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► To cite this version:

Norah Anthony, Victorine Lenclume, Adrian Fianu, Nathalie Le Moullec, Xavier Debussche, et al.. Association between prediabetes definition and progression to diabetes: the REDIA follow-up study. Diabetes Epidemiology and Management, 2021, 3, pp.100024. 10.1016/j.deman.2021.100024 . hal-03423927

HAL Id: hal-03423927

<https://hal.univ-reunion.fr/hal-03423927>

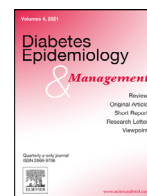
Submitted on 10 Nov 2021

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Original article

Association between prediabetes definition and progression to diabetes: The REDIA follow-up study



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ARTICLE INFO

Article History:

Received 15 October 2021

Revised 31 October 2021

Accepted 3 November 2021

Available online 7 November 2021

Keywords:

Prediabetes

Type 2 diabetes mellitus

Secondary prevention

Screening

ABSTRACT

Aim To determine which prediabetes definition is the best predictor of progression to diabetes in Reunion Island where 10% of the population has treated diabetes.

Methods This follow-up study used data from the REDIA cross-sectional study, a population-based study conducted in two stages. Participants were enrolled in 1999–2001 (REDIA-1) and followed-up years later in 2006–2009 (REDIA-2). Odds ratios (OR) for prediabetes were estimated with their 95% confidence interval (95%CI) from logistic regression models. REDIA-1 participants with no previously identified diabetes in REDIA-1 were assessed for new pharmacologically treated diabetes in REDIA-2. We evaluated several biological definitions of prediabetes, each based on the combination of fasting plasma glucose (FPG), 2-h post-load plasma glucose (2hPG), and/or HbA1c: FPG-ADA (American Diabetes Association), FPG-WHO (World Health Organization), 2hPG, HbA1c-ADA, HbA1c-IEC (International Expert Committee), FPG-WHO/2hPG, and FPG-WHO/HbA1c-ADA.

Results A total of 432 participants met all inclusion criteria. Of these, 102 (23.6%) were classified as prediabetic using the FPG-WHO/2hPG definition, including 58 (56.9%) with isolated impaired glucose tolerance, 17 (16.6%) with isolated impaired fasting glucose, and 27 (26.5%) with both impairments. A total of 54 (12.5%) participants became treated diabetics and in descending order, the ORs for the FPG-WHO/2hPG, 2hPG, FPG-WHO, FPG-WHO/HbA1c-ADA, FPG-ADA, HbA1c-ADA, and HbA1c-IEC definitions were 6.96 [3.72–13.03], 5.91 [3.24–10.77], 5.82 [2.86–11.81], 4.68 [2.38–9.19], 4.37 [2.34–8.17], 3.24 [1.72–6.10], and 2.74 [1.32–5.70], respectively.

Conclusion The FPG-WHO/2hPG definition had the highest strength of association with the progression to treated diabetes, closely followed by the 2hPG and FPG-WHO definitions. Our findings highlight the importance of performing both FPG test and OGTT to diagnose prediabetes in primary care.

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Introduction

In the last decades, diabetes has become a global epidemic and a major threat for populations [1]. New efforts combining research and public health interventions are welcome to improve the management of diabetes and to decrease its incidence [2,3].

One proven approach for the reduction of the diabetes disease burden is to focus public health interventions on prediabetes [4], a

silent pathological stage between normoglycemia and diabetes. Subjects with prediabetes are at high risk of diabetes [5], with the ADA (American Diabetes Association) expert panel estimating that up to 70% will eventually become diabetic [6]. Several studies have shown that lifestyle interventions combining both improved nutrition and increased physical activity can reduce the progression from prediabetes to diabetes [7]. Since prediabetes is completely asymptomatic, affected subjects must be identified through routine screening in the primary care setting. So far, general practitioners (GPs) do not have access to a clear, standardized definition of prediabetes.

Indeed, there now coexist several biological definitions of prediabetes, the use of which depends on local health recommendations and clinical or epidemiological objectives. These definitions are based

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on the presence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and/or elevated glycated hemoglobin (HbA1c) levels - three metabolic abnormalities detected by measuring fasting plasma glucose (FPG), 2-h postload plasma glucose (2hPG) using the oral glucose tolerance test (OGTT), and HbA1c, respectively [8–10]. The cutoff values of FPG, 2hPG, and HbA1c used in current biological definitions of prediabetes are shown in Table 1. Since biological definitions of prediabetes moderately overlap and are not equally effective in predicting the progression to diabetes [11,12], discussions are ongoing regarding which should be favored. This is the case even in France, where the national health authority recommends screening for prediabetes using the FPG test or both FPG and OGTT. Public health interventions aimed at reducing the disease burden of diabetes should provide GPs with the definition of prediabetes that shows the best association.

To help identify the most useful definition of prediabetes, we reviewed data from the population-based study Réunion DIAbetes (REDIA) [13], which was conducted in 1999–2001 and 2006–2009 in Reunion Island. This French overseas department located in the South-West Indian Ocean is of particular interest for two reasons. First, it is the French department with the highest prevalence of diabetes, with about 8% of Reunionese treated for diabetes [14,15]. Second, it is inhabited by a mixed population of European, African, and Asian origin [16,17]. Given these specificities, the probability of observing the progression to diabetes is higher in Reunion Island than in metropolitan France, and Reunionese are likely more representative of the global population.

The primary objective of the present study was to determine which definition of prediabetes is the best predictor of progression to diabetes in Reunion Island. The secondary objective was to identify factors associated with the progression to diabetes in the Reunionese population.

Material and methods

Study design

The population-based REDIA (Réunion DIAbetes) study was conducted in two stages in Reunion Island. REDIA-1 (from May 1999 to September 2001) was a cross-sectional study aimed at identifying the clinical and behavioral factors associated with diabetes and its control in the multiethnic Reunionese population. REDIA-2 (from April 2006 to June 2009) was a follow-up study aimed at estimating the risk of health events among REDIA participants [13].

REDIA-1

The population and data collection of REDIA-1 have been described previously [18,19]. Briefly, the population was a random representative sample of 4610 Reunionese people aged 18–69 years (2017 men and 2593 women). Data were collected on demographic characteristics, clinical variables (medical history, treatments, and anthropometrics), lifestyle habits, and glycemic parameters (FPG, 2hPG, and HbA1c). The study was approved by the ethical committee

of Montpellier [18], and informed written consent was obtained from all participants.

In the first phase of REDIA-1 (screening), clinical data were collected and capillary blood glucose (CBG) and HbA1c levels (DCA 2000, Ames, Bayer Diagnostics, Basingstoke, England) were measured in all participants. Participants were classified as having known diabetes (based on self-reporting), suspected diabetes, or normoglycemia. Suspected diabetes was defined by CBG levels ≥ 1.10 g/l (1.40 g/l if the person had not fasted) and/or HbA1c levels $\geq 6\%$. Overweight was defined as a body mass index (BMI) higher than or equal to 25 kg/m² and obesity as a BMI higher than or equal to 30 kg/m². Waist circumference was considered high when it exceeded 94 cm for men and 80 cm for women. In the second phase (check-up), the FPG test and the OGTT were performed in a balanced sample of participants with known diabetes, suspected diabetes, or normoglycemia (controls). Both tests were conducted using the glucose oxidase method.

REDIA-2

REDIA-2 follow-up took place seven years on average after participant enrollment in REDIA-1. Among the survivors eligible to follow-up, 624 refused to participate (overall participation rate of 83.3%). The same demographic characteristics, clinical variables, and anthropometrics were gathered as in REDIA-1 and some glycemic parameters were also measured but only in a sub-sample of participants.

Eligibility criteria

The criteria for inclusion in the present study were:

- not having been diagnosed or treated for diabetes (either pharmacological treatment and/or lifestyle modifications) at the time of REDIA-1 study;
- having no missing data on FPG, 2hPG, or HbA1c in REDIA-1;
- having no missing data on diabetes status in REDIA-2;

Study endpoints

Participants were classified as having normoglycemia, prediabetes, or diabetes based on the results of the HbA1c test conducted in the first phase of REDIA-1 and the results of the FPG test and the OGTT performed in the second phase of REDIA-1. Diagnosis of glycemic status was established using the glycemic parameter cutoff values shown in Table 1.

The evaluated definitions of prediabetes were: FPG-ADA, FPG-WHO (World Health Organization), 2hPG, HbA1c-ADA, HbA1c-IEC (International Expert Committee), FPG-WHO/2hPG, and FPG-WHO/HbA1c-ADA.

The primary outcome (diabetes status in REDIA-2) was being treated pharmacologically for a newly diagnosed diabetes at the time of REDIA-2 follow-up.

Table 1
Cutoff values of FPG, 2hPG, and HbA1c used in current biological definitions of prediabetes.

	Normoglycemia	Prediabetes	Diabetes
FPG (WHO)	FPG < 1.10 g/L (< 6.1 mmol/L)	IFG: FPG 1.10 - 1.25 g/L (6.1 - 6.9 mmol/L)	FPG \geq 1.26 g/L (\geq 7 mmol/L)
2hPG	2hPG < 1.40 g/L (< 7.8 mmol/L)	IGT: 2hPG 1.40 - 1.99 g/L (7.8 - 11.0 mmol/L)	2hPG \geq 2 g/L (\geq 11.1 mmol/L)
FPG (ADA)	FPG < 1.00 g/L (< 5.6 mmol/L)	IFG: FPG 1.00 - 1.25 g/L (5.6 - 6.9 mmol/L)	FPG \geq 1.26 g/L (\geq 7 mmol/L)
HbA1c (ADA)	HbA1c < 5.7%	HbA1c 5.7–6.4%	HbA1c \geq 6.5%
HbA1c (IEC)	HbA1c < 6.0%	HbA1c 6.0–6.4%	HbA1c \geq 6.5%

FPG: Fasting plasma glucose; WHO: World Health Organization; IFG: Impaired fasting glucose; 2hPG: 2-h postload plasma glucose; IGT: Impaired glucose tolerance; ADA: American Diabetes Association; HbA1c: Glycated hemoglobin; IEC: International Expert Committee.

The secondary outcome were clinical and lifestyle factors measured at REDIA-1.

Statistical analysis

The study sample was described using mean and standard deviation for quantitative variables and frequency and percentage for qualitative variables.

For each definition of prediabetes, the strength of association between the study outcome and prediabetes was estimated using odds ratios (ORs) and 95% confidence intervals (95%CI). Normoglycemia was taken as reference category.

In a bivariate analysis, clinical and lifestyle factors associated with the progression from non-diabetes in REDIA-1 to diabetes in REDIA-2 were assessed using the Student's *t*-test or Mann-Whitney tests for quantitative variables and the chi-square test or Fisher's exact test for qualitative variables, as appropriate.

Finally, for each definition of prediabetes, the OR of the study outcome was estimated using a multivariate logistic regression model adjusted for the time interval between REDIA-1 and REDIA-2 for each participant and all factors with a *p*-value < 0.20 in the bivariate analysis. Only the factors associated with a *p*-value < 0.05 after a backward stepwise procedure were retained in the final model. All these analyses were performed in R version 4.0.0.

Results

Definition of prediabetes which has the highest strength of association with the progression to diabetes

A total of 432 REDIA participants met the inclusion criteria for the present study (Fig. 1). Of these, 269 (62.3%) were female and 163 (37.7%) were male. Mean age was 46.4 (11.6) years. Obesity was found in 21.3% of participants, and an elevated waist circumference was observed in 47.9% of men and 75.7% of women. A first-degree family history of diabetes was found in 54.3% of participants and a history of treated high blood pressure in 19.4% of them. A large majority of participants reported being physically active, 80.7% moderate to very high daily professional or domestic physical activity and 43.6% sport activity (Table 2). A total of 54 (12.5%) subjects were pharmacologically treated for diabetes at the time of the REDIA-2 follow-up, which met our primary outcome. Depending on the definition that was evaluated, the prevalence of prediabetes ranged from 10.2% (FPG-WHO definition) to 34.3% (FPG-ADA definition). For instance, the FPG-WHO/2hPG definition identified 102 (23.6%) participants with prediabetes, including 58 (56.9%) with isolated IGT, 17 (16.6%) with isolated IFG, and 27 (26.5%) with both IGT and IFG (Table 3).

Whatever the definition used, subjects with prediabetes had a significantly higher risk of progressing to diabetes compared to

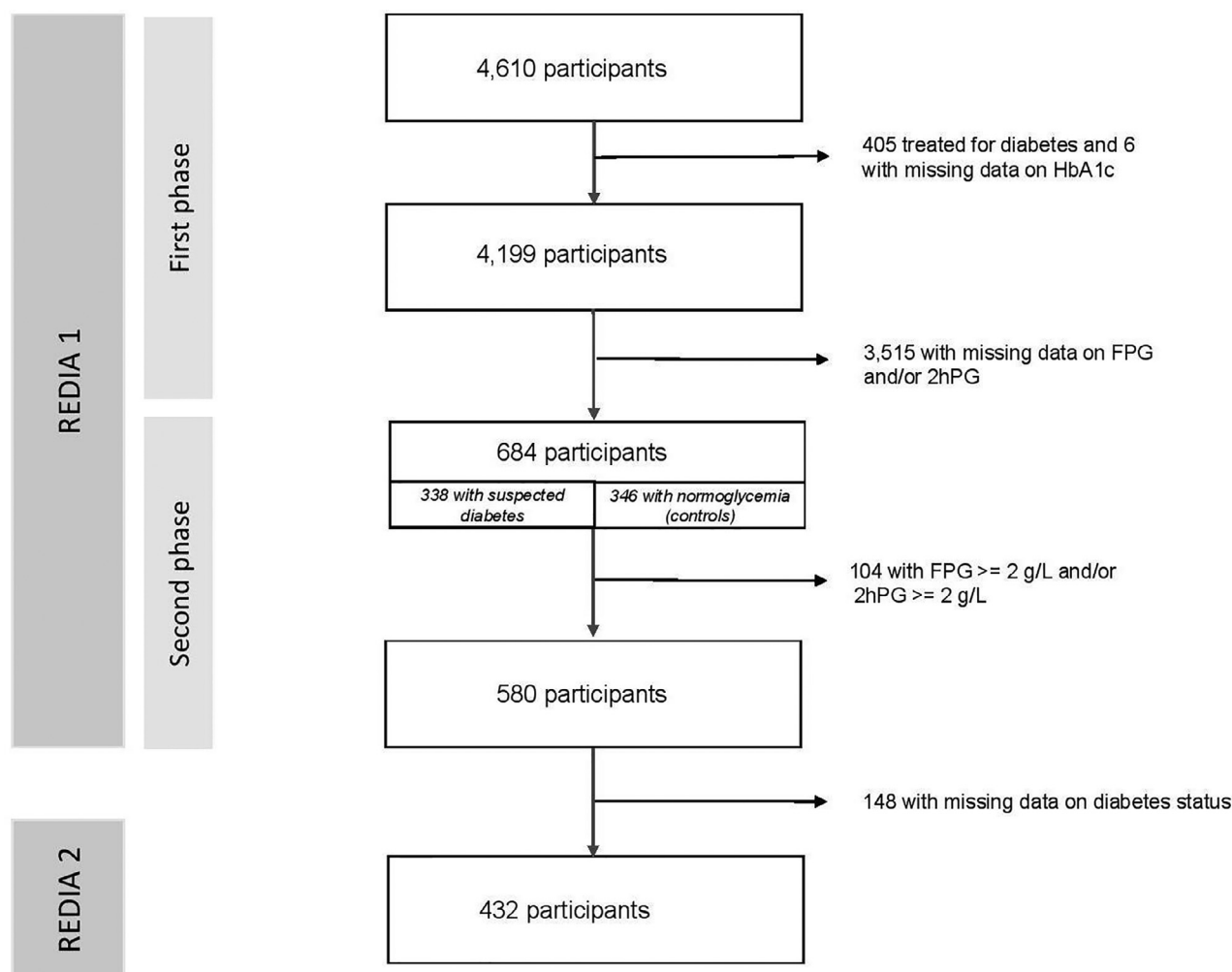


Fig. 1. flowchart of participant inclusion

HbA1c: Glycated hemoglobin; FPG: Fasting plasma glucose; 2hPG: 2-h postload plasma glucose.

Table 2
Baseline characteristics of the 432 included subjects.

	Total (N = 432) N (%) or *mean \pm SD
Sex (female/male)	269/163 (62.3/37.7)
Age (years)	46.4 \pm 11.6*
History of treated high blood pressure	84 (19.4)
BMI (kg/m²)	
<25	187 (43.3)
[25–30[153 (35.4)
\geq 30	92 (21.3)
Waist circumference (cm)	91.4 \pm 12.6*
Missing	1
Waist circumference in men (cm)	
< 94	85 (52.1)
\geq 94	78 (47.9)
Waist circumference in women (cm)	
< 80	65 (24.3)
\geq 80	203 (75.7)
Family history of diabetes	
Missing	5
None	161 (37.7)
Yes, second-degree or more distant	34 (8.0)
Yes, first-degree	232 (54.3)
Smoking status	
Current smoker	74 (17.1)
Former smoker	74 (17.1)
Never smoked	284 (65.7)
Daily professional or domestic physical activity	
Missing	1
Low	83 (19.3)
Moderate to very high	348 (80.7)
Sport activity	188 (43.6)

BMI: Body mass index.

normoglycemic subjects. In descending order, the crude (unadjusted) ORs of diabetes for the FPG-WHO/2hPG, 2hPG, FPG-WHO, FPG-WHO/HbA1c-ADA, FPG-ADA, HbA1c-ADA, and HbA1c-IEC definitions were 6.96 [95%CI: 3.72–13.03], 5.91 [3.24–10.77], 5.82 [2.86–11.81], 4.68

Table 3

Classification of the 432 included subjects into normoglycemia, prediabetes, and diabetes based on current biological definitions of prediabetes.

	Total (N = 432) N (%)
FPG-ADA	
Normoglycemia	276 (63.9)
Prediabetes	156 (36.1)
FPG-WHO	
Normoglycemia	380 (88.0)
Prediabetes	52 (12.0)
2hPG	
Normoglycemia	341 (78.9)
Prediabetes	91 (21.1)
HbA1c-ADA	
Normoglycemic	277 (64.1)
Prediabetes	135 (31.2)
Diabetes (newly diagnosed)	20 (4.6)
HbA1c-IEC	
Normoglycemic	357 (82.6)
Prediabetes	55 (12.7)
Diabetes (newly diagnosed)	20 (4.6)
FPG-WHO/2hPG	
Normoglycemic	322 (74.5)
Prediabetes	102 (23.6)
Diabetes (newly diagnosed)	8 (1.9)
FPG-WHO/HbA1c-ADA	
Normoglycemic	267 (61.8)
Prediabetes	141 (32.6)
Diabetes (newly diagnosed)	24 (5.6)

FPG: Fasting plasma glucose; ADA: American Diabetes Association; WHO: World Health Organization; 2hPG: 2-h post-load plasma glucose; HbA1c: Glycated hemoglobin; IEC: International Expert Committee.

Definitions of prediabetes

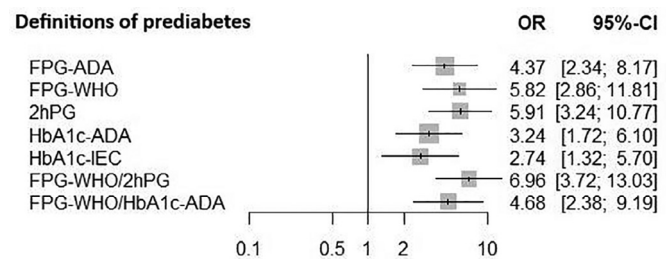


Fig. 2. Definitions of prediabetes and risk of progression to diabetes

OR: Odds ratio; CI: Confidence Interval. FPG: Fasting plasma glucose; ADA: American Diabetes Association; WHO: World Health Organization; 2hPG: 2-h postload plasma glucose; HbA1c: Glycated hemoglobin; IEC: International Expert Committee.

[2.38–9.19], 4.37 [2.34–8.17], 3.24 [1.72–6.10], and 2.74 [1.32–5.70], respectively (Fig. 2). Considering the FPG-WHO/2hPG definition which is associated with the highest risk of developing diabetes, 31 (43.7%) of REDIA-1 prediabetics became treated diabetics at REDIA-2.

Clinical factors associated with the progression to diabetes

Subjects who were pharmacologically treated for diabetes in REDIA-2 had significantly higher BMI ($p = 0.001$), waist circumference ($p < 0.001$), first-degree family history of diabetes ($p < 0.001$), and history of treated high blood pressure ($p = 0.017$) than the rest of the study population (Table 4). However, lower levels of daily professional or domestic physical activity as lack of sports activity were not associated with the risk for progression to diabetes.

After the backward stepwise procedure, adjusted ORs for the different definitions of prediabetes were consistent with unadjusted ORs (Appendix A). Note that since BMI and waist circumference are correlated, only BMI was included in the model to avoid multicollinearity.

Discussion

In our study, the FPG-WHO/2hPG prediabetes definition had the highest association in predicting the progression to diabetes over an average of 7 years, followed by the 2hPG and FPG-WHO definitions. This finding suggests that performing the OGTT in addition to the FPG test (using WHO cutoff values) greatly improves the detection of individuals at risk of diabetes. In fact, individuals with isolated IGT accounted for the majority of subjects in our sample (56.9%), meaning that performing the FPG test alone would result in missing more than half of prediabetes cases in Reunion Island. It is also important to note that according to the FPG-WHO/2hPG definition, about 43.7% of prediabetics became diabetic seven years later on average and similar findings are found in the literature [20,21].

The determinants that were statistically associated with the progression to diabetes were family history of diabetes, history of treated high blood pressure, BMI, and waist circumference. It is reassuring to note that these determinants are those found in the clinical score FINDRISC, recommended in France to identify subjects at risk of developing diabetes [22]. Unfortunately, despite the National Health Authority recommendation, the FINDRISC is neither widely known nor used by GPs in Reunion Island [23].

Diabetes is also a major public health concern in Mauritius, Reunion's neighboring island [24,25], whose population is characterized by similar ethnic diversity and nutritional habits (mainly originating in India) as the Reunionese population. In line with our findings, a longitudinal population-based study carried out in Mauritius found IGT to be a better predictor of diabetes than IFG [26]. Another study conducted in Mauritius found IGT to be more prevalent than IFG, with a higher proportion of women having isolated IGT and a higher proportion of men having isolated IFG [27]. This latter finding is of

Table 4

Factors associated with being pharmacologically treated for diabetes in REDIA-2, N = 432.

	Not pharmacologically treated for diabetes in REDIA-2 (N = 378) N (%)	Pharmacologically treated for diabetes in REDIA-2 (N = 54) N (%)	Total (N = 432) N (%)	p
Sex (female/male)	233/145 (61.6/38.4)	36/18 (66.7/33.3)	269/163 (62.3/37.7)	0.476
Age (years)	46.1 ± 11.8*	48.4 ± 9.9	46.4 ± 11.6	0.173
History of treated high blood pressure	67 (17.7)	17 (31.5)	84 (19.4)	0.017
BMI (kg/m²)				0.001
<25	173 (45.8)	14 (25.9)	187 (43.3)	
[25–30[134 (35.4)	19 (35.2)	153 (35.4)	
≥30	71 (18.8)	21 (38.9)	92 (21.3)	
Waist circumference (cm)	90.3 ± 12.5	98.4 ± 11.5	91.4 ± 12.6	<0.001
Missing	1	0	1	
Family history of diabetes				<0.001
Missing	3	2	5	
None	151 (40.3)	10 (19.2)	161 (37.7)	
Yes, second-degree or more distant	33 (8.8)	1 (1.9)	34 (8.0)	
Yes, first-degree	191 (50.9)	41 (78.8)	232 (54.3)	
Smoking status				0.545
Current smoker	67 (17.7)	7 (13.0)	74 (17.1)	
Former smoker	66 (17.5)	8 (14.8)	74 (17.1)	
Never smoked	245 (64.8)	39 (72.2)	284 (65.7)	
Daily professional or domestic physical activity				0.105
Missing	1	0	1	
Low	77 (20.4)	6 (11.1)	83 (19.3)	
Moderate to very high	300 (79.6)	48 (88.9)	348 (80.7)	
Sport activity	168 (44.6)	20 (37.0)	188 (43.6)	0.297

BMI: Body mass index. * Mean ± SD.

particular interest, as treated diabetes is more prevalent in women than men in Reunion Island [15], further highlighting the importance of performing both the FPG test and the OGTT when screening for prediabetes.

At present, the French Health Authority recommends screening for prediabetes and diabetes using the FPG test alone or in combination with the OGTT. In practice, however, the OGTT is rarely performed. In a recent study conducted in Reunion Island in primary care, many GPs were unaware of official recommendations for prediabetes screening and/or did not know the 2hPG-based definition of prediabetes. They therefore used the OGTT only marginally [23]. This suggests that the prevalence of IGT is widely underestimated in Reunion Island.

From a public health perspective, failure to use the OGTT for the screening of prediabetes is counterproductive because individuals with isolated IGT have been shown to be more receptive to lifestyle interventions than those with isolated IFG [28]. Since individuals with isolated IGT are the best target for preventive actions to reduce the diabetes burden, GPs should clearly be encouraged to use the OGTT.

Some significant disadvantages of using the FPG-WHO/2hPG definition must nevertheless be acknowledged. First, combining the FPG test with the OGTT is not the most efficient approach for the screening of prediabetes [29]. In the context of population-based screening, the decision to use this less efficient strategy should be made based on available resources. Second, subjects screened using this strategy are not only required to fast prior to taking the FPG test, but must also wait at least 2 h in the laboratory while taking the OGTT. To this is added the fact that minor side effects after glucose uptake during the OGTT have been reported [30]. Interestingly, some researchers have raised the possibility of using 1-h postload plasma glucose instead of 2hPG to increase acceptability of the OGTT [31]. Another disadvantage of the FPG-WHO/2hPG definition is the relatively high intra-individual variability over time of FPG and 2hPG levels compared to HbA1c levels [32]. Indeed, HbA1c reflects plasma glucose levels for the preceding three months, whereas FPG and 2hPG are glycemic values at a given time. To this is added the fact that the

HbA1c test is easier to perform than OGTT. Yet, in France, the HbA1c test is recommended only for the monitoring of patients with diagnosed diabetes and still not for diagnosis. Importantly, in our sample, HbA1c-based definitions of prediabetes were the least effective in predicting the progression to diabetes, and adding the HbA1c-ADA definition to the FPG-WHO definition did not increase predictive performance. In short, while the HbA1c test is easy to perform and yields more reproducible results than the FPG test and the OGTT, our results suggest that it is less effective in detecting subjects at risk of diabetes. In fact, several studies have documented a low concordance between HbA1c levels and 2hPG levels, which is likely explained by the fact that these two parameters identify different risk profiles [33–35].

Conflicting results have been reported regarding the effectiveness of HbA1c-based definitions in predicting the progression to diabetes. Both an individual participant data meta-analysis and a Cochrane meta-analysis found these definitions to have a better predictive value than our study did [36,37]. In both meta-analyses, however, the outcome was diabetes defined based on a combination of self-reporting, measures of glycemic parameters (FPG, 2hPG, and HbA1c), and/or use of anti-diabetic drugs. Using HbA1c to define both baseline prediabetes and the study outcome is problematic as a positive correlation is expected between these two HbA1c values. In fact, it has been demonstrated that due to hemoglobin glycation acceleration [38], HbA1c levels increase with age independently of plasma glucose levels [35,39]. Since HbA1c levels tend to increase following the diagnosis of prediabetes and because of aging, using current HbA1c-based definitions likely results in overestimating the risk of progression to diabetes. In view of this, age-appropriate HbA1c cutoff values may be needed for the diagnosis of prediabetes and diabetes. Finally, ethnicity has been shown to impact the predictive performance of HbA1c-based definitions of prediabetes, with HbA1c levels being higher in non-whites independently of plasma glucose values [40,41]. This could explain the lower strength of association of HbA1c-based definitions in our multiethnic population.

A recent meta-analysis assessed the predictive value of definitions of prediabetes for other outcomes, including all-cause mortality, cardiovascular disease, coronary heart disease, and stroke. The FPG-

WHO/2hPG and 2hPG definitions were found to have higher predictive value than HbA1c-based definitions [42]. Though diabetes was defined in our study based on the use of pharmacological treatment, the consistency of our results with those of this meta-analysis supports the interest of using the OGTT for prediabetes screening.

In our study, several limitations can be cited. First, from a statistical perspective, ORs parameters were used instead of relative risks or hazard ratios because time intervals between REDIA-1 and REDIA-2 fluctuated for each participant who were only seen at two times (and not followed between) and the precise date of diabetes diagnosis was not documented. In fact, the REDIA survey is more a succession of two cross-sectional studies rather than a longitudinal study. Second, since the prevalence of the primary outcome was quite high (12.5% participants of the study developed diabetes as defined in the method section), ORs might slightly overestimate the real relative risks. However and despite of this, it is important to emphasize that the two biological definitions which include 2hPG have the confidence interval with the highest lower limit. This is consistent with the fact that a majority of prediabetics can be diagnosed only with OGTT. Finally, it can be noted that the sample of our study is mostly made up of women (62.3%) as is common in health surveys. However, diabetes in Reunion Island affects more women [15] and therefore it seems unlikely that the over-representation of women in the sample biases the main result.

The main strength of our study is that it is one of the few to look at the respective associations of currently used definitions of prediabetes with diabetes occurrence in a sample composed mainly of mixed-race individuals.

In order to improve the detection of subjects at risk of diabetes while ensuring high acceptability of prediabetes screening in the population, a strategy combining the FINDRISC, the FPG test, and the OGTT could be implemented. In this strategy, subjects with a high FINDRISC would first be offered the FPG test, and those with a high FINDRISC and normal FPG levels would then be offered the OGTT. The effectiveness of this strategy, which would have to be evaluated, would require better communication on the interest of using the FINDRISC routinely in primary care.

In conclusion, all definitions of prediabetes evaluated in our study were able to predict the progression to diabetes in Reunion Island. The FPG-WHO/2hPG definition had the highest association, followed by the 2hPG and FPG-WHO definitions. Our study also found that using the FPG test alone would result in missing more than half of prediabetes cases in the Reunionese population. These findings suggest that better communication on the importance of using both the FPG test and the OGTT for the screening of prediabetes could considerably reduce the burden of diabetes. While this strategy is clearly needed in Reunion Island, where the prevalence of diabetes is especially high, we believe it would likely also be effective in other multi-ethnic populations.

Declaration of Competing Interest

None of the authors had any conflict of interest.

Funding

This project is co-financed by the European Union and the Regional Council of Réunion.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.deman.2021.100024.

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Appendix A

Risk of progression to diabetes according to definition of prediabetes: non-adjusted and adjusted odds ratios.

Definition of prediabetes	Non-adjusted ORs	Adjusted ORs*
FPG-ADA	4.37 [2.34; 8.17]	5.19 [2.66;10.61]
FPG-WHO	5.82 [2.86; 11.81]	5.46 [2.51;11.81]
2hPG	5.91 [3.24; 10.77]	5.89 [3.09;11.37]
HbA1c-ADA	3.24 [1.72; 6.10]	2.58 [1.30;5.16]
HbA1c-IEC	2.74 [1.32; 5.70]	2.23 [0.96;4.88]
FPG-WHO/2hPG	6.96 [3.72; 13.03]	6.99 [3.59;13.96]
FPG-WHO/HbA1c-ADA	4.68 [2.38; 9.19]	4.29 [2.14;8.97]

* OR were adjusted for time intervals between REDIA-1 and REDIA-2, age, history of high blood pressure, BMI, and familial history of diabetes. OR: Odds ratio; FPG: Fasting plasma glucose; ADA: American Diabetes Association; WHO: World Health Organization; 2hPG: 2-h postload plasma glucose; HbA1c: Glycated hemoglobin; IEC: International Expert Committee.