DIABETES PRIMARY PREVENTION PROGRAM: NEW INSIGHTS FROM DATA ANALYSIS OF RECRUITMENT PERIOD

Juan J Gagliardino[1*], Jorge F Elgart[1], Marcelo Bourgeois[2], Graciela Etchegoyen[2], Gabriel Fantuzzi[1], Matías Ré[1], Juan P Ricart[1], Silvia García[1], Cecilia Giampieri[1], Lorena González[1], Florencia Suárez-Crivaro[3], Peter Kronsbein[4], Julieta M Angelini[5], Camilo Martínez[5], Jorge Martínez[5], Alberto Ricart[6] and Eduardo Spinedi[1]

[1]CENEXA. Center for Experimental and Applied Endocrinology (UNLP-CONICET La Plata), Faculty of Medical Sciences (UNLP), La Plata, Argentina; [2]Chair of Epidemiology - INUS Center, Faculty of Medical Sciences (UNLP), La Plata, Argentina; [3]Laboratory, Secretariat of Health and Social Medicine, Municipality of La Plata, La Plata, Argentina; [4]Faculty of Nutrition, Food and Hospitality Sciences, Niederrhein University of Applied Sciences, Mönchengladbach, Germany; [5]Faculty of Medical Sciences, National University of La Plata (UNLP), La Plata, Argentina; [6]IdIHCS. Institute of Research in Humanities and Social Sciences (UNLP-CONICET La Plata), Faculty of Humanities and Cs of Education (UNLP), La Plata, Argentina.

Running title: Primary prevention of diabetes

***Address for Correspondence**:
Dr. Juan J. Gagliardino,
CENEXA (UNLP-CONICET La Plata), Facultad de Ciencias Médicas - UNLP.
60 y 120 – 4to. Piso, (1900) La Plata, Argentina.
Fax: (54-221) 422-2081
e-mail: cenexaar@yahoo.com.ar

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/dmrr.2943

Abstract word counts: 245

Text word counts: 2,151

Number of tables/figures: 4

Number of references: 21

Abstract

Objectives: Primary Prevention of Diabetes Program in Buenos Aires Province (PPDBA) evaluates the effectiveness of adopting healthy lifestyle to prevent type 2 diabetes (T2D) in people at high risk of developing it. We aimed to present preliminary data analysis of FINDRISC and laboratory measurements taken during recruitment of people for the PPDBA in the cities of La Plata, Berisso and Ensenada, Argentina.

Methods: People were recruited through: *Population approach* (house to house survey by FINDRISC in randomized areas) and *opportunistic approach* (FINDRISC completed by participants during consultations for non-related pre-diabetes/diabetes symptoms in public and private primary care centers of cities involved). In people with FINDRISC score ≥13 points we evaluated blood concentrations of HbA1c, creatinine, lipids and an oral glucose tolerance test (OGTT).

Results: 3415 individuals completed the FINDRISC populational survey and 344 the opportunistic survey; 43% of the two groups scored over 13 points; 2.8 and 75.4% of them, respectively, took the prescribed OGTT. 53.7% of the OGTT showed normal values and 5.2% unknown T2D. The remaining cases showed 69.5% impaired fasting glucose (IFG), 13.6% impaired glucose tolerance (IGT) and 16.9% both impairements. HbA1c values showed significant differences compared to normal glucose tolerance (NGT; 4.96±0.43%), pre-diabetes (5.28±0.51%) and T2D (5.60±0.51%). Participants with pre-diabetes and T2D showed a predominant increase in LDL-cholesterol values. In pre-diabetes, > 50% showed insulin resistance (IR).

Conclusions: People with pre-diabetes/T2D had dyslipidemia associated with IR which promotes the development of T2D and cardiovascular disease. Thus, it merits its appropriate treatment.

Key words: Diabetes primary prevention, pre-diabetes, dyslipidemia in pre-diabetes, FINDRISC score

1. INTRODUCTION

Diabetes prevalence in Argentina grew from 8.4 to 9.8% between 2005 and 2013 [1], mainly conditioned by type 2 diabetes (T2D). The frequent association of T2D with other cardiovascular risk factors (CVRF) facilitates development/progression of chronic complications responsible for their high morbidity and mortality and economic cost [2,3].

T2D develops in people with genetic predisposition exposed to unhealthy diets and physical inactivity [4]; therefore, adoption of healthy lifestyles is the most effective way to prevent the disease, a concept supported by the successful reduction, up to 58%, of T2D development through implementation of primary prevention programs in different countries and ethnical groups [5]. Based on such experience, there is a strong European movement towards promoting diabetes prevention programmes implementation in their region that even has developed a tool kit to use for that purpose [6]. Despite strong evidence of the preventive effectiveness of lifestyle changes in people at high risk of developing T2D, before implementing such programs at national level, it is necessary to verify how they work in our environment, identify potential difficulties/barriers to preventive goals to avoid or neutralize them, and estimate the program's cost.

Consequently, and given the lack of national evidence, we initiated the Pilot Program for Primary Prevention of Diabetes of Buenos Aires Province (PPDBA), aiming to evaluate the effectiveness of healthy lifestyle adoption on the clinical manifestation of T2D in people at increased risk of developing the disease. This report shows preliminary analysis of data obtained during recruitment of people for the PPDBA in three cities of Buenos Aires province.

2. MATERIALS AND METHODS

The characteristics of the PPDBA were previously reported [7]. Briefly, it is a prospective, randomized cohort study to evaluate the benefits of adopting healthy lifestyles (healthy meal plan and regular practice of physical activity) on the transition from pre-diabetes (impaired glucose tolerance [IGT], impaired fasting glycaemia [IFG], or both) to T2D. This study recruits men and women between 45 and 75 years of age with pre-diabetes according to the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD)[8] in three municipalities of Buenos Aires province (La Plata, Berisso and Ensenada). For recruitment we used two different procedures:

1. *Populational approach*: we randomly selected census areas in each municipality as explained in the previous publication [7]; in these areas, previously trained students of the

last year of the School of Medicine of La Plata National University visited homes to administer the FINDRISC [9].

2. *Opportunistic approach*: This scheme was used previously for pre-diabetes and cardiovascular risk factor detection [10]; in our case, people visiting a physician's office for reasons other than pre-diabetes/diabetes filled out the FINDRISC. To facilitate this approach we invited physicians in Primary Care Centers (CAPs) of the participant municipalities and in private groups in La Plata. Consequently, the sample included persons from both public health and social security sectors.

In both approaches, people with a FINDRISC score ≥13 points (cut-off value indicated by Prof. Jakko Tuomilheto, PPDBA advisor) were invited to receive free of charge an oral glucose tolerance test (OGTT) following WHO recommendations [11]. In the OGTT fasting blood sample we also measured concentrations of HbA1c (by HPLC technique), creatinine, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride using commercial kits. All blood samples were processed in a single laboratory (CentraLab, CABA, Argentina) within 24 hours after extraction.

People with normal glucose tolerance (NGT) were advised to repeat the OGTT in one year, whereas those with a diagnosis of T2D were referred to their own physician for appropriate treatment. Those who presented pre-diabetes (IFG, IGT or both) and met the PPDBA inclusion criteria were invited to participate in the PPDBA after acceptance and signing of the informed consent. Thereafter, these people were randomly assigned to one of our two study groups (*Intensified* and *Self-administered* intervention) as previously reported [7].

2.1 Ethical issue

The study protocol was analyzed and approved by the Bioethical Committee of the National University of La Plata and the Central Ethics Committee of the Ministry of Health of the province of Buenos Aires. The study was developed according to the Good Practice Recommendations (International Harmonisation Conference) and the ethical guidelines of the Helsinki Declaration. All subjects gave their written informed consent to participate in the study, and this was signed before blood samples were collected.

2.2 Statistical analysis

With the FINDRISC and laboratory data collected during the early recruitment period (2014-2015), a descriptive and inferential statistical analysis was performed using SPSS (Statistical Package for Social Sciences), version 15.0 for Windows (SPSS Inc, Chicago, IL, US). Continuous variables are presented as means and standard deviations (SD) and categorical variables as proportions. Differences in continuous variables were assessed using parametric and non-parametric tests according to the normal distribution of the variables (Kolmogorov-Smirnoff test), using the χ^2 test to evaluate the differences in proportions. Differences with p values <0.05 were considered significant..

3. RESULTS

FINDRISC: 3415 questionnaires were completed with the *Populational approach* and 344 with the *opportunistic* one. Their results showed a normal distribution with 43% of participants scoring ≥13 points; 23% and 3%, respectively, had high and very high scores of risk (FINDRISC criteria) [9]) of developing T2D (Figure 1). Whereas in the *populational approach* only 2.8% of people prescribed the OGTT did it, 75.4% of people in the *opportunistic approach* in the same condition took the OGTT.

Comparing FINDRISC results from people below and above 13 points, we found an asymmetric percentage distribution of each of the 8 questions within the two groups: people in the latter group had a higher percentage of:

- physical inactivity
- medication taken to control blood pressure
- age (were older)
- BMI corresponding to overweight/obesity
- waist circumference above the normal cut-off value
- low daily consumption of fruits and vegetables
- history of hyperglycemia.

The largest percentage corresponded to waist circumference (81%) and physical inactivity (74%) while history of hypoglycemia was recorded only in 20% of the this group.

According to the OGTT results and cut-off values suggested by the ADA-EASD, our sample included three categories of people: 1) with normal glucose tolerance (NGT), 2) with pre-diabetes (IFG/IGT or both) and 3) with undiagnosed/untreated T2D (Figure 2). Although we only prescribed OGTT for people with a score ≥13, 53.7% of them showed normal results.

Figure 2 also shows that 5.2% of the individuals evaluated had unknown/ undiagnosed and consequently untreated T2D. Further data analysis showed that in 63% of cases of T2D and in 62% of pre-diabetes identified, diagnosis was based on the fasting blood glucose value of the OGTT.

HbA1c values recorded to date showed significant differences when comparing the 3 following groups: people with NGT (4.96±0.43%), with pre-diabetes (5.28±0.51%) and with T2D (5.60±0.51%) (Figure 3).

Participants with pre-diabetes and T2D showed a similar abnormal lipid profile characterized by total cholesterol, LDL-c and triglyceride levels above those recommended by international guidelines (Table 1). Increased LDL-c levels was the most frequently detected change in the pre-diabetes group, this frequency comparable to that observed in people with T2D.

We did not measure insulinemia, therefore, we have no direct indicator of insulin resistance (IR) in people with pre-diabetes. We instead used two indirect measures: a clinical (waist circumference) [12] and a laboratory test (Triglyceride/HDL-c ratio) using cut-off values validated in our population [13]. According to waist circumference (men> 102 and women> 88 cm), 78% of participants with pre-diabetes had IR whereas that figure was 51% for the Triglyceride/HDL-c ratio (values >3.5 and >2.5 for men and women, respectively). Thus, independent of the index applied, more than half of our pre-diabetes population displayed IR.

4. DISCUSSION

Current PPDBA data show: barriers to participants' recruitment; evidence of diabetes diagnostic inefficiency in our care system; and some novel data.

While the FINDRISC data shows similar results for the two collection approaches, adherence to OGTT prescription was significantly higher with the *opportunistic approach* (75.4 *vs.* 2.8%). Adherence failure could be attributed to: a) subjectively "healthy" persons reject the diagnosis of a serious but asymptomatic disease after a medical student asked 8 questions; b) inadequate population and health system promotion of preventive practices considering the absence of symptoms (especially pain); and c) the subjective inclination to follow their physician's prescriptions more readily than those of an unfamiliar health agent. Therefore, the opportunistic rather than the populational approach is more advisable for use in similar studies implemented in our culture.

FINDRISC, with low cost and easy performance, decreased the prescription of OGTT (57%), thereby optimizing resources. Although the weakness of this assumption is that the FINDRISC has not yet been validated in our local population, it has been used in Caucasian,

Spanish and other Latin American populations [14]; these studies also yielded data comparable to those currently recorded. In any case, the cut-off value currently used rendered 53.7% of normal OGTT, thus it would require an adaptation of this value to our population in order to optimize outcomes. This assumption is supported by some European authors´conclusions that the FINDRISC is currently the best available tool for use in clinical practice but may require modifications if applied to different ethnic groups [15]. The asymmetry of positive answers in people below and above the cut-off value indicates that this adaptation requires recalculation of the weight given to each question and then the resetting of the cut-off value according to the results of the OGTT. However, for the time being, the FINDRISC with its current score is still a useful and effective tool at the primary care level.

Another important aspect of our FINDRISC data analysis is that family history of diabetes, which represents the effect of inheritance on the incidence of pre-diabetes/T2D development, is reported by people at high risk in a markedly lower proportion than waist circumference and physical inactivity related to the mass and function of visceral adipose tissue and metabolic modulators released by physical activity. These data support the concept that epigenetic alterations facilitate the development of pre-diabetes and its progression to T2D [16,17].

The 3 different pre-diabetes stages identified by OGTT (IFG, IGT, and both) have a different annual transition rate to T2D: 12% for the third stage and 4 and 6% for the other two, respectively [18]. Therefore, the implementation of preventive strategies is correspondingly more or less imperative. In our case, most people with dysglycemia presented IFG (69.5%), a finding also reported by other authors who showed that these people have significantly larger values of waist circumference, blood pressure and frequency of dyslipidemia and cardiovascular disease [19]. It has been also reported that they have already lost 50% of their β-cell mass [20]. Thus, when planning to implement a primary prevention intervention and having low availability of human and economic resource, systematic measurement of fasting blood glucose might be an incomplete but still reasonable approach to identify people with pre-diabetes.

Using the sequence FINDRISC-OGTT we identified 5% of people with T2D who were unaware of their disease and untreated; these results could suggest the advisability of systematic prescription of OGTT for diabetes detection. However, 63% of people with undiagnosed with T2D and 62% of those with pre-diabetes were identified by fasting glycemia values. Therefore, ongoing awareness of health care team members concerning the importance of careful analysis of fasting blood glucose values by searching for diagnostic values recommended by national and international guidelines could overcome the problem.

The importance of this awareness is further supported by the report that late diagnosis increases the risk of cardiovascular morbidity and mortality more than late treatment [21].

Based on the recommendations of the Experts Committee convened by ADA, EASD and International Diabetes Federation (IDF) to redefine diabetes diagnosis by HbA1c values [22], different countries established their own cut-off values for pre-diabetes and T2D diagnosis. Current HbA1c values result from the first local study of this type.

Participants with pre-diabetes and T2D displayed similar dyslipidemia characterized by abnormal changes in all lipid fractions; an increase in the LDL-c fraction was the most frequently detected, indicating a high risk for developing atherosclerotic cardiovascular disease (CVD). Thus, pre-diabetes stage is a risk for developing T2D but also for CVD [23]. Since we found no marked differences between the frequency of increased LDL-c in people with pre-diabetes and T2D, its presence in the former stage could be more a cause than a consequence of β-cell dysfunction. Identification of plasma lipoprotein receptor in pancreatic β cells involved in their binding/processing and the report that LDL particles reduce insulin mRNA levels, β-cell proliferation, and induce a dose-dependent increase in their apoptotic rate support this assumption. Conversely, HDL-c particles antagonize the proapoptotic effect of LDL-c. Therefore, the deleterious effect of increased LDL-c on β-cell function/mass could be potentiated by the simultaneous decrease in HDL-c concentration [24,25].

Finally, using two indirect measurements (waist circumference and TG/HDL-c ratio), we demonstrated that most people with pre-diabetes have IR.

We recognize that although our evidence is clear, it is based on certain circumstances and on a low number of cases. However, its statistical significance suggests that it is unlikely to be the result of chance.

In conclusion, early results of PPDBA implementation demonstrate that: 1) sequential performance of FINDRISC-OGTT is an effective strategy to identify people with pre-diabetes or T2D who were unaware of their disease; 2) people with pre-diabetes present a state of IR associated with dyslipidemia that favors development of T2D and CVD, thus this a stage of disease rather than pre-disease stage that merits its immediate treatment; 3) in our media, and probably in other ones with similar socioeconomic characteristics, the opportunistic approach implemented through primary care physicians was a more effective strategy to identify people with pre-diabetes; 4) health authorities must be aware of pre-diabetes and T2D underestimation occurring at the primary care level in order to correct this deficiency; and 5) final PPDBA data will more accurately define national HbA1c cut-off

values for pre-diabetes and T2D diagnosis. Our data contribute to develop effective strategies to decrease the diabetes burden.

Acknowledgments: The authors thank Adriana Di Maggio, Lucas Bertulo, and Marcelo Lopez for their collaboration in the logistics and communication of the PPDBA, the health care teams, the authorities of the Health Secretariats of La Plata, Berisso and Ensenada cities, and the Health Ministry of Buenos Aires Province for their valuable cooperation. GF, MR and JPR are fellows/theses of MINCYT (PID-2012-0051). LG is a PhD fellow from CONICET. JJG, GE, JFE, and ES are CONICET Career Researchers.

Funding: The PPDBA is supported by PID-2012-0051, which receives contributions from the Ministry of Science, Technology and Productive Innovation (MINCYT), National Scientific and Technical Research Council (CONICET) and the Sanofi Company.

Conflict of interest: None of the authors has any conflict of interest related to this project.

References

1. Galante M, Konfino J, Ondarsuhu D, et al. Principales resultados de la tercera Encuesta Nacional de Factores de Riesgo de enfermedades no transmisibles en Argentina. Rev Argent Salud Pública, 2015; 6(24): 22-29
2. Morsanutto A, Berto P, Lopatriello S, et. al. Major complications have an impact on total annual medical costs of diabetes: results of a database analysis. J Diabetes Complications 2006; 20:163-169.
3. Elgart JF, Asteazarán S, De La Fuente JL, et al. Direct and indirect costs associated to type 2 diabetes and its complications measured in a social security institution of Argentina. Int J Public Health. 2014; 59(5):851-857.
4. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am 2004;88:787–835
5. Baker MK, Simpson K, Lloyd B, Bauman AE, Fiatarone Singh MA. Behavioral strategies in diabetes prevention programs: A systematic review of randomized controlled trials. Diabetes Res. Clin Practice 2011; 91:1-12
6. Lindström J, Neumann A, Sheppard KE, et al. Take action to prevent diabetes--the IMAGE toolkit for the prevention of type 2 diabetes in Europe. Horm Metab Res. 2010; 42 Suppl 1:S37-55
7. Gagliardino JJ, Etchegoyen G, Bourgeois M, Fantuzzi G, García S, González L, Elgart JF, Ré M, Ricart A, Ricart JP y Spinedi E. Prevención primaria de diabetes tipo 2 en Argentina: estudio piloto en la provincia de Buenos Aires. Rev Argent Endocrinol Metab. 2016; 53:135-141
8. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2012; 35:1364–1379.
9. Saaristo T, Peltonen M, Lindström J, et al. Cross-sectional evaluation of the Finnish Diabetes Risk Score: a tool to identify undetected type 2 diabetes, abnormal glucose tolerance and metabolic syndrome. Diabetes Vasc Dis Res. 2005; 2:67-72.
10. Zhang Y, Hu G, Zhang L, Mayo R, Chen L. A novel testing model for opportunistic screening of pre-diabetes and diabetes among U.S. adults. PLoS One. 2015; 10(3):e0120382.

11. WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Geneva: World Health Organisation; 1999. Report No 99.2.
12. Alberti KG, Eckel RH, Grundy SM, et al; International Diabetes Federation Task Force on Epidemiology and Prevention; Hational Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120:1640-1645,
13. Salazar MR, Carbajal HA, Espeche WG, et al. Comparison of the abilities of the plasma triglyceride/high-density lipoprotein cholesterol ratio and the metabolic syndrome to identify insulin resistance. Diab Vasc Dis Res. 2013; 10:346-352.
14. Barengo NC, Tamayo DC, Tono T, Tuomilehto J. A Colombian diabetes risk score for detecting undiagnosed diabetes and impaired glucose regulation. Prim Care Diabetes. 2016. pii: S1751-9918(16)30100-0. doi: 10.1016/j.pcd.2016.09.004.
15. Schwarz PE, Li J, Lindstrom J, Tuomilehto J. Tools for predicting the risk of type 2 diabetes in daily practice. Horm Metab Res. 2009; 41(2):86-97
16. Reddy MA, Zhang E, Natarajan R. Epigenetic mechanisms in diabetic complications and metabolic memory. Diabetologia. 2015; 58:443-455.
17. Rönn T, Ling C. DNA methylation as a diagnostic and therapeutic target in the battle against Type 2 diabetes. Epigenomics 2015;7:451-460.
18. Gerstein HC, Santaguida P, Raina P, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. Diabetes Res Clin Practice 2007; 78(3):305-312.
19. Sinnott M, Kinsley BT, Jackson AD, et al. Fasting plasma glucose as initial screening for diabetes and prediabetes in irish adults: The Diabetes Mellitus and Vascular health initiative (DMVhi). PLoS One. 2015; 10(4):e0122704
20. Butler AE, Janson J, Bonner-Weir S, Ritzel R, Rizza RA, Butler PC. -Cell deficit and increased -cell apoptosis in humans with type 2 diabetes. Diabetes 2003; 52:102–110
21. Herman WH, Ye W, Griffin SJ, et al. Early Detection and Treatment of Type 2 Diabetes Reduce Cardiovascular Morbidity and Mortality: A Simulation of the Results of the

Anglo-Danish-Dutch Study of Intensive Treatment in People With Screen-Detected Diabetes in Primary Care (ADDITION-Europe). Diabetes Care. 2015; 38:1449-1455.

22. International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes Diabetes Care 2009; 32: 1327-1334.
23. DeFronzo RA, Abdul-Ghani M. Assessment and Treatment of Cardiovascular Risk in Prediabetes: Impaired Glucose Tolerance and Impaired Fasting Glucose. Am J Cardiol. 2011; 108(suppl):3B-24B.
24. Kruit JK, Brunham LR, Verchere CB, Hayden MR. HDL and LDL cholesterol significantly influence beta-cell function in type 2 diabetes mellitus. Curr Opin Lipidol 2010; 21:178-185,
25. Abderrahmani A, Niederhauser G, Favre D, et al. Human high-density lipoprotein particles prevent activation of the JNK pathway induced by human oxidised low-density lipoprotein particles in pancreatic beta cells. Diabetologia 2007; 50:1304-1314.

Table 1. Lipid profile of the different subgroups of pre-diabetes and T2D

Fraction / Condition		IFG (n=71)	IGT (n=15)	Both (n=19)	T2D (n=15)
Total Cholesterol (mg/dl)	Mean ± SD	197 ± 39	208 ± 30	205 ± 58	215 ± 52
	%*	44	60	47	47
c-HDL (Men)	Mean ± SD	44 ± 14	--	42 ± 10	59 ± 27
	%**	29		44	33
c-HDL (Women)	Mean ± SD	53 ± 15	51 ± 15	57 ± 14	53 ± 18
	%**	36	53	50	58
c-LDL	Mean ± SD	119 ± 37	128± 20	127 ± 51	129 ± 41
	%#	59	87	68	71
Triglycerides	Mean ± SD	154 ± 98	144 ± 68	165 ± 61	163 ± 115
	%†	38	33	47	40

Mean ± standard deviation (SD). Values represent % of people with values of * Total Cholesterol > 200 mg/dL; ** c-HDL < 50 mg/dl (female) and < 40 mg/dl (male); # c-LDL > 100 mg/dL and † Triglycerides (TG) > 150 mg/dL.

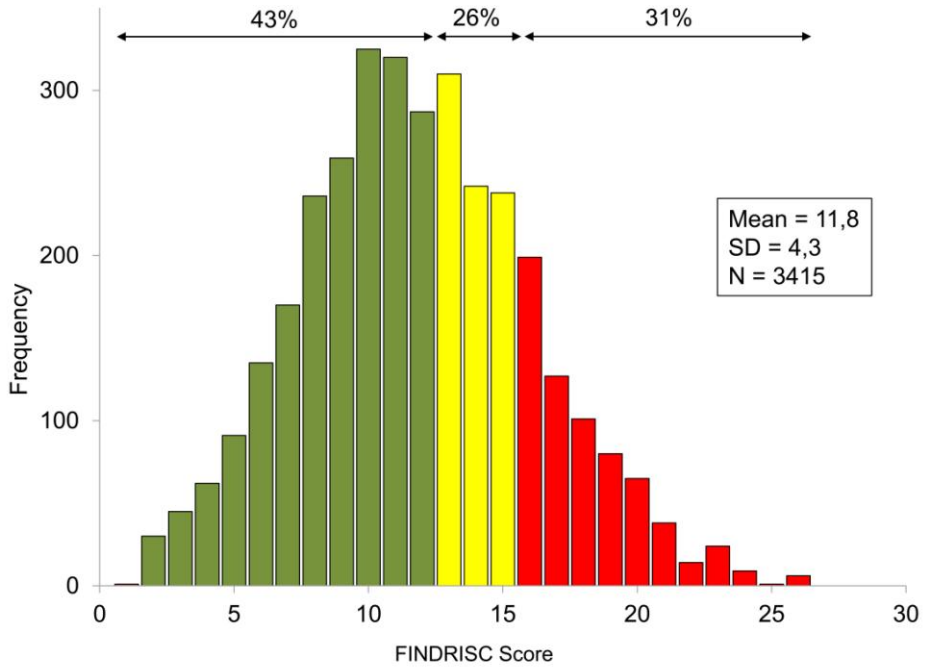

Figure 1. Distribution of risk percentage of FINDRISC

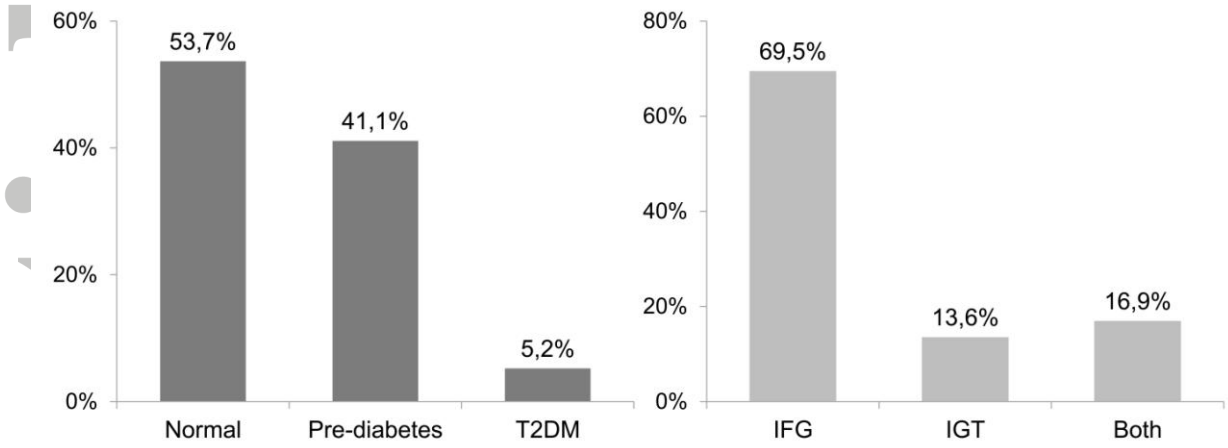

Figure 2. Results of the OGTT N (total) = 287; N (Pre-diabetes) = 118

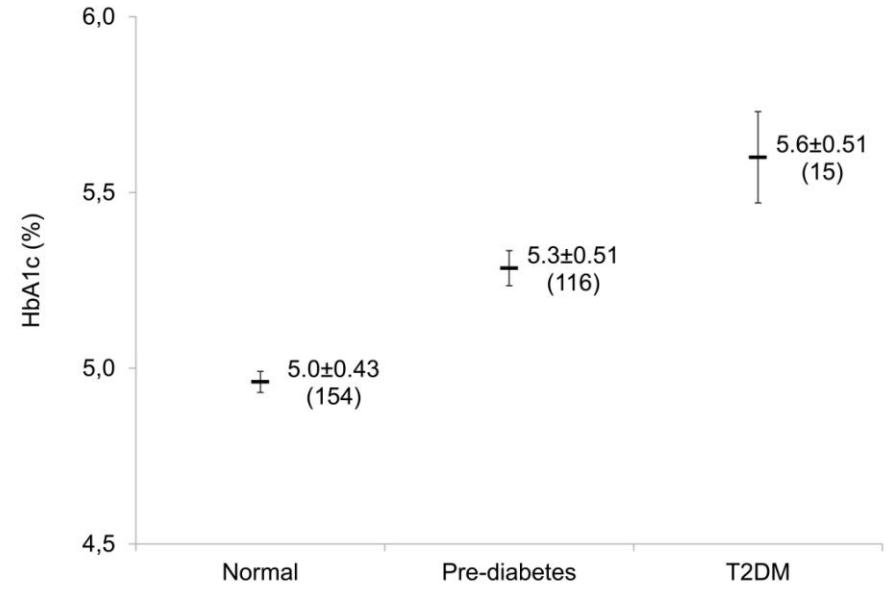

Figure 3. HbA1c differences by category.Values are mean ± standard deviation (N=group size, in parentheses).