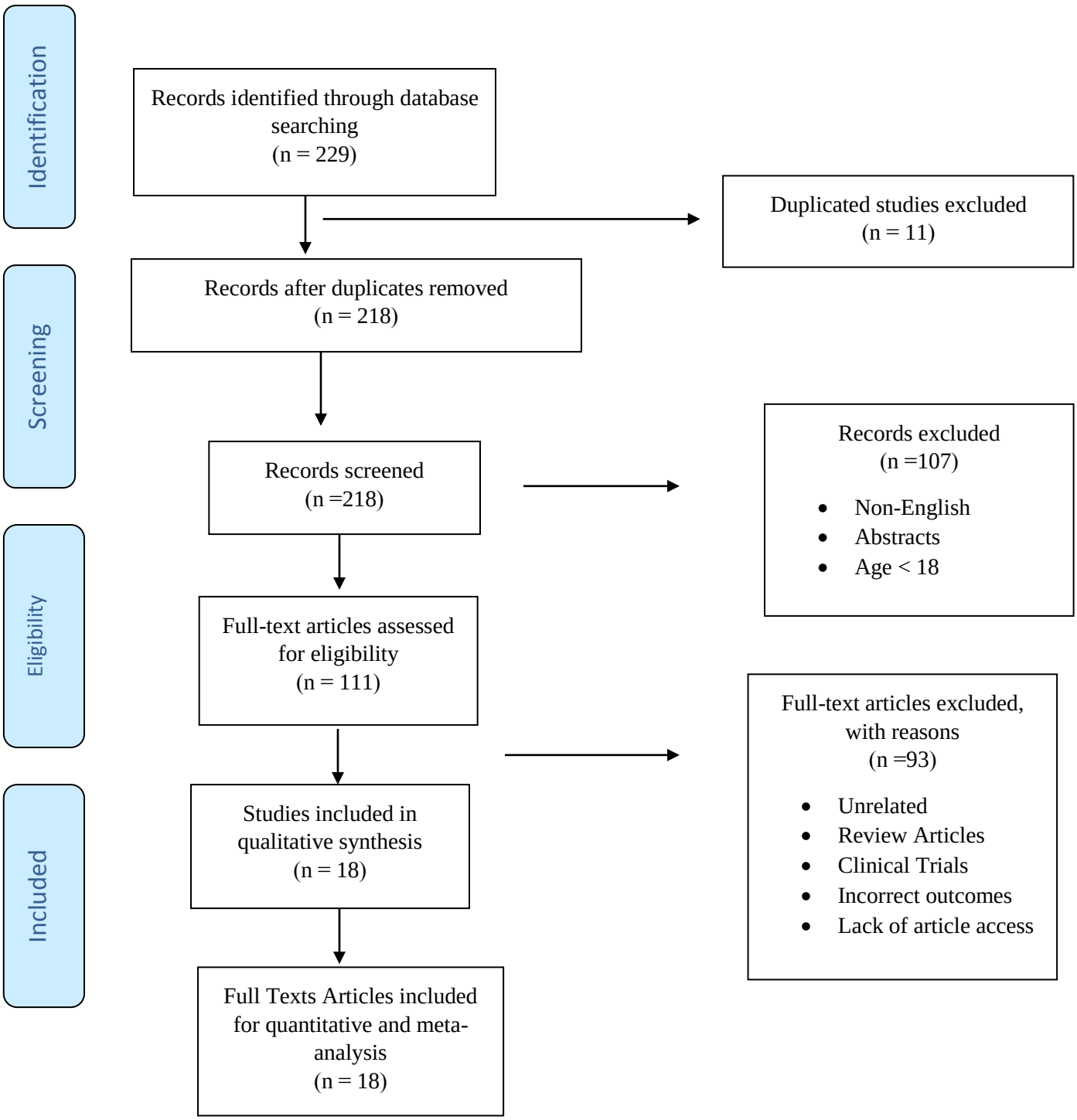

Figure 1 : PRISMA flowchart of study selection for meta-analysis of prevalence of depression among diabetic patients in Malaysia from 2005-2021

Table 1. Characters of the included studies, and corresponding NOS scores

Study (Author, year) [Ref]	Study design / Setting	Sample Size	Age (mean ± SD)	Males (n (%)	State	Depression Assessment	Cut-Off score	Prevalence (% (95% CI)	NOS score
Miskan, M. and Ambigga, K., (9)	Cross-sectional/ Hospital-based	382	47.9±11.4	44%	KL	HADS-D	≥8	26% (22 - 31)	9
Lee, K.W et al , (19)	Cross-sectional/ Hospital-based	526	32.4±4.9	50%	Kuala Selangor	DASS-21	>10	12% (9 - 15)	8
Woon, L.S.C et al., (24)	Cross-sectional/ Hospital-based	300	63 ± 16	158 (52.7%	KL	BDI-II	>10	20% (16 - 25)	8
Shuhaida, M.H.N et al. (21)	Cross-sectional/ Hospital-based	338	60.9±10.3	126 (37.3%)	KL	DASS-21	>9	15.4% (12 :20)	9
Radzi, A.M et al. (23)	Cross-sectional/ Hospital-based	511	64.5±7	53.8%	Kedah	M-GDS-14	>5	32.1% (28 - 36)	9
Tohid, H et al. (40)	Cross-sectional/ Hospital-based	331	60±14	47.4%	Sabah	DASS-21	>9	4.5% (3 - 7)	8
Md Aris, M. A. (38)	Cross-sectional/ Hospital-based	103	58±8.4	49.5%	Kuantan (Pahang)	DASS-21	>5	12.6% (7 - 21)	9
Devarajooh, C et al., (32)	Cross-sectional/ Hospital-based	371	55.33 ± 10.9	38%	Hulu Selangor	PHQ-9	>10	4.3% (2 - 7)	8
Husin, H et al. (41)	Cross-sectional/ Hospital-based	164	56±8	43 (53.8%)	Perak	HADS-D	≥8	36.8% (29 - 44)	9
Chew, B.H et (33)	Cross-sectional/ Hospital-based	752	56.9 ± 10	43.4%	Selangor	PHQ-9	>5	41.7% (38 - 45)	8
Hashim, N.A., et al., (36)	Cross-sectional/ Hospital-based	204	57.8±15.1		KL	DSM-IV		15.7% (11 - 21)	8
Tan, K.C et al., (25)	Cross-sectional/ Hospital-based	320	57.1 ± 10.84	150(46.8%)	Melaka	DASS-21	>9	26.6% (22 - 32)	8
Radeef, A.S et al., (39)	Cross-sectional/ Hospital-based	200	40.3±15.6	91 (45.5%)	Pahang	DASS-42	>10	13.5% (9 - 19)	8
Ganasegeran, K et al., (34)	Cross-sectional/ Hospital-based	169	36.9±15.9	99 (58.6%)	Selangor	HADS-D	≥8	31.4% (24 - 39)	9
Kaur, G et al., (35)	Cross-sectional/ Hospital-based	2508	56.6±10.67	975 (38.9%)	Klang Valley Selangor	DASS-21	>9	11.5% (10 - 13)	8
Hasan, S.S et al., (42)	Cross-sectional/ Hospital-based	320	50.±7		Seremban Negeri Sembilan)	DASS-21 + CES-D-10	>9 >11	16.25% (12 - 21)	8
Mohamed, R, et al . (43)	Cross-sectional/ Hospital-based	260	50.9±6.3	124 (47.7%)	Penang	HADS-D	≥8	12.3% (9 - 17)	8
Khai, N.T., et al. (32)	Cross-sectional/ Hospital-based	110	40±9	40 (44%)	Kedah	BDI-II	≥13	22% (15 - 31)	8

HADS-D= Hospital Anxiety and Depression Scale , **DASS-21**= Depression Anxiety Stress Scales – Short Form , **BDI-II**= Beck Depression Inventory , **PHQ-9**= Patient Health Questionnaire**,** **CES-D-10**= Center for Epidemiological Studies-Depression, M-GDS-14= The Malay version of Geriatric Depression Scale, **NOS** = Newcastel Ottawa Scale

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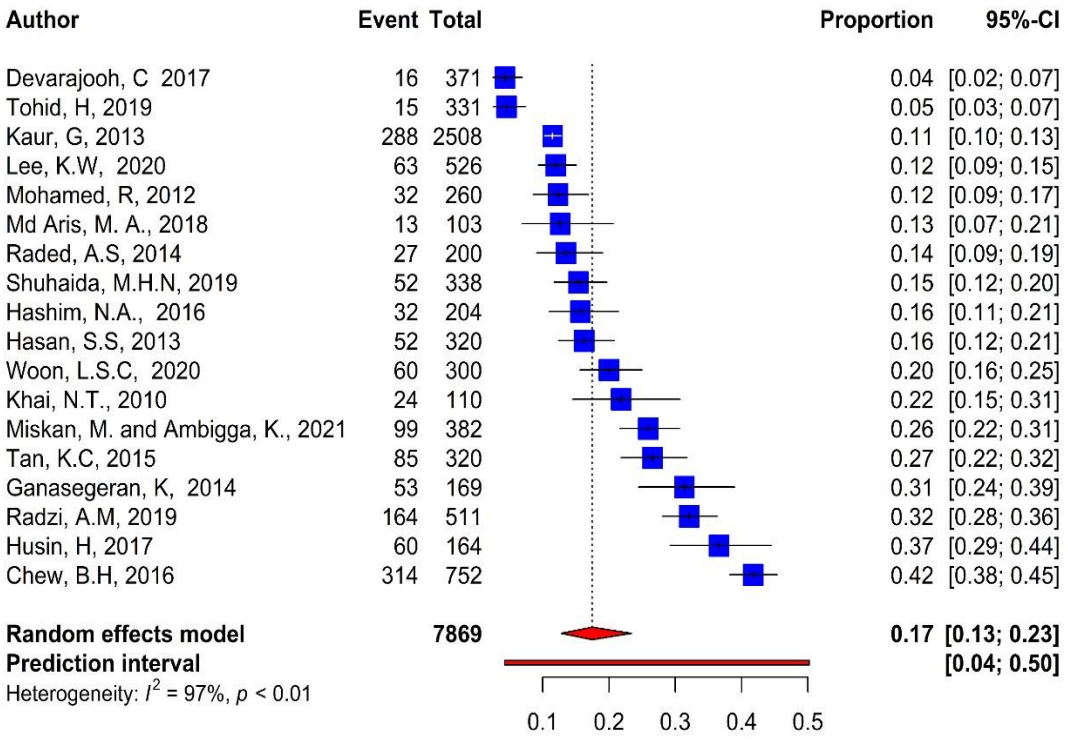

Figure 2: Prevalence of depression in the studies based on the random effect model

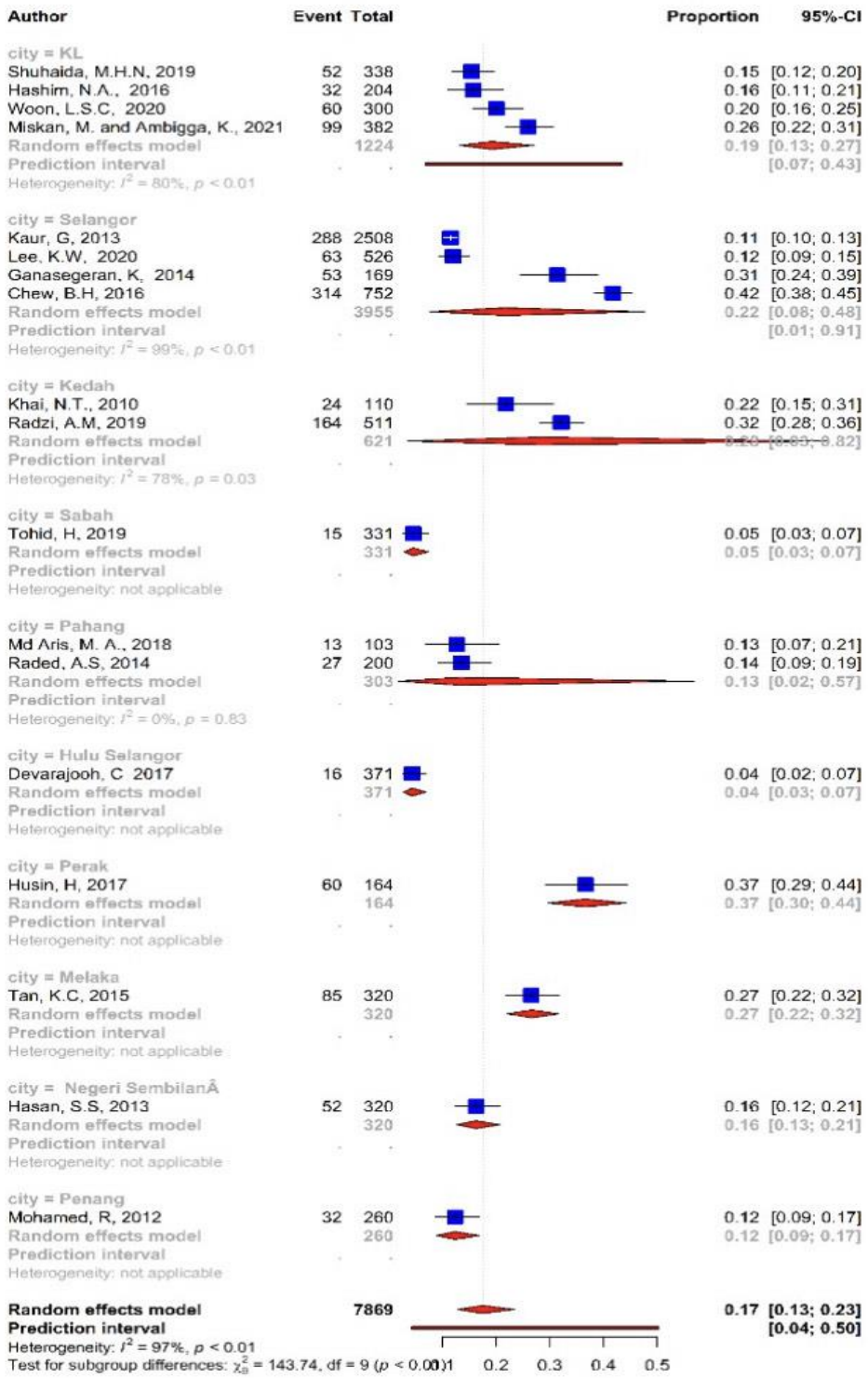

Figure 3: Prevalence of depression among various Malaysian regions based on the random effect model

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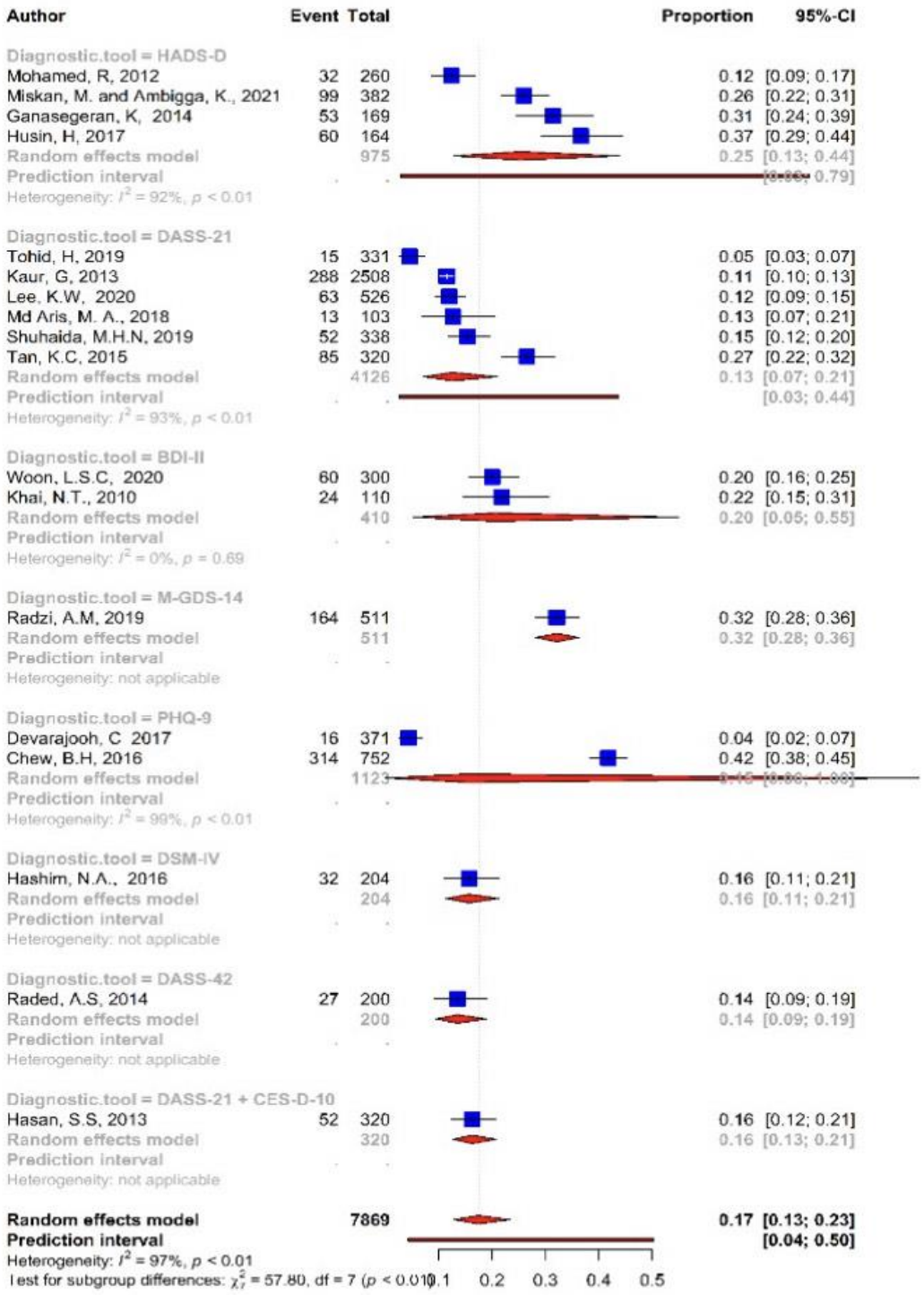
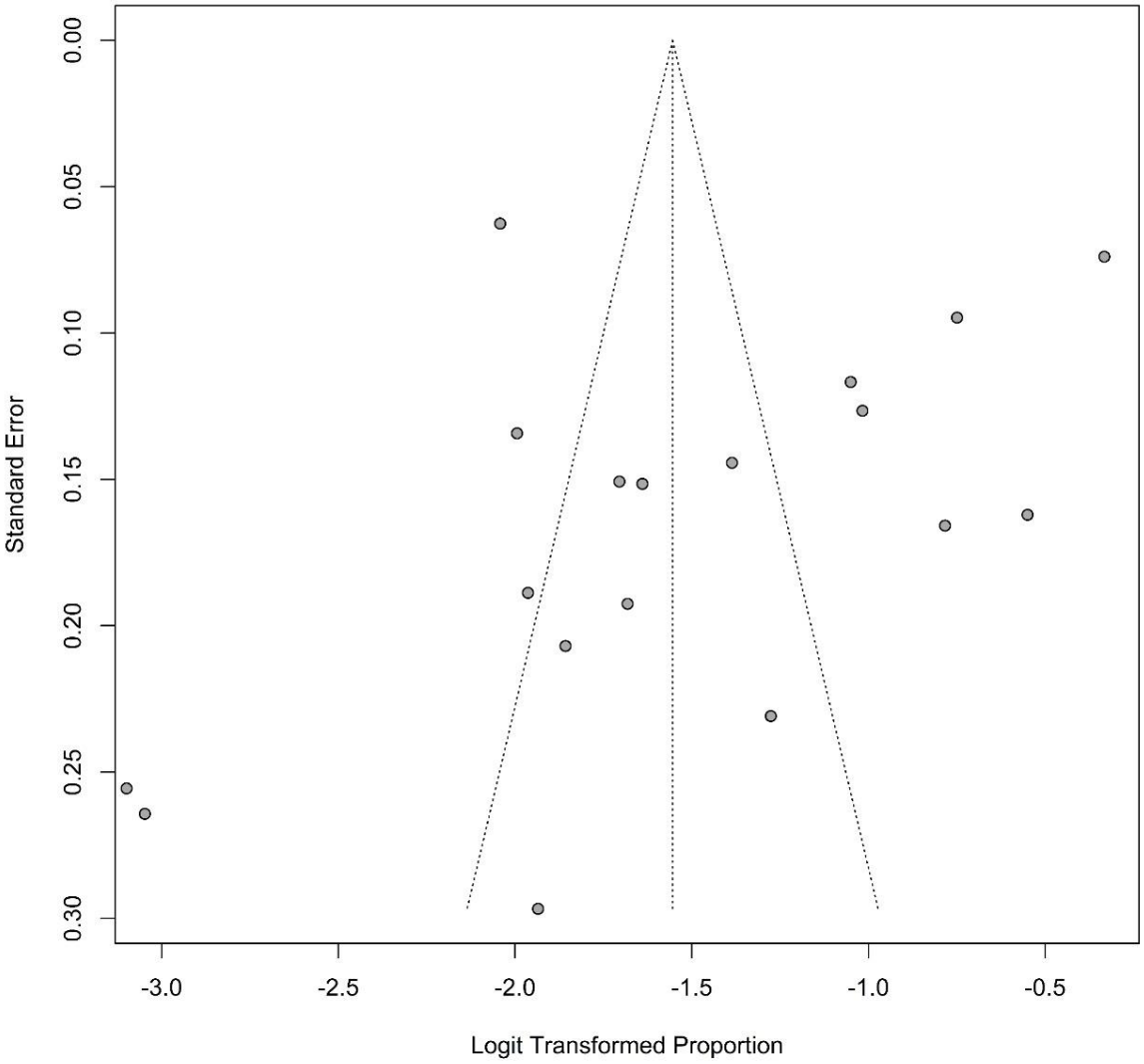


Figure 4 : Prevalence of depression in the diagnostic tools based on the random effect model

Figure 5: Funnel plot of prevalence of depression among studies



Discussion

Depression is a common comorbid disorder among diabetic patients [4]. Diabetes and comorbid depression are linked to an increased risk of death and mortality [45]. Because there is a lack of data on depression comorbidity in patients with chronic diseases in general and diabetic patients in particular, this meta-analysis predicts the overall pooled prevalence of depression among Malaysian type 2 diabetic patients.

The research results of these 18 studies, which included 7869 patients, indicated that the overall pooled prevalence of T2DM was 17% (95%CI; 13- 23). This finding is similar to one previous meta-analysis conducted by Ali, S et al., [46] which included 51331 diabetic patients and reported a pooled prevalence of depression of 17.6%.

On the other hand, our findings are lower than three other meta-analysis studies conducted in Ethiopia by Teshome, H.M et al., [47], Saudi Arabia by Alanazi, E.O et al [48], and Iran by Khaledi, M et al., [49]

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which found overall prevalence of depression of 39.73% (95% CI: 28.02 – 51.45) , 38.06% (95% CI: 31 – 45), and 28% (95% CI: 27 – 29) respectively.

Numerous studies conducted in other countries contradicted our findings, including Sun, N., et al [50], who performed a cross-sectional study in China and noted a depression prevalence of (56.1%). Some other cross-sectional studies conducted in Vietnam included 412 elderly diabetic patients and confirmed a depression prevalence of 79.4% [51, 52] completed a cross-sectional study of about 3978 diabetic patients in New Zealand and determined that depression was prevalent (18%). Similarly, Nanayakkara, N et al. [53] enrolled data from Australian National Diabetes Audit (ANDA) of 2552 adults with T2DM and discovered that depression was prevalent (29%). A previous meta-analysis conducted by Ali et al [46] found a global prevalence of depression (17.6%) among patients with T2DM.

According to this meta-analysis, Perak state in Malaysia has the highest prevalence of depression among T2DM, at 36.8% (95% CI; 29.5-44.2), followed by Kedah state at 28.3 % (95% CI; 6.95-66.66). Furthermore, the state of Hulu Selangor had the lowest prevalence 4.3% (95%CI; 26.6- 69.2). Husin, H. et al. [41] reported that their high rate of depression is associated with sexual impotence and illiteracy.

Due to the lack of national investigation into this subject, the interaction between these studies and other literatures cannot be determined. We propose that differences in glycemic control, education, socioeconomic status, healthcare services, and other socio-cultural factors explaining the variation among Malaysian states. Nonetheless additional population based research is needed to confirm the regional differences in depression prevalence among diabetic patients and to assess the factors that contribute to these differences. Additionally, this could aid in the development of strategies for primary prevention.

Our findings indicated that the most frequently used diagnostic tool in studies was the DASS-21, which had an overall prevalence of 12.51 % (95%CI; 7.15-20.98), while only one study used the CES-S to diagnose depression comorbidity 16.25 % (95%CI; 12.6- 20.71). This finding contrasted with those of De Joode, J.W et al. [54] and Alanazi, E.O et al. [48] who reported that PHQ-9 was the most frequently used diagnostic tool in their meta-analysis to approximate the prevalence of depression in type 2 diabetic patients.

Strength and limitation

Our search was based on the PRISMA guidelines, and we were able to locate all studies that had the potential to be included. We used subgroup analyses to compare and contrast the results of each study's geographical region and the diagnostic tools used.

Despite the fact that our ability to investigate numerous differences was limited by a lack of available data on the causes of depression in diabetic patients and across regions, our pooled estimates indicated a significantly increased risk of depression among patients with T2DM in comparison to the general population and compared different regions of Malaysia and diagnostic tools for depression.

Research methodology was varied, with a wide range of diagnostic tools and cut-off points used to interpret the wide range of

heterogeneity found in our results. Finally, our review was limited to diagnostic tool and state sub-groups and excluded other sub-groups such as DM duration, complications, co-morbidity, and stressful life events.

Conclusion

The systematic review and meta-analysis revealed a high prevalence of depression in type 2 diabetic patients across Malaysia's different states. Depression prevalence varied by region in the country; Perak state had the highest prevalence, followed by Kedah state, while the Sabah and Hulu Selangor states had the lowest prevalence. Additional research is required to ascertain the precise causes of these differences. Moreover, health education provided by healthcare professionals at all levels should assist T2DM patients who are experiencing mental health difficulties.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Disclosure statement

Nil

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