First versus second drop of capillary blood for monitoring blood glucose: A meta-analysis and systematic review

Keywords
monitoring, nursing, care, health, blood glucose

Abstract

Introduction

The accuracy of first or second drop of capillary blood for blood glucose monitoring remains unclear. This meta-analysis aimed to compare and evaluate the accuracy of first or second drop of capillary blood for blood glucose monitoring, to provide evidence for the clinical blood glucose monitoring and nursing care.

Material and methods

Two authors searched PubMed, Clinical trials, Cochrane Library, Clinical Evidence, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang and Weipu database for relevant literatures about the comparison of blood glucose values of the first capillary blood from the establishment of each database until November 10, 2023. After screening, extracting data and evaluating the quality of the literature, Revman 5.4 software was used for meta-analysis.

Results

23 studies involving a total of 3121 patients were finally included in this meta-analysis. There was no significant difference in the measured value of blood glucose between the first drop and the second drop of capillary blood [MD= -0.01, 95% CI (- 0.04, 0.03), P = 0.73]. There was no publication bias in the synthesized outcome tested by Begg's regression analysis (P = 0.152). The result of subgroup analysis showed that there was no difference in the blood glucose values of the first two drops of blood measured by different blood glucose meters and different cleaning methods (all P>0.05).

Conclusions

Current evidence suggests that when using capillary blood to monitor blood glucose, the first drop of capillary blood can be directly used to measure blood glucose.

Title page

Title: First versus second drop of capillary blood for monitoring blood glucose: A meta-analysis and systematic review

Running title: glucose monitoring & care

Authors: Xiaowan Dong[*1], Chen Zhang[*1], Tiantian Wu[*1], Baimei Zhu[#1]

[1], Department of Emergency, Children's Hospital of Nanjing Medical University, Nanjing, China.

[*], Equal contributor

[#], Corresponding author

Corresponding to: Baimei Zhu, lnlf42@sina.com, Children's Hospital of Nanjing Medical University, Nanjing, China.

Address: No. 72, Guangzhou Road, Gulou District, Nanjing, Jiangsu Province, China.

Telephone: 13603261266

Ethics approval and consent to participate

In this study, all methods were performed in accordance with the relevant guidelines and regulations. Ethics approval and consent to participate are not necessary because this study is a meta-analysis and systematic review.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article. The original data will be available from corresponding authors on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study did not receive any funding in any form.

Author contributions

X D, C Z designed research; X D, C Z, T W, B Z conducted research; X D, C Z analyzed data; X D, B Z wrote the first draft of manuscript; B Z had primary responsibility for final content. All authors read and approved the final manuscript.

Acknowledgments

None.

First versus second drop of capillary blood for monitoring blood glucose: A meta-analysis and systematic review

Abstract

Introduction: The accuracy of first or second drop of capillary blood for blood glucose monitoring remains unclear. This meta-analysis aimed to compare and evaluate the accuracy of first or second drop of capillary blood for blood glucose monitoring, to provide evidence for the clinical blood glucose monitoring and nursing care.

Methods: Two authors searched PubMed, Clinical trials, Cochrane Library, Clinical Evidence, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang and Weipu database for relevant literatures about the comparison of blood glucose values of the first capillary blood from the establishment of each database until November 10, 2023. After screening, extracting data and evaluating the quality of the literature, Revman 5.4 software was used for meta-analysis.

Results: 23 studies involving a total of 3121 patients were finally included in this meta-analysis. There was no significant difference in the measured value of blood glucose between the first drop and the second drop of capillary blood [MD= -0.01, 95% CI (- 0.04, 0.03), P = 0.73]. There was no publication bias in the synthesized outcome tested by Begg's regression analysis (P = 0.152). The result of subgroup analysis showed that there was no difference in the blood glucose values of the first two drops of blood measured by different blood glucose meters and different cleaning methods (all P>0.05).

Conclusions: Current evidence suggests that when using capillary blood to monitor blood glucose, the first drop of capillary blood can be directly used to measure blood glucose.

Keywords: blood glucose; monitoring; care; nursing; health.

Introduction

Diabetes is one of the diseases that seriously endanger human health. By 2022, there are about 526 million diabetes patients worldwide and about 124 million diabetes patients in China[1, 2]. Blood glucose monitoring is the basis and important link of intensive treatment for patients with diabetes. Patients with poor blood glucose control need to have blood glucose monitoring more than 4 times a day[3]. In addition to diabetes patients, severe patients, postoperative fasting patients also need to monitor blood glucose every day[4]. At present, the clinical blood glucose monitoring methods mainly include capillary blood glucose monitoring (mainly fingertip blood glucose monitoring) and venous blood glucose monitoring. The determination of venous blood glucose value is an internationally recognized "gold standard" because of its high accuracy [5]. However, due to the shortcomings of complex operation, high blood demand, long waiting time for determination results, this process cannot be used as the main means of frequently monitoring blood glucose. The portable blood glucose meter is used to measure blood glucose at fingertips, which has the advantages of small volume, simple operation, low blood demand, fast collection results and less trauma [6-8], which is commonly used in hospital and home blood glucose monitoring. Although peripheral blood glucose is the most commonly used method for blood glucose monitoring, there is no unified standard for taking the first drop or the second drop of blood when collecting blood sample.

In 2010, the Ministry of Health of China has pointed out that the first drop of blood should be abandoned and the second drop of blood glucose should be used to detect blood glucose in the "Code of Management and Clinical practice of Portable Blood glucose Tester in Medical institutions "[9]. At present, a large number of studies at home and abroad have reported that there is no significant difference in the blood glucose value measured by the first two drops of blood. But some studies have reported that the blood glucose measured by the first two drops of blood is different, so the second drop of blood should be used to detect blood glucose. There are systematic reviews[10-12] to compare and analyze the differences in the effect of blood glucose determination between the first two drops of blood, but there are few reports included in the systematic evaluation, the heterogeneity of instruments and methodologies are not discussed, and the conclusions are not comprehensive. Different opinions and views make clinical workers confused in the implementation of treatment and health education. Therefore, the purpose of this study is to provide useful reference information for clinical blood glucose monitoring and nursing and health education by analyzing the difference of blood glucose detection between the first two drops of capillary blood by meta-analysis.

Methods

This meta-analysis and systematic review was conducted and reported based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement[13].

Literature criteria

The inclusion criteria of the literature for this meta-analysis were as follows: (1) the population of the study were patients who need to monitor their blood glucose; (2) the study was designed as a non-randomized controlled trial matched before and after, and the design of the study was reasonable; (3) the literature had reported the value of blood glucose in the first two drops of fingertips.

The exclusion criteria were as follows: (1) literature with poor quality and repeated reports; (2) reports whose original data were incomplete or unable to be extracted and used; (3) unmatched trials, simple case reports or nursing summaries, reviews.

Literature search

The two authors searched PubMed, Clinical trials, Cochrane Library, Clinical Evidence, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang and Weipu database. This study searched all the relevant literatures about the comparison of blood glucose values of the first capillary blood from the establishment of each database until November 10, 2023. The literature search formula of this study was as follows：(“diabetes mellitus” OR “capillary blood” OR “glucose” OR “blood glucose” OR “blood sugar”) AND (“first drop” OR “second drop” OR “monitoring” OR “blood glucose monitoring” OR “measurement”). In strict accordance with the purpose of the study and the inclusion criteria of the literature, the two researchers independently reviewed the titles and abstracts of the literature to determine whether the literature was included or not. For the literature with different opinions, the third person would intervene to reach an agreement after discussion. For the included literature, the basic information of the literature was extracted and sorted out by two researchers, including the first author, publication time, the general data of patients, such as included population, the number of matched cases, details of blood glucose monitoring and outcomes.

Literature quality assessment

The included literature quality evaluation was completed independently by two researchers, and the evaluation results were cross-reviewed and discussed. If there were any differences, the third researcher was consulted. The methodological index for non-randomized studies (MINORS) tool was used to evaluate the quality of the included studies. There were 12 evaluation indicators in the MINORS tool, each item was evaluated with a score of 0 to 2, and the highest score was 24. Score 0 indicated the item was not reported in the literature, score 1 indicated reported but insufficient information, score 2 indicated that the literature reported and provided sufficient information. The higher the evaluation score, the better the quality of the literature.

Statistical analysis

RevMan 5.4 software was used for meta-analysis in this study. This meta-analysis calculated the mean difference (MD) and its 95% confidence interval (CI) for continuous variable data. The heterogeneity included in the study was analyzed by chi-square test (the test level was $\alpha = 0.1$), and the heterogeneity was quantitatively judged by I^2 value. If there was no statistical heterogeneity ($I^2<50\%$, $P>0.1$) among the results of each study, the fixed effect model was used for meta-analysis. If there was statistical heterogeneity ($I^2\geq50\%$, $P<0.1$) between the results of each study, the source of heterogeneity was further analyzed. After excluding the obvious clinical heterogeneity, random effect model was used for Meta analysis. The publication bias of the results was analyzed by funnel plot and Egger regression test. $P<0.05$ indicated that there was significant difference between the two groups.

Results

Study selection

As presented in Figure 1, according to the retrieval strategy, this meta-analysis preliminarily retrieved 166 articles. After preliminary reading of titles and abstracts, 58 articles that met the inclusion criteria were selected. After reading the full text, 23 studies[14-36] were finally included in this meta-analysis.

Figure 1 The flow chart of study selection

Characteristics of included studies

As shown in Table 1, of the included 23 studies, a total of 3121 patients were included, the included studies reported 6340 cases for first and second drop of capillary blood respectively. The 23 studies included were from China, Turkey, India and Italy. The included studies had established clear inclusion and exclusion criteria, and reported the basic information of each group.

Table 1 The characteristics of included studies

Quality of included studies

All the included studies were self-paired non-randomized controlled studies. The items 6, 7 and 8 of MINORS tool were not reported in each trial, while other items were reported and provided the necessary information. The overall quality of the literature included was good (Table 2).

Table 2 The quality of included studies

Meta-analysis

All the included 23 literature reported the blood glucose value of first versus second drop of capillary blood. As presented in Figure 2, there was no significant difference in the measured value of blood glucose between the first drop and the second drop of capillary blood [MD= -0.01, 95% CI (- 0.04, 0.03), P = 0.73]. Funnel plot (Figure 3) and Begg's test results (P = 0.152) showed that there was no publication bias in the synthesized outcome.

Figure 2 The forest plot on the blood glucose value of first versus second drop of capillary blood

Figure 3 The funnel plot on the blood glucose value of first versus second drop of capillary blood

Among the 23 studies included, there were 8 literatures of glucose oxidase (GOD) method and 8 literatures of glucose dehydrogenase (GDH) method according to the blood glucose meter measurement method, and other 7 articles of other brand blood glucose meters were not reported and therefore were not included in the analysis. The results of meta-analysis showed that there was no significant difference in the first two drops of blood glucose between GOD blood glucose meter and GDH blood glucose meter.

Of the 23 studies included, 13 studies only used 75% ethanol to disinfect fingertips, 6 studies used flowing water to wash hands and then used 75% ethanol to disinfect hands, and 3 studies used hand washing only with flowing water. The subgroup analysis of three different cleaning methods showed that there was no significant difference in the blood glucose value in the first two drops among hand washing group, disinfection group and hand washing disinfection group ($P > 0.05$).

Sensitivity analysis

In this study, the results of one of the studies were removed in turn to observe the value of the combined effect of the remaining studies, and the combined effect of each group was within the 95%CI of the total combined effect, and the results did not change significantly, indicating that the results of the analysis were robust and reliable.

Discussions

Blood glucose monitoring provides information about the body's glucose metabolism, and its accuracy is essential for correct clinical decisions, especially in patients whose insulin dose is determined by blood glucose results[37, 38]. Venous blood glucose is considered to be a reliable monitoring index, but because it takes a long time to check blood glucose levels in hospital laboratories, which may lead to delayed treatment, bedside blood glucose meters are often used to measure blood sugar[39]. At present, the monitoring of blood glucose in fingertips is a simple, rapid and reliable method. It is observed that in clinic, nurses use different methods to collect blood samples for capillary blood glucose determination[40]. There is no standard practice in blood glucose measurement either in the literature or in clinical practice. Therefore, for health care workers and patients who are regularly monitored, it is very important to determine the correct blood glucose measurement technique to avoid inaccurate results. In this study, the blood glucose values measured by the first two drops of blood in 23 reports are analyzed by meta-analysis. The results have shown that there is no difference in blood glucose between the first drop and the second drop of blood, and both of them can be used for the determination of blood glucose.

In the past, many health care providers have thought that the first drop of fingertip blood should be abandoned because the first drop of fingertip blood is usually taken from the capillaries of the fingertips, and the blood sample contains interstitial and intracellular fluid, which was a mixture of arterioles, venules and capillaries[41]. When collecting blood samples, excessive squeezing of the fingertips will lead to the mixing of tissue fluid and blood samples, resulting in incorrect measurement results[42]. Besides, wiping off the disinfectant after disinfection cannot completely remove the residual disinfectant on the skin surface, and the first drop of peripheral blood is inevitably mixed with a small amount of disinfectant, thus affecting the accuracy of the measured value. Furthermore, the exudation of tissue fluid decreases with time, and the mixed tissue fluid of the second drop of peripheral blood may be lower than that of the first drop of peripheral blood[43]. At present, many nursing experts and educators recommend that patients wash their hands with water and soap and use the first drop of blood[44].

Some studies[45, 46] compare the values of the first drop and the second drop of blood in blood glucose self-monitoring with that of venous blood, and come to the conclusion that there is no difference in blood glucose value between venous blood and the first drop of blood. Under the condition that the patient's hands are clean, the first drop of blood is closer to the value of venous blood glucose[47, 48]. The first drop of fingertip blood is mostly natural flow, while for the second drop fingertip blood, if the needle depth is not enough, often need to use external force to force blood outflow, because external force extrusion can make too much tissue fluid exudation and hemodilution, hemodilution also makes other components that need to be tested to be diluted, resulting in poor test value[49]. If the needle depth is increased, it will increase the pain of patients, and the wound will also deepen. For patients who need to monitor blood glucose for a long time, it will increase the resistance of patients and reduce the compliance of regular blood glucose monitoring[50].

At present, the core technology of blood glucose meter mainly includes GOD and GDH. GOD blood glucose meter has high specificity to glucose and is not disturbed by other glucose, but is easily disturbed by oxygen. GDH blood glucose meter, easy to be disturbed by other glucose, but not easily disturbed by oxygen[51, 52]. Due to the difference in the principle of blood glucose detection between the two blood glucose meters, it may affect the blood glucose value of the first two drops of blood, and then affect the difference[53]. According to the subgroup analysis of different kinds of blood glucose meters, no matter GOD or GDH blood glucose meter, there is no significant difference in the rapid determination of blood glucose by using the first two drops of blood, and the first drop of blood can be used to detect blood glucose directly. Besides, this study has found that no matter whether the patient wash the hands or not, they can still choose the first drop of peripheral blood for blood glucose detection. The results of this study suggest that when using a rapid blood glucose meter to determine the blood glucose value, as long as it is operated correctly, it is not necessary to wipe off the peripheral blood of the first drop, but can directly use the first drop of peripheral blood to determine the blood glucose value. In the busy nursing work, this can not only save the trouble of wiping off the first drop of blood, reduce the consumption of disposable medical supplies and blood contamination, but also save more valuable working time, and reduce the patient's pain. However, it must be noted that the included studies do not report that the difference between the dosage in the first and second drop is similar also among different level of glycemia, we cannot calculate because of the limited data. Therefore, future studies should report more about the dosage in the first and second drop and identify the potential association with the different level of glycemia.

There are some limitations in this meta-analysis that are worth considering. Firstly, the included patients in the included studies have no obvious abnormal peripheral circulation and other special changes in blood glucose, so for patients with other disease types and special conditions, the difference of blood glucose values in the first two drops of fingertips also needs other studies to supplement the relevant data. In addition, most of the included studies did not report the corresponding venous blood glucose values. This study only compared the blood glucose values of the first two drops of blood, but did not include the venous blood glucose values. In the future, it is necessary to compare the blood glucose values of the first two drops of blood and venous blood glucose values respectively, and analyze which of the first two drops of fingertip blood is closer to the venous blood glucose value, to provide more reliable evidence for clinical blood glucose monitoring and nursing.

Conclusion

In conclusion, the results of meta-analysis show that there is no significant difference between the first drop of blood and the second drop of blood in the rapid determination of blood glucose, and it is not necessary to abandon the first drop of blood when measuring peripheral blood glucose. Measuring blood glucose with the first drop of blood not only helps to reduce the time pressure of nurses to detect blood glucose, reduce the waste of medical resources, but also reduce the inconvenience and pain of patients' daily diabetes management, which has certain social and economic benefits.

List of abbreviations

PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses

CNKI, China National Knowledge Infrastructure

MD, mean difference

CI, confidence interval

GOD, glucose oxidase

GDH, glucose dehydrogenase

Reference

1. Russo MP, Grande-Ratti MF, Burgos MA, Molaro AA, Bonella MB: **Prevalence of diabetes, epidemiological characteristics and vascular complications**. *Arch Cardiol Mex* 2023, **93**(1):30-36.

2. Ruze R, Liu T, Zou X, Song J, Chen Y, Xu R, Yin X, Xu Q: **Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments**. *Front Endocrinol*

(Lausanne) 2023, **14**:1161521.

3. Cloete L: **Diabetes mellitus: an overview of the types, symptoms, complications and management**. *Nurs Stand* 2022, **37**(1):61-66.

4. Hermanns N, Ehrmann D, Shapira A, Kulzer B, Schmitt A, Laffel L: **Coordination of glucose monitoring, self-care behaviour and mental health: achieving precision monitoring in diabetes**. *Diabetologia* 2022, **65**(11):1883-1894.

5. Miller EM: **Continuous Glucose Monitoring in Practice**. *J Fam Pract* 2023, **72**(6 Suppl):S13-S18.

6. Benhalima K, Mathieu C: **The role of blood glucose monitoring in non-insulin treated type 2 diabetes: what is the evidence?** *Prim Care Diabetes* 2012, **6**(3):179-185.

7. Hortensius J, van der Bijl JJ, Kleefstra N, Houweling ST, Bilo HJ: **Self-monitoring of blood glucose: professional advice and daily practice of patients with diabetes**. *Diabetes Educ* 2012, **38**(1):101-107.

8. Pullano SA, Greco M, Bianco MG, Foti D, Brunetti A, Fiorillo AS: **Glucose biosensors in clinical practice: principles, limits and perspectives of currently used devices**. *Theranostics* 2022, **12**(2):493-511.

9. Association DboCM: **Guidelines for clinical application of blood glucose monitoring in China**. *Chinese Medical Journal* 2011, **91**(10):656-664.

10. Ouyang X, Luo X, Li J: **Meta analysis of the difference of blood glucose measured by different blood collection methods** *General practice Nursing* 2020, **18**(28):6-9.

11. Su B, Bu H, Wang H: **Meta analysis of the effect of different blood collection methods on the results of rapid blood glucose meter**. *Prevention and Control of chronic Diseases*

in China 2007, **15**(6):547-549.

12. Xu M, Yang G, Zhang S: **Meta analysis of the difference between the first drop and the second drop of peripheral blood glucose value** *Chinese Journal of practical Nursing* 2016, **32**(1):2-4.
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE *et al*: **The PRISMA 2020 statement: An updated guideline for reporting systematic reviews**. *J Clin Epidemiol* 2021, **134**:178-189.
14. An L, Chen L, Shen H: **A multicenter clinical study on the difference of peripheral blood glucose value between the first drop and the second drop** *Advances in Modern Biomedicine* 2015, **31**(12): 6086-6090.
15. Chen Y: **Accuracy of detection of blood glucose in the first two drops of peripheral blood in patients with diabetes mellitus** *Chinese Journal of Gerontology* 2007, **19**(4):364-366.
16. Fruhstorfer H, Quarder O: **Blood glucose monitoring: milking the finger and using the first drop of blood give correct glucose values**. *Diabetes Res Clin Pract* 2009, **85**(1):e14-15.
17. Hong W, Xu Y, Zhu C: **Analysis of clinical value of rapid determination of blood glucose by peripheral blood**. *Modern practical Medicine* 2014, **26**(5):2-5.
18. Hortensius J, Slingerland RJ, Kleefstra N, Logtenberg SJ, Groenier KH, Houweling ST, Bilo HJ: **Self-monitoring of blood glucose: the use of the first or the second drop of blood**. *Diabetes Care* 2011, **34**(3):556-560.
19. Li G, Yang J, Li C: **A comparative study on the blood glucose value of the first two**

drops of peripheral blood in patients with diabetes mellitus. *General practice Nursing* 2009 **26**(11): 981-984.

20. Li H, Li J: **Difference of the first two drops of peripheral blood in micromethod for blood glucose detection**. *Chinese Journal of practical Nursing* 2005, **21**(23):16.

21. Li M, Wang X, Shan Z: **Deciding between using the first or second drop of blood for the self monitoring of blood glucose**. *Prim Care Diabetes* 2014, **8**(4):365-369.

22. Luo Q, Zhou L, Zhou S: **Difference between the first drop and the second drop of blood glucose in the detection of capillary blood glucose in pregnant women with gestational diabetes mellitus.** *New World of Diabetes* 2021, **24**(8):4-6.

23. Ma C, Zhang H, Zhang M: **Comparison of rapid blood glucose monitoring between the first drop of blood and the second drop of blood at fingertip**. *Contemporary Nurses* 2011, **28**(11):135-136.

24. Palese A, Fabbro E, Casetta A, Mansutti I: **First or Second Drop of Blood in Capillary Glucose Monitoring: Findings from a Quantitative Study**. *J Emerg Nurs* 2016, **42**(5):420-426.

25. Sagkal Midilli T, Ergin E, Baysal E, Ari Z: **Comparison of Glucose Values of Blood Samples Taken in Three Different Ways**. *Clin Nurs Res* 2019, **28**(4):436-455.

26. Saini S, Kaur S, Das K, Saini V: **Using the first drop of blood for monitoring blood glucose values in critically ill patients: An observational study**. *Indian J Crit Care Med* 2016, **20**(11):658-661.

27. Shen Z, Wang Q, Xiang F: **Correlation between peripheral blood and venous blood glucose monitoring** *Journal of Nurse Education* 2014, **29**(19):1774-1775.

28. Su X, Wu X, Zhou X: **Difference between the first and second drop of microvascular total blood glucose under different conditions** *New World of Diabetes* 2016, **24**(8):60-63.

29. Wang D, Zhuang X, Chi J: **Difference of immediate blood glucose detection between the first drop of blood and the second drop of blood at fingertip**. *Journal of Xining university* 2013, **18**(12):360-362.

30. Wang X, Wang Y, Ping L: **Comparison and analysis of the test results of the first drop of blood and the second drop of blood by portable blood glucose meter**. *Journal of practical Diabetes* 2014 **10**(2):25-26.

31. Wei X: **A comparative study on the first two drops of capillary blood glucose and venous blood glucose in patients with diabetes mellitus** *Chinese Medicine and Clinic* 2018, **23**(4):10-14.

32. Xu L, Huang J, Zhou P: **Comparison between the first drop and the second drop of peripheral blood collected by self-blood glucose monitoring**. *Guangdong Medicine* 2012, **32**(10):1526-1527.

33. Yang S, Zheng L, Li Y: **Comparative test of blood glucose value of the first and second drop of finger in patients with cerebral infarction complicated with diabetes mellitus** *Journal of practical Clinical Nursing* 2016, **15**(1):92-94.

34. Yang Y, Hu H, Liu X: **The effect of different blood glucose detection methods on the difference of blood glucose value**. *International Journal of Nursing* 2017, **36**(19):2734-2736.

35. Zhou C: **Analysis of the difference between the first drop and the second drop of peripheral blood and venous blood glucose value**. *Chinese and Foreign Medicine* 2015,

10(4):38-39.

36. Zhou Y: **The difference of blood glucose value between peripheral blood and venous blood between the first drop and the second drop**. *Acting Nurse* 2011, **12**(4):142-144.

37. Ahmadian N, Manickavasagan A, Ali A: **Comparative assessment of blood glucose monitoring techniques: a review**. *J Med Eng Technol* 2023, **47**(2):121-130.

38. Wang Y, Wu Y, Lei Y: **Microneedle-based glucose monitoring: a review from sampling methods to wearable biosensors**. *Biomater Sci* 2023, **11**(17):5727-5757.

39. Kieu A, King J, Govender RD, Ostlundh L: **The Benefits of Utilizing Continuous Glucose Monitoring of Diabetes Mellitus in Primary Care: A Systematic Review**. *J Diabetes Sci Technol* 2023, **17**(3):762-774.

40. Mathew TK, Zubair M, Tadi P: **Blood Glucose Monitoring**. In: *StatPearls.* edn. Treasure Island (FL) ineligible companies. Disclosure: Muhammad Zubair declares no relevant financial relationships with ineligible companies. Disclosure: Prasanna Tadi declares no relevant financial relationships with ineligible companies.; 2023.

41. Johannis W, Meyer A, Elezagic D, Streichert T: **Measuring capillary blood glucose concentration: Is the first blood drop really the right blood drop?** *Prim Care Diabetes* 2023.

42. Arias-Rivera S, Raurell-Torreda M, Fernandez-Castillo RJ, Campos-Asensio C, Thuissard-Vasallo IJ, Andreu-Vazquez C, Rodriguez-Delgado ME: **Blood glucose monitoring in critically ill adult patients: type of sample and method of analysis. Systematic review and meta-analysis**. *Enferm Intensiva (Engl Ed)* 2023.

43. Hussain FN, Raymond S, Feldman KM, Scarpelli-Shchur S, Strauss TS, Al-Ibraheemi Z,

Brustman L: **Comparison of an Intermittently Scanned (Flash) Continuous Glucose Monitoring System to Standard Self-Monitoring of Capillary Blood Glucose in Gestational Diabetes Mellitus**. *Am J Perinatol* 2023, **40**(11):1149-1157.

44. Kim JH, Lee KT: **Selective Application of Blood Glucose Monitoring After Free Flap Surgery: Potential Indications in Real-World Practice**. *Ann Plast Surg* 2023, **90**(6):585-591.

45. Qiu J, Su P, Wu L: **Research progress of fingertip blood collection and nursing for diabetic blood glucose monitoring**. *Contemporary Nurses* 2022, **29**(12):4-8.

46. Zhou L, Zhang Y, Di Y: **Research progress on pain nursing of diabetic patients with fingertip blood glucose detection**. *Evidence-based Nursing* 2021, **7**(18):4-6.

47. Zhang X, Wang S, Bo L: **Research progress of perioperative blood glucose monitoring index** *International Journal of Anesthesiology and Resuscitation* 2022, **43**(4):4-7.

48. Tang W, Zhang Z: **New progress of blood glucose monitoring technology in elderly patients with diabetes mellitus**. *Practical Geriatrics* 2022, **36**(10):978-982.

49. Xu Y, Jiang P, Chen J, Mu F: **Research progress and nursing points of blood glucose management in patients with diabetes mellitus** *Evidence-based Nursing* 2022, **8**(20):2763-2767.

50. Juneja D, Deepak D, Nasa P: **What, why and how to monitor blood glucose in critically ill patients**. *World J Diabetes* 2023, **14**(5):528-538.

51. Bilen H, Kilicaslan A, Akcay G, Albayrak F: **Performance of glucose dehydrogenase (GDH) based and glucose oxidase (GOX) based blood glucose meter systems at moderately high altitude**. *J Med Eng Technol* 2007, **31**(2):152-156.

52. Olateju T, Begley J, Flanagan D, Kerr D: **Effects of simulated altitude on blood glucose meter performance: implications for in-flight blood glucose monitoring**. *J Diabetes Sci Technol* 2012, **6**(4):867-874.

53. Tang Z, Louie RF, Lee JH, Lee DM, Miller EE, Kost GJ: **Oxygen effects on glucose meter measurements with glucose dehydrogenase- and oxidase-based test strips for point-of-care testing**. *Crit Care Med* 2001, **29**(5):1062-1070.

Figure legends

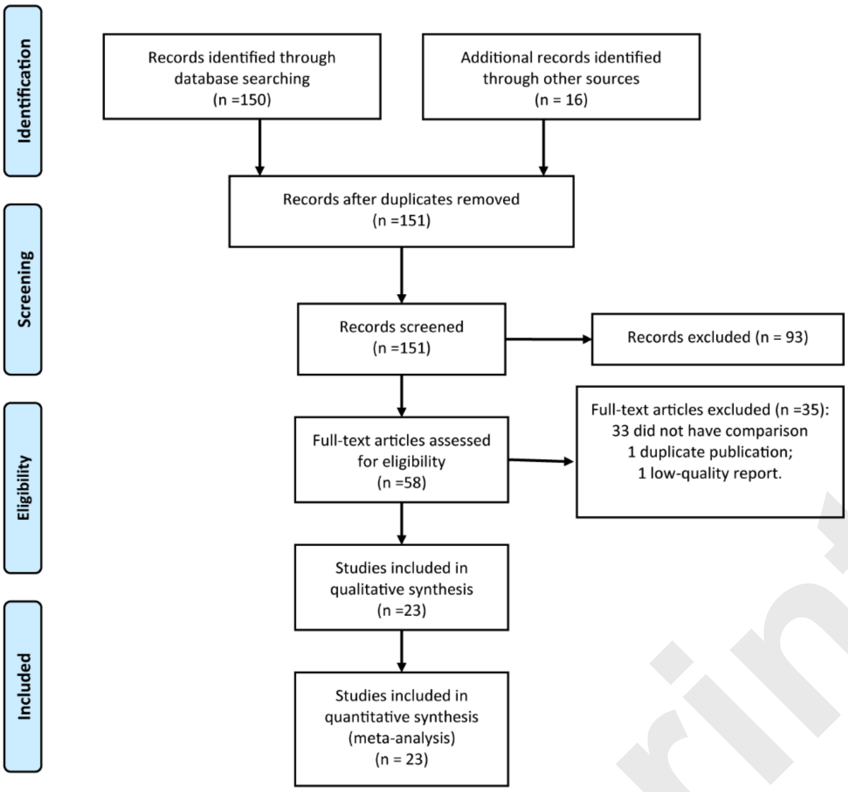


Figure 1 The flow chart of study selection

Study or Subgroup	First drop Mean	First drop SD	First drop Total	Second drop Mean	Second drop SD	Second drop Total	Weight	Mean Difference IV, Fixed, 95% CI
An 2015	14.51	1.9	1183	14.78	1.9	1183	6.0%	-0.27 [-0.42, -0.12]
Chen 2007	6.79	2.57	39	6.82	2.51	39	0.1%	-0.03 [-1.16, 1.10]
Fruhstorfer 2009	5.34	0.29	205	5.33	0.28	205	46.6%	0.01 [-0.05, 0.07]
Hong 2014	4.91	0.37	220	4.87	0.42	220	25.9%	0.04 [-0.03, 0.11]
Hortensius 2011	9.03	4.43	244	8.95	4.73	244	0.2%	0.08 [-0.73, 0.89]
Li 2005	8.68	2.49	100	8.85	2.53	100	0.3%	-0.17 [-0.87, 0.53]
Li 2009	8.4	0.8	50	8.6	0.4	50	2.3%	-0.20 [-0.45, 0.05]
Li 2014	14.51	1.9	459	14.78	1.9	459	2.3%	-0.27 [-0.52, -0.02]
Luo 2021	10.73	2.59	116	10.69	2.47	116	0.3%	0.04 [-0.61, 0.69]
Ma 2011	9.78	3.26	100	9.9	3.28	100	0.2%	-0.12 [-1.03, 0.79]
Midilli 2019	5.52	1.26	190	5.64	1.34	190	2.1%	-0.12 [-0.38, 0.14]
Palese 2016	10.24	3.5	195	10.42	3.61	195	0.3%	-0.18 [-0.89, 0.53]
Saini 2016	8.21	2.88	1470	7.99	2.86	1470	3.3%	0.22 [0.01, 0.43]
Shen 2014	9.87	2.19	400	9.72	2.85	400	1.1%	0.15 [-0.20, 0.50]
Su 2016	8.5	3.2	200	8.6	3	200	0.4%	-0.10 [-0.71, 0.51]
Wang 2013	4.91	0.37	50	4.87	0.42	50	5.9%	0.04 [-0.12, 0.20]
Wang 2014	11	3.29	100	11.22	3.39	100	0.2%	-0.22 [-1.15, 0.71]
Wei 2018	9.6	3	385	9.6	3.3	385	0.7%	0.00 [-0.45, 0.45]
Xu 2012	8.79	1.58	192	8.85	1.77	192	1.3%	-0.06 [-0.40, 0.28]
Yang 2016	10.08	3.22	74	10.09	3.18	74	0.1%	-0.01 [-1.04, 1.02]
Yang 2017	8.58	3.48	100	8.7	3.47	100	0.2%	-0.12 [-1.08, 0.84]
Zhou 2011	9.65	4.66	200	9.83	4.99	200	0.2%	-0.18 [-1.13, 0.77]
Zhou 2015	9.36	4.43	68	9.81	4.89	68	0.1%	-0.45 [-2.02, 1.12]
Total (95% CI)			**6340**			**6340**	**100.0%**	**-0.01 [-0.04, 0.03]**

Heterogeneity: $Chi^2 = 27.85$, df = 22 (P = 0.18); $I^2 = 21\%$

Test for overall effect: Z = 0.34 (P = 0.73)

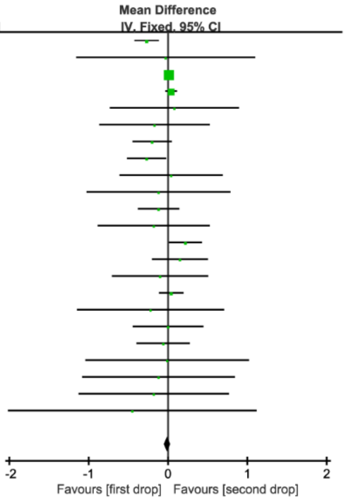
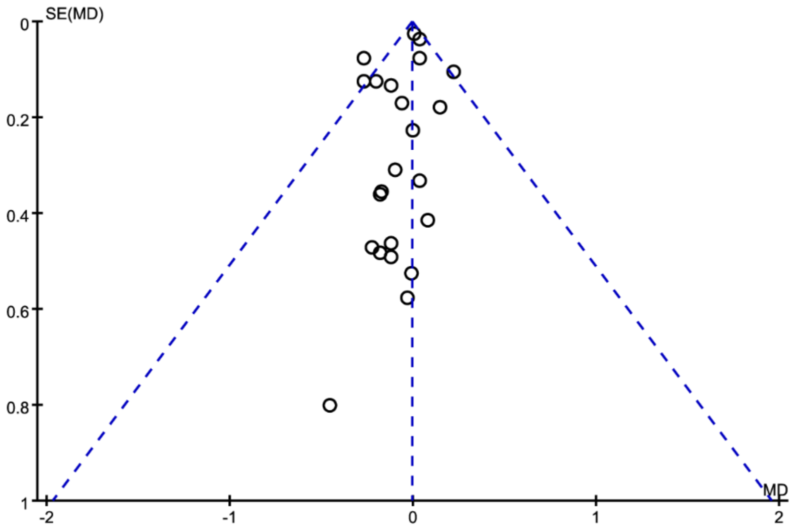


Figure 2 The forest plot on the blood glucose value of first versus second drop of capillary blood

422



423 Figure 3 The funnel plot on the blood glucose value of first versus second drop of capillary blood

Table 1 The characteristics of included studies

Study	Population	Sample size	Paired cases of blood glucose monitoring	Hand cleaning method	Types of blood glucose meters	First drop of blood glucose value (mmol/L)	Second drop of blood glucose value (mmol/L)
An 2015	Diabetic patients	240	1183	Hand washing and disinfection	NA	14.51 ± 1.90	14.78 ± 1.90
Chen 2007	Diabetic patients	39	39	Disinfection	NA	6.79 ± 2.57	6.82 ± 2.51
Fruhstorfer 2009	Adult patients	53	205	Hand washing	GDH	5.34 ± 0.29	5.33 ± 0.28
Hong 2014	Diabetic patients	100	220	Disinfection	GDH	4.91 ± 0.37	4.87 ± 0.42
Hortensius 2011	Diabetic patients	102	244	Hand washing	GDH	9.03 ± 4.43	8.95 ± 4.73
Li 2005	Diabetic patients	20	100	Disinfection	GOD	8.68 ± 2.49	8.85 ± 2.53

Li 2009	Diabetic patients	50	50	Disinfection	GDH	8.40 ± 0.80	8.60 ± 0.40
Li 2014	Diabetic patients	526	459	Disinfection	NA	14.51 ± 1.90	14.78 ± 1.90
Luo 2021	Patients with gestational diabetes mellitus	116	116	Disinfection	NA	10.73 ± 2.59	10.69 ± 2.47
Ma 2011	Diabetic patients	20	100	Hand washing and disinfection	GOD	9.78 ± 3.26	9.90 ± 3.28
Midilli 2019	Adult patients	190	190	Hand washing and disinfection	GDH	5.52 ± 1.26	5.64 ± 1.34
Palese 2016	Patients with type 1 diabetes	195	195	Hand washing and disinfection	GOD	10.24 ± 3.50	10.42 ± 3.61
Saini 2016	ICU patients	90	1470	Disinfection	NA	8.21 ± 2.88	7.99 ± 2.86
Shen 2014	Type 2 diabetes patients	100	400	Disinfection	GOD	9.87 ± 2.19	9.72 ± 2.85
Su 2016	Diabetic patients	200	200	Hand washing and	GOD	8.50 ± 3.20	8.60 ± 3.00

				disinfection			
Wang 2013	Inpatient	50	50	Disinfection	GOD	4.91 ± 0.37	4.87 ± 0.42
Wang 2014	Diabetic patients	100	100	Disinfection	GOD	11.00 ± 3.29	11.22 ± 3.39
Wei 2018	Diabetic patients	385	385	Disinfection	GDH	9.60 ± 3.00	9.60 ± 3.30
Xu 2012	Diabetic patients	103	192	Disinfection	NA	8.79 ± 1.58	8.85 ± 1.77
Yang 2016	Cerebral infarction complicated with diabetes mellitus	74	74	NA	NA	10.08 ± 3.22	10.09 ± 3.18
Yang 2017	Diabetic patients	100	100	Disinfection	GDH	8.58 ± 3.48	8.70 ± 3.47
Zhou 2011	Inpatient	200	200	Disinfection	GOD	9.65 ± 4.66	9.83 ± 4.99
Zhou 2015	Inpatient	68	68	Hand washing	GDH	9.36 ± 4.43	9.81 ± 4.89

Notes: NA, not available; GOD, glucose oxidase; GDH, glucose dehydrogenase.

Table 2 The quality of included studies

Study	1. The purpose of the study is clearly given.	2. Consistency of patient inclusion	3. Collection of expected data	4. The end point index can properly reflect the purpose of the study	5. The objectivity of the Evaluation of Endpoint Index	6. Is the follow-up time sufficient?	7. The rate of lost visits is less than 5%.	8. Is the sample size estimated?	9. Is the choice of the control group appropriate?	10. Is the control group synchronized?	11. Is the baseline between groups comparable?	12. Whether statistical analysis is appropriate
An 2015	2	2	2	2	2	0	0	0	2	2	2	2

Chen 2007	2	1	2	2	2	0	0	0	2	2	2	2
Fruhstorfer 2009	2	2	2	2	2	0	0	0	2	2	2	2
Hong 2014	2	2	1	2	2	0	0	0	2	2	2	2
Hortensius 2011	2	2	2	2	2	0	0	0	2	2	2	2
Li 2005	2	2	1	2	2	0	0	0	2	2	2	2
Li 2009	2	2	2	2	2	0	0	0	2	2	2	2
Li 2014	2	2	2	2	2	0	0	0	2	2	2	2
Luo 2021	2	2	2	2	2	0	0	0	2	2	2	2
Ma 2011	2	2	1	2	2	0	0	0	2	2	2	2
Midilli	2	2	2	2	2	0	0	0	2	2	2	2

2019												
Palese 2016	2	2	2	2	2	0	0	0	2	2	2	2
Saini 2016	2	2	2	2	2	0	0	0	2	2	2	2
Shen 2014	2	2	2	2	2	0	0	0	2	2	2	2
Su 2016	2	2	2	2	2	0	0	0	2	2	2	2
Wang 2013	2	2	2	2	2	0	0	0	2	2	2	2
Wang 2014	2	2	2	2	2	0	0	0	2	2	2	2
Wei 2018	2	2	2	2	2	0	0	0	2	2	2	2
Xu 2012	2	2	1	2	2	0	0	0	2	2	2	2
Yang 2016	2	2	2	2	2	0	0	0	2	2	2	2

Yang 2017	2	2	2	2	2	0	0	0	2	2	2	2
Zhou 2011	2	2	1	2	1	0	0	0	2	2	2	2
Zhou 2015	2	2	2	2	2	0	0	0	2	2	2	2

Study or Subgroup	First drop Mean	SD	Total	Second drop Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
An 2015	14.51	1.9	1183	14.78	1.9	1183	6.0%	-0.27 [-0.42, -0.12]
Chen 2007	6.79	2.57	39	6.82	2.51	39	0.1%	-0.03 [-1.16, 1.10]
Fruhstorfer 2009	5.34	0.29	205	5.33	0.28	205	46.6%	0.01 [-0.05, 0.07]
Hong 2014	4.91	0.37	220	4.87	0.42	220	25.9%	0.04 [-0.03, 0.11]
Hortensius 2011	9.03	4.43	244	8.95	4.73	244	0.2%	0.08 [-0.73, 0.89]
Li 2005	8.68	2.49	100	8.85	2.53	100	0.3%	-0.17 [-0.87, 0.53]
Li 2009	8.4	0.8	50	8.6	0.4	50	2.3%	-0.20 [-0.45, 0.05]
Li 2014	14.51	1.9	459	14.78	1.9	459	2.3%	-0.27 [-0.52, -0.02]
Luo 2021	10.73	2.59	116	10.69	2.47	116	0.3%	0.04 [-0.61, 0.69]
Ma 2011	9.78	3.26	100	9.9	3.28	100	0.2%	-0.12 [-1.03, 0.79]
Midilli 2019	5.52	1.26	190	5.64	1.34	190	2.1%	-0.12 [-0.38, 0.14]
Palese 2016	10.24	3.5	195	10.42	3.61	195	0.3%	-0.18 [-0.89, 0.53]
Saini 2016	8.21	2.88	1470	7.99	2.86	1470	3.3%	0.22 [0.01, 0.43]
Shen 2014	9.87	2.19	400	9.72	2.85	400	1.1%	0.15 [-0.20, 0.50]
Su 2016	8.5	3.2	200	8.6	3	200	0.4%	-0.10 [-0.71, 0.51]
Wang 2013	4.91	0.37	50	4.87	0.42	50	5.9%	0.04 [-0.12, 0.20]
Wang 2014	11	3.29	100	11.22	3.39	100	0.2%	-0.22 [-1.15, 0.71]
Wei 2018	9.6	3	385	9.6	3.3	385	0.7%	0.00 [-0.45, 0.45]
Xu 2012	8.79	1.58	192	8.85	1.77	192	1.3%	-0.06 [-0.40, 0.28]
Yang 2016	10.08	3.22	74	10.09	3.18	74	0.1%	-0.01 [-1.04, 1.02]
Yang 2017	8.58	3.48	100	8.7	3.47	100	0.2%	-0.12 [-1.08, 0.84]
Zhou 2011	9.65	4.66	200	9.83	4.99	200	0.2%	-0.18 [-1.13, 0.77]
Zhou 2015	9.36	4.43	68	9.81	4.89	68	0.1%	-0.45 [-2.02, 1.12]
Total (95% CI)			**6340**			**6340**	**100.0%**	**-0.01 [-0.04, 0.03]**

Heterogeneity: Chi² = 27.85, df = 22 (P = 0.18); I² = 21%
Test for overall effect: Z = 0.34 (P = 0.73)