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Leveraging Internet+ for diabetes medication treatment: A meta-analysis

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Abstract. Background Chronic disease diabetes is highly prevalent. The use of community or family health care to control diabetes will be hindered by problems such as lack of resources. The "Internet+" model, especially telemedicine, has the potential to improve treatment compliance and blood sugar control. More research is required to assess the effects of pharmaceutical services within this framework on the management of diabetes. **Methods** Computer search of CNKI, Wanfang, PubMed, VIP Database, Web of Science, Embase (To Augest 2023). It compared telemedicine with routine care of diabetes. The main results included in the study were reported HbA1C at three time points and three different intervention. **Result** Out of 470 citations, 12 eligible RCT were identified (n=1558). All remote medical studies achieved a significant reduction in HbA1C during the follow-up period, but it varied with intervention time and measures. **Conclusion** Compared with routine care, it was found that with remote medical intervention, the patient's HbA1C were significantly improved. Compared to telephone intervention and intelligent devices, pharmaceutical services based on the Internet model have shown better results. In addition, the study also found that the efficacy of this intervention continuously improves over time in the short term. However, if the intervention time exceeds 1 year, the efficacy will gradually decrease.

Keywords: Diabetes, Telemedicine, Pharmaceutical Care.

1. Introduction

T2D, accounting for around 90% of the worldwide cases of diabetes, affects a staggering 537 million individuals, necessitates extended drug administration and individualized healthcare services due to its prevalence as a chronic ailment [1]. By 2040, there is a projected significant increase in the global prevalence of diabetes, with the number of adults affected by the disease projected to exceed 700 million, marking a growth of more than 50% from the current 463 million [2]. Worryingly, the rapidly increasing trend of illness among children and young people (under 40 years old) [1]. Hence, timely identification and proactive disease control play a vital role in averting and minimizing the adverse effects of microvascular and macrovascular complications, while also alleviating the mortality burden.

Community pharmacies in England serve as the most commonly visited primary care facility by NHS patients, around 90% of the population is estimated to have convenient accessibility within a 20-minute walking distance [3]. At present, the ability of grass-roots or community management of diabetes is the key link to change the status of diabetes prevention and control in the context of hierarchical diagnosis and treatment. In the current community management of diabetes in grass-roots medical institutions,

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there are insufficient investment in chronic disease prevention and treatment, insufficient personnel and equipment, insufficient training of chronic disease management staff, and poor compliance of diabetes patients [4]. The failure to effectively control the blood sugar level of diabetes patients through community or family medical means may increase the risk of a series of diabetes complications and other health problems.

With the rapid development of the Internet, the Internet plus model has gradually been applied to pharmaceutical services, providing more convenient and efficient treatment for diabetes patients. Telemedicine refers to the utilization of telecommunications for the provision of healthcare services, encompassing interactive, consultative, and diagnostic services [5]. Remote diabetes medical intervention measures can include simple SMS reminder system or more complex network service interface. Through these interfaces, patients or family members (uploaded by medical staff during hospitalization) can upload blood glucose levels measured using home blood glucose meters and other correlated information such as medical history, drug consumption, and dietary patterns. Healthcare professionals have the ability to access this data and offer guidance regarding modifications in medication and lifestyle choices. Remote medicine can help patients monitor blood sugar and various physical signs, and improve their self-management abilities, thereby improving their compliance and quality of life [6].

The impact mechanism of pharmaceutical services under the Internet plus mode at home and abroad on the effectiveness of diabetes treatment includes information sharing and transmission, remote monitoring and intelligent equipment, multidisciplinary collaboration and team management, patient education and self-management. These mechanisms can improve the treatment compliance and blood sugar control level of diabetes patients and reduce the incidence of hypoglycemia and other complications. However, the current research still has some limitations. To better assess the influence of pharmaceutical services within the Internet plus framework on diabetes treatment, it is imperative to enhance the research design and refine the selection of samples.

Previous reviews describing telemedicine's role in diabetes management have been published [7]. However, some reviews only analyze that telemedicine has a positive impact on diabetes control [8] or focus on specific types of telemedicine, such as intelligent devices [9]. In recent years, the rapid progress in this field has led to the emergence of numerous novel clinical trials and the introduction of more advanced and innovative intervention strategies. Through systematic review, quantitative and qualitative synthesis of RCTs, we compared the different effects of telemedicine and conventional nursing based on the impact of HbA1C levels on the quality of life in individuals with diabetes mellitus.

2. Methods

2.1. Literature search

Computer search of CNKI, Wanfang, VIP Database, PubMed, Web of Science, Embase. The search terms are "Pharmaceutical care", "Diabetes", "Internet", "Pharmaceutical services", and all retrieved literature is manually screened. We conducted the search from the inception of the database until August 2023. To conduct the search, both Chinese and English databases were utilized, with a combination of relevant keywords and additional terms related to the topic. The search was performed separately for each language.

This article has retrieved a total of 470 articles: 9 articles from CNKI, 9 articles from Wanfang Database, 101 articles from PubMed Database, 56 articles from VIP Database, 66 articles from Web of Science Database, and 229 articles from Embase Database.

2.2. Criteria for inclusion and exclusion of literature

2.2.1. Inclusion criteria. Type of study: (1) Randomized controlled trial (RCT). (2) Subjects: According to the diagnostic criteria for diabetes recommended by the World Health Organization, patients diagnosed with diabetes were $\geq$ 18 years old. (3) Intervention measures: in the intervention group,

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patients received services under the “Internet plus+pharmaceutical service” mode implemented by pharmacists and (or) medical teams, including medication education, individualized medication, diet guidance, disease education, telephone follow-up and other related contents. (4) Outcome indicators: The outcome indicators are HbA1C, FBG, blood pressure, TG, TC, LDL-C, HDL-C ,SDACA, A-DQOL, BMI, etc.

Criteria: (1) Trials that were not randomized and controlled (non-RCTs) ;(2) Review literature and repetitive publications; (3) Literature with low quality or inability to extract outcome indicator data.

2.3. Literature selection and Extraction of data.

The researcher assesses the titles and abstracts of the literature, eliminating those that are clearly inappropriate. For potentially eligible literature, a thorough reading of the full text is conducted to determine its inclusion. Extract data from literature that ultimately meets the inclusion and exclusion criteria, including first author, publication year, sample size, intervention measures, research object, duration of intervention and outcome measures.

2.4. Literature quality evaluation.

All literature will be evaluated by evaluators according to the evaluation criteria of the Cochrane Version 5.4 system evaluation manual for randomized controlled trials. The evaluation content of this tool includes: (1) whether to achieve random sequence; (2) Whether to achieve hidden allocation; (3) Whether to use blind methods (including blinding the research subjects, researchers, and evaluators of results); (4) Whether the data is complete (whether there are reports of dropout or dropout cases and reasons for dropout); (4) Whether to selectively report research results; (6) Are there any other biases. The evaluator makes a high degree of bias, low degree of bias, and unclear judgment for each item. If the literature does not meet any of the aforementioned criteria, it is highly likely to be biased and will be excluded from the review

2.5. Statistical Methods

Data analysis was conducted using RevMan5.4. For continuous variable data, if the intervention methods used are inconsistent, use SMD (standardized mean difference) to represent and calculate the 95% confidence interval (CI); When conducting subgroup analysis, MD (difference in means) was used. Heterogeneity test, if P-value$>$0.1 and $I^2<50\%$, it suggests homogeneity among the studies. In such cases, a fixed effects model is selected for the meta-analysis. Conversely, if P-value$<$0.1 and $I^2>50\%$, it indicates heterogeneity among the studies. Subgroup analysis will be performed to investigate potential factors contributing to heterogeneity. To maintain consistency in clinical characteristics, any notable deviations will be excluded, and a random effects model will be utilized for the meta-analysis. In cases where the P-value is less than 0.1 and the source of heterogeneity cannot be identified, only qualitative analysis will be conducted.

For the main outcome indicator HbA1C, subgroup analysis was conducted based on the patient’s baseline characteristics (age, gender, and course of disease), intervention time, inclusion age, and intervention method to investigate potential sources of heterogeneity.

3. Results

3.1. Literature search results

The initial search yielded 470 relevant literature, including 396 in English and 74 in Chinese. The researcher conducted a deduplication process using EndNote, resulting in a total of 397 unique articles. Upon reviewing the titles and abstracts, 355 articles were excluded as they exhibited significant disparities with the predefined inclusion criteria. Following a thorough examination of the complete texts and conducting quality evaluations, 20 studies with incomplete data, low literature quality, and inconsistent outcome indicators were excluded. In the end, there were 12 [10-21] trials with complete and reliable data on HbA1C, which were included in the data analysis, including 5 in English and 7 in

Chinese. The study included a total of 1558 participants, with 778 individuals in the experimental group and 780 individuals in the control group (**Figure 1**).

3.2. Table of basic features included in the literature

Extract the following information from the literature (**Table 1**): the experimental features, the study details, including the study name, year, country, study design, duration, and sample size, will be recorded. Additionally, patient characteristics such as age, sex, and duration of diabetes will also be documented. And the results (HbA1c, FBS, SBP, DBP, weight (kg and BMI)).

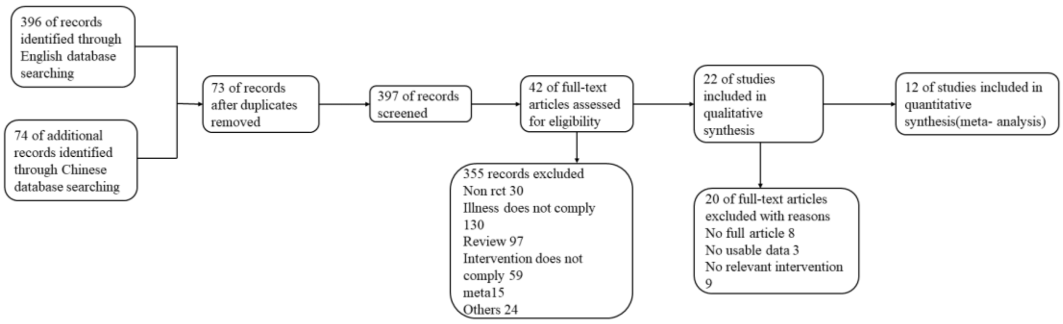

Figure 1. Diagram of the literature search procedure.

Table 1. Detailed information of the included literature.

Number	Author/Year	Number (in/con)	Duration of intervention	Intervention measures	Research object	Outcome indicators
1	Aguiar, P. M.,2018	40/40	2012.9-2014.4	Clinical pharmacist service, face-to-face or phone consultations (health education-related issues)	Type 2 diabetes, aged 40–79 years A1C level ≥ 7.0%.	AHEI
3	Crowley, M. J.,2016	25/25	2013.12-2014.4	Telemonitoring, medication management, self-management support, and depression management	Type 2 diabetes with maintenance of HbA1c continuously >9.0% for >1 year	AHI
5	Jiayu, 2022	100/103	2018.3-2019.3	Telephone, WeChat, medication education, medication exercise and adverse reaction reminders	≥40 years old, Proficient in using mobile WeChat	ABCKJR

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Table 1. (continued).

7	Lee, J. Y.,2020	120/120	2015.4-2016.6	Home gluco-telemonitors, self-management	Type 2 diabetes, aged 18~75 years oldHbA1c levels of ≥ 7.5%~11.0%	ABOGHKM
8	Limin,2018	65/64	2016.3-2016.8	Based on internet APP medication, diet, and exercise consultation management	Type 2 diabetes; Patients receiving initial insulin treatment	ABCFKM
9	Lu, Z.,2021	60/60	2019.1-2019.12	Mobile clinical pharmacy software, drug adjustment and simplification plan	(1) T2DM and HbA1c 7–10.0%; (2) age 18~75 years	ABHP
12	Qin,2023	90/90	2021.1-2022.1	WeChat phone health education promotion, check-in learning, and phone follow-up	Diabetes patients with definite diagnosis; Age 18-70 years old; hospitalization>10 days	ABFNJ
14	Rong, 2021	50/50	2019.1-2020.6	Implement nursing plans, nutritional interventions, health knowledge training, discharge blood glucose management	Type 2 diabetes	ABQK
16	Sarayani, A.,2018	50/50	2013.6-2015.1	Phone calls, drug therapy problems	Type 2 diabetes, use of oral hypoglycemic medications, and HbA1c ≥ 7%	AGIK

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Table 1. (continued).

19	Xiuqing, 2022	120/120	2021.2-2022.2	Telephone, WeChat, chronic disease education, medication exercise and adverse reaction reminders, follow-up every three months	≥40 years old; Proficient in using smartphones	ABCKR
21	Yanling, 2021	41/41	2018.1.1-2019.6.30	Medical health management platform monitoring blood sugar, knowledge popularization, and reasonable diet	Type 2 diabetes; disease≥ 10 years; Age 18-70 years old; HbA1c≥6.5% in the past 3 months	ABCQJ
22	Yanqing,2021	50/50	2019.5-2019.8	Technical optimization of medical maintenance management mode, blood glucose monitoring, diet and exercise education	Type 2 diabetes patients; Type 2 diabetes was ≥ 2 years; ③age ≥ 60~≤ 80 years old	ABCK

Ps:Outcome indicators: A:HbA1c; B:Fasting blood glucose (FBG); C:2hpG; D:HDL-C; E:LDL-C; F: weight (kg or BMI); G: lipids; H: blood pressure; I: medication adherence; J: Satisfaction with the Medicines Service; K: diet, exercise , diabetes self-efficacy; L: Knowledge of diabetes and drugs; M: Quality of life score; N: Humanistic indicators such as psychology and attitude ; O:renal function (eGFR) ; P: Adverse drug reaction (AdR); Q: TC; R: TG; S: Complication; T: Incidence of adverse drug reactions; U: Compliance; V: Mortality; W: Diabetes Medication Adherence Behavior.

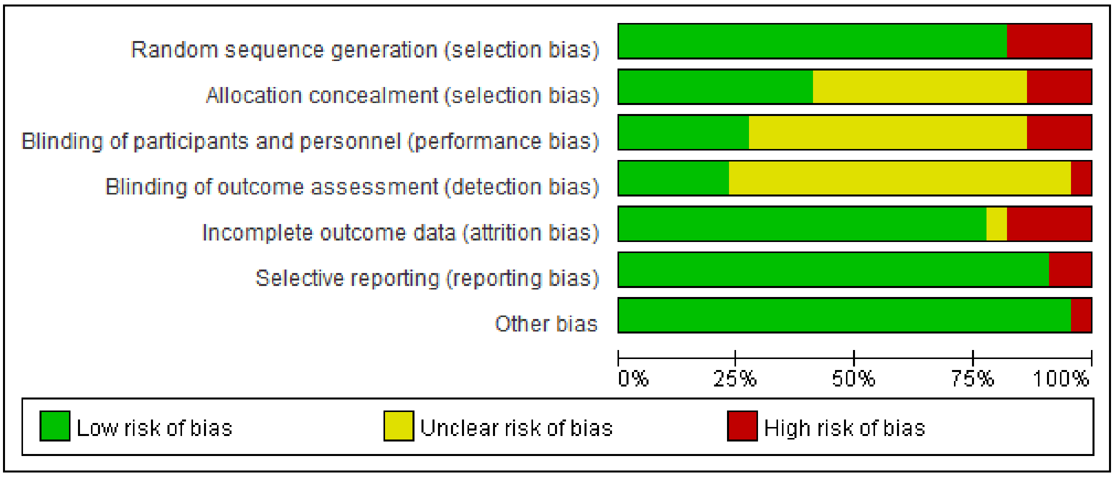

Figure 2. Risk assessment of internal bias.

3.3. *Risk assessment of internal bias in research*

Due to the impracticality of implementing blind treatment in remote medical interventions, all trials were conducted in an open-label manner, with participants being fully aware of their assigned treatments. Therefore, each experiment contains at least one bias risk factor **(Figure 2)**.

3.4. *Results*

3.4.1. HbA1c. Among the 12 studies included, HbA1c was utilized as an assessment parameter. The heterogeneity test yielded a significant result (P<0.00001, I^2=75%), indicating substantial variation among the studies. In the meta-analysis, a random effects model was utilized, and the findings indicated a statistically significant difference in HbA1c levels between the two groups [SMD=-0.55, 95% CI (-0.76, -0.35), P<0.00001].

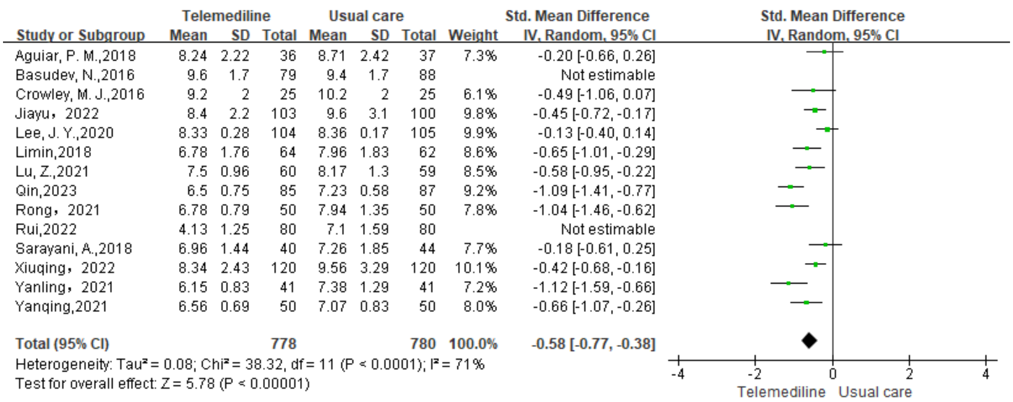

Figure 3. Meta-analysis results for HbA1c.

Conduct subgroup analysis on HbA1c at different follow-up times.4 studies were followed up for one year, and significant improvements in HbA1c levels were observed in the experimental group, with statistically significant differences [MD=-0.87, 95% CI (-1.19, -0.56), P=0.046].The follow-up time of 4 studies was 5-8 months, with MD=-1.01,95% CI (-1.33, -0.69), P=0.17. The follow-up period for more than one year was conducted in four studies with MD=-0.07,95% CI (-0.13, -0.01) and P<0.00001.

A statistically significant difference was observed, with significantly lower levels of HbA1c in the experimental group compared to the control group (**Figure 3**) .

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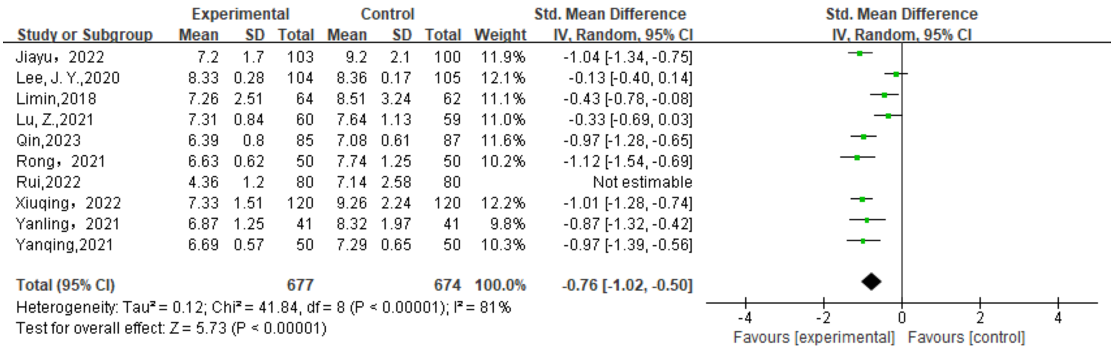

Figure 4. Meta-analysis results for FBG.

3.4.2. Fasting blood glucose (FBG). A total of 9 studies were included, evaluating FBG as an indicator. The heterogeneity test yielded a P-value＜0.00001 and I²=81%, denoting significant heterogeneity among the studies. Hence, a random effects model was utilized for the analysis, revealing a significant reduction in FBG levels in the experimental group compared to the control group, with a statistically significant difference [SMD=-0.76, 95% CI (-1.02, -0.5), P<0.00001] (**Figure 4**) .

3.4.3. 2hPBG. Including 4 studies, the evaluation indicator for analysis was 2hPBG. The heterogeneity test revealed a P-value＜0.00001 and I²=0%.No significant heterogeneity was observed among the included studies, indicating a lack of substantial variation. Therefore, a random effects model was selected for the analysis. The meta-analysis results demonstrated a significant reduction in 2PBG levels in the experimental group compared to the control group, with a statistically significant difference [SMD=-0.88, 95% CI (-1.04, -0.72), P<0.00001] (**Figure 5**) .

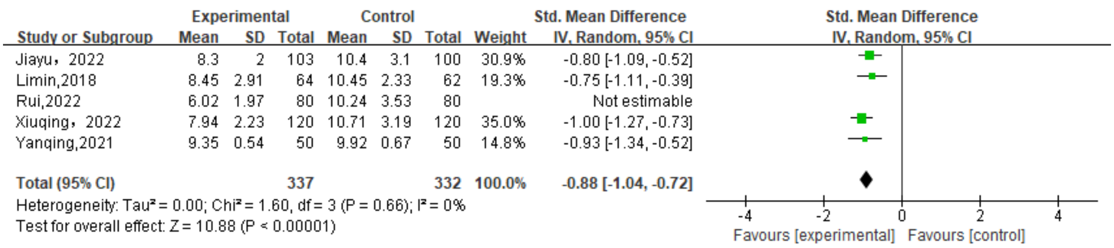

Figure 5. Meta-analysis results for 2hPBG.

3.4.4. Publication bias and sensitivity analysis. This study used HbAlc as an evaluation indicator. To investigate the origins of heterogeneity, we excluded the combined indicators that exhibited significant heterogeneity. Sensitivity analysis and meta-analysis were then conducted on a total of 14 articles. The results revealed [SMD= -0.64, 95% CI (-0.92, -0.35), I²=89%]. However, after excluding Basudev, N [22], and Rui [23], only the remaining 12 articles were subjected to meta-analysis and found to have an SMD of -0.58, confidence intervals of [-0.77, -0.38], I²=71%. This indicates that these two articles have a significant impact on heterogeneity in meta-analysis but have not had a significant impact on the conclusions of the data. Therefore, these two articles were not considered in data processing.

3.4.5. Subgroup analysis. Telephone intervention group, I²=74%, P=0.35, MD:-0.34 [-1.05, 0.37], indicating that in the overall effect test, the difference between the effect value and zero is not significant. The treatment of diabetes may not have a significant impact on the change of HbAlc levels. At the same time, there is some heterogeneity between studies, but the results of merging effects are relatively stable.

Internet Platform, I²=55%, P<0.00001, MD=:-0.96 [-1.23, -0.69], there is a significant correlation between the change of HbAlc and the treatment of diabetes, and the results of combined effects show that the average difference of variables ranges from -1.23 to -0.69.

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Smart device, $I^2 = 67\%$, P=0.46. In the overall effect test, the difference between the effect value and zero is not significant, and there may be no significant correlation between variables. MD: -0.34 [-1.26, 0.57], the average difference range of variables is between -1.26 and 0.57, but the results of combining effect quantities are relatively unstable. To establish a definitive relationship between variables, additional research is required (**Figure 6**).

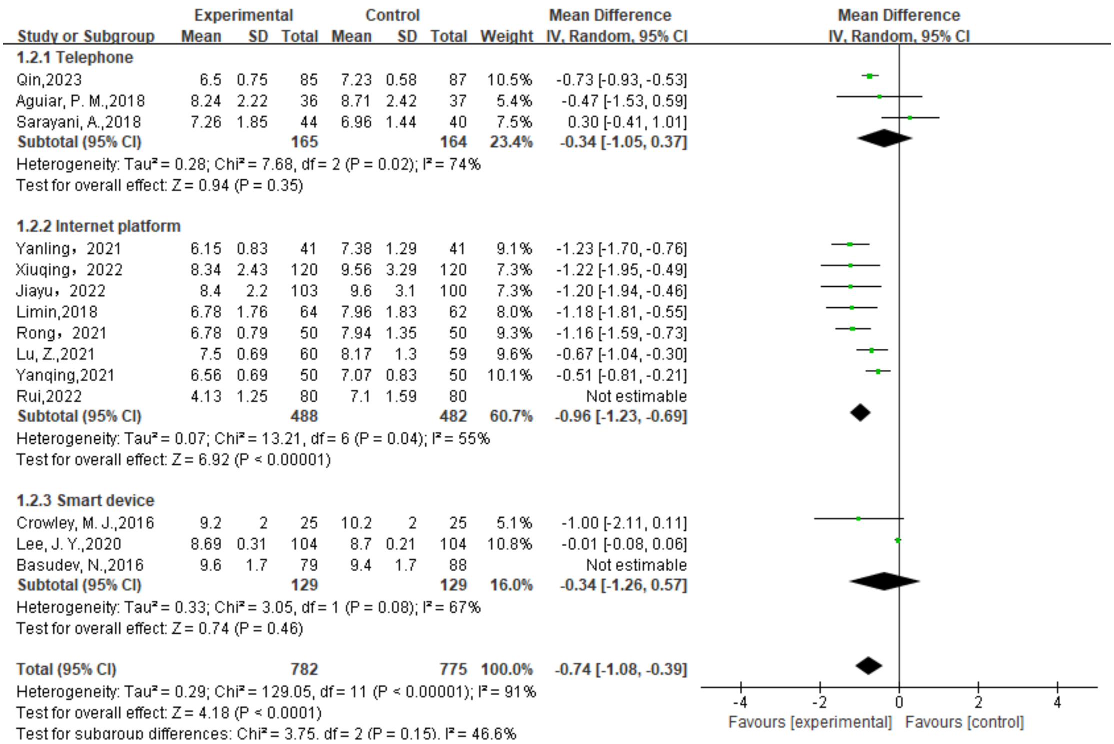

Figure 6. Result for sub-group analysis.

4. Discussion

The objective of this study is to perform a meta-analysis evaluating the efficacy of internet-based pharmaceutical services for the management of diabetes, both domestically and internationally. Through the analysis of data from 12 studies [10-21], the findings indicate a notable influence of the Internet+model on the therapeutic outcomes of individuals with diabetes.

Firstly, HbA1c was analyzed as an evaluation indicator. Through the implementation of the Internet+model, a significant reduction in HbA1c levels was observed in patients with diabetes. The analysis indicated a statistically significant distinction, with a mean difference of -0.55 and a confidence interval of (-0.76, -0.35). The obtained P-value was less than 0.00001.

Differences in the influence of various follow-up durations on HbA1c levels were observed through further subgroup analysis. In the experimental group, significant improvements in HbA1c levels were observed during a one-year follow-up period in four studies 12,15-16,19], with a mean difference of -0.87, a confidence interval of (-1.19, -0.56), and P=0.46. Similarly, during the 5-8 month follow-up period, four studies [11,14,18,20] reported a mean difference of -1.01, a confidence interval of (-1.33, -0.69), and P=0.17. During a follow-up period of over 1 year, four studies [10,13,17,21] showed a difference value of -0.07, a confidence interval of (-0.13, -0.01), and P<0.00001. The effectiveness of the Internet+model is influenced by the duration of follow-up, suggesting that the length of time patients is monitored and supported through this approach plays a role in its efficacy.

The efficacy of the Internet+model is influenced by the duration of the follow-up period. It was observed that in the short term, a longer follow-up period resulted in a more pronounced improvement in HbA1c levels when utilizing the Internet+model. However, during a follow-up period of more than one year, the efficacy of the Internet+model is relatively small.

It is important to acknowledge that the duration of follow-up can be influenced by additional variables, including patient adherence and treatment plan duration. Consequently, conducting further research and effectively controlling for these potential confounding factors may be essential for a more precise assessment of the relationship between follow-up time and the effectiveness of the Internet+ model.

FBG and 2hPBG were also analyzed as evaluation indicators. The impact of the Internet+model on these two parameters deserves attention. Analyzing nine studies [12-17,19-21], it was found that the experimental group exhibited a significant decrease in FBG levels compared to the control group. The mean difference was -0.76, with a confidence interval of (-1.02, -0.5) and $P < 0.00001$. Similarly, four studies [12-14,19-21]demonstrated a significant reduction in 2hPBG levels in the experimental group compared to the control group, with a mean difference of -0.88, a confidence interval of (-1.04, -0.72), and $P < 0.00001$.

Finally, a discussion was conducted on different pharmaceutical service intervention methods, and it was found that there were differences in the improvement effects of different pharmaceutical service methods on HbA1c levels. In the overall effect test, the results of the telephone intervention group did not show a significant difference between the effect value and zero. This suggests that there may not be a significant correlation between the treatment of diabetes and the change in HbA1c levels. This may be because the way of telephone intervention cannot provide enough personalized and real-time support, leading to its limited effect in improving the therapeutic effect of diabetes.

In contrast, the results of the Internet platform group show that there is a significant correlation between the change of HbA1c and the treatment of diabetes, and the pharmaceutical service of the Internet+model can significantly improve the blood sugar control level of diabetes patients. By leveraging the Internet platform, patients with diabetes can receive customized and up-to-date assistance and supervision, leading to improved diabetes management and ultimately better treatment outcomes. This result is consistent with the existing research and practical experience, and confirms the effectiveness of the Internet+model in the treatment of diabetes.

However, the results of the intelligent device group show that in the overall effect test, the difference between the effect value and zero is not significant, which may indicate that the improvement of intelligent devices on the treatment effect of diabetes is limited. Intelligent devices may not be able to provide enough personalized support and monitoring functions, leading to unstable effects in improving the therapeutic effect of diabetes.

5. Conclusion

There is certain degree of heterogeneity in this study, which may be caused by the divergences in sample distinguishing features, intervention measures, and follow-up time among different studies. It is crucial to acknowledge the limitations of this study, such as the inclusion of a restricted number of studies, variations in study quality, and the potential presence of publication bias.

This article reviewed the application of Internet+model in the treatment of diabetes and found that the follow-up time had a certain impact on its efficacy. Over time, the impact of the Internet+model on HbA1c levels becomes increasingly pronounced, with longer follow-up periods leading to more substantial improvements. However, during a follow-up period of more than one year, the efficacy of the Internet+model is relatively small. In addition, the improvement effect of different pharmaceutical care interventions on the level of HbA1c is also different. Pharmaceutical services on the Internet platform can significantly improve the blood sugar control level of diabetes patients, while telephone intervention and intelligent devices have limited effect.

There are differences in the effectiveness of pharmaceutical services for diabetes treatment under the Internet+model. The utilization of the Internet platform offers diabetes patients enhanced personalized and real-time assistance and monitoring, resulting in a notable impact on improving blood sugar control levels. However, the effectiveness of telephone intervention and smart devices is relatively limited and may require further improvement and optimization. Further research should investigate the influence of various pharmaceutical service models on the efficacy of diabetes treatment and develop more tailored and efficient pharmaceutical service strategies that align with individual circumstances.

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