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**DECREASE OF GLYCATED HEMOGLOBIN BASED ON EVALUATION OF DIABETES  
INTERVENTION PROGRAMS IN LOW-AND MIDDLE-INCOME COUNTRIES : A  
SYSTEMATIC REVIEW**

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## **Introduction**

While diabetes is increasing worldwide with over 415 million people affected<sup>1</sup>, its rise is particularly severe in low-and middle-income countries (LMICs), where more than 75% of people with diabetes live. We can already refer to a significant diabetes epidemic which is mostly related to the increasing urbanization of the world's population responsible for the rise of sedentary lifestyle and improper diets. This urbanization phenomenon has often occurred later but faster in LMICs than in high-income countries, leading to a dramatic increase in the number of people with diabetes, particularly in African countries where the expected number of people with diabetes is over 40 million by 2045.

Despite this significant rise of its incidence, diabetes remains often unrecognized in LMICs. Indeed, its diagnosis occurs generally at a late stage, during complications of the disease. It is estimated that nearly half of people with diabetes worldwide have not been diagnosed as such, with 83% of them living in LMICs<sup>2</sup>. Moreover, while this chronic disease requires lifelong care, most people in these countries do not have access to appropriate health care and thus cannot benefit from the consultations or analyzes necessary for the diagnosis and monitoring of diabetes. Indeed, only a small part of their GDP is allocated to health care, such as in India where the health system receives only 5% of the GDP<sup>3</sup>.

Although the death rate related to diabetes is more than twice higher in LMICs than in high-income countries<sup>4</sup>, diabetes awareness, sometimes wrongly considered as a disease affecting only elderly and wealthy people, is not a priority for LMICs. There are no specific public funds allocated nor international aid which is rather intended for communicable diseases such as HIV and tuberculosis, or for malaria.

This lack of resources and information explains why diabetes intervention techniques are often unknown and perfectible in LMICs. To this day, to our knowledge, no systematic review reviewed the interventional programs in LMICs. The main goal of our study was to identify and describe studies about diabetes interventional programs conducted in LMICs. The secondary goals were estimating the effectiveness of these intervention programs and identifying factors that may influence these results.

## **Methodology**

### Databases and keywords

A systematic review has been performed by including articles published in English and French on the following databases: Medline, Google Scholar, Web of Science, Cochrane Library, and Scopus. The following formulation of the queries has been used: (“diabetes mellitus”) AND (“program evaluation” OR “health survey” OR “health education” OR “disease management” OR “capacity building”) AND (“a country” OR “LMICs” OR “developing countries”), with “a country” being successively replaced by each country from LICs (34), Lower-Middle Income Countries (LMICs, 47), and UMICs (56), for a total of 137 countries, according to the classification by the World Bank in 2018.

### Inclusion and non-inclusion criteria

Once extracted from the databases, the selected publications have been processed using Rayyan to include articles based on the title and the abstract, and then based on the whole text in accordance with PRISMA guidelines. The titles and the abstracts have been considered by two independent reviewers. The inclusion criteria required the study to be about type 2 diabetes intervention programs in one of the 137 LMICs and to have been published between 2009 and 2019. The evidence level was determined using criteria summarized in Supplementary Table 1, which come from a systematic review of Jost and colleagues<sup>4</sup> (2018). The articles regarding other aspects of support for people with diabetes, such as prevention, screening, and diagnosis, have not been included.

### Variables of interest

For each program, the following variables have been noted when available: year, country, income level of the country, intervention area, intervention type, evidence level, primary outcome, sample size, number of patients in the intervention group, HbA1c level before and after intervention in each group, duration, average monthly variation of HbA1c, average monthly variation of HbA1c compared to control group, p value, and follow-up percentage.

## **Results**

### Literature review

The inclusion process has been summarized in the flow chart (figure 1). Following the literature review, the information regarding variables of interest have been noted and grouped in a table (Supplementary Table 2).

#### Geographical distribution of the studies

Among 137 eligible countries, only 21 are mentioned in at least one article. Nearly 69% (n=51) of the interventions were about one of nine Asian countries mentioned in this study. By themselves, Iran, China, and India aggregated nearly half (49%, n=36) of intervention sites. The rest concerned America (18%, n=13) and Africa (14%, n=10). This unbalanced distribution is even more obvious when looking at income level. It benefits UMICs which represent more than 77% (n = 57) of intervention sites as against 20% (n=15) for LMICs and only 3% (n=2) for LICs. Also, a high proportion of these interventions (70%, n=52) took place in urban areas while only 15% (n=11) occurred in rural areas, and the location of the remaining interventions (n=11) has not been specified.

#### Intervention types

While several intervention types have been included in this study, most (77%, n=57) were patient education projects. However, this intervention category covered diverse situations. Indeed, these interventions can be led by various professionals such as nurses, pharmacists<sup>5</sup>, nutritionists, psychologists<sup>6</sup>, or dentists<sup>7</sup>. They also differ by the way they are led, with the majority carried out as individual or group information sessions, but they can also occur remotely by means of phone messages<sup>8</sup> or other electronic applications<sup>9</sup>.

#### Primary outcomes

Various indicators can be used to measure an intervention's efficiency. The most widely used is the glycated hemoglobin (HbA1c) level which reflects the patient's state of glycemic control. Thus, HbA1c level was one of the primary outcomes for 54% of the interventions (n=40).

#### HbA1c level evolution for patients in the intervention group

In 42 studies, HbA1c level evolution was interpretable for patients having benefited from the intervention. In one of these studies<sup>10</sup>, there are two intervention groups, one being encouraged to exercise (yoga) and one benefiting from peer support. HbA1c level evolution for the group having undergone the intervention was thus measured 43 times.

We noticed that in 42 cases, HbA1c level decreased after the intervention. This drop was significant in 45% of cases (n=19) while it was not in 7% (n=3). For the remaining cases (48%, n=20), there was no available p value.

The only exception was the group benefiting from peer support from the study with two intervention groups<sup>10</sup>, where HbA1c level increased non-significantly. Overall, out of 43 interventions, there was an average monthly decrease of 0.162% in HbA1c level.

#### HbA1c level evolution for patients of the intervention group compared to control group

In 36 studies, there was a control group allowing the interpretation of HbA1c level evolution compared to that of the intervention group. Given the study with two intervention groups<sup>10</sup>, there were therefore 37 interventions to compare. In 92% of cases (n = 34), there was a negative difference between the HbA1c level evolution for the intervention group and that of the control group, suggesting that HbA1c level drop was more pronounced when patients underwent the intervention. These results were significant in most cases (53%, n=18) while they were not in 38% (n=13). For the remaining 9% of cases (n=3), p value was missing. HbA1c level drop was thus more pronounced in the control group only in 8% of cases (n=3), with this drop being significant in only a single case. When considering all 37 interventions, there was an average monthly decrease of 0.156% in HbA1c level in the intervention group compared to the control group.

#### Average values of HbA1c level in different groups

The average value of HbA1c was mostly stable in control groups, from 8.57 % before the intervention to 8.62 % afterwards. Intervention programs allowed a significant drop in the average value of HbA1c level for patients belonging to intervention groups, from 8.34 % before the intervention to 7.79 % afterwards.

## **Discussion**

The education programs displayed a real effectiveness in lowering HbA1c level. This is consistent with the results of other systematic reviews such as that of Pimouguet and colleagues from 2011<sup>11</sup> which highlighted a decrease of 0.38% in HbA1c level in patients having undergone the intervention. Nevertheless, despite this improvement in glycemic control, the resulting level remained below the 7% recommended by the “Haute Autorité de Santé” for most people with type 2 diabetes in France. This high value is explained by causes such as late diabetes diagnosis in LMICs, thus starting with a clearly unbalanced diabetes with high HbA1c level.

However, it would have been interesting to have information about other criteria such as the cost-efficiency ratio of these interventions which is particularly important in LMIC as health authorities have only limited means and

a large part of the population lacks health insurance. Only two interventions have studied this ratio in this review: one in South Africa<sup>12</sup> suggesting that group education displayed a better cost-efficiency ratio, and the other in American Samoa<sup>13</sup> describing a model which reduces the cost of HbA1c level decrease. Furthermore, glycemic control would not have a favorable cost-efficiency ratio for patients over 55 years old according to a study of Li and colleagues<sup>14</sup> from 2010. Thus, it would have been relevant to have information on other criteria than glycemic control by HbA1c decrease in this systematic review.

This systematic review showed that all types of education programs reduced HbA1c level and could therefore be used indifferently for populations. Yet, according to an article by Grillo and colleagues<sup>15</sup> from 2013, group education should be favored as it results in an HbA1c decrease equivalent to that of individual education, while reaching more patients.

There was also a significant geographical imbalance. Four countries (Iran, China, India, and Brazil) accounted for 60% of the articles. This imbalance favored Asia (69% of articles), at the expense of Africa which was the least represented continent (13% of articles). This imbalance was detrimental since Africa is experiencing the largest explosion in the rate of people with diabetes: it is estimated that by 2040, this rate will have increased by 140% there<sup>1</sup>.

Likewise, there is an imbalance according to the income level at the expense of LICs which only represented 3% of interventions. The imbalance at the expense of rural areas (15% of interventions) is also detrimental. Indeed, it would have been interesting to have more information about these territories to be able to measure a possible influence of access to infrastructure and of the lifestyle on the results of interventions compared to those in urban areas (70% of interventions).

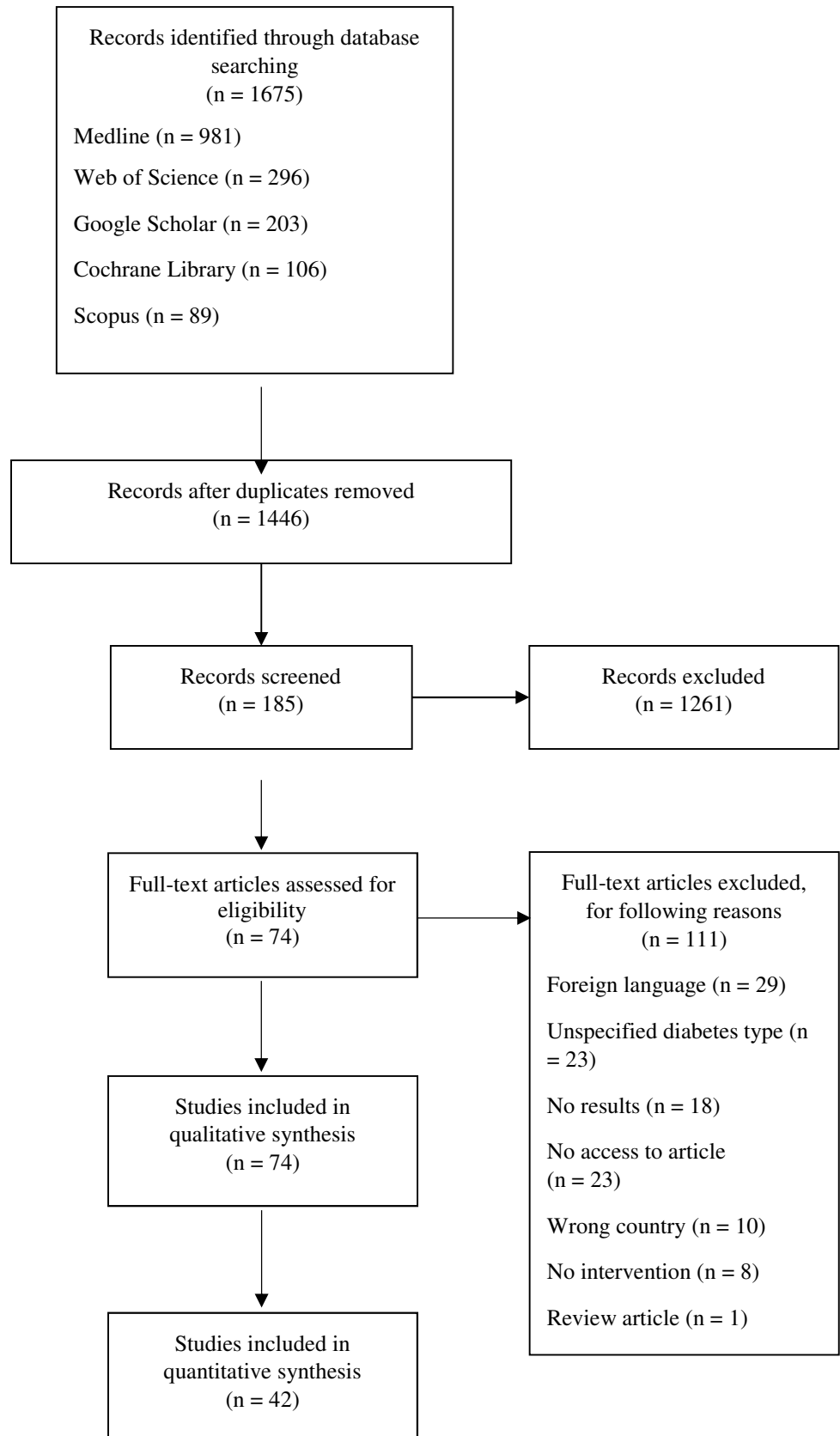
Thereby, we managed to identify articles dealing with intervention programs in LMICs and to show their efficiency over glycemic control. Other studies are still required to establish their efficiency over other criteria such as cost-efficiency ratio. These studies will also enable to deepen our knowledge about LICs, American countries and rural areas to have a more precise idea of the factors influencing the results obtained.

We declare no competing interests

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**Figure 1.** Flow chart describing the literature review of diabetes interventional programs