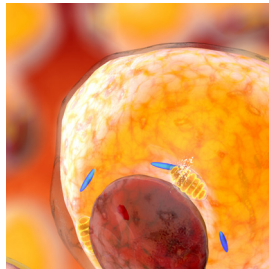


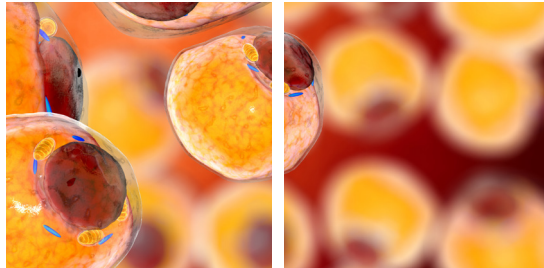
# Scientific Highlights of the 2019 LATAM Diabetes Management Workshop

A satellite symposium held during the  
**17<sup>th</sup> Congress of the Latin American  
Diabetes Association**



Friday, 1 November 2019  
from 17.00 to 18.30

Punta Cana,  
Dominican Republic





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## **INTRODUCTION**

Professor Yulino Castillo Núñez opened the meeting by outlining the learning objectives of this satellite symposium. The program is designed to update current knowledge of the epidemiology of pre-diabetes and diabetes, to highlight modifiable risks for diabetes – that is, insulin resistance, obesity and unhealthy lifestyle factors – to present data generated from landmark diabetes prevention trials, including data on therapeutic options, and to provide insight into helping patients implement lifestyle changes that can alter their disease projection.



## **CHAIR**

Yulino Castillo Núñez

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## L1

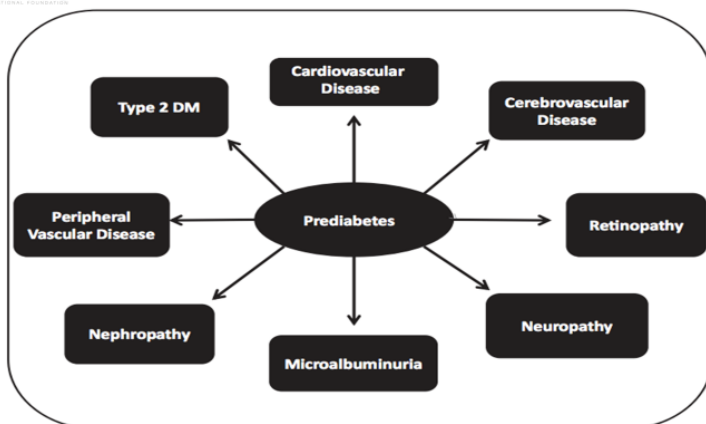
### Pre-diabetes: A risk factor or a disease?


Patricio Lopez-Jaramillo

FOSCAL and MASIRA Research Institutes,  
University of Santander, Colombia

Worldwide rates of diabetes are increasing year on year, and are predicted to continue increasing to 2040 and beyond in each area of the world. Although the epidemic of diabetes is ubiquitous, the prevalence of diabetes varies with the income of different countries – with low income countries having a higher incidence of diabetes than higher income countries.<sup>1</sup> Pre-diabetes rates also differ by country income, a fact not accounted for by conventional risk factors. Obesity is one of the main risk factors for developing dysglycemia, and one of the drivers of this relationship is the low muscle strength often found in obese subjects associated with their increased fat mass and metabolic risk factors. As body mass index increases, levels of C-reactive protein increase,<sup>2,3</sup> and systolic blood pressure rises.<sup>3</sup> In addition, as waist circumference increases, levels of leptin increase, and levels of adiponectin decrease.<sup>4</sup> Pre-diabetes is not just associated with type 2 diabetes (T2DM), but with several other disorders, including cardiovascular disease (CVD) and kidney disease. The risk of CVD starts to increase when a patient's HbA1c level enters the pre-diabetes range.

Figure 1: The impact of pre-diabetes





In Columbia, prevalence of impaired glucose tolerance (IGT) and impaired fasting glycemia is ~10%, which translates into >3 million adults with pre-diabetes out of a population of ~50 million – 2/3 of individuals with pre-diabetes are undiagnosed. Progression from IGT to diabetes is 18.3% per year in Asian Indians, higher than Finnish patients (6% per year) and Americans (11% per year).<sup>5</sup> Use of metformin in a clinical trial reduced the progression rate of IGT to diabetes in the Asian Indian population.<sup>5</sup>

Alteration in glucose metabolism is a risk factor for acute myocardial infarction (AMI) and a factor for poor prognosis following AMI.<sup>6</sup> Indeed, among patients with AMI, the majority have hyperglycemia and among those with hyperglycemia, a high percentage have pre-diabetes. The leptin-to-adiponectin ratio is already impaired in patients with pre-diabetes, but this ratio is improved by use of metformin, which may also improve prognosis in these patients.<sup>7</sup> Data suggest that Latin-Americans may benefit most from intervention to prevent diabetes.

In conclusion, pre-diabetes should be considered a disease in itself, and the avoidance of sarcopenia should be a main goal of interventions to prevent diabetes.



## L2

### **Eat well and move yourself! Obesity management for diabetes prevention**

G.E. Umpierrez

Diabetes and Endocrinology Department,  
Emory University, Atlanta, USA

Lifestyle changes may prevent diabetes in 30–50% of people with pre-diabetes. These changes include reducing body weight by 5%–10% and maintaining this weight loss over the long term, and implementing a regular moderate-intensity physical activity for 30–60 minutes daily, at least 5 days a week. USA Government guidelines published in 2008 advocated the term ‘physical activity’ rather than ‘exercise’ to make the concept more inclusive, with the precept that some is better than none, and that anything counts.

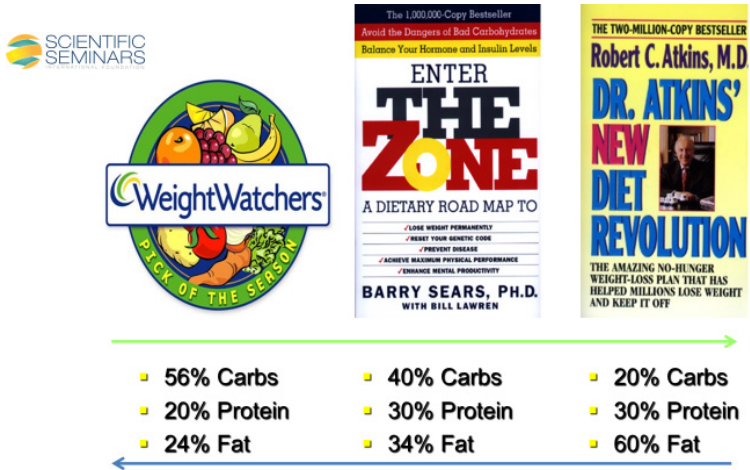
Lifestyle intervention in people with pre-diabetes has been shown to reduce progression to diabetes – a systematic review and meta-analysis of trials has found that after one and three years of lifestyle intervention, there is a 36–54% lower risk of progressing to T2DM compared with patients’ usual treatment.<sup>8</sup>

Inflammation is apparent in those with pre-diabetes, but this is ameliorated by weight loss, which also reduces blood glucose levels. In an older (but still relevant) study, Mayer-Davis *et al* showed that individuals with higher levels of physical activity had greater insulin sensitivity (less insulin resistance) and lower fasting insulin levels compared with individuals who had lower levels of activity. They suggested that ongoing physical activity—not just isolated bouts of physical activity—may be key determinants of insulin sensitivity.<sup>9</sup>

The Diabetes Prevention Program, which enrolled >3000 patients with IGT compared the impact of placebo versus metformin versus intensive lifestyle intervention. The study found that over the average follow-up of 2.8 years, intensive lifestyle intervention was the most effective strategy for preventing progression from IGT to T2DM, especially as people age.<sup>10</sup>

Although evidence supports lifestyle intervention as the most effective way to prevent diabetes, in the long term, compliance is a big problem. Therefore, finding the right diet that a patient will continue to follow in the long-term is the key to success. There is a plethora of published diets, with different guidelines advising on the optimal combination of protein, carbohydrate and fat for maximum weight loss (Figure 2).

Figure 2: Examples of popular diets



However, there are no clear data showing that any one diet is better than another. Adherence is the key for a diet to work, but it is difficult to follow dietary modification, and high levels of participants do not maintain their diet over the long term.



### L3

## Can we prevent more diabetes by using drugs on top of lifestyle interventions?

Nicola Napoli

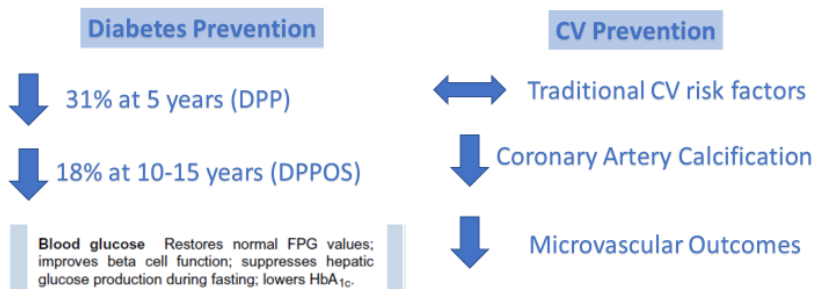
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There is extensive evidence for the benefit of lifestyle intervention to prevent diabetes. Analysis of the long-term data (15 years) from the Diabetes Prevention Program suggests that use of metformin is associated with less progression to overt T2DM and greater weight loss, as well as cost saving versus placebo.<sup>11</sup> Further analysis has found that risk of microvascular disease, nephropathy and retinopathy, increases in proportion to the rise in HbA1c already in the pre-diabetes range,<sup>12</sup> and treatment with metformin is associated with reduced microvascular disease, a finding that holds also for people with pre-diabetes. Further post-hoc findings of the Diabetes Prevention Program include the finding that the use of metformin is associated with lower prescriptions of anti-depressant medication, and that metformin may protect against coronary atherosclerosis in pre-diabetes and early diabetes mellitus in men.<sup>13</sup> Coronary artery calcification is increased in pre-diabetes, increasing the risk of CVD, morbidity and mortality (Figure 3).


Figure 3:



## Conclusions: Metformin







Other medications used in pre-diabetes include pioglitazone and acarbose. Pioglitazone use in pre-diabetes has been shown to prevent progression from IGT to T2DM by 72% over a median follow-up period of 2.4 years,<sup>14</sup> and has been associated with cardiovascular and liver benefits; however, it has also been associated with increased risk of heart failure, fractures, edema and weight gain.<sup>14,15</sup> Acarbose has been trialled in patients with pre-diabetes, and although it produced an 18% reduction in the risk of diabetes with no main side-effects, it was not associated with any cardiovascular protective properties.

So, in answer to the question posed at the start of this presentation - can we prevent more cases of diabetes by using drugs in addition to lifestyle interventions? Yes, we can, but adherence to treatment is essential to achieve the expected benefits.



## REFERENCES

1. Dagenais GR, et al. Variations in diabetes prevalence in low-, middle-, and high-income countries: Results from the prospective urban and rural epidemiological study. *Diabetes Care*. 2016 May;39(5):780–7.
2. Garcia RG, et al. Plasma concentrations of asymmetric dimethylarginine (ADMA) in metabolic syndrome. *Int J Cardiol* 2007 Nov 15;122(2):176–8.
3. López-Jaramillo P, et al. Inter-relationships between body mass index, C-reactive protein and blood pressure in a Hispanic pediatric population. *Am J Hypertens* 2008 May;21(5):527–32.
4. Rueda-Clausen CF, et al. The presence of abdominal obesity is associated with changes in vascular function independently of other cardiovascular risk factors. *Int J Cardiol*. 2010 Feb 18;139(1):32–41.
5. Lopez-Jaramillo P. Defining the research priorities to fight the burden of cardiovascular diseases in Latin America. *J Hypertens*. 2008 Sep;26(9):1886–9.
6. Gomez-Arbelaez D, et al. [Hyperglycaemia is associated with worse outcomes in Latin-American individuals with acute myocardial infarction]. *Clin Investig Arterioscler* 2016 Jan-Feb;28(1):9–18. [Article in Spanish, English abstract]
7. Sardu C, et al. Pericoronary fat inflammation and Major Adverse Cardiac Events (MACE) in prediabetic patients with acute myocardial infarction: effects of metformin. *Cardiovasc Diabetol* 2019 Sep 30;18(1):126.
8. Glechner A, et al. Effects of lifestyle changes on adults with prediabetes: A systematic review and meta-analysis. *Prim Care Diabetes* 2018 Oct;12(5):393–408.
9. Mayer-Davis EJ, et al. Intensity and amount of physical activity in relation to insulin sensitivity: The Insulin Resistance Atherosclerosis Study. *JAMA* 1998;279:669–674.
10. Knowler WC, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002 Feb 7;346(6):393–403.
11. Aroda VR, et al. Metformin for diabetes prevention: insights gained from the Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study. *Diabetologia* 2017 Sep;60(9):1601–1611.
12. Perreault L, et al. Regression from prediabetes to normal glucose regulation and prevalence of microvascular disease in the Diabetes Prevention Program Outcomes Study (DPPOS). *Diabetes Care* 2019 Sep;42(9):1809–815.
13. Goldberg RB, et al. Effect of long-term metformin and lifestyle in the Diabetes Prevention Program and its outcome study on coronary artery calcium. *Circulation* 2017 Jul 4;136(1):52–64.

14. DeFronzo RA, et al. Pioglitazone for diabetes prevention in impaired glucose tolerance. *N Engl J Med* 2011 Mar 24;364(12):1104–15.
15. Liao HW et al. Pioglitazone and cardiovascular outcomes in patients with insulin resistance, pre-diabetes and type 2 diabetes: a systematic review and meta-analysis. *BMJ Open*. 2017 Jan 5;7(1):e013927.



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