Impacts of nurse-led clinic and nurse-led prescription on hemoglobin A1c control in type 2 diabetes
A meta-analysis
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Abstract
Background: To evaluate the impacts of nurse-led clinic and nurse-led prescription on hemoglobin A1c (HbA1c) control in type 2 diabetes.

Methods: We searched relevant publications in English and Chinese database and conducted meta-analysis by Stata 12.0. We divided the case groups of included studies into 2 categories according to the role of nurse: nurse-led clinic and nurse-led prescription. Nurse-led clinic was implemented on the basis of standard diabetes care provided by doctor, and control group also receive the standard diabetes care but without nurse-led clinic. The doctor mentioned above might work alone or in a health care team. Nurse-led prescription was prescribed by nurse independently and compared with that of doctor.

Results: The meta-analysis shown that, compared with the standard diabetes care, nurse-led clinic significantly decreases HbA1c level (standard mean difference [SMD]=−0.767; 95% confidence interval [CI]: −1.062, −0.471; \( P < .001 \)). In subgroup analysis, nurse-led clinic also had positive impacts on controlling HbA1c level, no matter in developed countries (SMD = −0.353; 95% CI: −0.6, −0.106; \( P = .005 \)) or developing countries (SMD = −1.114; 95% CI: −1.498, −0.73; \( P < .001 \)). Additionally, there was no significant difference between nurse-led prescription and doctor prescription in controlling HbA1c levels (SMD = −0.203; 95% CI: −0.434, 0.029; \( P = .086 \)).

Conclusion: The nurse-led clinic had positive significance for HbA1c control. Meanwhile, the impact of nurse-led prescription on controlling HbA1c is comparable to that of doctor. It is valuable to provide nurse-led clinic on the basis of standard diabetes care provided by doctor to better control HbA1c, and nurse-led prescription should be provided when doctor-led service is limited.

Abbreviations: HbA1c = hemoglobin A1c, SMD = standard mean difference, T2DM = type 2 diabetes.

Keywords: hemoglobin A1c, meta-analysis, nurse, type 2 diabetes

1. Introduction
Type 2 diabetes (T2DM) is a global epidemic that causes a great burden in human health and economy.\cite{1} The number of T2DM patients has doubled worldwide in the past 20 years. According to the International Diabetes Federation, there were 415 million T2DM patients in 2015, and by 2040, this number will be approximately 642 million.\cite{2} The rapid increase in the incidence of diabetes and limited healthcare resources are great challenges in diabetes management. In the traditional standard diabetes care, the role of nurses is not very crucial. In recent years, some countries have expanded the roles of nurses, including nurse-led clinic and nurse-led prescription.\cite{3,4} Nurses can operate nurse-led clinic on the basis of standard diabetes care provided by doctors or can prescribe medications instead of doctors. The functions of nurse-led clinic include setting behavioral goal, establishing individualized care plan, and providing relevant diabetes knowledge education for patients.\cite{5,6} Nurse-led prescriptions include ordering laboratory tests, prescribing medications, and adjusting medication dosages.\cite{7,8} Many studies have investigated the effects of nurse-led clinic or nurse-led prescription on hemoglobin A1c (HbA1c) control in T2DM.\cite{5,9,10} With inconsistent results being reported, we searched relevant randomized controlled trials (RCTs) and conducted a meta-analysis on these topics.

2. Materials and methods

2.1. Search strategy
Our research was conducted by reviewing previous papers, thus ethical approval is not required. The literature searches were...
operated by 2 reviewers independently in PubMed, Web of Science, Science Direct, Cochrane Central Register of Controlled Trials, and Chinese Databases, including China National Knowledge Infrastructure, China Biology Medicine disc, Chongqing VIP, and Wan Fang Data (updated to March 17, 2019) with the following keywords: “diabetes” and “hemoglobin A1c” and “nurse.” Relevant review studies, meta-analysis, and cited references were also estimated for potential studies, any disagreement was reached to agreement after discussion.

2.2. Inclusion and exclusion criteria

Studies included in current meta-analysis met the following inclusion criteria:

1. RCT;
2. T2DM patients;
3. the outcome measure was HbA1c, and provided changes in HbA1c levels or the changes can be calculated;
4. the control group receive standard diabetes care conducted by doctors, who work alone or work in a health care team;
5. nurse-led clinic or nurse-led prescription was operated on case group.

The exclusion criteria were as follows:

1. non-RCT;
2. the outcome measures without HbA1c;
3. no sufficient data.

2.3. Data extraction and study quality assessment

Two investigators collected the relevant data independently, and any inconsistency was reached to consistency by discussion. The following information was extracted from each included study: first author; year of publication, country, sample size, follow-up time, components of intervention team, the role of nurse, treatments of case and control groups, and changes in HbA1c level. The Jadad composite scale was applied on assessment of included RCT quality, which assigned scores for reported randomization, blinding, and withdrawals.[12] This is a 5-point scale with a score of at least 3 for high-quality trials and a score of 2 or less for low-quality trials.[13] Any disagreement was resolved by discussion to reach agreement.

2.4. Statistical analysis

We divided the case groups of included studies into 2 categories according to the role of nurse: nurse-led clinic and nurse-led prescription. Nurse-led clinic was implemented on the basis of standard diabetes care provided by doctor, and control group also receive the standard diabetes care but without nurse-led clinic. The doctor mentioned above might work alone or in a health care team. Nurse-led prescription was prescribed by nurse independently and compared with that of doctor in 2 RCTs. Additionally, there was no significant difference between nurse-led prescription and doctor prescription in controlling HbA1c level, no matter in developed countries (SMD = 0.916, 95% CI: −0.767, −0.471; P < .001) (Fig. 2A). No publication bias was found (P = .073) (Fig. 3). When subgroup analysis was operated based on different countries, the nurse-led clinic also had positive impacts on controlling HbA1c level, no matter in developed countries (SMD = −0.535; 95% CI: −0.6, −0.106; P = .005) (Fig. 2B) or developing countries (SMD = −1.114; 95% CI: −1.498, −0.73; P < .001) (Fig. 2C). Significant heterogeneity was also found in the studies of developed countries (I² = 76.5%, P < .001) and developing countries (I² = 89.2%, P < .001).

3. Results

3.1. Study characteristics

We initially identified 5021 articles and finally 177 studies for full-text review, from which 17 RCTs with 2701 patients[4,6,9–11,15–24] met the inclusion and exclusion criteria of our meta-analysis. An overview of the methodology of the literature review is presented as PRISMA flow diagram in Figure 1. Among the included RCTs, 8 were Chinese studies, 6 studies were from developed countries, other 3 studies were from the Netherlands and Ireland. There was no statistically significant difference in baseline HbA1C between case and control groups in all studies. The quality of studies was assessed by Jadad score, and 8 RCTs ≥3 scores with high quality, while 9 RCTs less than 3 scores with low quality. The main characteristics and Jadad score of included studies were shown in Table 1.

3.2. Impact of nurse-led clinic on HbA1c control

In 15 RCTs, nurse-led clinic was implemented on the basis of standard diabetes care provided by doctor, and control group also receive the standard diabetes care but without nurse-led clinic. Significant heterogeneity was detected among studies and random-effects model was used (I² = 91.6%, P < .001). Compared with the standard diabetes care, nurse-led clinic significantly decreases HbA1c level (SMD = −0.767; 95% CI: −1.062, −0.471; P < .001) (Fig. 2A). When subgroup analysis was operated based on different countries, the nurse-led clinic also had positive impacts on controlling HbA1c level, no matter in developed countries (SMD = −0.353; 95% CI: −0.434, 0.029; P = .086; I² = 48.1%) (Fig. 2D).

3.3. Effect of nurse-led prescription on HbA1c control

Nurse-led prescription was prescribed by nurse independently and compared with that of doctor in 2 RCTs. Additionally, there was no significant difference between nurse-led prescription and doctor prescription in controlling HbA1c levels (SMD = −0.203; 95% CI: −0.434, 0.029; P = .086; I² = 48.1%) (Fig. 2D).

4. Discussion

T2DM, which accounts for more than 90% of diabetes cases, causes microvascular diseases and leads to progressive damage in various organs. T2DM not only results in serious physical and psychological problems to patients but also is a heavy burden to the medical field.[23] Although the risk factors and prevention of T2DM are popularly increasing, its incidence is still increasing.[24] HbA1c results from the glycation of hemoglobin and requires glycemic control in the past 2 to 3 months.[25] HbA1C and glycemic control are very crucial for treating diabetes. Most T2DM patients are outpatients, and many clinic doctors do not have enough time to impart diabetes-related knowledge to patients, especially in developing countries. Furthermore, most patients lack knowledge about diabetes and self-management ability. These inevitably lead to unfavorable HbA1C and glycemic control.[26] The nurse-led clinic, as a novel approach to manage diabetic patients, has been implemented on the basis of
standard diabetes care provided by doctors. The nurse-led clinic can provide detailed knowledge of diabetes to patients as well as guidance on diet, exercise, glycemic monitoring, and medication to improve HbA1C and glycemic control in T2DM patients. In another case, nurses, instead of doctors, can order laboratory tests, prescribe medications, and adjust the dosages of medications.

A relevant English meta-analysis published in 2017 only included 7 RCTs from developed countries and did not include RCTs from developing countries, and the result showed that nurse-led clinic did not significantly reduce HbA1c level compared with standard diabetes care. In a Chinese meta-analysis published in 2016, 13 RCTs from developed countries and 8 from developing countries were included. Although this meta-analysis showed that nurse-led clinic can better control HbA1c level, it combined 2 nurse-led prescription-associated RCTs with nurse-led clinic-associated RCTs to conduct a meta-analysis. This inevitably led to deviations on the conclusions.

Overall, 17 RCTs were included in our current meta-analysis, 9 from developed countries and 8 from developing countries. The included RCTs were divided into the following 2 categories according to the role of nurses: nurse-led clinic and nurse-led prescription. Nurse-led clinic and nurse-led prescription were performed on the case group in 15 RCTs and 2 RCTs, respectively. Our meta-analysis confirmed that compared with standard diabetes care, the nurse-led clinic significantly decreases HbA1c level. The subgroup analysis based on different countries suggested that nurse-led clinic had positive effects on controlling HbA1c level, regardless if it comes from developed countries or developing countries. Although the nurse-led clinic of developing countries is not as progressive as that of developed countries, it is affiliated to the hospitals with abundant medical resources, and relevant nurses are proficient in their clinical work. Furthermore,
## Table 1

The main characteristics and Jadad score of included studies.

| First author | Year | Country | Case (N) | Control (N) | Follow-up, mo | Intervention team | The role of nurse | Treatment of case group | Treatment of control group | Hemoglobin A1c changes (mean, SD) | Jadad score |
|--------------|------|---------|----------|-------------|---------------|-------------------|------------------|-------------------------|-----------------------------|-----------------------------|-----------|
| Aubert RE    | 1998 | America | 71       | 67          | 12            | Nurse case managers Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -1.7 1.33 | -0.6 1.33 | 2         |
| Litaker D    | 2003 | America | 79       | 78          | 12            | Nurse practitioners Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -0.63 1.5 | -0.15 1 | 4         |
| Taylor OB    | 2003 | America | 61       | 66          | 12            | Nurse case managers Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -1.14 2.34 | -0.35 2.43 | 4         |
| Krein SL     | 2004 | America | 106      | 103         | 18            | Nurse case managers Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -0.02 2.02 | -0.16 1.89 | 4         |
| Gabbay RA    | 2006 | America | 150      | 182         | 12            | Nurse case managers Physicians Diabetes nurse educators Dieticians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -0.01 1.59 | 0.04 1.4 | 3         |
| MacMahon Tone J | 2009 | Ireland | 101      | 99          | 12            | Nurse specialist in diabetes Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -0.34 0.97 | 0.12 0.97 | 4         |
| Welch G      | 2011 | America | 21       | 18          | 12            | Nurse specialist in diabetes Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | 1-h diabetes care visits | -1.6 1.4 | -0.6 1.1 | 4         |
| Zhang Y      | 2011 | China   | 90       | 91          | 12            | Nurse case managers Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -3.5 0.95 | -1.8 1.2 | 2         |
| Liu C        | 2013 | China   | 74       | 74          | 6             | Nurse case managers Physicians | Nurse-led clinic | Standard diabetes care | Standard diabetes care | -2.1 1.41 | -1.41 1.54 | 2         |

(continued)
### Table 1 (continued)

| First author | Year | Country | Case (N) | Control (N) | Follow-up, mo | Intervention team | The role of nurse | Treatment of case group | Treatment of control group | HbA1c changes (mean, SD) | Jadad score |
|--------------|------|---------|----------|-------------|---------------|-------------------|-------------------|------------------------|--------------------------|--------------------------|-------------|
| Zhou L       | 2013 | China   | 40       | 40          | 6             | Nurse case managers Physicians | Nurse-led clinic | Establishing outpatient files and follow up monthly | Standard diabetes care | −3.58 0.97 | −1.56 1.08 | 2           |
| Li W         | 2013 | China   | 68       | 66          | 6             | Nurse case managers Physicians | Nurse-led clinic | Explaining diabetes knowledge Directing diet, exercise, medications and psychological problems | Standard diabetes care | −3.5 1.4  | −1.5 3.8  | 2           |
| Wang P       | 2013 | China   | 120      | 120         | 12            | Nurse case managers Physicians | Nurse-led clinic | Giving individual advice on diet based on glycemic level | Standard diabetes care | −3.1 1     | −1.4 1.1  | 2           |
| Dong L       | 2014 | China   | 148      | 148         | 3             | Nurse case managers Physicians | Nurse-led clinic | Explaining diabetes knowledge Directing diet, exercise, medications and psychological problems Encouraging patients to do aerobic exercise | Standard diabetes care | −2.02 1.59 | −1 1.74  | 2           |
| Dong G       | 2015 | China   | 25       | 25          | 12            | Nurse case managers Physicians | Nurse-led clinic | Explaining diabetes knowledge Directing diet, exercise, medications and psychological problems Encouraging patients to communicate with each other. | Standard diabetes care | −1.61 0.77 | −0.77 0.77 | 2           |
| Dong W       | 2015 | China   | 40       | 40          | 12            | Nurse case managers Physicians | Nurse-led clinic | Explaining diabetes knowledge Directing diet, exercise, medications and psychological problems | Standard diabetes care | −2.84 1.76 | −0.97 1.97 | 2           |
| Houweling ST | 2009 | Netherlands | 46    | 38          | 12            | Nurse specialist in diabetes | Nurse-led prescription | Nurse prescribe medication based on the guidelines† | Standard diabetes care Nurse education | −1.5 1.35 | −0.9 1.22 | 3           |
| Houweling ST | 2011 | Netherlands | 102  | 104         | 14            | Practice nurses | Nurse-led prescription | Nurse prescribe 14 medications and adjusting dosages of 30 medications Nurse were not permitted to prescribe insulin, but were can adjust the dosage Nurse order laboratory tests | Standard diabetes care | −0.09 0.97 | 0.03 1.39 | 5           |

SD = standard deviation.

† The standard diabetes care mentioned above were all provided by doctor, who might work alone or in a health care team.

† The guidelines are from the Dutch College of General Practitioners and the Dutch Diabetes Federation.
compared with the high expenses and the inconvenient approach of medical treatment in developed countries, the lower cost and convenience of medical treatment in developing countries are more likely to gain the trust and recognition of patients. Therefore, it is possible to enhance the knowledge about diabetes among patients and improve the adherence of patients in developing countries, thus improving HbA1C and glycemic control among T2DM patients. Additionally, our study found that there was no significant difference between nurse-led prescription and doctor-led prescription in controlling HbA1c levels. This result indicated that the HbA1C control provided by nurses was comparable to that provided by doctors. It is valuable to provide nurse-led prescription when doctor-led service is limited.

Our study evaluated the effect of nurse-led clinic and nurse-led prescription on HbA1c control in T2DM patients, and the results confirmed the positive significance of nurse-led clinic and the feasibility of nurse-led prescription. However, our study had several limitations. First, significant heterogeneity was detected among the included RCTs. Second, only 2 nurse-led prescription-associated RCTs were included in our study; hence, the effect of nurse-led prescription on HbA1c control should be carefully considered. More RCTs should be conducted to verify this result. Additionally, most T2DM patients live in developing countries; however, the quality of included RCTs in developing countries was commonly poor. Therefore, high-quality RCTs in developing countries are needed to confirm the role of nurse-led clinic in controlling HbA1c in T2DM patients.

5. Conclusion

The nurse-led clinic significantly decrease the HbA1c level compared with standard diabetes care, no matter in developed countries or developing countries. Meanwhile, the impact of nurse-led prescription on controlling HbA1c is comparable to that of doctor. It is valuable to provide nurse-led clinic on the
basis of standard diabetes care provided by doctor to better control HbA1c, and nurse-led prescription should be provided when doctor-led service is limited.

Acknowledgment
The authors thank Editage English service for language editing services.

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