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# Risk Factors for Type 2 Diabetes Mellitus and Diabetic Foot Syndrome

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## Abstract

**Introduction:** Type 2 Diabetes Mellitus is the most prevalent type of DM worldwide and the diabetic foot syndrome is one of the complications.

**Objective:** To identify the most incident risk factors in type 2 Diabetes analyzing the different type risk factors prevalence and to analyze the diabetic foot syndrome predominance in type 2 DM at world.

**Methodology:** By collecting quantitative data through a bibliographic search. A total of 20 publications were selected.

**Results:** Risk factors that showed more incidents values were hypertension followed by high body mass index. In addition, the world-wide prevalence of the diabetic foot syndrome ranges from 1,2% to 12,1%.

**Conclusion:** Type 2 Diabetes Mellitus is a pathology with prevention plans with modifiable risk factors. Diabetic foot syndrome is a complication that presents a lower predominance showing world level prevalence in relation to other complications derived.

***Keywords:*** *Type 2 Diabetes Mellitus; Diabetic Foot Syndrome; Risk Factors; Complications of Diabetes; Primary Prevention*

## Introduction

Diabetes Mellitus (DM) is a chronic and progressive pathology made up of a group of diseases characterized by an increase in plasma glucose concentration as a result of alterations in insulin secretion, insulin action, or both. There are different types of DM due to factors such as genetics, environmental factors and lifestyle choices [1]. Worldwide, according to data from the International Diabetes Federation (IDF) in 2014, DM had a prevalence of 8.3% [2].

Type 2 DM, also called non-insulin dependent, is due to an ineffective use of insulin [3]. The risk of suffering from this pathology is determined by a combination of modifiable risk factors such as overweight, obesity, poor diet, sedentary lifestyle and smoking together with non-modifiable risk factors such as genetics, race and age [4].

Type 2 DM represents 85 - 90% of DM cases in developed countries worldwide [2]. At the European level, it affects approximately 5 - 10% of the population, especially people over 75 years of age [5]. According to the study carried out in Spain, diabetes in 2011, the prevalence of type 2 DM is 13.8% [6].

It is estimated that between 20% and 40% of diabetics will develop peripheral vascular disease and/or neuropathy as a consequence of poor glycemic control [7]. One of the consequences of these disorders suffered by patients with type 2 DM is Diabetic Foot (PD).

The WHO defines PD as a syndrome in which they arise: ulcer, infection or loss of tissues associated with neuropathy and peripheral vascular pathology [2]. PD causes the appearance of foot ulcers and, it is estimated that approximately 15% of diabetics will develop an ulcer of this type throughout their lives and, on the other hand, 70% of amputations that are performed they are due to DM [7].

## Objective of the Study

The objectives of the study were to identify the most common risk factors in type 2 DM and to analyze the predominance of PD Syndrome as a complication of type 2 DM.

## Materials and Methods

### Design

A Systematic Review (SR) of scientific studies that included quantitative analyzes about the risk factors of type 2 DM and those that addressed prevalence data on complications in this pathology was carried out, considering PD Syndrome among these.

### Search strategy

A bibliographic search was carried out in the period between the months of November 2017 to February 2018. This was carried out in two phases: the first phase aimed to search for studies which provide analytical information about the risk factors of type 2 DM. For the collection of these, a search was carried out in the biomedical database PubMed, LILACS and in the Center of Resources for Learning and Research (CRAI) of the University of Barcelona. Additionally, articles were identified in Editorial Elsevier and finally a detailed search was carried out in "Revista Clínica Española". The selection process is shown in the flow chart (Figure 1).

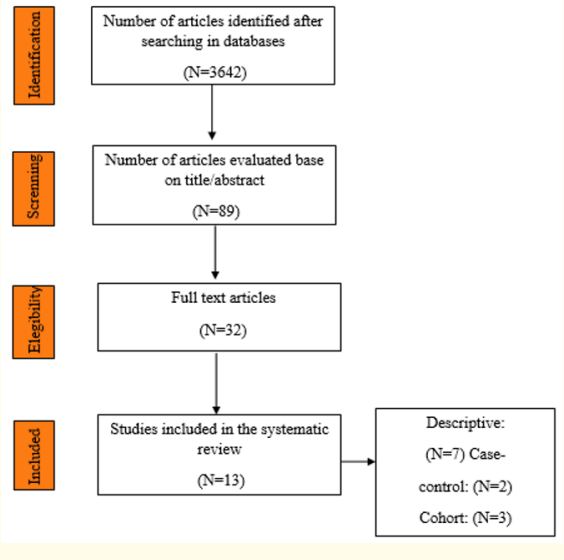


***Figure 1:*** *Flowchart of the study selection process to analyze the first objective.*

The objective of the second phase of the literature search was to compile studies that would provide us with information about the prevalence of PD Syndrome in type 2 DM as well as other complications. This search was carried out in the databases: PubMed and the CRAI of the University of Barcelona, as well as in the Elsevier publishing house. The selection process is shown in the flow chart (Figure 2).

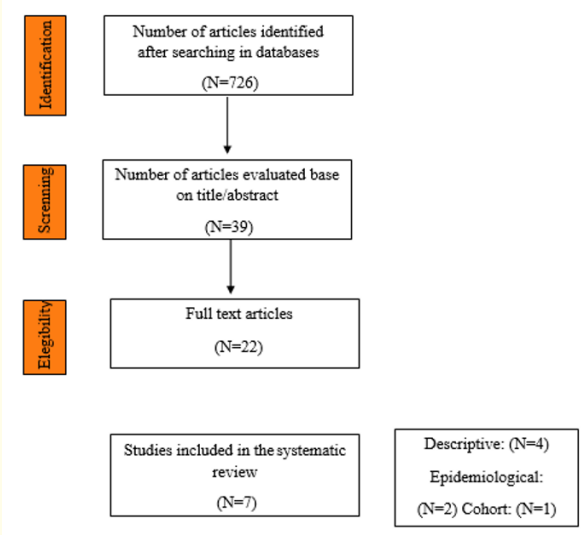


***Figure 2:*** *Diagram of the flow of the study selection process to analyze the second objective.*

Resolution of the first objective, it was decided to apply a series of requirements that the studies had to fulfill for the validity of these in the SR, which were the following: to include patients diagnosed with type 2 DM, to offer quantitative data about the factors of risk of type 2 DM and had been published between the years 2008-2018. On the other hand, the exclusion criteria selected were: those articles that made reference to any type of DM that was not type 2 DM, did not offer quantitative data on the risk factors for type 2 DM and carry out the study on a population without prior diagnosis of the disease.

For the choice of articles that provide us with information for the resolution of the second objective proposed in this work, the following inclusion criteria were established: articles that provide quantitative data regarding the prevalence of PD Syndrome in a population diagnosed with type 2 DM and had been published between the years 2008-2018. Referring to the exclusion criteria, the following were established: those articles that did not offer data expressed in a quantitative way and those that made reference to PD Syndrome on any type of DM that was not type 2 DM.

Regarding language, no restrictions were applied, except during the search for studies that would help us answer the first objective, in the PubMed database.

## Data extraction

Due to the diversity of risk factors for type 2 DM in the literature, in order to limit the study to the main risk factors, the "Update Guide on Type 2 Diabetes Mellitus" from the Network of Groups of Diabetes Study (GDPS) of 2016, which provided us with risk factors with a 2+ level of evidence and a grade D recommendation [8]. In addition, in combination with this guide on type 2 DM, to contrast the information

collected and provide new information, the "Clinical Practice Guide on Type 2 Diabetes" provided by the National Health System (SNS) was used and the government of the Basque Country in 2008, which gave us sex as a risk factor with a level of evidence of grade 3 [9].

The risk factors extracted from both guidelines and considered for their analysis can be seen in table 1.

| No modificables | Modificables |
|---|---|
| Age | Body Mass Index (BMI)<br>High |
| Race/ethnicity | Abdominal obesity |
| Genetic susceptibility | Sedentary lifestyle |
| Gestational DM history | Smoking |
| Polycystic ovary syndrome | Dietary patterns |
| Sex | Disorders of the regulation of glucose |
| | Hypertension arterial (HTA) |
| | Low birth weight |
| | Drugs (atypical antipsychotics, combination of β-blockers and diuretics and other drugs such as glucocorticoids, antiretrovirals or oral contraceptives) |
| | Heart disease |

***Table 1:*** *Risk factors considered for analysis.*

From the risk factors of interest, data were extracted referring mainly to their prevalence and also their p-value and Odds Ratio (OR), measures that relate the association between the risk factor and type 2 DM.

Finally, for the resolution of the second objective of this SR, data were extracted from studies about both chronic and acute complications in type 2 DM with the aim of estimating the prevalence of PD Syndrome in this pathology and its predominance over other complications.

## Results

### Most prevalent risk factors in type 2 DM

A total of 13 articles were used to resolve the first objective set out in this SR.

The analysis carried out from the data extracted from the studies shows us that the most prevalent risk factors in type 2 DM are modifiable, since six of the seven risk factors that were found to be the most prevalent were modifiable, among which are: hypertension, sedentary lifestyle, high BMI, high glycosylated hemoglobin level, and unhealthy diet [10-20]. On the other hand, only sex turned out to be the only non-modifiable risk factor that was more prevalent in two of the 13 studies [21,22]. This represents that only non-modifiable risk factors were observed to be more prevalent in 15.4% of the articles analyzed.

Specifically, the most prevalent risk factor found was hypertension, presenting as the most prevalent in four of the 13 articles, which represents that it was the one that was most affected in people with type 2 DM, in 30.8% of the studies included in the SR, as shown in figure 4 [10-13]. The second most prevalent risk factor was elevated BMI, which was the most prevalent risk factor in three of the 13 studies, representing 23.1% of the studies analyzed (Figure 3) [14-16].

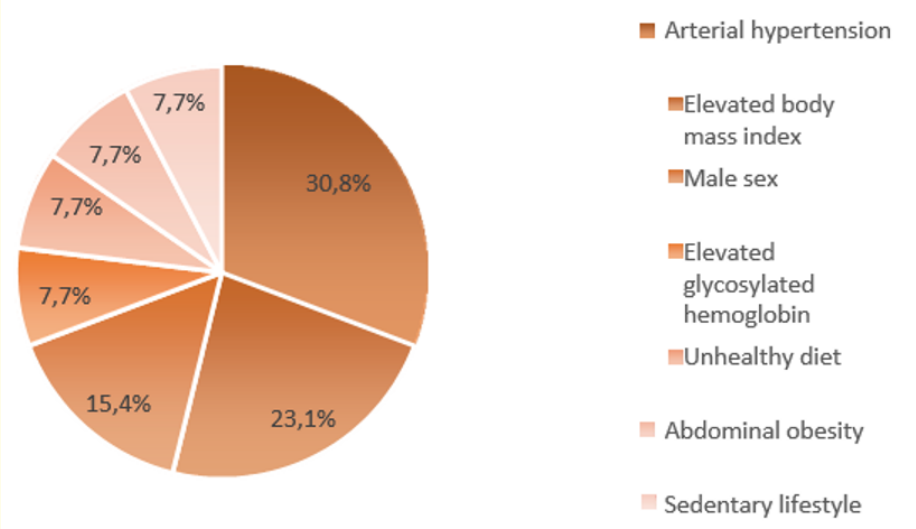


***Figure 3:*** *Percentage of the most prevalent risk factors in relation to items used in the RS.*

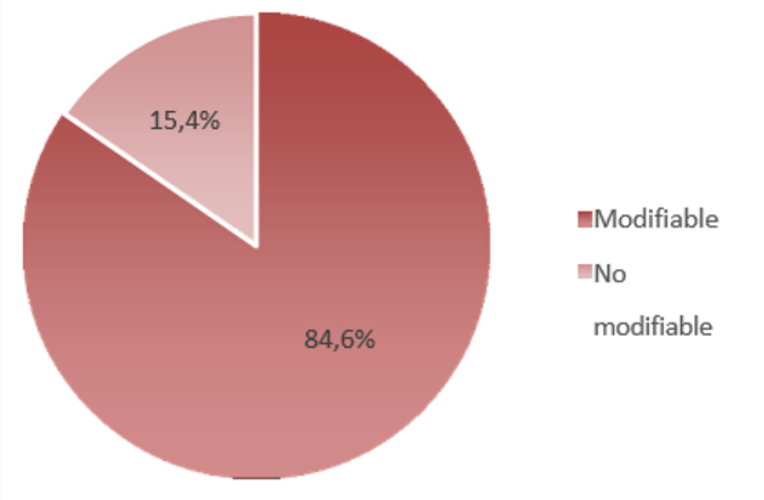


***Figure 4***

Referring to the statistical analysis using the p-value and the OR of the risk factors found to be the most prevalent, HTN showed statistically significant values in six of the eight articles that analyzed the p-value since values < 0.05 were shown [10-12,15,18,20]. Regarding the OR, the two studies that showed values for this variable presented statistically significant data [11,18].

Regarding high BMI, all the studies that offered us data about the p-value showed significant values [10-12,15,16,18,20-22], on the other hand, referring to the OR variable, this was significant in all studies that analyzed this statistical concept [11,18]. Lastly, the statistical data offered by the studies about sex (male) revealed values < 0.05 in five of the seven articles that showed us this value [10-12,21,22]. The OR was only analyzed in the study by Baena JM., *et al*. [16], presenting statistically significant values.

The characteristics of the 13 studies can be observed in Appendix A and in a more synthesized way, are the data of the most prevalent risk factors of each study in table 2.

| Most prevalent risk factors | Author/ Country/Year | Article | Results | | | | Type of risk factor |
|---|---|---|---|---|---|---|---|
| | | | Sample | % | p- value | OR | |
| HTA | Wang S., *et al*. China. 2016 [10] | Association between obesity indices and type 2 diabetes mellitus among middle-aged and elderly people in Jinan, China: a cross-sectional study | N = 284 | 67,3 | 0,034 | * | |
| | Sicras A et al. Spain. 2014 [11] | Clinical and economic characteristics associated with type 2 diabetes | N = 3760 | 67,2 | < 0,001 | 2,4 (IC 95%: 2,2 - 2,6) | Modifiable |
| | Rosado J., *et al*. Spain. 2012 [12] | Prevalence of diabetes in an adult population of Madrid (Spain). MADRIC Study (Madrid Cardiovascular Risk). | N = 139 | 72,5 | < 0,001 | * | |
| | Aggramonte M. Cuba. 2009 [13] | Prevalence of risk factors for atherosclerosis in diabetic patients type 2 | N = 219 | 74,0 | * | * | |
| IMC High | Paper K., *et al*. Thailandia. 2016 [14] | Incidence and risk factors for type 2 diabetes in transitional Thailand: results from the Thai cohort study | N = 698 | 42,1 | * | * | Modifiable |
| | Mariño AL *et al*. Cuba. 2012 [15] | Clinical, anthropometric and laboratory characterization women with type 2 diabetes mellitus | N = 58 | 94,8 | 0,023 | * | |
| | Baena JM *et al*. Spain. 2011 [16] | Altered basal blood glucose and risk of diabetes mellitus 10 years old. Cohort study. | N = 33 | 57,6 | 0,047 | * | |
| Diet does not healthy | Rule ID, *et al*. Brazil. 2008 [17] | Risk factors in patients with diabetes mellitus type 2. | N = 66 | 69,7 | * | * | Modifiable |
| Abdominal obesity | Saadati H., *et al*. Iran. 2013 [18] | Evaluation of risk factors for type 2 diabetes in population living in city of Yazd: a case-control study. | N = 200 | 87,0 | 0 | 3,44 (IC 95% 2,07-5,71) | Modifiable |
| Sedentary | Ferreira D., *et al*. Brasil. 2011 [19] | Prevalence of Risk Factors and Complications of Type 2 Diabetes Mellitus in Users of a Family Health Unit. | N = 70 | 71,4 | * | * | Modifiable |
| HbA1c elevated | Gil E., *et al*. Spain. 2015 [20] | Incidence of type 2 diabetes and associated factors in adult population of the Community of Madrid. PrediMERC Cohort. | N = 44 | 77,3 | 0 | * | Modifiable |
| Sex (male) | Watanabe Y., *et al*. Japan.2016 [21] | Risk of future diabetes in Japanese people with high-normal fasting plasma glucose levels: a 4-year follow- up study. | N = 133 | 74,4 | 0,168 | * | No Modifiable |
| | Sung K., *et al*. South Korea. 2012 [22] | Combined influence of insulin resistance, overweight/ obesity, and fatty liver as risk factors for type 2 diabetes. | N = 223 | 89,0 | 0,001 | * | |

***Table 2:*** *Synthesis of the characteristics of studies included in the RS on risk factors in type 2 DM.*
*N→ Sample/ *→ No data/ significant p-value→ p < 0,05.*

### Prevalence of PD as a complication in type 2 DM

For the resolution of the second objective, a total of seven studies have been obtained, which have provided us with a sample size of 45,632 patients affected by type 2 DM, taking into account that in the study carried out by Mundet X., *et al*. [23] only the prevalence data from the last sample have been taken into account as it is the most recent.

Through the prevalence data observed in each study, it can be observed that PD as a complication is placed behind other complications such as neuropathy, retinopathy, nephropathy and heart disease in most studies and it can also identify a worldwide prevalence ranging between 1.2% and 12.1%. The characteristics of the studies included in this SR can be seen in Appendix B and in a more synthesized way in table 3.

| Author/Country/Year | Article | Sample | Prevalence of Diabetic Foot (%) |
|---|---|---|---|
| Mundet X., *et al*. 2008. Spain [23] | Prevalence and incidence of chronic complications and mortality in a cohort of type 2 diabetic patients in Spain | N = 182 | 2,2 |
| Bermudez J., *et al*. Honduras. 2016 [24] | Comorities in patients with type 2 DM from the National Diabetic Institute, April-June 2016, Tegucigalpa, Honduras. | N = 382 | 5,2 |
| Pérez A., *et al*. Spain. 2014 [25] | Glycaemic control in patients with type 2 DM in Spain. | N = 5382 | 2,6 |
| Rahman A., *et al*. Saudi Arabia. 2014 [26] | Prevalence of chronic complication among type 2 diabetics attending primary health care centers of Al- Ahsa district of Saudi Arabia: A Cross sectional survey. | N = 506 | 12,1 |
| Arrieta F., *et al*. Spain. 2011 [27] | Descriptive study of the clinical-care evolution of the population with type 2 DM in the Community of Madrid. Diabetic follow-up study type 2 (ESD- 2). | N = 3268 | 9,9 |
| Lauterbach S., *et al*. 2010. United Kingdom [28] | Prevalence of diabetic foot syndrome and its risk factors in the UK. | N = 34198 | 8,5 |
| She was afraid of M., *et al*. 2009. Polonia [29] | Characteristics of patients with type 2 diabetes of short duration in Poland. | N = 1714 | 2,2→ treated sample by general medicine<br><br>1,2→ treated sample by doctors DM specialists. |
| Leal E., *et al*. 2018. Cuba [30] | Chronic complications in patients with recent diagnosis of type 2 diabetes mellitus | N = 200 | 5,5 |
| Ramirez D. 2018. Peru [31] | Main chronic complication of type 2 diabetes mellitus in the internal medicine service of the National Hospital Hipólito Unanue between August and December 2017 | N = 85 | 6,1 |

***Table 3:*** *Synthesis of the characteristics of studies included in the RS on DP in type 2 DM.*

*N→ Sample.*

## Discussion

Type 2 DM is a disease caused by various risk factors. This SR was carried out in order to determine which are the risk factors for type 2 DM most present in the population that suffers from this pathology and also to assess the prevalence of PD Syndrome as a complication.

In the study by Sicras A., *et al*. [11], which presented the largest sample of patients with type 2 DM with respect to the total of the included studies, with a total of 3,760 affected by the disease, hypertension was the most prevalent risk factor affecting 67.2% of the population who presented the pathology. Wang S., *et al*. [10], which reveals the characteristics of 282 people with type 2 DM included in their study, hypertension was identified as the risk factor most present in the population, affecting a total of 191 people, which it represents

67.3% of the population studied. The articles by Rosado J., *et al*. [12] and Agramonte M [13] also concluded that hypertension was the most prevalent risk factor in the population with type 2 DM, affecting 72.5% and 74.0% respectively in each publication.

Regarding elevated BMI, in the study carried out by Papier K., *et al*. [14] made up of a sample of 698 people, being overweight was the risk factor with the highest prevalence, affecting 42.1% of the population studied. Continuing with this variable, according to Mariño AL., *et al*. [15], obesity was the most prevalent risk factor, affecting 94.8% of the sample included in their study, which was made up of women. Baena JM., *et al*. [16] followed up for 10 years patients with altered baseline blood glucose, of which 33 developed type 2 DM. The analysis carried out found that obesity was the most prevalent risk factor, affecting 57.6%.

The studies carried out by Watanabe Y., *et al*. [21] and Sung K., *et al*. [22] both of Asian origin, were the only ones to point out a non-modifiable risk factor as the most incident. This was the sex, specifically being male, obtaining a prevalence of 74.4% and 89.0% respectively.

The synthesis of the studies included in this SR identifies HT as the most incident risk factor in type 2 DM, showing prevalence values greater than 50.0% of the sample in all the studies analyzed. High BMI was established as the second most prevalent modifiable risk factor, however, the data do not offer us a clear consensus regarding its prevalence since we found very high values.

Dispersed both for obesity, showing prevalence values that range from 20.3% to 94.8%, and for overweight, for which the values vary between 5.2% and 44.0%. For this estimate, the study carried out by Sung K., *et al*. [22] since it does not establish a differentiation between overweight and obesity, showing the prevalence of BMI without distinction of the two parameters. Regarding the prevalence of sex (male), as well as the prevalence of high BMI, there is no clear unanimity since the prevalence's shown by the studies range between 32.9% and 89.0%.

Of the different risk factors analyzed, it should be noted that smoking was consolidated in most of the studies as one of the least incident risk factors, showing prevalence values lower than 25.0% in 69.3% of the studies that showed values for this risk factor [10-12,14,16-20]. Furthermore, a non-significant p-value was observed in almost all the studies that showed us this data [10,12,15,16,18,20].

The results of this SR show that patients with type 2 DM have a high risk of suffering from some cardiovascular disease, as indicated by Sicras A., *et al*. [11], type 2 DM associated with a high BMI or hypertension increases cardiovascular risk since they are considered risk factors in both pathologies.

On the other hand, after studying the quantitative data on PD Syndrome in different countries, 85.7% of the studies showed prevalence values lower than 10.0% [23-25,27-29] and furthermore, no showed as more prevalent in none of the studies.

The study by Rahman A., *et al*. [26] showed the highest prevalence of this complication, reaching 12.1%, placing it as the fifth most frequent complication after heart disease, nephropathy, retinopathy and neuropathy. The value shown by this study is not significantly different from those shown in the studies by Arrieta F., *et al*. [27] and Lauterbach S., *et al* [28]. Arrieta F., *et al*. [27] ranked PD Syndrome as the third most frequent complication with a prevalence of 9.9%, surpassed by erectile dysfunction and heart disease. In the study carried out by Lauterbach S., *et al*. [28], the PD showed the second highest value with respect to the other complications analyzed, showing a prevalence of 8.5%, although it should be noted that only three complications were analyzed.

Bermúdez J., *et al*. [24], which studied the population with type 2 DM in Honduras, placed PD Syndrome lower than neuropathy and showed the same value as retinopathy, 5.2%. Regarding the situation of PD Syndrome in Spain, Pérez A., *et al*. [25] made his study of 5,382 patients with type 2 DM in the Spanish geography, establishing the PD prevalence at 2.6% of the population, it should be noted that this

complication was ranked as the least prevalent of the eight analyzed. On the other hand, other studies carried out in Spain, such as the one carried out in the Community of Madrid by Arrieta F., *et al*. [27] previously named, showed different values with respect to the article by Pérez A., *et al* [25]. Mundet X., *et al*. [23] which prepared its study on the population of Barcelona, concluded in a similar way to the study by Pérez A., *et al*. [25], showing a prevalence of PD of 2.2% and placing it as one of the less frequent complications occupying the penultimate position with respect to the total of complications studied.

The data analyzed allow us to observe a prevalence of this complication that is close to that reported in the article by Lauterbach S., *et al*. [28] in which data on the prevalence of this complication were collected from different studies carried out around the world, concluding that it was between 2.2% and 13.7%. Bała M., *et al*. [29], placed the PD Syndrome in the last position both in the examination performed by specialist physicians and in that performed by general practitioners with a prevalence of 1.2% and 2.2%, respectively.

## Study Limitations

- There are few studies that analyze the prevalence of type 2 DM risk factors, so the data used in this work have been extracted from the information that characterized the sample of each study.
- When screening studies showing us the prevalence of DP Syndrome, there was a lack of consensus on the definition of PD as several included amputation within this complication, so they had to be excluded from the study.

## Future Lines of Research

Once the most incident risk factors have been identified, this work may lead to the creation of a health education project in order to apply prevention methods on the most incident risk factors in type 2 DM, thus, reduce the prevalence of this pathology.

## Conclusion

- Type 2 DM is a preventable pathology in some patients as it is the modifiable factors that are placed as the most incidents. Specifically, HTA is the risk factor showing higher prevalence's, followed by high BMI. In addition, people with type 2 DM have a high risk of cardiovascular disease.
- PD Syndrome is low in predominance over other complications of type 2 DM, estimating a prevalence of this complication globally ranging from 1.2% to 12.1%.

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