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LETTER

Diagnostic criteria should be considered when reviewing the effect of diabetes prevention studies

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Keywords Cardiovascular complications · Diabetes prevention study · Fasting plasma glucose · Impaired glucose tolerance · Vascular complications

Abbreviations
FPG Fasting plasma glucose
IFG Impaired fasting glucose
IGT Impaired glucose tolerance

To the Editor: Nathan and colleagues recently published a review of diabetes prevention trials, specifically looking at their long-term effects on reducing the diabetes-related vascular complications [1]. Data from nine diabetes prevention studies were thoroughly and comprehensively analysed to investigate the association of diabetes prevention with microvascular or cardiovascular complications. The majority of participants enrolled in the nine studies had either impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) or both. We found that in Table 1 of their review [1], Nathan et al included details of the specific diagnostic criterion for IFG, which was a fasting plasma glucose (FPG) level of 5.3–6.9 mmol/l in the Diabetes Prevention Program (DPP) trial, but no details were given for other trials. In fact, the definitions given for IFG or IGT in terms of the range of FPG were inconsistent across studies.

We have adjusted the table to provide the FPG ranges of the definitions (Table 1). The definition of IGT in terms of 2 h plasma glucose (7.8–11.0 mmol/l) was the same in nine studies, but the diagnostic criterion for IFG or IGT in term of FPG was different across studies. In particular, in the Da Qing Diabetes Prevention Study (DQDPS), Finnish Diabetes Prevention Study (FDPS) and the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM), some of the original participants who were enrolled decades ago with an FPG of 7.0–7.7 mmol/l should have been diagnosed with diabetes, rather than prediabetes, according to the current diabetes diagnostic criterion as set out in 1999 [2]. Reviewing these diabetes prevention cohorts without a concrete interpretation of the diagnostic criteria may, to some extent, lead to an insufficient understanding of their original results. These minor differences in the IFG or IGT diagnostic criterion according to FPG may at least partly explain the discrepant results between these diabetes prevention studies. Therefore, we have added the information regarding the criteria in Table 1 as a supplement to the work by Nathan et al.

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Table 1 Description of major diabetes prevention studies reporting long-term complications

Study	Total number of participants	Cohort	IFG diagnostic criterion	IGT diagnostic criteria[f]		Duration[a]	Post-trial follow-up[b]	Intervention	HR (95% CI)[c]	HbA_{1c} at study end[d], active vs control (%) (mmol/mol)
			FPG (mmol/l)	FPG (mmol/l)	2 h PG (mmol/l)					
DQDPS	577	IGT	–	<7.8	≥7.8 & <11.1	6		Lifestyle	0.49 (0.33, 0.73)	
DQDPOS							20	Lifestyle	0.57 (0.41, 0.81)	NA
DQDPOS	–	–				–	30	Lifestyle	0.61 (0.45, 0.83)	NA
DPP	3234	IGT + IFG[e] + BMI ≥24[g]	≥5.3 & <7.0	–	≥7.8 & <11.1	2.8		Lifestyle	0.42 (0.34, 0.52)	5.9 vs 6.1 (41 vs 43)
								Metformin	0.69 (0.57, 0.83)	6.0 vs 6.1 (42 vs 43)
DPPOS							15	Lifestyle	0.73 (0.65, 0.83)	6.2 vs 6.3 (44 vs 45)
								Metformin	0.82 (0.72, 0.93)	6.1 vs 6.3 (43 vs 45)
FDPS	522	IGT + BMI >25[g]	–	<7.8	≥7.8 & <11.1	3.9	–	Lifestyle	0.42 (0.3, 0.7)	NA
NAVIGATOR	9306	IGT + IFG + CVD or CVD risk factors[h]	≥5.3 & <7.0	<7.0	≥7.8 & <11.1	5	–	Nateglinide	1.07 (1.0, 1.15)	6.1 vs 6.3 (43 vs 45)
								Valsartan	0.86 (0.8, 0.92)	NA
ACE	6522	IGT + CHD	–	<7.0	≥7.8 & <11.1	5	–	Acarbose	0.82 (0.71, 0.94)	5.88 vs 5.94 (41 vs 41)
ACT NOW	602	IGT + IFG + BMI ≥25	≥5.3 & <7.0	–	≥7.8 & <11.1	2.3	–	Pioglitazone	0.28 (0.16, 0.49)	5.50 vs 5.70 (37 vs 39)
STOP-NIDDM	1429	IGT + IFG + BMI ≥25	≥5.6 & <7.8	–	≥7.8 & <11.1	3.3	–	Acarbose	0.75 (0.63, 0.90)	NA
ORIGIN	1456	CVD + IGT or IFG	≥6.1 & <7.0	<7.0	≥7.8 & <11.1	6.2	–	Glargine	0.72 (0.58, 0.90)	6.3 vs 6.5 (45 vs 48)
DREAM	5269	IGT and or IFG	≥6.1 & <7.0	<7.0	≥7.8 & <11.1	3	–	Rosiglitazone	0.38 (0.33, 0.44)	NA
								Ramipril	0.91 (0.80, 1.03)	

The bold red font in the table denotes new additions or corrections to Table 1 in Nathan et al [1]. The three changes in the 'Cohort' column represent corrections regarding the inclusion criteria

[a] Duration of original controlled clinical trial in years

[b] Total follow-up from randomisation in years

[c] HR of active intervention vs control for annual incidence (all studies except ORIGIN, which reports OR) for diabetes development. All studies represent reduction in annual incidence (95% CI) except DREAM and NAVIGATOR, which analysed differences in prevalence at study end. All reductions in diabetes incidence significant ($p < 0.05$) compared with control group except for nateglinide in NAVIGATOR study and ramipril in DREAM

[d] HbA_{1c} levels between active and control groups at study end, except in DPPOS where HbA_{1c} is the mean over the entire 15 years of follow-up, in ACE where the HbA_{1c} difference is at 1 year and in ORIGIN where HbA_{1c} is at 6 years

[e] IFG in DPP was a fasting plasma glucose of 5.3–6.9 mmol/l (95–125 mg/dl)

[f] Participants needed to meet both criteria (FPG and 2 h PG) to be classed as having IGT

[g] Reported in [1] as ≥25

[h] IFG was not reported to be one of the inclusion criteria in [1]

NA, not available; CHD, coronary heart disease

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