diabetesresearchandclinicalpractice xxx (xxxx) xxx

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice

International Diabetes Federation Position Statement on the 1-hour post-load plasma glucose for the diagnosis of intermediate hyperglycaemia and type 2 diabetes☆,☆☆

Michael Bergman[a,*], Melania Manco[b], Ilhan Satman[c], Juliana Chan[d], Maria Inês Schmidt[e], Giorgio Sesti[f], Teresa Vanessa Fiorentino[g], Muhammad Abdul-Ghani[h], Ram Jagannathan[i], Pramod Kumar Thyparambil Aravindakshan[j], Rafael Gabriel[k], Viswanathan Mohan[l], Martin Buysschaert[m], Abdullah Bennakhi[n], Andre Pascal Kengne[o], Brenda Dorcely[p], Peter M. Nilsson[q], Tiinamaija Tuomi[r,s], Tadej Battelino[t], Akhtar Hussain[u,v,w,x,y], Antonio Ceriello[z], Jaakko Tuomilehto[k,aa,bb,cc]

[a] NYU Grossman School of Medicine, Departments of Medicine and of Population Health, Division of Endocrinology, Diabetes and Metabolism, VA New York Harbor Healthcare System, New York, NY, USA
[b] Predictive and Preventive Medicine Research Unit, Bambino Gesù Children's Hospital IRCCS, Rome, Italy
[c] Istanbul University Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Istanbul, Turkey
[d] The Chinese University of Hong Kong, Faculty of Medicine, Department of Medicine and Therapeutics, Hong Kong Institute of Diabetes and Obesity, Hong Kong, China
[e] Postgraduate Program in Epidemiology, School of Medicine and Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
[f] Department of Clinical and Molecular Medicine, University of Rome-Sapienza, 00189 Rome, Italy
[g] Department of Medical and Surgical Sciences, University Magna Graecia of Catanzaro, 88100 Catanzaro, Italy
[h] Division of Diabetes, University of Texas Health Science Center at San Antonio, San Antonio Texas, USA
[i] Hubert Department of Global Health Rollins, School of Public Health, Emory University, Atlanta, GA, USA
[j] Department of Research Operations and Diabetes Complications, Madras Diabetes Research Foundation, Chennai, India
[k] Department of International Health, National School of Public Health, Instituto de Salud Carlos III, Madrid, Spain
[l] Dr. Mohan's Diabetes Specialities Centre and Madras Diabetes Research Foundation, Chennai, India
[m] Department of Endocrinology and Diabetology, Université Catholique de Louvain, University, Clinic Saint-Luc, Brussels, Belgium
[n] Dasman Diabetes Institute Office of Regulatory Affairs, Ethics Review Committee, Kuwait
[o] South African Medical Research Council, Francie Van Zijl Dr, Parow Valley, Cape Town, 7501, South Africa
[p] NYU Grossman School of Medicine, Department of Medicine, Division of Endocrinology, Diabetes and Metabolism, New York, NY, USA
[q] Department of Clinical Sciences and Lund University Diabetes Centre, Lund University, Skåne University Hospital, Malmö, Sweden
[r] Folkhälsan Research Center, Helsinki, Finland
[s] Abdominal Center, Endocrinology, Helsinki University Central Hospital, Research Program for Diabetes and Obesity, Center of Helsinki, Helsinki, Finland
[t] Faculty of Medicine, University of Ljubljana, Slovenia
[u] Faculty of Health Sciences, Nord University, Bodø, Norway
[v] Faculty of Medicine, Federal University of Ceará (FAMED-UFC), Brazil
[w] International Diabetes Federation (IDF), Brussels, Belgium
[x] Diabetes in Asia Study Group, Post Box: 752, Doha-Qatar
[y] Centre for Global Health Research, Diabetic Association of Bangladesh, Dhaka, Bangladesh
[z] IRCCS MultiMedica, Milan, Italy
[aa] Public Health Promotion Unit, Finnish Institute for Health and Welfare, Helsinki, Finland
[bb] Department of Public Health, University of Helsinki, Helsinki, Finland
[cc] Saudi Diabetes Research Group, King Abdulaziz University, Jeddah, Saudi Arabia

☆ **Referees:** Guillermo Arreaza-Rubin (Division of Diabetes, Endocrinology and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, USA); Elaine Chow (Phase 1 Clinical Trial Centre, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China); Louis Monnier (Medical School of Montpellier, University of Montpellier, Montpellier, France); Antonio Nicolucci (Center for Outcomes Research and Clinical Epidemiology [CORESEARCH], Pescara, Italy); Kohjiro Ueki (Diabetes Research Center, National Center for Global Health and Medicine, Tokyo, Japan).

☆☆ **Coordinators:** Akhtar Hussain (Faculty of Health Sciences, Nord University, Bodø, Norway; Faculty of Medicine, Federal University of Ceará (FAMED-UFC), Brazil; International Diabetes Federation (IDF), Brussels, Belgium; Diabetes in Asia Study Group, Post Box: 752, Doha-Qatar; Centre for Global Health Research, Diabetic Association of Bangladesh, Dhaka, Bangladesh). Antonio Ceriello (IRCCS MultiMedica, Milan, Italy).

* Corresponding author.
E-mail address: michael.bergman@nyulangone.org (M. Bergman).

https://doi.org/10.1016/j.diabres.2024.111589

0168-8227/Published by Elsevier B.V.

A B S T R A C T

Many individuals with intermediate hyperglycaemia (IH), including impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT), as presently defined, will progress to type 2 diabetes (T2D). There is confirmatory evidence that T2D can be prevented by lifestyle modification and/or medications, in people with IGT diagnosed by 2-h plasma glucose (PG) during a 75-gram oral glucose tolerance test (OGTT). Over the last 40 years, a wealth of epidemiological data has confirmed the superior value of 1-h plasma glucose (PG) over fasting PG (FPG), glycated haemoglobin (HbA_{1c}) and 2-h PG in populations of different ethnicity, sex and age in predicting diabetes and associated complications including death. Given the relentlessly rising prevalence of diabetes, a more sensitive, practical method is needed to detect people with IH and T2D for early prevention or treatment in the often lengthy trajectory to T2D and its complications. The International Diabetes Federation (IDF) Position Statement reviews findings that the 1-h post-load PG $\geq$ 155 mg/dL (8.6 mmol/L) in people with normal glucose tolerance (NGT) during an OGTT is highly predictive for detecting progression to T2D, micro- and macrovascular complications, obstructive sleep apnoea, cystic fibrosis-related diabetes mellitus, metabolic dysfunction-associated steatotic liver disease, and mortality in individuals with risk factors. The 1-h PG of 209 mg/dL (11.6 mmol/L) is also diagnostic of T2D. Importantly, the 1-h PG cut points for diagnosing IH and T2D can be detected earlier than the recommended 2-h PG thresholds. Taken together, the 1-h PG provides an opportunity to avoid misclassification of glycaemic status if FPG or HbA_{1c} alone are used. The 1-h PG also allows early detection of high-risk people for intervention to prevent progression to T2D which will benefit the sizeable and growing population of individuals at increased risk of T2D. Using a 1-h OGTT, subsequent to screening with a non-laboratory diabetes risk tool, and intervening early will favourably impact the global diabetes epidemic. Health services should consider developing a policy for screening for IH based on local human and technical resources. People with a 1-h PG $\geq$ 155 mg/dL (8.6 mmol/L) are considered to have IH and should be prescribed lifestyle intervention and referred to a diabetes prevention program. People with a 1-h PG $\geq$ 209 mg/dL (11.6 mmol/L) are considered to have T2D and should have a repeat test to confirm the diagnosis of T2D and then referred for further evaluation and treatment. The substantive data presented in the Position Statement provides strong evidence for redefining current diagnostic criteria for IH and T2D by adding the 1-h PG.

Introduction

The International Diabetes Federation (IDF) estimates that 537 million individuals or 10.5 % of the global adult population were living with diabetes in 2021; 783 million or 12.2 % of adults are expected to have diabetes by 2045 [1]. In addition, an estimated 541 million individuals or 10.6 % of the global adult population had impaired glucose tolerance (IGT) in 2021 and are considered at increased risk for developing type 2 diabetes (T2D) with an expectation that this could increase to 730 million, or 11.4 % in 2045 [1].

The IDF Position Statement on the 1-hour post-load plasma glucose (1-h PG) for the diagnosis of intermediate hyperglycaemia (IH) and T2D is based on considerable evidence that an elevated 1-h PG during a 75 g oral glucose tolerance test (OGTT) can identify individuals with normal glucose tolerance (NGT) (defined by glycated haemoglobin (HbA_{1c} < 5.7 % [38.8 mmol/mol]) or fasting PG(FPG) < 100 mg/dL (5.6 mmol/L) or 2-h PG < 140 mg/dL (7.8 mmol/L) who have undiagnosed T2D or are at increased risk for T2D. It is well known that people with T2D have increased risk of micro- and macrovascular complications, obstructive sleep apnoea (OSA), cystic fibrosis-related diabetes mellitus (CFRD), metabolic dysfunction-associated steatotic liver disease (MASLD), and premature mortality. The 1-h PG has been the subject of review articles [2–12] including a published petition advocating its adoption to replace current diagnostic criteria [8]. The IDF Position Statement on the 1-hour post-load Plasma Glucose (1-h PG) for the Diagnosis of Intermediate Hyperglycaemia (IH) and T2D was prepared by an international IDF Task Force and reviewed by a panel of independent external experts.

1. What are the inadequacies of current diagnostic criteria for IH?

Despite the considerable proven benefit of lifestyle modification in thwarting the insidious progression to T2D, many individuals with IH, as presently defined, will nevertheless continue to progress. Furthermore, the preponderance of individuals at risk for developing T2D are not promptly identified and those that are, frequently do not receive adequate referral concerning lifestyle intervention. Therefore, it is paramount to screen individuals at increased risk with a more sensitive and practical method capable of identifying IH and T2D at an earlier time point than currently to initiate appropriate intervention as early as possible.

T2D can be prevented by intensive lifestyle modification and/or use of glucose-lowering drugs such as biguanides (e.g. metformin) and alpha-glucosidase inhibitors (acarbose) [13,14]. Recent analyses demonstrated that most individuals with IH, defined as IGT, benefitted from lifestyle intervention [15–17]. In the same vein, intensive glycemic control in individuals with newly diagnosed T2D will have legacy effect regarding long-term complications [18–22]. In many populations, the diagnosis of IH and T2D can be best done with a post-challenge PG during an OGTT [23]. The reliance on FPG and/or HbA_{1c} alone to diagnose IH and T2D can lead to missed opportunities for early diagnosis and prevention. Current diagnostic modalities are discrepant as they may identify different individuals depending on whether post-challenge PG, FPG or HbA_{1c} determinations are employed [24–26]. Table 1 illustrates that there is currently no international consensus on the definition of IH as the American Diabetes Association (ADA), World Health Organization (WHO) and the informal International Expert Committee (IEC) propose different criteria [27].

The different definitions of IH have varying sensitivities and specificities that identify different, although, overlapping, populations. The prevalence of IH by different ADA/WHO diagnostic criteria was determined in the 2005–2008 National Health and Nutrition Examination Surveys. The crude prevalence of IH in adults aged $\geq$ 18 years was 14.2 % for HbA_{1c} 5.7–6.4 % (39—46 mmol/mol), 26.2 % for FPG (IFG_{ADA}) 100–125 mg/dL (5.6–6.9 mmol/L), 7.0 % for FPG 110–125 mg/dL (IFG_{WHO}) (6.1–6.9 mmol/L), and 13.7 % for OGTT 140–199 mg/dL (7.8–11.1 mmol/L) (IGT) [28].

Table 1
Definitions of Intermediate Hyperglycaemia [27]

	ADA*	WHO	IEC
IFG (FPG)	100–125 mg/dL (5.6–6.9 mmol/L)	110–125 mg/dL (6.1–6.9 mmol/L) and 2-h PG <140 mg/dL (<7.8 mmol/L); if 2-h PG is measured	
IGT (2-h PG) after 75 g OGTT	140–199 mg/dL (7.8–11.0 mmol/L)	140–199 mg/dL (7.8–11.0 mmol/L)	
HbA_{1c}	5.7–6.4 % (39–46 mmol/mol)		6.0–6.4 % (42–46 mmol/mol)

Abbreviations: ADA, American Diabetes Association; WHO, World Health Organization; IEC, International Expert Committee; IFG, impaired fasting glucose; FPG, fasting plasma glucose; IGT, impaired glucose tolerance; 2-h PG, 2-hour plasma glucose; OGTT, oral glucose tolerance test; HbA_{1c}, glycated haemoglobin, A_{1c}.
*ADA definitions do not explain how to classify people who have both IFG and IGT.

Some individuals with T2D detected by an OGTT may no longer be classified as such when using HbA_{1c} criteria ($HbA_{1c} \geq 6.5$ %; 48 mmol/mol) and vice versa. Several medical conditions can affect the HbA_{1c} measurement including haematological disorders, renal failure, hypertriglyceridemia in addition to variability due to age and ethnicity. Lack of standardization of assays in many under-resourced settings also limits the diagnostic accuracy of HbA_{1c} [29]. Furthermore, progression rates to diabetes appear to differ by IH definitions with a HbA_{1c} level between 6.0 and 6.4 % (42–46 mmol/mol) possibly identifying individuals at lower risk than with IFG_{WHO} and IGT criteria [30]. Furthermore, longitudinal studies have shown that 50–60 % of individuals with IH based on current criteria did not progress to diabetes in approximately 10 years whereas 30–40 % of those with newly diagnosed diabetes had NGT at baseline [31,32].

By employing current definitions of IH, when based mainly on FPG and/or HbA_{1c}, individuals at increased risk may inadvertently be diagnosed relatively late in the gradual progression to diabetes. The delayed diagnosis obviates the potential benefit of earlier intervention when β-cell function is more intact particularly given the evidence that β-cell function is reduced at glucose levels below established thresholds for IFG or IGT [33–38]. Therefore, diagnostic measures with a greater sensitivity are needed to identify individuals with increased risk of developing T2D at an earlier stage [39–41].

FPG below ADA and WHO threshold for T2D defining IFG has also been found to predict increased risk for T2D in otherwise healthy people [42]. Physiologic FPG and 2-h PG levels associated with optimal β-cell function are considerably lower than presently proposed for IFG and IGT [43]. Although IH diagnosed by FPG or HbA_{1c} is associated with increased risk for cardiovascular disease (CVD) and other complications, post-load PG is considerably more robust than FPG in this regard [44,45]. Therefore, implementation of lifestyle intervention before PG levels achieve current critical thresholds for IH may be more effective in thwarting progression to diabetes, reducing complications, and improving health outcomes and quality of life [34–36]. This should enhance benefit beyond that demonstrated in global diabetes prevention programs in those with IGT, particularly since interventions are less effective for prevention of T2D in people with isolated IFG than in people with IGT, with or without IFG [46,47].

2. What is the background for recommending the 1-h post-load PG level for predicting progression to T2D?

Numerous observational studies worldwide consistently demonstrate a direct association between 1-h PG ≥ 155 mg/dL (8.6 mmol/L) during an OGTT with incident T2D. Notably, this association is more robust compared with those observed for FPG or 2-h PG. Studies investigating the 1-h PG are listed in Table 2 [2,9]. Abdul Ghani et al. demonstrated the predictive power of the 1-h PG compared with FPG and 2-h PG values with incident diabetes over 8 years in a high-risk Mexican American cohort [48]. Furthermore, combining 1-h PG (≥155 mg/dL [8.6 mmol/L]) and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria for the metabolic syndrome (i.e., at least three of the following criteria: waist circumference > 102 cm in men or > 88 cm in women, plasma triglycerides ≥ 150 mg/dL [1.7 mmol/L], HDL cholesterol < 40 mg/dL [1.03 mmol/L] in men or < 50 mg/dL [1.29 mmol/L] in women, blood pressure ≥ 130/85 mm Hg, and FPG ≥ 110 mg/dL [6.1 mmol/L]) [49] significantly improved the identification of high-risk individuals for T2D [48]. The Botnia Study in Finland and the Malmö Preventive Project (MPP) in Sweden have also provided evidence that FPG and 2-h PG were less efficient predictors than the 1-h PG of incident T2D and that the 1-h PG was a more efficient screening tool for selecting individuals at increased risk for developing T2D [50]. This evidence, based on prospective cohorts, strongly supports the effectiveness of 1-h PG ≥ 155 mg/dL (8.6 mmol/L) to detect high-risk individuals for T2D and its associated complications for early intervention.

The clinical benefit of the 1-h PG was compared with other markers for predicting T2D [66]. The Botnia Prospective Study confirmed that the 1-h PG (AUC = 0.75, sensitivity 75 %, specificity 68 %) predicted progression to T2D more accurately than FPG (AUC = 0.63, sensitivity 55 %, specificity 64 %) or 2-h PG (AUC = 0.68, sensitivity 56 %, specificity 73 %) levels. Another analysis of the improvement in combined sensitivity, specificity and PPV to predict future T2D risk proffered by the 1-h PG > 155 mg/dL (8.6 mmol/L) versus IFG and IGT in the San Antonio Heart Study (SAHS) and Botnia Study is shown in Table 3 [67]. The two were prospective longitudinal studies in which people without diabetes (Caucasians and Mexican Americans in the SAHS and Caucasians in the Botnia Study) were followed for 7–8 years.

Moreover, the predictive power of the 1-h PG was comparable with a multivariate model consisting of six metabolic markers (AUC = 0.78, sensitivity 67 %, specificity 75 %). Including 1-h PG with these markers outperformed the 1-h PG alone. HbA_{1c} showed a non-significant slightly lower performance than the 1-h PG (AUC = 0.67, sensitivity 65 %, specificity 64 %) [64]. The combination of 1-h PG and HbA_{1c} (AUC = 0.76, sensitivity 78 %, specificity 68 %) was comparable to 1-h PG alone but significantly outperformed HbA_{1c} alone. Finally, a model combining 1-h PG, HbA_{1c} and six other metabolic markers was significantly better in terms of predictive performance than 1-h PG and HbA_{1c} [66]. The authors concluded that the 1-h PG, alone or in combination with metabolic markers, is a robust predictor for determining the future risk of T2D. Taking the evidence into consideration, the 1-h PG outperforms the 2-h PG and is cheaper to measure than metabolites. While the 30-minute PG, HbA_{1c}, and mannose were statistically comparable to the 1-h PG, they showed slightly lower performance. The authors thus concluded that international diabetes organizations should consider shortening the standard 75-g OGTT to 1-h to improve the convenience of the test without decreasing the predictive value for IH and diabetes [66].

Furthermore, reproducibility of the 1-h PG was assessed by Briker et al. in 119 African people. When the second OGTT was performed within 11 days of the initial study, the reproducibility of the 1-h PG was equivalent to the FPG and 2-h PG. The κ -statistics (95 %CI) for reproducibility were: FPG ≥ 100 mg/dL (5.6 mmol/L) = 0.586 (0.428–0.743); 1-h PG ≥ 155 mg/dL (8.6 mmol/L) = 0.628 (0.488–0.768);2-h PG ≥ 140 mg/dL (7.8 mmol/L) = 0.640 (0.498–0.783).The concordance between baseline, 1-h PG and 2 h-PG concentrations for OGTT-1 and OGTT-2 were r = 0.92, r = 0.85 and r = 0.92 (all $p < 0.001$), respectively [63]. Kasturi et al. found in adolescent girls with obesity that the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) had similar reproducibility and 1-year predictive ability for IH compared with standard fasting and 2-h OGTT criteria. They concluded that "the shortened 1-hour OGTT may provide diagnostic equivalence for IH risk with the additional advantage of a less time-consuming risk assessment [68]."

3. Why was the 2-h PG level selected instead of the 1-h PG?

In 1979, the National Diabetes Data Group (NDDG) recommended that an intermediate PG level (30 min, 1-h, or 1 1/2-h) be measured to diagnose IGT defined by a 2-h value ≥ 140 mg/dL (7.8 mmol/L) but < 200 mg/dL (11.1 mmol/L) [69]. Due to the impracticality of measuring multiple intermediate PG values, the NDDG recommended a modification whereby IGT could be diagnosed if FPG was in the non-diabetic range and the 2-h PG levels met pre-specified threshold levels. Furthermore, as the 2-h PG during the OGTT was found to be more reproducible and provided a more sensitive and specific indicator of diabetes status than the 1-h PG, the latter measurement was abandoned [70,71]. However, as noted above, the reproducibility of the 1-h PG was more recently found to be equivalent to FPG and 2-h PG in studies by Briker et al. and Kasturi et al. [63,68]. The WHO and ADA criteria subsequently considered the 2-h PG as the only post-load value required. It should be noted that the criteria then did not require that the selection of the 1-h or 2-h PG be based on the presence of diabetes complications.

Table 2
Odds ratios, hazard ratios and C-statistics for T2D prediction of 1-h PG in cohort studies.

1st author, Year of publication	Study Cohort	N (sample size)	Follow-up (years)	1 h-PG Cutoff mg/dL (mmol/L)	Findings			
					OR/HR T2D	Sensitivity T2D	Specificity T2D	C-statistics
Abdul-Ghani et al 2008 [48]	SAHS	1,611 MexicanAmericans	8	155(8.6)	(a) without Metabolic Syndrome NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h PG < 155 mg/dL (8.6 mmol/L) OR [95 %CI]: 3.4[1.8–6.4] (b) with Metabolic Syndrome NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h PG < 155 mg/dL (8.6 mmol/L) OR [95 %CI]: 15.2 [7.8–29.3]	75 %	79 %	NA
Abdul-Ghani et al 2010 [51]	SAHS and Botnia Study	3,450 Mexican AmericansFinnish	7–8	150(8.3)	FPG < 90 mg/dl and 1-h PG > 150 mg/dL (8.3 mmol/L) OR [95 %CI]: 7.1 [3.3–17] FPG 90–100 mg/dL(5.0–5.6 mmol/L) and 1-h PG > 150 mg/dL (8.3 mmol/L) OR [95 %CI]: 11.3 [5.0–25.8] FPG > 100 mg/dL(5.6 mmol/L) and 1-h PG > 150 mg/dL (8.3 mmol/L) OR [95 %CI]: 17.7 [7.5–41.9]	NA	NA	NA
Priya et al 2013 [52]	Data from tertiary diabetes center	1,179NGT Indians	4.0	155(8.6)	NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h PG < 155 mg/dL (8.6 mmol/L)Proportion (n, %): 98 (19.5) vs. 50 (8.0) OR [95 %CI]: 2.18 [1.23–3.89]	66 %	61 %	NA
Alyass et al 2015 [50]	Botnia Study	2,603 Finnish	4.94	160(8.9)	OR [95 %CI]: 8.0 [5.5–11.6]	75 %	73 %	AUC_{ROC} 0.83 [95 % CI: 0.80—0.86]
Alyass et al 2015 [50]	MPP	2,386Swedish	23.5	151(8.4)	OR [95 %CI]: 3.8 [3.1–4.7]	62 %	70 %	AUC_{ROC} 0.74 [95 % CI: 0.72—0.77]
Fiorentino et al 2015 [53]	CATAMERI study and EUGENE2 Study	392Caucasians	5.2	155(8.6)	NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h PG < 155 mg/dL(8.6 mmol/L) HR [95 %CI]: 4.02 [1.06–15.26]	NA	NA	NA
Bergman et al. 2016 [37]	GOH Study	853 multiethnic individuals without diabetes	24	155(8.6)	NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h PG < 155 mg/dL (8.6 mmol/L) OR [95 %CI]: 4.35 [2.50–7.73]	55.6 %	77.2 %	AUC_{ROC} 0.736 [95 %CI 0.699, 0.773]
Oka et al 2016 [54]	Historical cohort study.	1,445 Japanese workers	4.5	#205 (11.4)	1-h PG Q4 vs. Q1: HR [95 % CI]: 42.5 [5.7–315.2] Compared with the first quartile, the HR for future diabetes in the fourth quartile of 1-h PG was 42.5 [95 % CI: 5.7–315.2 (p < 0.05)] and the HR in the fourth quartile of 2-h PG was 4.4 [95 % CI: 1.8–10.8 (p < 0.05)], after adjustments for covariates including FPG.	NA	NA	AUC_{ROC} 0.88 [95 %CI 0.84, 0.91]
Oh et al. 2017 [55]	KoGES	5,703NGT Koreans	12	144(8.0)	NGT1-h PG > 144 mg/dL (8.0 mmol/L) vs. NGT1-h PG < 144 mg/dL (8.0 mmol/L)	70 %	68 %	AUC_{ROC} 0.74 [95 %CI: NA]

(*continued on next page*)

Table 2 (*continued*)

1st author, Year of publication	Study Cohort	N (sample size)	Follow-up (years)	1 h-PG Cutoff mg/dL (mmol/L)	Findings			
					OR/HR T2D	Sensitivity T2D	Specificity T2D	C-statistics
					HR [95 %CI]: 2.84 [2.34–3.45]			
Paddock et al. 2017 [56]	SWNA Study	1,946 people from Arizona	12.8#	168(9.3)	NGT1-h PG > 168 mg/dL (9.3 mmol/L)vs. NGT1-h PG < 168 mg/dL (9.3 mmol/L) HR [95 %CI]: 1.71 [1.60–1.82]	Reported for different cutpoints	Reportedfor different cutpoints	AUC_{ROC} 0.672 [95 %CI: NA] at 5 years AUC_{ROC} 0.728 [95 %CI: NA]at 25 years
Pareek et al 2018 [57]	MPP	Population based cohort of 4,867 Swedish men	12 and 39	155(8.6)	NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h < PG 155 mg/dL (8.6 mmol/L) HR [95 %CI]: 3.87 [2.16–6.93] after 12 y NGT1-h PG > 155 mg/dL (8.6 mmol/L) vs. NGT1-h < PG 155 mg/dL (8.6 mmol/L) HR [95 %CI]: 2.93 [2.48–3.46] after 39 y	NA	NA	C-index 0.698 at 12 yearsC-index 0.637 at 39 y
Sai Prasanna et al 2017 [58]	Data from Electronic Health Records	1,356 Indians	5.6	153(8.5)	NGT1-h > 153 mg/dL (8.5 mmol/L) OR [95 %CI]: 1.026 [1.019–1.033]	64 %	66 %	AUC_{ROC}: 0.716 [95 % CI: NA]
Strandberg et al 2011 [59]	Helsinki BusinessmenStudy	2,756	37#	161(8.9)	NGT1-h > 161 mg/dL (8.9 mmol/L) and BMI < 30 kg/m^2 HR [95 %CI]:4.71 [3.36–6.60] NGT1-h > 161 mg/dL(8.9 mmol/L) and BMI ≥ 30 kg/m^2 HR [95 %CI]:10.13 [6.46–18.59]	NA	NA	NA
Thewjitcharoen et al 2019 [60]	Data from tertiary diabetes center	220Thai people	>12	155(8.6)	Thai cardiovascular risk score validation NGT1-h < 155 mg/dL (8.6 mmol/L) (DM risk score 7.6 and CVD risk score 4.1) NGT1-h > 155 mg/dL (8.6 mmol/L)(DM risk score 9.1 and CVD risk score 6.7)	NA	NA	NA
Kumpatla et al 2019 [61]	Data from Electronic Health Records	4,023	11	155(8.6)	During follow-up period, 10.8 % of subjects in NGT 1-h PG < 155 mg/dL (8.6 mmol/L) and 44.4 % in NGT1-h PG > 155 mg/dL (8.6 mmol/L) converted to diabetes. NGT1-h PG > 155 mg/dL (8.6 mmol/L) incident diabetes OR [95 %CI]:7.9 [2.2–28.1] Individuals with NGT1-h PG > 155 mg/dL(8.6 mmol/L) remained free of diabetes for a median period of 7.6 years (95 % CI 5.8–7.8), whereas NGT subjects with NGT1-h PG > 155 mg/dL (8.6 mmol/L) remained free for 10 years (95 % CI 8.5–10.0).	NA	NA	NA
Manco et al 2019 [62]	RISC cohort	797	3	155(8.6)	NGT1-h PG < 155 mg/dL (8.6 mmol/L) vs. NGT1-h > 155 mg/dL (8.6 mmol/L) after adjusting age, sex, BMI. OR [95 %CI]:2.19 [1.49–3.20]	NA	NA	AUC 0.67 [95 % CI]: NA
Briker et al 2020 [63]	Africans in America cohort	434	NA	155(8.6)	Assess variations in glucometabolic profiles. 17 % of NGT individuals, 72	NA	NA	NA

(*continued on next page*)

Table 2 (*continued*)

1st author, Year of publication	Study Cohort	N (sample size)	Follow-up (years)	1 h-PG Cutoff mg/dL (mmol/L)	Findings			
					OR/HR T2D	Sensitivity T2D	Specificity T2D	C-statistics
					% of pre-diabetic individuals, and 96 % of diabetic individuals had 1-hour glucose levels ≥ 155 mg/dL (8.6 mmol/L) NGT individuals with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) exhibited worse insulin resistance and β-cell function compared to NGT 1- h < 155 mg/dL (8.6 mmol/L) Second OGTT was performed in 27 % (119/434) of participants 10 ± 7 days after the first to check reproducibility.There was substantial agreement (κ=0.628) between the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) in the two OGTTs, indicating consistent results			
Saunajoki et al 2020 [64]	Oulu45Finland cohort	654	12	160(8.9)	In total, 1-h PG with a cut-point of 160 mg/dL (8.9 mmol/L) predicted 76.6 % (82/107), whereas 2-h PG with cut- point 122 mg/dL(6.8 mmol/L) predicted 62.6 %(67/107) of new cases with diabetes	NA	NA	AUC_{ROC} [95 % CI]: 0.81 [0.76–0.86]
Rong et al 2021 [65]	Chinese population	928 Male, ≥55 years	20	155(8.6)	NGT and 1-h PG ≥ 155 mg/dL (8.6 mmol/L)vs. NGT and 1-h PG < 155 mg/dL (8.6 mmol/L), HR for incidence of T2D at 10 years and 20 years (after adjustment for age, BMI, waist circumference, systolic BP, triglyceride, HDL-C, history of hypertension, glucose tolerance and FPG): HR [95 % CI]: 1.300 [1.236–1.367] at 10 y and HR [95 % CI]: 1.269 [1.214–1.327] at 20 y.	NA	NA	AUC_{ROC} [95 % CI]: 0.778 [0.748–0.807] at 10 years AUC_{ROC} [95 % CI]: 0.766 [0.736–0.796] at 20 years

Abbreviations: T2D, type 2 diabetes; 1-h PG, 1-hour plasma glucose; OR, odds ratio; HR, hazard ratio; SAHS, San Antonio Heart Study; NGT, normal glucose tolerance; CI, confidence interval; FPG, fasting plasma glucose; AUC_{ROC}, area under the receiver-operating characteristic curve; MMP, Malmö Preventive Project; CATAMERI, CATAnzaro Metabolic Risk factors; EUGENE2, European Network on Functional Genomics of T2D; GOH, Glucose Intolerance Obesity and Hypertension; KoGES, Korean Genome and Epidemiology Study; SWNA, Southwestern Native American; C index, concordance index; BMI, body mass index; DM, diabetes mellitus; CVD, cardiovascular disease; RISC, Relationship between Insulin Sensitivity and Cardiovascular Risk; OGTT, oral glucose tolerance test.
Notes: NA: not available from the manuscript. Follow-up time is reported as mean otherwise # refers to median value. C-statistics refers to the area under the receiver-operating characteristic curve (AUC_{ROC}) for 1-h PG for future diabetes.

This question was addressed by Paddock et al. who compared the 1- and 2-h PG levels for predicting diabetic retinopathy [72]. The prevalence and incidence of diabetic retinopathy, based on direct ophthalmoscopy, changed in a similar manner across the distributions of 1-h PG and 2-h PG concentrations. Receiver operating characteristics (ROC) analysis showed that the ability of 1-h PG and 2-h PG to predict the prevalence and incidence of retinopathy was similar. Similarly, data from a Finnish population-based study showed that retinopathy prevalence was associated with 30 min PG, 1-h PG and 2-h PG in people without diabetes [73], and started to increase at approximately 162 mg/dL (9 mmol/L) with the 1-h PG, i.e. already in people with IH. However, after adjustment for systolic blood pressure, only 30 min PG, 1-h PG and 2-h insulin levels were associated with retinopathy.

As the 1-h PG can shorten the time needed for an OGTT, has economic and practical advantages, Paddock et al. recommended that the 1-h PG should be considered as an alternative post-glucose load time point to identify those at elevated risk for diabetic retinopathy [72].

4. Is the 1-h PG level preferable to HbA_{1c} and other post-load PG values such as shape of the glucose curve or the incremental area under the glucose concentration curve $\Delta_{(G0\text{-}120)}$?

The effectiveness of HbA_{1c} and the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was assessed for identifying dysglycaemia in 212 people in a real-life

Table 3
Sensitivity, specificity, and PPV of various diabetes prediction models [67].

Model	SAHS				Botnia Study			
	Sensitivity (%)	Specificity (%)	Sensitivity and specificity	PPV (%)	Sensitivity (%)	Specificity (%)	Sensitivity and specificity	PPV (%)
SADPM	88.8	52.0	140.8	19.4	97.4	18.2	115.6	5.7
IFG and/or IGT	64.4	86.9	151.3	39.0	77.5	46.4	123.9	6.8
IFG	31.6	91.5	123.1	41.2	68.5	51.2	119.7	6.9
IGT	45.6	91.2	136.8	39.1	39.2	85.6	124.8	12.8
1-h PG > 155 mg/dL	75.0	78.7	153.7	45.9	62.0	81.3	143.3	14.5
Two-step model	77.7	77.4	155.1	44.8	75.8	71.6	147.4	11.9

SAHS, San Antonio Heart Study; PPV, positive predictive value; SADPM, San Antonio Diabetes Prediction Model; IFG, impaired fasting glucose; IGT, impaired glucose tolerance, 1-h PG, 1-hour plasma glucose.

clinical setting [74]. When comparing the accuracy of HbA_{1c}, defined by ADA and IEC criteria (Table 1), FPG and 2-h PG with an elevated 1-h PG during the OGTT, the level of agreement was two-fold greater for the elevated 1-h PG [74]. The 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was therefore found to be superior for detecting high-risk individuals compared with HbA_{1c}. Furthermore, HbA_{1c} was a less precise correlate of insulin sensitivity and β-cell function than the 1-h PG and correlated poorly with the 2-h PG. Abdul-Ghani et al, in a study of 687 people free of T2D, demonstrated that although the HbA_{1c} alone is a significant predictor of future risk of T2D, its predictive power was weaker when compared with the 1-h PG with a significantly lower AUC_{ROC} (0.73 vs 0.84) [75].

Alyass et al [50] evaluated the performance of fourteen OGTT-PG traits from the longitudinal Botnia and MPP cohorts including post-load PG at different time points (30, 60, 90 min along with FPG and 2-h PG), shape of the glucose curve and AUC $glucose_{0\text{-}120}$ in predicting T2D. The 1-h PG alone outperformed the prediction model of multiple clinical risk factors (age, sex, BMI, family history of T2D) in the Botnia Study and MPP (AUC_{ROC} 0.75 [0.72, 0.79] and 0.67 [0.64, 0.70]), respectively. Using this rigorous mathematical approach, the study demonstrated the 1-h PG as the most relevant OGTT-derived trait for classifying middle-aged European adults at increased risk for T2D [50].

5. What is the 1-h threshold level during the OGTT that identifies individuals at risk for T2D?

Longitudinal studies summarized in Table 2 have robustly demonstrated that individuals with NGT having a 1-h PG ≥ 155 mg/dL (≥8.6 mmol/L) during the OGTT were at increased risk to develop T2D [48,50,57,59,63–65].

The 1-h PG threshold of 155 mg/dL (8.6 mmol/L) was initially identified in 1,611 participants without diabetes in the SAHS [48] where it predicted risk of T2D in the subsequent 7–8 years with higher accuracy than in those with IGT (threshold 140 mg/dL [7.8 mmol/L]). A predictive model based on 1-h PG during the OGTT and the presence or absence of the metabolic syndrome, independent of 2-h PG, performed equally well in stratifying individuals for future risk of T2D compared with the model that included 2-h PG. The AUC_{ROC} was 0.84 for 1-h PG > 155/ mg/dL (>8.6 mmol/L) vs. 0.79 for IGT. In addition, another report of 1,551 individuals without diabetes from the SAHS confirmed that 1-h PG was a good predictor for future T2D and had a greater AUC_{ROC} compared with 2-h PG. The AUC_{ROC} was 0.84 for 1-h PG > 155 mg/dL(8.6 mmol/L) vs. 0.79 for IGT. When a cut point for continuous variables was used as a threshold for predicting future T2D, 155 mg/dL (8.6 mmol/L) was determined to be the most accurate 1-h PG value with the sensitivity 75 % and specificity 79 % to predict incident T2D, while the 2-h PG of 140 mg/dL (7.8 mmol/L) had the sensitivity 51 % and specificity 92 % [76].

As another example, the 1-h PG of 155 mg/dL (8.6 mmol/L) was identified as most predictive of T2D in mixed populations of Caucasians and Hispanics [51]. The 1-h PG of 161 mg/dL (8.95 mmol/L) was found to be optimal in the pan-European population of the Relationship between Insulin Sensitivity and Cardiovascular disease risk (RISC) study [77]. Nevertheless, the 1-h PG of 155 mg/dL (8.6 mmol/L) may represent a reasonable compromise in terms of sensitivity and specificity for predicting T2D in multi-ethnic detection and prevention programs for T2D.

In combined populations of the Botnia (N = 2,603) and MPP (N = 2,386) studies, the 1-h PG was confirmed as the best predictor of incident T2D among 14 OGTT derived indices of risk over a follow-up period of 4.94 years and 23.5 years, respectively [50]. Of 75 % who progressed to T2D in the Botnia cohort, 30 % had a 1-h PG above the threshold of 160 mg/dL (8.9 mmol/L) at baseline. In the MPP, 37 % had a 1-h PG ≥ 151 mg/dL (8.4 mmol/L) at baseline and 33.3 % developed T2D. This compared with 11.8 % in participants with 1-h PG < 151 mg/dL (8.4 mmol/L) at baseline. Of people progressing to T2D during a 23.5-year follow-up, 62 % had a 1-h PG ≥ 151 mg/dL (8.4 mmol/l) at baseline [50].

In a larger sample from the MPP cohort (N = 4,867), in people with NGT at baseline but having a 1-h PG ≥ 155 mg/dL (8.6 mmol/L), the cumulative T2D incidence per 1,000 person years was 2.2 after 12 years follow-up and increased to 8.8 after 39 years [57]. The cumulative incidence was even higher in those with IGT and 1-h PG > 155 mg/dL (8.6 mmol/L), i.e., 6.3 and 9.6 after 12- and 39-years follow-up, respectively. The 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was associated with greater discriminative ability to predict T2D than 2-h PG at both 12- and 39-years follow-ups. Noteworthy, the presence of an elevated 1-h PG > 155 mg/dL (8.6 mmol/L) together with IFG or IGT was associated with greater risk of T2D than IFG or IGT alone. People with IGT at baseline but with a 1-h PG below the threshold constituted a minority; very few of these individuals progressed to T2D while all individuals with IGT who progressed to T2D were captured by a 1-h PG > 155 mg/dL (8.6 mmol/L).

A 1-h PG was evaluated as an alternative in European patients with coronary artery disease (CAD), with an algorithm created based on HbA_{1c}, FPG and 1-h PG limiting the need for a 2-h PG [78]. A 2-h PG ≥ 200 mg/dL (11.1 mmol/L) was the reference for undiagnosed T2D. The yield of HbA_{1c}, FPG and 1-h PG was compared with the 2-h PG. In ROC analysis, a 1-h PG ≥ 216 mg/dL (12 mmol/L) balanced the sensitivity and specificity for detecting T2D (both 82 %; the positive and negative predictive values 40 % and 97 %). A combination of FPG < 117 mg/dL (6.5 mmol/L) and 1-h PG < 200 mg/dL (11 mmol/L) excluded 99 % of people with undiagnosed T2D. A combination of FPG > 144 mg/dL (8.0 mmol/L) and 1-h PG > 270 mg/dL (15 mmol/L) identified 100 % of people with undiagnosed T2D.

6. How does the 1-h PG compare with other diagnostic criteria for predicting complications?

A 1-h PG cut point of 155 mg/dL (8.6 mmol/L) may identify a category of high-risk individuals comparable to IFG and IGT. A threshold value for IFG of 110 mg/dL (6.1 mmol/L) was chosen

arbitrarily as it represented "*near the level above which acute phase insulin secretion is lost in response to intravenous administration of glucose and is associated with a progressively greater risk of developing micro- and macrovascular complications*" [79]. Similarly, individuals with NGT with a 1-h PG > 155 mg/dL(8.6 mmol/L) have impaired β-cell responsiveness to a glucose stimulus while being insulin resistant and, as such, are at increased risk of developing T2D [53,79].

As to the diagnosis of overt diabetes, the diagnostic 2-h PG cut off value of 200 mg/dL (11.1 mmol/L) was justified "largely because at approximately that point in glucose distribution where the prevalence of the microvascular complications considered specific for hyperglycaemia (i.e., retinopathy) started to increase dramatically" [79]. For example, the Whitehall survey found that retinopathy developed after 6–8 years follow-up in individuals with a 2-h PG at baseline ≥ 229 mg/dL (12.7 mmol/L) [80]. Studies in Pima Indians [81,82], Egyptians [83], and data from the National Health and Nutrition Examination Survey III (NHANES III) [79] demonstrated the robust association between high FPG and increased risk of retinopathy over time. Threshold values of FPG ranging from 121 mg/dL (6.7 mmol/L) to 129 mg/dL (7.2 mmol/L) were predictive of increased risk for T2D. Therefore, the ADA Expert Committee agreed on a FPG value of 126 mg/dL (7.0 mmol/L) as reasonably equivalent to the 2-h PG diagnostic cut off in terms of enhanced risk for retinopathy [79].

Nonetheless, robust evidence demonstrates that high 1-h PG is also associated with increased risk of retinopathy. In the MPP cohort, the adjusted hazard ratios (HRs) for incident diabetic retinopathy during 39 years follow-up was significantly higher in NGT participants with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) (HR 5.23, 95 %CI 3.24–8.43; p < 0.001) and IGT participants with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) (HR 4.67, 95 %CI 1.75–12.48; p < 0.001). The risk of retinopathy was not increased in those with IGT having a 1-h PG below the threshold < 8.6 mmol/L compared with NGT alone [57]. (See Supplementary Data, Table S7). In a longitudinal study of an American Indian community, the ability of 1-h PG and 2-h PG to predict retinopathy was investigated with cross-sectional ($n = 2,895$) and longitudinal ($n = 1,703$) analyses of the prevalence and incidence of diabetic retinopathy, respectively, based on direct ophthalmoscopy. ROC analysis showed that 1-h PG and 2-h PG did not have different predictive values for identifying retinopathy cases. More importantly, the 1-h PG cut points of 230 mg/dL (12.8 mmol/L) and 173 mg/dL (9.6 mmol/L) did not have different accuracies compared with the 2-h PG cut points of 200 mg/dL (11.1 mmol/L) and 140 mg/L (7.8 mmol/L), respectively [72].

There are few published studies analyzing the association, or the predictive value, between 1-h PG and nephropathy (kidney function or microalbuminuria), in comparison with FPG and/or 2-h PG. Succurro et al. [84] reported that estimated GFR adjusted for age and gender was significantly lower in individuals with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) than in individuals with 1-h PG < 155 mg/dL (8.6 mmol/L). People with higher 1-h PG values also showed an increased risk for chronic kidney disease (CKD) compared with people with lower values. Indeed, people who had 2-h NGT, but 1-h PG ≥ 155 mg/dL (8.6 mmol/L) also showed a higher risk for CKD compared with people having 1-h PG < 155 mg/dL (8.6 mmol/L).

Recently, Cassano et al [85], reported a link between 1-h PG ≥ 155 mg/dL (8.6 mmol/L) during an OGTT and possible increased risk for CKD in people with newly diagnosed T2D. 1-h PG was a major predictor of estimated glomerular filtration rate (e-GFR) justifying 23.6 % of its variation (p < 0.0001). In another study, Saunajoki et al. [86], compared people free of known diabetes without albuminuria with people with albuminuria. The latter had significantly higher 1-h PG and 2-h PG levels, but not FPG or HbA_{1c} levels. An elevated 1-h PG increased the estimated odds ratio of albuminuria more than three times in people with IH (OR 3.60; 95 % CI 1.70–7.64) and diabetes (OR 3.05; 95 % CI 1.29–7.23).

In the follow-up analysis of the Finnish Diabetes Prevention Study, the incidence of cardiovascular disease (CVD) among people with IGT at baseline was associated with an updated mean (i.e., mean value at every recording of a new glucose measurement and includes all follow-up recordings prior to the event or end of follow-up) HbA_{1c}, 1-h PG and 2-h PG HR per 1 unit SD of 1.57 (95 % CI 1.16 to 2.11), p = 0.0032, 1.51 (1.03 to 2.23), p = 0.036 and 1.60 (1.10 to 2.34), p = 0.014, respectively. There was no association between updated mean FPG and CVD incidence (p = 0.11) [87]. In analyses of the last value prior to the CVD event, the same three glycemic measurements were associated with CVD events, with HRs per 1 unit SD of 1.45 (1.06 to 1.98), p = 0.020, 1.55 (1.04 to 2.29), p = 0.030 and 2.19 (1.51 to 3.18), p,0.0001, respectively.

7. What is known about the prevalence of the 1-h PG ≥ 155 mg/dL (8.6 mmol/L)?

Several observational studies in different ethnic groups have analysed the proportion of individuals with NGT (i.e., normal FPG and 2-h PG) having a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) (Table 4). The frequency of 1-h post-load PG ≥ 155 mg/dL (8.6 mmol/L) in those with NGT varies based on the study design, ranging from 11 to 16 % in population-based studies of obese youth to 25–42 % in cohorts enriched with high-risk people.

It is noteworthy that the frequency of individuals with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was demonstrated in the CATAMERI Study to increase with worsening glucose tolerance being 56.6 % in those with

Table 4
Proportion of people with NGT and a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) in various studies.

Study name	Mean age	Sex (% women)	Proportion of individuals with NGT and 1-hour post-load PG ≥ 155 mg/dL (8.6 mmol/L)(%)
SAHS (N = 1611) [48]	NA	NA	16.7
Botnia Study (N = 2442) [88]	46 ± 0.3	54	15.8
Chiba Foundation for Health Promotion & Disease Prevention (N = 4970) [89]	38.8 ± 9.4	41	10.8
CATAMERI Study (N = 3020) [90]	48 ± 13	53	25.4
Section of Endocrinology, University of Florence (N = 1062) [91]	NA	NA	24.0
GENFIEV (N = 926) [92]	NA	NA	39.0
Israel GOH Study (N = 853) [37]	48.1 ± 6.8	48	25.4
Dr. Mohan's Diabetes Specialties Centre, India (N = 1179) [52]	NA	NA	42.6
The New York University Langone Diabetes and Endocrine Associates (N = 236) [39]	55.7 ± 12.8	69	28.9
MMP (N = 4867) [57]	48 (median age)	0	33.2
SOLAR (N = 233) [93]	11.1 ± 1.7	43	35.2
Bambino Study (N = 1038) [94]	11.3 ± 2.8	NA	11.4
RISC Study (N = 1205) [77]	44 ± 8	56.1	20.0

Abbreviations: MMP, Malmö Preventive Project; SAHS, San Antonio Heart Study; CATAMERI, CATAnzaro Metabolic Risk factors; GENFIEV, Genetic, Physiopathology and Evolution of Type 2 Diabetes; GOH, Israel Study of Glucose Intolerance, Obesity and Hypertension; SOLAR, Study of Latino Adolescents at Risk of Type 2 Diabetes; RISC, Relationship between Insulin Sensitivity and Cardiovascular Risk.

isolated IFG, 77.6 % in those with isolated IGT, 93.8 % in those with combined IFG + IGT, and 98.8 % in those with newly diagnosed T2D [90]. Similar findings were seen in the Israel Study of Glucose Intolerance, Obesity and Hypertension (GOH) [37] demonstrating the incremental cohort distribution shift towards the high 1-h PG value as the severity of dysglycaemia progresses (Table 5).

8. What is the evidence that the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) precedes IGT and T2D?

To test the hypotheses that the 1-h PG is an earlier marker of IH and T2D than the 2-h PG, Ha et al. analysed a longitudinal dataset of OGTTs from studies of Southwestern Native American (SWNA) over several decades [95]). To estimate individual glucose trajectories for diabetes risk prediction over time, a linear mixed effects model was used to: [1] determine the order of elevation of 1-h PG vs. 2-h PG for predicting IH; and [2] evaluate the timing of elevation of 1-h PG vs. 2-h PG for prediction of IH and T2D.

The 1-h PG threshold of 155 mg/dL (8.6 mmol/L) for defining IH was crossed a median 1.6 years earlier (mean, 5.3 years) than the 2-h PG threshold of 140 mg/dL (7.8 mmol/L), the current diagnostic threshold for IGT. Applying the 1-h PG threshold could therefore result in earlier detection and enhance intervention in individuals at high-risk for IH and T2D. The finding that a high 1-h PG represents an intermediate state between NGT and IGT was confirmed in a longitudinal study of the RISC cohort which found that a subset of individuals progressing from NGT to IGT after 3 years had 1 h-PG ≥ 155 mg/dL (8.6 mmol/L) at baseline, implying that a high 1-h PG occurred first [95]. Furthermore, the risk of progressing to IGT was higher in people with high 1-h PG than in those with low 1-h PG. Since most (74 %) crossed the 1-h PG threshold first, screening using the 1-h PG would identify people at risk who might benefit from early preventive intervention since insulin sensitivity and β-cell function are already impaired in individuals with NGT but high 1-h PG (see Section 9).

Similarly, the proposed 1-h PG cut-point of 209 mg/dL (11.6 mmol/L) for diagnosing T2D (see Section 19) was crossed a median 1 year earlier (mean 1.6 years) than the standard 2-h PG threshold of 200 mg/dL (11.1 mmol/L). Thus, using 1-h PG to diagnose T2D may also facilitate earlier initiation of glucose lowering therapy when reversal from T2D and adequate glycaemic control are more likely to be achieved [95,96].

9. What is known regarding the pathophysiology of NGT with 1-h PG ≥ 155 mg/dL (8.6 mmol/L)?

The natural history of progression from normal glucose homeostasis to T2D is characterised by three different phases [97]. The first phase occurs when β-cell function compensates for increased insulin demand owing to reduced insulin sensitivity. The second phase occurs when β-cell function is still maintained but β-cell mass becomes depleted leading finally to irreversible impairment of β-cell responsiveness. This leads to the third phase where insulin secretion from β-cells can no longer maintain glucose homeostasis and diabetes develops. The entire process may take more than a decade when FPG and 2-h PG levels remain in the normal range. There are, however, individuals with normal FPG and 2-h PG at the baseline observation who may develop T2D faster, and a continuum of risk for developing T2D across the spectrum of 2-h PG exists. As post-challenge PG increases, there is a decline in β-cell glucose sensitivity, a measure of the dependence of the insulin response to a glucose stimulus although sufficient insulin secretion may be maintained [98].

Table 5
Number of people in each glycemic category in the 2-h OGTT according to normal vs. high 1-h PG in the Israel GOH Study [37].

2-h OGTT	1-h PG	
	< 155 mg/dL (8.6 mmol/L) n (%)	≥155 mg/dL (8.6 mmol/L) n (%)
NGT	667 (81.9)	147 (18.1)
IFG	455 (59.9)	305 (40.1)
IGT	36 (35.0)	67 (65.0)
IFG + IGT	47 (16.7)	234 (83.3)
T2D	8 (4.1)	185 (95.9)

Abbreviations: 1-h PG, 1-hour plasma glucose; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2D, type 2 diabetes.

The RISC study [77] found that there was a progressive and significant decline in insulin sensitivity and β-cell glucose sensitivity (i.e., representing the dependence of insulin secretion on absolute glucose concentration) progressing from NGT with normal 1-h PG, to NGT with high 1-h PG, and to individuals with IGT while basal and total insulin secretion significantly increased. No differences were found in β-cell rate sensitivity (i.e., representing the dependence of insulin secretion on the rate of change of glucose concentration) and the potentiation factor (accounting for higher insulin secretion on the descending phase of OGTT hyperglycaemia than at the same glucose concentration on the ascending phase) between NGT with high 1-h PG and IGT. This suggests that NGT with a high 1-h PG represents a risk for T2D which may or may not be related to IGT with reduced β-cell glucose sensitivity as the phenotypic signature and pathogenetic cause. On the other hand, early β-cell dysfunction appeared to be a predominant feature in Asian populations who progressed to T2D [99–101]. A 10-year population-based study in Korea, using homeostatic model assessment for β-cell function and insulin resistance (HOMA-β and HOMA-IR), demonstrated that while HOMA-IR increased with age, people developing T2D could not mount an insulin response to overcome the resistance [40]. In many populations, particularly in Asians, over 50 % of individuals with screen-detected T2D were diagnosed based on 2-h PG during an OGTT, not by FPG [23].

Longitudinal studies have also investigated individuals with both IGT and high 1-h PG. In particular, the MPP [57] demonstrated that the hazard ratio (HR) of developing diabetes during a 12-year follow-up was higher in NGT with a high 1-h PG (HR 3.87; 95 %CI 2.16–6.93) and in people with IGT with a high 1-h PG (HR 9.0; 95 %CI 3.83–21.16) compared with individuals with IGT having a normal 1-h PG at baseline. After 39 years of follow-up, individuals with NGT and IGT with a high 1-h PG had higher HR (2.93, 95 %CI 2.48–3.46 vs. 2.76, 95 %CI 1.87–4.06), while it was lower and non-significant in the IGT group with normal 1-h PG (HR 1.17, 95 %CI 0.43–3.15). (See Supplementary Data Tables S1-S4, S8, S10). There was a small number of individuals with IGT who had a normal 1-h PG, only a few who progressed to diabetes, consistent with findings from the Israel GOH study [37]. Table 5 confirms that with worsening dysglycaemia, the prevalence of high 1-h PG increased in the Israel GOH Study; a minority of individuals with IFG and IGT had a 1-h PG < 155 mg/dL (8.6 mmol/L). (See Supplementary Data Fig. S4).

The significant increase in the incidence of T2D with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) progressing from NGT to IFG to IGT was shown in the SAHS and Botnia Study (Fig. 1) [48,88]. People with NGT in the SAHS had a low risk for T2D (5.0 %). However, people with NGT and a 1-h PG > 155 mg/dL (8.6 mmol/L) had significantly increased risk (15.3 %) for future T2D compared with people with 1-h PG < 155 mg/dL (8.6 mmol/L) (2.9 %) (P 0.0001) [48]. People with IFG and a 1-h PG > 155 mg/dL (8.6 mmol/L) had a 37.3 % incidence of T2D, while people with IFG and a 1-h PG < 155 mg/dl had a 10.8 % incidence. People with IGT and a 1-h PG > 155 mg/dL (8.6 mmol/L) had a 35.5 % T2D incidence, while people with IGT and a 1-h PG < 155 mg/dL (8.6 mmol/L) had a 17.8 % incidence rate [48].

In the Botnia Study, people with NGT had a low risk for developing T2D (2.4 %). However, people with NGT and a 1-h PG > 155 mg/dL (8.6 mmol/L) had a significantly increased risk (8.5 %) for future T2D compared with people with NGT and a 1-h PG < 155 mg/dL (8.6 mmol/

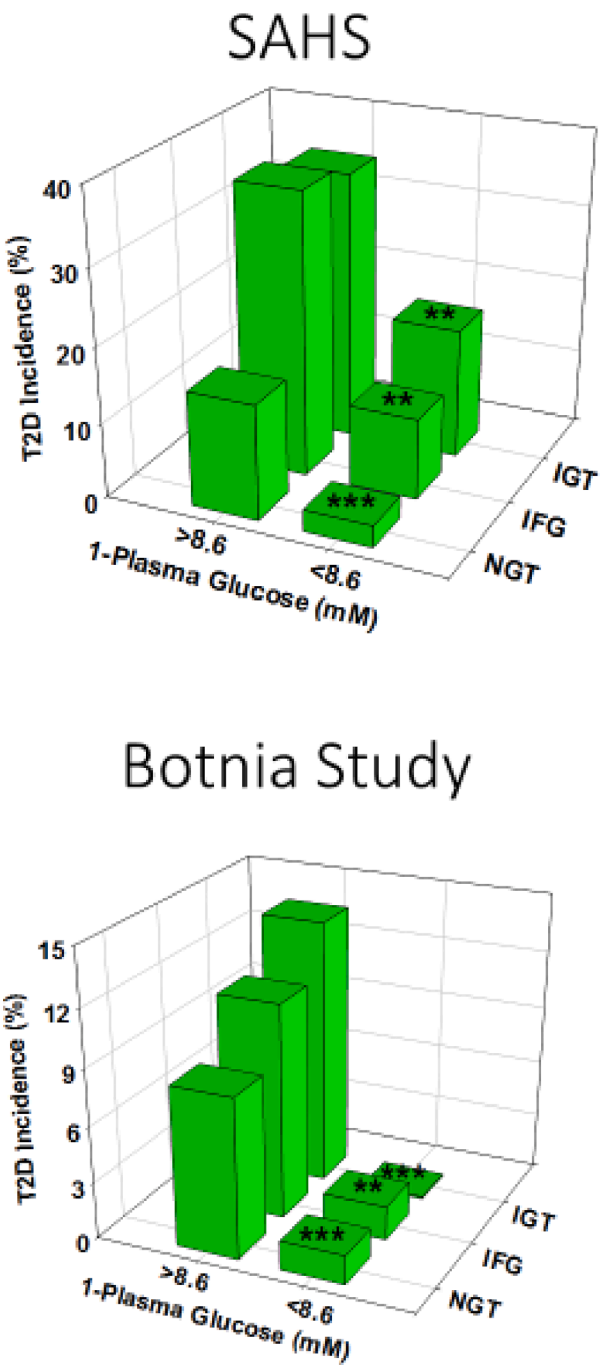

Fig. 1. 1-h PG and the incidence of T2D in the SAHS and Botnia Study (adapted from [48,88]. p values represent difference in T2D incidence in each category between people with high 1-h PG versus low 1-h PG: *p < 0.05, **p < 0.001, ***p < 0.0001.

L) (1.3 %) (P < 0.0001) [88]. People with IFG and a 1-h PG > 155 mg/dL (8.6 mmol/L) had a significantly increased risk (11.4 %) for future T2D compared with people with IFG and a 1-h PG < 155 mg/dL (8.6 mmol/L) (1.8 %). People with IGT and a 1-h PG > 155 mg/dL (8.6 mmol/L) had a significantly increased risk (14 %) for future T2D compared with people with IGT and a 1-h PG < 155 mg/dL (8.6 mmol/L) (0 %) [88].

Thus, individuals with NGT with a high 1-h PG have reduced β-cell glucose sensitivity but still maintained NGT due to sufficient residual β-cell mass and preserved second phase insulin secretion. The subsequent loss of second phase insulin secretion results in IGT and gradually overt T2D.

The Diabetes Research on Patient Stratification (DIRECT) trial [102] included among IH categories a subgroup of participants (30.6 % of 2,111 people) with a 1-h PG ≥ 155 mg/dL (8.6 mmol/L), with normal FPG, 2-h PG and HbA_{1c} <5.7 % (<39 mmol/mol). This group with a high 1-h PG showed differences in both insulin sensitivity and β-cell function compared with the other groups with isolated IH defects (IFG, or elevated HbA_{1c}), though a comparison with IGT was not possible due to low numbers. The group with the high 1-h PG demonstrated lower secretion at a reference glucose (rounded mean basal glucose in all participants) of 108 mg/dL (6.0 mmol/L). Moreover, β-cell glucose sensitivity was significantly impaired in those with an elevated 1-h PG, noted in the RISC study, as was the potentiation factor (index of OGTT insulin secretion potentiation) compared with those with IFG or HbA_{1c}-defined IH. The 1-h PG ≥ 155 mg/dL (8.6 mmol/L) subgroup may therefore identify an IH phenotype with metabolic defects, specifically greater β-cell dysfunction compared with people with IH having other single defect in glycaemia regulation [102].

Consistent with these observations, insulin sensitivity in muscle, liver and adipose tissue was not different in non-obese (body mass index; BMI < 25 kg/m^2) Japanese men with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) compared with those having 1-h PG < 155 mg/dL (8.6 mmol/L). However, compared with the latter group, the insulinogenic index ($\Delta insulin_{30}$ / $\Delta glucose_{30}$) was significantly lower in the high 1-h group (1.4 ± 1.2 vs 0.7 ± 0.3), indicating impaired early insulin secretion. Adiponectin level was significantly lower (1.8 ± 1.2 vs 1.1 ± 0.8 ng/mL) in the high 1-h PG group and did not significantly correlate with the insulinogenic index. Multiple regression analysis demonstrated that the insulinogenic index and adiponectin were independently associated with 1-h PG [103]. Thus, study participants with a high 1-h PG during an OGTT had reduced early insulin secretion than participants with a low 1-h PG, but insulin sensitivity and fat distribution were comparable between the groups. Thus, in non-obese Japanese men, impaired early insulin secretion might be an underlying mechanism of an elevated 1-h PG during an OGTT.

The pattern of the PG response curve during an OGTT has prognostic significance. Compared with a "monophasic" pattern, the "biphasic" pattern is associated with greater insulin sensitivity/secretion and a reduced risk of progression to diabetes. Jalleh et al. measured PG, glucagon-like peptide-1 (GLP-1), glucose dependent insulinotropic polypeptide (GIP) and insulin levels as well as speed of gastric emptying in 36 adults without diabetes aged over 65 years [104]; at baseline, 22 participants had a "monophasic" and 14 a "biphasic" glucose response during the OGTT. The 1-h PG response curve was greater and the GLP-1 $AUC_{0–120\ min}$ and insulin secretion were lower in the monophasic group. There were no differences in gastric emptying, GIP, or insulin sensitivity. At 5.8 ± 0.1 years follow-up, the 1-h PG response curve was greater while GLP-1 $AUC_{0–120\ min}$ was lower in the monophasic group. A biphasic curve was associated with a lower 1-h PG response curve and an increase in GLP-1, but there was no difference in either GIP or gastric emptying rate. Therefore, a biphasic PG curve following a 75 g OGTT is associated with an increase in GLP-1 and insulin secretion and a reduction in 1-h PG response. These observations suggest that an increased GLP-1 response may be central to the reduced risk of dysglycaemia known to be associated with biphasic, compared to monophasic, glucose responses. These gastrointestinal and hormonal responses in the monophasic group further support the predictive value of 1-h PG ≥ 155 mg/dL (8.6 mmol/L) for T2D [104].

10. Is the 1-h post-load PG ≥ 155 mg/dL (8.6 mmol/L) associated with cardio-metabolic risk factors and target organ damage?

A large body of evidence suggests that individuals with NGT but having an elevated 1-h PG exhibit an unfavourable cardio-metabolic risk profile, with elevated plasma biomarkers of systemic inflammation increasing the risk of cardiovascular target-organ damage [105]. Furthermore, studies in cells, animals, and humans suggest that an

elevated 1-h PG is a sufficient stimulus for several cardiovascular risk factors including inflammation, thrombosis, and endothelial dysfunction, with oxidative stress generation as the possible pathogenetic factor [106]. These findings are summarized in Table 6.

Recently, Cassano et al reported that people with NGT and 1-h PG ≥ 155 mg/dL (8.6 mmol/L) exhibited levels of oxidative stress, endothelial dysfunction and platelet activation that were significantly higher compared with people with NGT and 1-h PG < 155 mg/dL (8.6 mmol/L) but comparable with those found in people with IGT [85]. The worse oxidative profile found in people with NGT and 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was associated with a decreased eGFR. These results are in agreement with Succurro et al. showing that compared to people with 1-h PG < 155 mg/dL (8.6 mmol/L), people with 1-h PG ≥ 155 mg/dL (8.6 mmol/L), independent of the 2-h PG, demonstrated decreased eGFR and increased risk of CKD (OR 3.72 [95 % CI 1.02 to 13.58]) [84]. Another cross-sectional study in 496 people subdivided into two groups according to presence of albuminuria, assessed by urinary albumin-to-creatinine ratio, reported that people with albuminuria displayed significantly higher 1-h PG and 2-h PG, but not FPG or HbA_{1c} compared with people without albuminuria. Additionally, stratifying people according to the 1-h PG cut-off for IH and diabetes ([<155 mg/dL (8.6 mmol/L), 155–208 mg/dL (8.6–11.6 mmol/L) and ≥ 209 mg/dL (11.6 mmol/L]), a 3-fold increased risk of albuminuria was found in people with 1-h PG defined IH and diabetes compared with people with 1-h PG < 155 mg/dL (8.6 mmol/L) (OR 3.60; 95 % CI 1.70–7.64 and OR 3.05; 95 % CI 1.29–7.23, respectively) [86].

Cross-sectional population-based studies have shown that an elevated 1-h PG is associated with CVD. In the CATAMERI study comprising 1,010 individuals without diabetes, a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) was associated with prevalent CVD, including CAD and cerebrovascular disease, independent of classical risk factors both in individuals with normal HbA_{1c} (<5.7 %; 39 mmol/mol) as well as in those with HbA_{1c}-defined IH (HbA_{1c} 5.7-6.4 %; 39–46 mmol/mol) ($p < 0.001$) [149]. In a logistic regression analysis, the odds ratios (OR) adjusted for several CVD risk factors revealed that individuals with HbA_{1c} < 5.7 % (39 mmol/mol) and 1-h PG ≥ 155 mg/dL (8.6 mmol/L) and those with HbA_{1c} 5.7 − 6.4 % (39–46 mmol/mol) and 1-h PG ≥ 155 mg/dL had a 4.5-fold (OR: 4.54) and 6.2-fold (OR: 6.19) increased risk of composite CVD and 6.2-fold (OR: 6.16) and 8.0-fold (OR: 8.04) increased risk of CAD, respectively, in comparison with individuals with HbA_{1c} < 5.7 % (39 mmol/mol) and 1-h PG < 155 mg/dL(8.6 mmol/L) [149].

Hospital-based cross-sectional studies in people with CAD have also shown that elevated 1-h PG is also independently associated with worse clinical outcome. Among people admitted to a coronary care unit due to ACS, an OGTT including both 1-h and 2-h PG values identified individuals with the most severe in-hospital risk profile, adverse remodeling and longer hospitalization [152]. Among people with CAD who underwent coronary angiography, those with NGT but 1-h PG ≥ 155 mg/dL (8.6 mmol/L) exhibited greater severity of coronary artery lesions and an increased risk of re-admission with adverse CVD events [148].

Several longitudinal studies have evaluated the impact of 1-h PG on CVD and all-cause mortality. In the Helsinki Businessmen Study comprising 2,756 healthy men without diabetes at baseline followed for 44 years, a strong association between 1-h PG and CVD mortality was observed ($p < 0.001$). Individuals with BMI < 30 kg/m^2 and 1-h PG concentration > 161 mg/dL (8.9 mmol/L) exhibited a 1.33-fold increase in all-cause mortality, compared with those having a BMI < 25 kg/m^2 and 1-h PG ≤ 161 mg/dL (8.9 mmol/L) after adjusting for age and

Table 6
Association of 1-h post-load PG ≥ 155 mg/dL (8.6 mmol/L) with cardiovascular risk factors, target organ damage, and adverse outcomes.*.

Association with cardiovascular risk factors:

- Insulin resistance [63,77,107,108]
- Obesity and visceral adiposity [109–112]
- Metabolic syndrome [111–113]
- Pro-atherogenic lipid profile [114,115]
- Increased uric acid [116]
- Increased viscosity [117]
- Reduced Vitamin D [118]
- Increase in pro-inflammatory markers [119,120]
- Increase in oxidative stress markers [85,121]
- Reduction in molecules with anti-inflammatory properties [119,122]
- Increase in platelet activation markers [85]
- Increase in advanced glycated end-products (AGEs) and decrease in endogenous secretory receptor for advanced glycation end products secreted RAGE (esRAGE) [123,124]
- Decrease in circulating adiponectin [103]

Association with target-organ damage:

- Subclinical atherosclerosis [125–127]
- Increased pulse pressure [127]
- Vascular (arterial) stiffness [89,127–129]
- Left ventricular hypertrophy [130]
- Impaired diastolic cardiac function [131]
- Right ventricular dysfunction [132]
- Subclinical left atrial myocardial dysfunction [133]
- Impaired insulin-stimulated myocardial glucose metabolism [134]
- Impaired myocardial mechano-energetic efficiency [135]
- Morpho-functional subcortical brain alterations and poor memory performance tests [136]
- Decline in kidney function [84,85]
- Increased albuminuria [86]
- Diabetic retinopathy [57,72]
- Increased liver enzymes, MASLD (formerly called non-alcoholic fatty liver disease or NAFLD), and metabolic dysfunction-associated steatohepatitis (MASH, formerly, non-alcoholic steatohepatitis; NASH) [109,110,137–139]
- Cystic fibrosis-related diabetes (CFRD) [140–145]

Capability of predicting progression to:

- Macrovascular complications [57,146–152]
- All cause-mortality [57,59,130,146,147,150,151,153–155]

* Modified from reference [2].

smoking [59]. In the population-based Erfurt Male Cohort Study (ERFORT), 1,125 men aged 40 to 59 years without diabetes were followed for 30 years [153]. Individuals with a 1-h PG > 200 mg/dL (11.1 mmol/L) exhibited a 1.49-fold increased risk for death compared with men having 1-h PG ≤ 200 mg/dL (11.1 mmol/L) after multiple adjustments [153].

The Israel GOH Study followed 1,945 individuals without diabetes at baseline for 33 years [154]. 1-h PG was determined after a 100-g OGTT. Individuals with NGT at baseline but having the 1-h PG > 155 mg/dL (8.6 mmol/L) exhibited a 1.32-fold increased risk for death compared with NGT individuals having a 1-h PG ≤ 155 mg/dL (8.6 mmol/L) after multiple adjustments. In the MPP after 39 years follow-up, NGT individuals with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) exhibited a 1.24-fold increased risk for incident myocardial infarction and fatal CAD and a 1.29-fold increased risk for all-cause mortality compared with NGT individuals with 1-h PG level < 155 mg/dL (8.6 mmol/L) after multiple adjustments [57]. Furthermore, in the MPP, the 1-h PG, but not FPG or 2-h PG, was found to be an independent predictor of CVD death (HR: 1.09) and all-cause mortality (HR: 1.10). Addition of 1-h PG to clinical risk factors significantly improved their capability to predict CVD and all-cause mortality [155] (See Supplementary Tables S5, S6, S9).

In a cohort of 39,573 people without diabetes participating in the Chicago Heart Association Detection Project in Industry, high 1-h PG after a 50-gr oral glucose load was associated with an increased risk of stroke, CAD and increased CVD and all-cause mortality during a follow-up of 22 years in both men and women. This was independent of several traditional CVD risk factors [146]. These observations are consistent with results of the Honolulu Heart Program comprising 6,394 Japanese-American men without diabetes followed for 12 years that demonstrated 1-h PG after a 50-gr OGTT was directly associated with fatal and nonfatal CAD events [147].

The OPERA project in Finland elucidated risk of atherosclerosis in a population-based study encompassing middle-aged people with hypertension and randomly selected age- and sex-matched control people followed for 24 years. The 1-h PG was an independent and better predictor of CVD morbidity and mortality with slightly over 50 % more CVD endpoints that were not recognized by FPG or 2-h PG [150]. In a cohort of 862 Chinese men without diabetes at baseline having a median age of 74 years, an elevated 1-h PG was associated with a greater risk of developing CVD (adjusted HR: 1.097) and all-cause mortality (adjusted HR: 1.196) after a follow-up of 20 years [151]. Compared with 2 h-PG, 1 h-PG was a stronger independent predictor of CVD and all-cause mortality after adjusting for various traditional risk factors [151].

Overall, the evidence supports that the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) is capable of independently detecting individuals at risk of cardiovascular target organ damage, adverse CVD outcomes, and mortality (see Supplementary Data; Tables S5, S6, S9).

11. What is known about the association of the 1-h PG with obstructive sleep apnoea?

Cross-sectional studies in people with NGT have reported an association between 1-h PG ≥ 155 mg/dL (8.6 mmol/L) and severity of obstructive sleep apnoea (OSA). An analysis performed in overweight/obese people without diabetes attending the Sleep Disorders Center in Ruijin Hospital, Shanghai showed that 1-h PG was significantly increased in people with mild to moderate OSA, and also in those with severe OSA [156]. Additionally, 1-h PG, but not FPG or 2-h PG, was significantly associated with parameters of OSA severity including apnoea-hypopnoea index (AHI), oxygen desaturation index, and percentage of lowest nocturnal oxygen saturation [156]. Pamidi at al. found similar results in a study [157] comprising people without diabetes having OSA; amongst individuals with NGT, 1-h PG was directly associated with severity of OSA assessed by AHI after adjustment for BMI. Moreover, the prevalence of 1-h PG ≥ 155 mg/dL (8.6 mmol/L) increased with worsening OSA, with the majority of people with an elevated 1-h PG having moderate to severe OSA in both NGT (76 %) and IH groups (85 %) [157]. The association between elevated 1-h PG and severity of OSA has recently also been described in children and adolescents with obesity [158].

12. What is known about association of the 1-h PG with cystic fibrosis-related diabetes?

Several studies have demonstrated that elevated 1-h PG is associated with worse pulmonary function in people affected by cystic fibrosis (CF). A cross-sectional study in 101 children with CF undergoing CF-related diabetes (CFRD) screening with an OGTT, demonstrated that pulmonary function, assessed by percent predicted forced expiratory volume in 1 sec (FEV_1), was inversely correlated with 1-h PG but not with FPG or 2-h PG [140]. Adjusted for BMI, predicted FEV_1 was reduced 1% for every 10 mg/dL (0.6 mmol/L) increase in 1-h PG. Subsequently, the same investigators performed a retrospective analysis in 80 paediatric patients with CF followed for 5 years and found that children with elevated 1-h PG ≥ 160 mg/dL (8.9 mmol/L) were more likely to have worse predicted FEV_1% than those with lower 1-h PG [144].

Aside from its association with worse pulmonary function and its faster decline, a greater value of 1-h PG has been shown to be associated with an impaired β-cell function [142,145], and an increased risk for developing CFRD [141,143,144]. In a longitudinal study in Germany including 385 youths with CF, individuals with NGT and 1-h PG > 200 mg/dL (11.1 mmol/L) had a 3-fold increased risk of developing CFRD during a follow up of 3.6 years compared with counterparts with 1-h PG < 200 mg/dL (11.1 mmol/L) (OR: 2.81, 95% CI: 1.43–5.51) [143]. A retrospective study in children attending The Children's Hospital of Philadelphia Cystic Fibrosis Center confirmed this outcome and also demonstrated that a 1-h PG > 160 mg/dL (8.9 mmol/L) was associated with a greater risk of CFRD during a 5-year follow-up [144]. Moreover, a retrospective longitudinal analysis of 158 children with CF attending the Children's Hospital of Colorado CF Center demonstrated that an elevation in 1-h PG preceded the increase in 2-h PG and that 1-h PG ≥ 140 mg/dL (7.8 mmol/L) predicted development of CFRD over the subsequent five years in children with NGT at baseline [141].

13. What is known about the association of the 1-h PG with metabolic dysfunction-associated steatotic liver disease (MASLD)?

Several studies have demonstrated an association between elevated 1-h PG and MASLD and MASH [109,110,137–139], conditions broadly recognized to confer an increased risk of both hepatic and extra-hepatic morbidity and mortality [159,160]. In the CATAMERI study, individuals with NGT and 1-h PG ≥ 155 mg/dL (8.6 mmol/L) displayed higher levels of liver damage biomarkers, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT) in comparison with those with 1-h PG < 155 mg/dL (8.6 mmol/L) adjusted for confounding factors [109]. Furthermore, a cross-sectional analysis of 700 individuals undergoing ultrasound evaluation for hepatic steatosis showed that participants with NGT but 1-h PG ≥ 155 mg/dL (8.6 mmol/L) displayed a significant 1.7-fold increased risk of hepatic steatosis compared with those with NGT and having 1-h PG < 155 mg/dL (8.6 mmol/L). A high 1-h PG was associated with elevated ALT, GGT, and high sensitivity C-reactive protein (hs-CRP) levels as well as increased hepatic insulin resistance [110]. The 1-hour PG ≥ 155 mg/dL (8.6 mmol/L) in people with NGT has also been associated with hepatic steatosis assessed by transient elastography [161] which is considered a safe, non-invasive tool that can risk-stratify people with a high 1-h PG with a high level of accuracy [161].

The capacity of the 1-h PG ≥ 155 mg/dL (8.6 mmol/L) to identify hepatic steatosis was also seen in people within HbA_{1c}-defined categories [137]. In a study of 1,108 adults, people with HbA_{1c} < 5.7 % (39 mmol/mol) but 1-h PG ≥ 155 mg/dL (8.6 mmol/L) had a 1.61-fold

increased risk of hepatic steatosis compared with those with lower 1-h PG value (OR adjusted for age and sex: 1.62) [138]. Similarly, people having HbA_{1c}-defined IH, those with elevated 1-h PG ≥ 155 mg/dL (8.6 mmol/L) were more likely to have hepatic steatosis and greater levels of AST, ALT, GGT, hs-CRP, complement C3, and lower level of insulin-like growth factor-1 (IGF-1) [138].

An Italian study evaluating hepatic steatosis with ultrasonography assessed by western blot duodenal abundance of the glucose carrier sodium/glucose co-transporter 1 (SGLT-1) during upper gastrointestinal endoscopy [137]. Individuals with hepatic steatosis displayed increased levels of 1-h PG but not increased FPG or 2-h PG [137]. Accordingly, 1-h PG was associated with an increased risk of MASLD fibrosis risk, steatosis and considered as a surrogate indicator of hepatic fibrosis [137]. Moreover, a short-term exposure to high glucose concentrations was shown to promote intracellular lipid accumulation in Huh7 hepatic cells and resulted in an upregulation of endoplasmic reticulum (ER) stress-related responses and pro-inflammatory pathways implicated in the pathogenesis of liver fibrosis [162]. This observation suggested that early post-prandial hyperglycemia may contribute to hepatic steatosis, and its progression to more severe forms of liver damage. An observational study performed in 101 Indian adults with NGT, obesity and hepatic steatosis reported an association between 1-h PG ≥ 155 mg/dL (8.6 mmol/L) and a higher degree of fatty liver disease assessed by ultrasonography [163]. Furthermore, in 2,335 Caucasian individuals with varying glucose tolerance, 1-h PG ≥ 155 mg/dL (8.6 mmol/L) identified those harboring a higher risk of advanced hepatic fibrosis estimated by the non-invasive index of fibrosis FIB-4 in those with NGT or isolated IFG. The 1-h PG has shown a greater sensitivity and specificity for risk of hepatic fibrosis than FPG, 2-h PG, and HbA_{1c} [139].

14. Should classifying IH be based on 1-h PG or on both 1-h PG and 2-h PG levels?

The sensitivity, specificity, and net predictive values for the 1-h and 2-h PG values were derived from the MPP and Israel GOH Study [9]. The sensitivity was considerably greater for the 1-h PG level although somewhat less specific when contrasted with the 2-h PG values in both studies. The sensitivity and specificity relationships were more optimal in both cohorts for the 1-h PG. Individuals in the MPP and Israeli GOH Study having a 1-hour PG ≥ 155 mg/dL (8.6 mmol/L) combined with IGT had the greatest risk for microvascular disease, diabetes, and mortality possibly indicating the effect of an increased duration of exposure to hyperglycemia as IGT occurs later that the elevation in the 1-h PG level [9].

Venn diagrams in the Supplementary Data demonstrate the association between the 1-h PG, IFG and IGT for the CATAMERI Study (Suppl. Fig. S1) [90]), MPP (Suppl. Fig. S2 and S3) [57],and Israel GOH Study (Suppl. Fig. S4) [37]. The scatterplot in the Supplementary Data (Fig. S5) depicts the association between the 1-h PG and 2-h PG in the MPP [57].

15. What are the health economic implications regarding the 1-h PG for detecting IH?

People with high 1-h PG represent a phenotype akin to IGT but exhibit a higher incidence of T2D. The major T2D prevention programs have robustly demonstrated the efficacy of lifestyle intervention in delaying the onset of T2D and reducing associated morbidity in people with IGT [164–168]. However, as noted earlier, diabetes prevention trials have been less effective in those with isolated IFG [46–47]. Hence, there is interest in ascertaining the benefits of intervention in people with high 1-h PG. The STOP DIABETES study [169], confirmed the efficacy of lifestyle intervention in delaying the onset of T2D in people with high 1-h PG. Therefore, the implication of early identification and lifestyle intervention in individuals with high 1-h PG are projected to be substantial, both in terms of direct and indirect cost reduction for society. It is reasonable that cost-effectiveness of screening would be dramatically enhanced if screening is performed in people with known risk factors for diabetes including obesity and metabolic abnormalities.

Andellini et al. [170] estimated the benefits arising from early identification of people with high 1-h PG and subsequent low-cost lifestyle interventions in a population that simulated a general one followed for years. The primary focus was the reversal of IH, delay in progression to T2D and development of cardiovascular comorbidities. A robust structured health economic analysis was used to estimate the cost-effectiveness of 1-h PG measurements in comparison to the conventional 2-h PG for screening of diabetes risk over a 35-year period. The primary outcome was the cost per quality-adjusted life year (QALY) gained.

The authors developed a Monte Carlo-based Markov simulation model, which forecasted the long-term effects of two distinct strategies concerning both clinical and cost-effectiveness outcomes. The simulation model extracted data from the MPP regarding T2D progression and all-cause mortality [57,164,167], from the DPP Outcomes Study (DPPOS) [165] for the effect of metformin and lifestyle interventions on disease progression, and from the United Kingdom Prospective Diabetes Study (UKPDS) for data related to the development of diabetes complications [19], diabetes-related deaths and regression from IGT to NGT [171]. The cohort included 20,000 simulated people with a 35-year follow-up.

The analysis projected that the 1-h PG would increase the number of years free from clinical T2D by 2 years, delay the onset of T2D by 1 year per person and to decrease the incidence of T2D complications by 40 % (relative risk 0.6) per person resulting in an overall increase of 0.58 QALY gained per person when a high 1-h PG was used to screen people for risk of T2D and lifestyle intervention implemented. Despite expenditures associated with 1-h PG testing (a 5-time-point OGTT repeated every three years in people with NGT with low 1-h PG and yearly in people with IGT and NGT with high 1-h PG) and preventive treatment, long-term costs, related to diabetes and associated complications, would be reduced by simulated low-cost (lifestyle intervention plus metformin) interventions.

The lifetime cost saving for those who were diagnosed with high 1-h PG and treated by lifestyle intervention and metformin was approximately 31, 225,719.82 €. The incremental cost-effectiveness ratio for the overall population was estimated at −8,214.7€ per each QALY gained, signifying the potential cost savings and health benefits associated with the 1-h PG screening strategy [170].

Simulation models are widely used to assess long-term effects and future costs of an intervention compared to standard of care to inform decisions that impact care. In the case of 1-h PG, the simulation model found that it was clinically superior and more cost-effective compared to the conventional 2-h PG. It is worth noting that this study [170] did not consider the reduction of indirect costs of T2D or improvement in quality of life and increased life expectancy. Therefore, this analysis likely provided an underestimation of cost-effectiveness.

16. What is known about the 1-h PG for detecting youths and adolescents at high-risk for T2D?

The incidence of T2D in youth is very low and characterized by accelerated deterioration in insulin secretion and an increased development of complications [172]. Young people who progressed to overt diabetes presented a steady decline in the disposition index (DI) while those who reverted to NGT experienced a steady increase that persisted after completion of pubertal transition [93,173,174]. Thus, it is crucial to screen young individuals who are overweight or obese for IH and diabetes to ensure early diagnosis and targeted interventions to prevent or delay progression to T2D and onset of complications [175].

The incidence of IH and diabetes depends on whether FPG, 2-h PG, or HbA_{1c} is used for screening. Using only one of these methods can result in an underestimation in the incidence of IH [176]. In a group of 154

children and adolescents from the "Bambino" study with follow-up data, addition of the 1-h PG to FPG and 2-h PG following an OGTT achieved 100% sensitivity to detect incident IGT over a median follow-up of 2 years [177]. High 1-h PG delineates in youths, as in adults, a phenotype of IH characterized by reduced first phase secretion, insulin sensitivity and DI not different from IGT [178–180] Importantly, it is also a marker of CVD risk [178,179,181] and fatty liver disease [177]. In two large studies of white non-Hispanic children and adolescents, lipid profiles and blood pressure values in those with NGT and different high 1-h PG cut points were similar to those with IGT [178] and/or IFG [179]. The "Bambino" study [177] also demonstrated significantly higher values of ALT in those with high 1-h PG suggesting that this phenotype is associated with fatty liver disease, likely in a bi-directional relationship as it is for IGT and overt diabetes. These observations strongly suggest that young individuals with high 1-h PG have a cardio-metabolic risk profile similar to people with IGT.

Factors that can influence diagnostic accuracy of 1-h PG in youths and explain discrepancies among paediatric studies with respect to those in adults include age and puberty-related changes of insulin metabolism, ethnicity, length of follow-up, and endpoint used in the prediction analyses to define the disease.

The large fluctuation in insulin sensitivity and secretion at the pubertal transition may account for a lower diagnostic threshold defining high 1-h PG in youths compared with adults. In a cross-sectional study [178] investigating diagnostic accuracy of high 1-h PG in youth by ROC analysis, the best 1-h PG cut point identifying those with IGT was 132.5 mg/dL (7.36 mmol/L). In a training set of 920 individuals, the test had an AUC of 0.86, sensitivity 80.8% and specificity 74.3%. In a validation set of individuals from the same population, the threshold identified those with IGT with an AUC of 0.81, sensitivity 70.3% and specificity 80% [178]. The same threshold predicted IH in a multi-ethnic cohort (34% Caucasian, 31% Hispanic, 32% African American) of 202 young individuals with obesity [181] with an AUC of 0.63 for the high 1-h PG to predict incident IH, with the sensitivity 65% and specificity 62%. Of note, AUCs of FPG, 2-h PG and HbA_{1c} were low, 0.545, 0.563 and 0.599, respectively. The 83 individuals (41%) with high 1-h PG defined at baseline with the 132.5 mg/dL (7.4 mmol/L) threshold, presented about a three times higher risk to develop IH (i.e., IGT and/or IFG) over a 2-year follow up, independent of confounders. The adult cut point of 155 mg/dL (8.6 mmol/L) had a low diagnostic sensitivity of 20%, while the specificity was high, 86%, as expected, and was not associated with increased odds of developing IH.

A cohort study investigated the diagnostic accuracy of the adult threshold for high 1-h PG in Latino youths [93]. The high 1-h PG defined as $\geq$ 155 mg/dL (8.6 mmol/L) was associated with a greater reduction in β-cell function and 2.5 times greater likelihood of developing IH over 8 years of follow up. The pattern of change for people with high 1-h PG was characterized by a steady decline in DI resulting in a 55% decrease in this parameter by year 8. There was an initial decline in the DI also in youths with low 1-h PG, followed by a successive increase that produced a 29% higher DI than baseline.

The "Bambino" study addressed the potential influence of age and puberty-related changes in a cohort of 154 white non-Hispanic young individuals with obesity exploring with ROC analysis the diagnostic accuracy of age-, sex- and pubertal stage-specific values of 1-h PG [177]. Threshold values ranged from a minimum of 129 mg/dL (7.2 mmol/L) in prepubertal children (AUC 0.90, sensitivity 100% and specificity 76%) to a maximum of 194 mg/dL (10.8 mmol/L) in girls (AUC 0.77, sensitivity 95% and specificity 85%). In the entire sample, the threshold value of 159 mg/dL (8.8 mmol/L) had an AUC 0.82, sensitivity 86% and specificity 79% [177].

Tricò et al. explored the potential influence of ethnicity/race on 1-h PG diagnostic accuracy and observed similar predictive power for IH in Caucasian, African-American, and Hispanic people despite well-known ethnic-related differences in insulin sensitivity and secretion [181]. Length of follow-up and the definition of the disease, i.e., IH or T2D, were also important factors to consider. In large cohorts of adults [50,55,56] the optimal cut point for the 1-h PG to maximize both the sensitivity and specificity ranged from 130 to 161 mg/dL (7.2 to 8.9 mmol/L) with T2D as the endpoint.

In paediatric cohort studies with IH (IFG and/or IGT) as the endpoint, follow-up ranged from 2 to 8 years [93,177,181]. The threshold value of 155 mg/dL (8.6 mmol/L) has been proposed in young individuals, although long-term (i.e., decades) cohort studies with overt diabetes and/or micro-angiopathy as endpoints, are lacking. Indeed, the value of 155 mg/dL (8.6 mmol/L), would not capture a very large segment of the population. In the study of Tricò et al. [181] and the "Bambino" study (n = 2,295) [177], the prevalence of a high 1-h PG defined by the cut off of ~ 132.5 mg/dL (7.36 mmol/L) was 40% and 36%, respectively. In the Bambino study, the prevalence of a high 1-h PG defined by the threshold of 155 mg/dL (8.6 mmol/L) was 15 %. Furthermore, in a US multi-ethnic population (n = 129) of Hispanic (82%), African American (30%) and Asian (17 %), modelling of 1-h PG based on the 132.5 mg/dL (7.36 mmol/L) threshold showed a significant association with changes in DI similar in magnitude to the 155 mg/dL (8.6 mmol/L) threshold value. However, as only the higher 1-h PG threshold value was associated with increased odds of IH, lends further support to 155 mg/dL (8.6 mmol/L) for use in screening [182]. The 1-h PG has been proven to be reproducible in the short-term (i.e., six weeks) with a better correlation coefficient than the 2-h PG (0.42 vs. 0.28, respectively) [68].

Thus, the evidence supports screening with the 1-h PG cut point of 155 mg/dL (8.6 mmol/L) in young individuals for risk of IH and T2D, since this will capture those likely to experience a progressive decline in β-cell function toward overt diabetes. Nevertheless, there is need for a large multi-ethnic cohort study to confirm the diagnostic value of 1-h PG in youth [177].

17. What is the importance of post-challenge glucose in older people?

While there are no specific studies on the 1-h PG in the elderly, information about post-challenge PG may be extrapolated from studies that have evaluated its importance in older people, since both 1-h PG and 2-h PG are highly correlated. The pooled data from several European populations without known diabetes showed that the mean post-challenge 2-h PG concentration in the OGTT rose with aging increasing particularly after 50 years of age [183]. FPG level changed little with age. Similar results were observed in Asian Indian, Chinese and Japanese populations [184]. Thus, it can be concluded that the steep increase in prevalence of T2D with age is mainly driven by the elevation in post-challenge glucose.

The Rancho Bernardo Study in California examined the frequency of isolated post-challenge hyperglycaemia in men and women aged 50–89 years with no history of myocardial infarction or diabetes [185]. Of new screen-detected people with diabetes, 60 % had isolated high 2-h PG. The US Cardiovascular Health Study found that more than half of new screen-detected people with diabetes aged 65–80 years had isolated post-challenge hyperglycemia [186]. A Korean study found that people $\geq$ 65 years had a higher homeostatic level of pancreatic β-cell function (i.e., higher fasting and 2-hour insulin, and C-peptide levels and better β-cell function [HOMA-β scores]) compared with people < 65 years [187]. The older group had the lowest diagnostic yield when using FPG (46%) and the highest with 2-h PG (85%). These results were mostly due to the higher frequency of isolated post-challenge hyperglycaemia in older people.

IGT is a common condition in older people. A population-based study in Finland with a 22-year follow-up among people with an average age of 73 years showed that the prevalence of isolated IGT was 15.8%, combined IFG and IGT was 4.2%, and isolated IFG was 4.0% using the WHO criteria [188].

Thus, to detect hyperglycaemia in older people without diabetes, it is

especially important to perform an OGTT with determination of post-challenge 1-h or 2-h PG.

18. What is the evidence that intervention in individuals with a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) is effective?

The STOP DIABETES study [169] was a retrospective observational study in a community practice in southern California of 422 individuals at increased risk of T2D with well-established risk factors. Participants had an OGTT and were risk stratified based on the presence and severity of insulin resistance, impaired β-cell function, and 1-h PG ≥ 155 mg/dL (8.6 mmol/L).

Glycaemic response was defined as normal if the participant had NGT according to ADA criteria and a 1-h PG < 155 mg/dL (8·6 mmol/L). Moderate impairment in glucose tolerance was defined by the presence of NGT and 1-h PG ≥ 155 mg/dL (8·6 mmol/L), or IFG or IGT, or both, and 1-h PG < 155 mg/dL (8·6 mmol/L). A severe abnormality in glucose tolerance was defined by IFG or IGT, or both, and 1-h PG> 155 mg/dL (8.6 mmol/L).

Approximately 25% of participants had NGT combined with 1-h PG ≥ 155 mg/dL (8·6 mmol/L). The annual incidence of T2D in these individuals was higher (4.8%) than in those with IFG or IGT, or both (3.8%). The incidence of T2D was equally reduced in these two groups by treatment with metformin and pioglitazone (to 1·7% and 1·9%, respectively) and metformin, pioglitazone, and GLP-1 receptor agonist (to 0% and 0·7%). The annual incidence of T2D in those receiving only lifestyle therapy was 4.1%. NGT was restored in 39% receiving lifestyle therapy only, 52% receiving metformin and pioglitazone and 77% receiving metformin, pioglitazone, and GLP-1 receptor agonist [169].

Although relatively few people completed the follow-up of seven years, the STOP DIABETES study nonetheless identified a subgroup of individuals with NGT and a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) who should be considered as having IH and documented that effective interventions were associated with lower risk of progression to T2D. However, there is lack of high-quality data from large-scale prospective trials in this area.

19. What is the evidence that the 1-h PG can diagnose T2D?

A *meta*-analysis of 15 studies comprising 35,551 participants with Caucasian, American Indian, Japanese, Mexican American, and South Asian ethnicities (54% Caucasian) was performed to determine the optimal 1-h PG cutoff equivalent to the gold standard 2-h PG 200 mg/dL (≥11.1 mmol/L), diagnostic of T2D [96]. The cutoff of 209 mg/dL (11.6 mmol/L) had a sensitivity of 0.92, specificity of 0.91, AUC 0.939, and a positive predictive value of 45%. The 1-h PG correctly classified 31,164 of 32,246 (91%) individuals as not having diabetes and as many as 3,082 (9%) individuals who did not have T2D by current criteria as having diabetes [96].

The OGTT would be impractical and costly if performed as the initial screening test for T2D or IH. Prescreening with validated diabetes risk screening calculators based on questionnaires (e.g., Finnish Diabetes Risk Score - FINDRISC; ADA risk score, etc.) [33,189] to identify high-risk individuals is suggested to decrease the proportion of false positive cases and to exclude people who are at a low risk of T2D from glycaemia testing. Further laboratory measurements should be considered in those subsequently determined to be high-risk with a risk score. The diagnosis at the next step should be confirmed with a second test, as recommended by ADA and WHO [190]. In this way, the burden of glycaemia testing can be reduced very significantly without increasing the number of false negatives [191]. A cross-sectional study validated the diabetes risk score using the 1-h PG in addition to FPG and $HbA1_c$ in a Saudi population to detect IH or T2D combined (i.e., dysglycaemia) with a reasonable AUC of 0.76 (95 % confidence interval 0.73–0.79) [192]. Of people with dysglycaemia, 58 % were identified with 1-h PG ≥ 155 mg/dL (8.6 mmol/L) alone.

Additional studies involving age, sex, and ethnicity as well as assessing risk factors for complications of hyperglycemia should be considered. As the proposed 1-h PG cut-point of 209 mg/dL (11.6 mmol/L) for diagnosing T2D (see Section 8) was crossed a median of 1 year earlier (mean 1.6 years) than the standard 2-h PG threshold of 200 mg/dL (11.1 mmol/L), this may facilitate earlier initiation of therapy when adequate glycaemic control is easier to achieve and reversal from diabetes more likely [95,96].

20. Conclusions: Current OGTT criteria for IH and T2D should be redefined with a 1-h post-load PG level

Table 7 summarizes the benefits inherent by screening with the 1-h post-load PG for the diagnosis of IH and T2D reviewed in this IDF Position Statement. As the current diagnostic criteria are suboptimal for the early detection of IH and T2D, we propose that the 1-h post-load PG level during the 75-g OGTT will serve as a novel screening tool that could replace the 2-h OGTT (Table 8). The 1-h PG determination is either better than or equivalent to the 2-h PG so a 1-h OGTT alone would suffice. However, the 2-h OGTT can be used, if preferred. Adding the 1-h PG to the 2-h OGTT, which could improve risk stratification, would increase complexity in the assessment of glycaemia and is not formally recommended.

Health services should consider developing a policy for screening for IH based on local human and technical resources. People detected to be at high-risk for T2D (e.g., achieved high score on validated screening questionnaire, overweight or obesity, family history, age 35 years or older, history of gestational diabetes, polycystic ovary syndrome, hypertension, sedentary, CVD) should undergo a 75-gram 1-h OGTT after an overnight fast. People with a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) are considered to have IH and should be prescribed lifestyle intervention and referred to a diabetes prevention program. People with a 1-h PG ≥ 209 mg/dL (11.6 mmol/L) are considered to have T2D and should have a repeat test to confirm the diagnosis of T2D and then referred for further evaluation and treatment.

Considerable evidence presented suggests that a 1-h PG ≥ 155 mg/dL (8.6 mmol/L) detects individuals with NGT having reduced β-cell function. Identifying the earliest time point on the IH continuum is

Table 7
Overview: The 1-h PG ≥ 155 mg/dL (8.6 mmol/L) for diagnosis of Intermediate Hyperglycaemia and T2D.

1. Defines high-risk of T2D in adults, children, and youth
2. Associates with worsened metabolic and atherogenic profiles
3. Identifies risk for micro- and macrovascular complications and mortality
4. Identifies risk for OSA, CFRD, MASLD, and severity of hepatic fibrosis
5. Occurs *before* the onset of IGT
6. Merits identification *before* IGT occurs
7. Cost-effective for high-risk screening
8. Provides opportunity for earlier detection and intervention in high-risk populations identified with primary screening tools (FINDRISC, ADA)
9. May benefit from lifestyle and pharmacologic interventions to reduce progression to T2D
10. Reduces diagnostic complexity and confusion with current diagnostic criteria for IH
11. Shortens OGTT from 2 to 1 hour making it more practical and clinically acceptable
12. Threshold ≥ 209 mg/dL (11.6 mmol/L) defines T2D

Table 8
Screening algorithm for IH and T2D.

1. Screen high-risk population with validated questionnaire (FINDRISC, ADA)
2. High-risk people should undergo laboratory screening:
a. 1-h 75-gram OGTT or,
b. 2-h 75-gram OGTT (i.e., FPG + 2-h PG) or,
c. FPG or,
d. HbA_{1c}
3. People with a 1-h PG $\geq$ 155 mg/dL (8.6 mmol/L) are considered to have IH and should be prescribed lifestyle intervention and referred to a diabetes prevention program.
4. People with a 1-h PG $\geq$ 209 mg/dL (11.6 mmol/L) are considered to have T2D and should have a repeat test to confirm the diagnosis of T2D and then referred for further evaluation and treatment.t.

critical to avoid progressive and insidious deterioration in β-cell function. An elevated 1-h PG level provides an opportunity for early identification of a large population at increased risk and people with previously undiagnosed T2D. The 1-h PG $\geq$ 155 mg/dL (8.6 mmol/L) has been shown to occur some years before the development of IGT and T2D. Therefore, when the 1-h PG level is elevated, lifestyle intervention that has been proven to be effective for people with IGT who have an elevated post-challenge glucose, may have the greatest benefit for preserving or reversing the deterioration in β-cell function and to prevent further progression to IH and diabetes.

An elevated 1-h post-load PG level has been confirmed to be a better or at least equally as good predictor of T2D than isolated HbA_{1c} or 2-h PG in various populations. In addition, epidemiologic studies have consistently shown that a 1-h PG $\geq$ 155 mg/dL (8.6 mmol/L) predicted an increased risk for microvascular disease, myocardial infarction, fatal CAD, and mortality when the 2-h PG level was < 140 mg/dL (7.8 mmol/L). An elevated 1-h PG is also associated with other conditions such as OSA, CFRD, and MASLD.

A 1-h 75-g OGTT may also have a future role for detection of gestational diabetes mellitus (GDM) [5,193]. The 1-h PG threshold of 160 mg/dL (8.9 mmol/L), with a sensitivity of 62 % and specificity of 94 % identifying 8.6 % of pregnant women as positive, was found to have the same diagnostic performance as the conventional 2-h PG of 140 mg/dL (7.8 mmol/L) for detecting GDM in a Brazilian cohort of 4,998 pregnant women. The authors concluded that the 1-h OGTT could be simpler, less costly and improve adherence to pregnancy screening protocols [193]. In addition, a retrospective study of 769 Portuguese women with GDM [194] found that postpartum, the 1-h PG $\geq$ 142 mg/dL (7.9 mmol/L) had a sensitivity of 91.4 %, specificity of 75.1 % and an AUC of 0.90 (CI 95 %: 0.86—0.93) to predict changes at 2-h in the reclassification test. Although these findings are promising, the 1-h OGTT requires further assessment during pregnancy and postpartum before it can be implemented for screening and diagnosis.

Additional related publications are summarized in references [195–207].

The evidence presented in the Position Statement justifies a valuable opportunity to extend the diagnosis of IH and T2D using the 1-h PG. A growing population of individuals at increased risk for T2D can be identified earlier in the lengthy trajectory to diabetes with the 1-h PG determination. The substantial evidence gathered over 40 years summarized in this Position Statement strongly supports redefining current screening and diagnostic recommendations for IH and T2D with the 1-h PG level during 75 g OGTT. This will reduce misclassification and maximize opportunities for early detection and prevention.

Observations presented in this Position Statement lay the foundation for advancing global public health beyond the significant achievements in diabetes prevention studies. Given the relentlessly rising prevalence of diabetes, urgent action is needed to stop or delay diabetes, prevent premature death and disabilities, make healthcare sustainable, ensure societal productivity and reduce human suffering. Against this background, despite challenges inherent in implementing the 1-h OGTT, there is considerable upside potential to support its use to diagnose high-risk individuals subsequent to general screening with a risk scoring questionnaire (FINDRISC; ADA) [189] thereby enabling early interventions which will favourably impact the global diabetes epidemic. Shortening of the OGTT from 2 to 1 hour does not make the OGTT less informative but will have many advantages.

Contributions

MB and JT conceptualized the IDF Position Statement, wrote the original draft, reviewed and edited subsequent drafts of the paper. MM, IS, JC, MIS, GS, VF, MAG RJ, PKTA, and RG wrote the original draft, reviewed and edited subsequent drafts of the paper. VM, MaBu, AB, APK, BD, PMN, TT, and TB reviewed and edited subsequent drafts of the paper. AC, AH conceptualized the paper and reviewed and edited the paper.

Funding source

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

Ms. Irene Jung, B.A. is gratefully acknowledged for her excellent technical skills in preparing the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2024.111589.

References

[1] Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119. https://doi.org/10.1016/j.diabres.2021.109119. Epub 2021 Dec 6. Erratum in: Diabetes Res Clin Pract. 2023 Oct;204:110945. PMID: 34879977.
[2] Jagannathan R, Buysschaert M, Medina JL, Katz K, Musleh S, Dorcely B, et al. The 1-h post-load plasma glucose as a novel biomarker for diagnosing dysglycemia. Acta Diabetol 2018;55(6):519–29.
[3] Fiorentino TV, Marini MA, Succurro E, Andreozzi F, Perticone M, Hribal ML, et al. One-hour postload hyperglycemia: implications for prediction and prevention of type 2 diabetes. J Clin Endocrinol Metab 2018;103(9):3131–43.
[4] Bergman M, Abdul-Ghani M, DeFronzo RA, Manco M, Sesti G, Fiorentino TV, et al. Review of methods for detecting glycemic disorders. Diabetes Res Clin Pract 2020;165:108233.
[5] Bergman M. The 1-hour plasma glucose: common link across the glycemic Spectrum. Front Endocrinol (Lausanne) 2021;12:752329.
[6] Buysschaert M, Bergman M, Valensi P. 1-h post-load plasma glucose for detecting early stages of prediabetes. Diabetes Metab 2022;48(6):101395.
[7] Jagannathan R, Neves JS, Dorcely B, Chung ST, Tamura K, Rhee M, et al. The oral glucose tolerance test: 100 years later. Diabetes Metab Syndr Obes 2020;13:3787–805.
[8] Bergman M, Manco M, Sesti G, Dankner R, Pareek M, Jagannathan R, et al. Petition to replace current OGTT criteria for diagnosing prediabetes with the 1-

hour post-load plasma glucose ≥ 155 mg/dl (8.6 mmol/L). Diabetes Res Clin Pract 2018;146:18–33.
[9] Bergman M, Jagannathan R, Buysschaert M, Pareek M, Olsen MH, Nilsson PM, et al. Lessons learned from the 1-hour post-load glucose level during OGTT: Current screening recommendations for dysglycaemia should be revised. Diabetes Metab Res Rev 2018;34(5):e2992.
[10] Bergman M, Jagannathan R, Buysschaert M, Medina JL, Sevick MA, Katz K, et al. Reducing the prevalence of dysglycemia: is the time ripe to test the effectiveness of intervention in high-risk individuals with elevated 1 h post-load glucose levels? Endocrine 2017;55(3):697–701.
[11] Jagannathan R, Bergman M. Use of 1-h post-load plasma glucose concentration to identify individuals at high risk of developing type 2 diabetes. Diabet Med 2017; 34(7):877–8.
[12] Dorcely B, Katz K, Jagannathan R, Chiang SS, Oluwadare B, Goldberg IJ, et al. Novel biomarkers for prediabetes, diabetes, and associated complications. Diabetes Metab Syndr Obes 2017;10:345–61.
[13] Chan JCN, Lim LL, Wareham NJ, Shaw JE, Orchard TJ, Zhang P, et al. The lancet commission on diabetes: using data to transform diabetes care and patient lives. Lancet 2020;396(10267):2019–82.
[14] Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007;334(7588):299.
[15] Herman WH, Ye W. Precision prevention of diabetes. Diabetes Care 2023;46(11): 1894–6.
[16] Rooney MR, Fang M, Ogurtsova K, Ozkan B, Echouffo-Tcheugui JB, Boyko EJ, et al. Global prevalence of prediabetes. Diabetes Care 2023;46(7):1388–94.
[17] Zhang L, Zhang Y, Sa S, Wang X, Dong L, Li Q, et al. Safety and effectiveness of metformin plus lifestyle intervention compared with lifestyle intervention alone in preventing progression to diabetes in a chinese population with impaired glucose regulation: a multicentre, open-label, randomised controlled trial. Lancet Diabetes Endocrinol 2023;11(8):567–77.
[18] Chan JCN, Paldánius PM, Mathieu C, Stumvoll M, Matthews DR, Del Prato S. Early combination therapy delayed treatment escalation in newly diagnosed young-onset type 2 diabetes: a subanalysis of the VERIFY study. Diabetes Obes Metab 2021;23(1):245–51.
[19] Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359(15): 1577–89.
[20] Laiteerapong N, Ham SA, Huang ES, Karter AJ. The legacy effect in type 2 diabetes: impact of early glycemic control on future complications (the Diabetes & Aging study). Diabetes Care 2019;42(3):416–26.
[21] Lind M, Imberg H, Coleman RL, Nerman O, Holman RR. Historical hba1c values may explain the type 2 diabetes legacy effect: Ukpds 88. Diabetes Care 2021;44 (10):2231–7.
[22] Matthews DR, Paldánius PM, Proot P, Chiang Y, Stumvoll M, Del Prato S. Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial. Lancet 2019;394(10208):1519–29.
[23] Qiao Q, Nakagami T, Tuomilehto J, Borch-Johnsen K, Balkau B, Iwamoto Y, et al. Comparison of the fasting and the 2-h glucose criteria for diabetes in different Asian cohorts. Diabetologia 2000;43(12):1470–5.
[24] Bergman M, Buysschaert M, Schwarz PEH, Albright A, Narayan KMV, Yach D. Diabetes prevention: global health policy and perspectives from the ground. Diabetes Manag (Lond) 2012;2(4):309–21.
[25] Cohen RM, Haggerty S, Herman WH. HbA1c for the diagnosis of diabetes and prediabetes: is it time for a mid-course correction? J Clin Endocrinol Metab 2010; 95(12):5203–6.
[26] Herman WH, Cohen RM. Racial and ethnic differences in the relationship between HbA1c and blood glucose: implications for the diagnosis of diabetes. J Clin Endocrinol Metab 2012;97(4):1067–72.
[27] Makaroff LE. The need for international consensus on prediabetes. Lancet Diabetes Endocrinol 2017;5(1):5–7.
[28] James C, Bullard KM, Rolka DB, Geiss LS, Williams DE, Cowie CC, et al. Implications of alternative definitions of prediabetes for prevalence in U.S. Adults Diabetes Care 2011;34(2):387–91.
[29] Mostafa SA, Davies MJ, Srinivasan BT, Carey ME, Webb D, Khunti K. Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation? Postgrad Med J 2010;86(1021): 656–62.
[30] Morris DH, Khunti K, Achana F, Srinivasan B, Gray LJ, Davies MJ, et al. Progression rates from HbA1c 6.0-6.4% and other prediabetes definitions to type 2 diabetes: a meta-analysis. Diabetologia 2013;56(7):1489–93.
[31] Anjana RM, Rani CSS, Deepa M, Pradeepa R, Sudha V, Nair HD, et al. Incidence of diabetes and prediabetes and predictors of progression among asian indians: 10-year follow-up of the Chennai urban rural epidemiology study (CURES). Diabetes Care 2015;38(8):1441–8.
[32] Unwin N, Shaw J, Zimmet P, Alberti KGMM. Impaired glucose tolerance and impaired fasting glycaemia: the current status on definition and intervention. Diabet Med 2002;19(9):708–23.
[33] Bergman M, Buysschaert M, Ceriello A, Hussain A, Mohan V, Sesti G, et al. Current diagnostic criteria identify risk for type 2 diabetes too late. Lancet Diabetes Endocrinol 2023;11(4):224–6.
[34] Bergman M. Inadequacies of absolute threshold levels for diagnosing prediabetes. Diabetes Metab Res Rev 2010;26(1):3–6.
[35] Bergman M. The early diabetes intervention program - is early actually late? Diabetes Metab Res Rev 2014;30(8):654–8.
[36] Bergman M, Dankner R, Roth J, Narayan KMV. Are current diagnostic guidelines delaying early detection of dysglycemic states? Time for new approaches Endocrine 2013;44(1):66–9.
[37] Bergman M, Chetrit A, Roth J, Jagannathan R, Sevick M, Dankner R. One-hour post-load plasma glucose level during the OGTT predicts dysglycemia: observations from the 24 year follow-up of the Israel study of glucose intolerance, obesity and hypertension. Diabetes Res Clin Pract 2016;120:221–8.
[38] Bergman M, Dorcely B. Remission of prediabetes via lifestyle intervention. Lancet Diabetes Endocrinol 2023;11(11):784–5.
[39] Jagannathan R, Sevick MA, Li H, Fink D, Dankner R, Chetrit A, et al. Elevated 1-hour plasma glucose levels are associated with dysglycemia, impaired beta-cell function, and insulin sensitivity: a pilot study from a real world health care setting. Endocrine 2016;52(1):172–5.
[40] Ohn JH, Kwak SH, Cho YM, Lim S, Jang HC, Park KS, et al. 10-year trajectory of β-cell function and insulin sensitivity in the development of type 2 diabetes: a community-based prospective cohort study. Lancet Diabetes Endocrinol 2016;4 (1):27–34.
[41] Priya MM, Amutha A, Pramodkumar TA, Ranjani H, Jebarani S, Gokulakrishnan K, et al. β-Cell function and insulin sensitivity in Normal glucose-tolerant subjects stratified by 1-hour plasma glucose values. Diabetes Technol Ther 2016;18(1):29–33.
[42] Tirosh A, Shai I, Tekes-Manova D, Israeli E, Pereg D, Shochat T, et al. Normal fasting plasma glucose levels and type 2 diabetes in young men. N Engl J Med 2005;353(14):1454–62.
[43] Ferrannini E, Manca ML. Identifying glucose thresholds for incident diabetes by physiological analysis: a mathematical solution. Am J Physiol Regul Integr Comp Physiol 2015;308(7):R590–6.
[44] The DECODE Study Group. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. The DECODE study group. European Diabetes Epidemiology Group. Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe. Lancet (Lond). 1999;354(9179):617-21.
[45] The DECODE Study Group. Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and noncardiovascular diseases? Diabetes Care 2003;26(3):688–96.
[46] Sathish T, Khunti K, Narayan KMV, Mohan V, Davies MJ, Yates T, et al. Effect of conventional lifestyle interventions on type 2 diabetes incidence by glucose-defined prediabetes phenotype: an individual participant data meta-analysis of randomized controlled trials. Diabetes Care 2023;46(11):1903–7.
[47] Weber MB, Ranjani H, Staimez LR, Anjana RM, Ali MK, Narayan KMV, et al. The stepwise approach to diabetes prevention: results from the D-CLIP randomized controlled trial. Diabetes Care 2016;39(10):1760–7.
[48] Abdul-Ghani MA, Abdul-Ghani T, Ali N, DeFronzo RA. One-hour plasma glucose concentration and the metabolic syndrome identify subjects at high risk for future type 2 diabetes. Diabetes Care 2008;31(8):1650–5.
[49] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and Management of the Metabolic Syndrome. Circulation 2005;112 (17):2735–52.
[50] Alyass A, Almgren P, Akerlund M, Dushoff J, Isomaa B, Nilsson P, et al. Modelling of OGTT curve identifies 1 h plasma glucose level as a strong predictor of incident type 2 diabetes: results from two prospective cohorts. Diabetologia 2015;58(1): 87–97.
[51] Abdul-Ghani MA, Stern MP, Lyssenko V, Tuomi T, Groop L, DeFronzo RA. Minimal contribution of fasting hyperglycemia to the incidence of type 2 diabetes in subjects with Normal 2-h plasma glucose. Diabetes Care 2010;33(3):557–61.
[52] Priya M, Anjana RM, Chiwanga FS, Gokulakrishnan K, Deepa M, Mohan V. 1-hour venous plasma glucose and incident prediabetes and diabetes in asian indians. Diabetes Technol Ther 2013;15(6):497–502.
[53] Fiorentino TV, Marini MA, Andreozzi F, Arturi F, Succurro E, Perticone M, et al. One-hour postload hyperglycemia is a stronger predictor of type 2 diabetes than impaired fasting glucose. J Clin Endocrinol Metab 2015;100(10):3744–51.
[54] Oka R, Aizawa T, Miyamoto S, Yoneda T, Yamagishi M. One-hour plasma glucose as a predictor of the development of type 2 diabetes in Japanese adults. Diabet Med 2016;33(10):1399–405.
[55] Oh TJ, Lim S, Kim KM, Moon JH, Choi SH, Cho YM, et al. One-hour postload plasma glucose concentration in people with normal glucose homeostasis predicts future diabetes mellitus: a 12-year community-based cohort study. Clin Endocrinol 2017;86(4):513–9.
[56] Paddock E, Hohenadel MG, Piaggi P, Vijayakumar P, Hanson RL, Knowler WC, et al. One-hour and two-hour postload plasma glucose concentrations are comparable predictors of type 2 diabetes mellitus in southwestern native americans. Diabetologia 2017;60(9):1704–11.
[57] Pareek M, Bhatt DL, Nielsen ML, Jagannathan R, Eriksson KF, Nilsson PM, et al. Enhanced predictive capability of a 1-hour Oral glucose tolerance test: a prospective population-based cohort study. Diabetes Care 2018;41(1):171–7.
[58] Sai Prasanna N, Amutha A, Pramodkumar TA, Anjana RM, Venkatesan U, Priya M, et al. The 1h post glucose value best predicts future dysglycemia among normal glucose tolerance subjects. J Diabetes Complications 2017;31(11): 1592–6.
[59] Strandberg TE, Pienimäki T, Strandberg AY, Salomaa VV, Pitkälä KH, Tilvis RS, et al. One-hour glucose, mortality, and risk of diabetes: a 44-year prospective study in men. Arch Intern Med 2011;171(10):941–3.
[60] Thewjitcharoen Y, Elizabeth Jones A, Butadej S, Nakasatien S, Chotwanvirat P, Wanothayaroj E, et al. Elevated 1-h post-load plasma glucose levels in thai people

with normal glucose tolerance associated with high diabetes and cardiovascular risk. Diabet Med 2020;37(4):705–6.
[61] Kumpatla S, Parveen R, Stanson S, Viswanathan V. Elevated one hour with normal fasting and 2 h plasma glucose helps to identify those at risk for development of Type2 Diabetes-11 years observational study from South India. Diabetes Metab Syndr 2019;13(4):2733–7.
[62] Manco M, Mari A, Petrie J, Mingrone G, Balkau B. One hour post-load plasma glucose and 3 year risk of worsening fasting and 2 hour glucose tolerance in the RISC cohort. Diabetologia 2019;62(3):544–8.
[63] Briker SM, Hormenu T, Dubose CW, Mabundo LS, Chung ST, Ha J, et al. Metabolic characteristics of Africans with normal glucose tolerance and elevated 1-hour glucose: insight from the Africans in America study. BMJ Open Diabetes Res Care 2020;8(1):e000837.
[64] Saunajoki AE, Auvinen JP, Bloigu AH, Timonen MJ, Keinänen-Kiukaanniemi SM. Evaluating the 1-h post-load glucose level to predict future type 2 diabetes. Diabetes Res Clin Pract 2020;160:108009.
[65] Rong L, Luo N, Gong Y, Tian H, Sun B, Li C. One-hour plasma glucose concentration can identify elderly Chinese male subjects at high risk for future type 2 diabetes mellitus: a 20-year retrospective and prospective study. Diabetes Res Clin Pract 2021;173:108683.
[66] Peddinti G, Bergman M, Tuomi T, Groop L. 1-hour post-OGTT glucose improves the early prediction of type 2 diabetes by clinical and metabolic markers. J Clin Endocrinol Metab 2019;104(4):1131–40.
[67] Abdul-Ghani MA, Abdul-Ghani T, Stern MP, Karavic J, Tuomi T, Bo I, et al. Two-step approach for the prediction of future type 2 diabetes risk. Diabetes Care 2011;34(9):2108–12.
[68] Kasturi K, Onuzuruike AU, Kunnam S, Shomaker LB, Yanovski JA, Chung ST. Two- vs one-hour glucose tolerance testing: predicting prediabetes in adolescent girls with obesity. Pediatr Diabetes 2019;20(2):154–9.
[69] National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes. 1979;28(12):1039-57.
[70] Rushforth NB, Bennett PH, Steinberg AG, Miller M. Comparison of the value of the two- and one-hour glucose levels of the oral GTT in the diagnosis of diabetes in Pima Indians. Diabetes 1975;24(6):538–46.
[71] Bartoli E, Fra GP, Carnevale Schianca GP. The oral glucose tolerance test (OGTT) revisited. Eur J Intern Med 2011;22(1):8–12.
[72] Paddock E, Looker HC, Piaggi P, Knowler WC, Krakoff J, Chang DC. One-hour plasma glucose compared with two-hour plasma glucose in relation to diabetic retinopathy in american indians. Diabetes Care 2018;41(6):1212–7.
[73] Saunajoki A, Auvinen J, Saarela V, Uusitalo JJ, Leiviska I, Keinanen-Kiukaanniemi S, et al. Association of glucose metabolism and retinopathy signs in non-diabetic individuals in midlife-the northern Finland birth cohort 1966 study. PLoS One 2020;15(10):e0240983.
[74] Jagannathan R, Sevick MA, Fink D, Dankner R, Chetrit A, Roth J, et al. The 1-hour post-load glucose level is more effective than HbA1c for screening dysglycemia. Acta Diabetol 2016;53(4):543–50.
[75] Abdul-Ghani MA, Abdul-Ghani T, Müller G, Bergmann A, Fischer S, Bornstein S, et al. Role of glycated haemoglobin in the prediction of future risk of T2DM. J Clin Endocrinol Metab 2011;96(8):2596–600.
[76] Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? Diabetes Care 2007;30(6):1544–8.
[77] Manco M, Panunzi S, Macfarlane DP, Golay A, Melander O, Konrad T, et al. One-hour plasma glucose identifies insulin resistance and β-cell dysfunction in individuals with Normal glucose tolerance: cross-sectional data from the relationship between insulin sensitivity and cardiovascular risk (RISC) study. Diabetes Care 2010;33(9):2090–7.
[78] Gyberg V, De Bacquer D, Kotseva K, De Backer G, Schnell O, Tuomilehto J, et al. Time-saving screening for diabetes in patients with coronary artery disease: a report from EUROASPIRE IV. BMJ Open 2016;6(12):e013835.
[79] The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997;20(7):1183-97.
[80] Sayegh HA, Jarrett RJ. Oral glucose-tolerance tests and the diagnosis of diabetes: results of a prospective study based on the Whitehall survey. Lancet 1979;2 (8140):431–3.
[81] McCance DR, Hanson RL, Charles MA, Jacobsson LTH, Pettitt DD, Bennett PH, et al. Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. BMJ 1994;308 (6940):1323–8.
[82] Pettitt DJ, Knowler WC, Lisse JR, Bennett PH. Development of retinopathy and proteinuria in relation to plasma-glucose concentrations in Pima Indians. Lancet 1980;2(8203):1050–2.
[83] Engelgau MM, Thompson TJ, Herman WH, Boyle JP, Aubert RE, Kenny SJ, et al. Comparison of fasting and 2-hour glucose and HbA1c levels for diagnosing diabetes. Diagnostic criteria and performance revisited. Diabetes Care 1997;20 (5):785–91.
[84] Succurro E, Arturi F, Lugarà M, Grembiale A, Fiorentino TV, Caruso V, et al. One-hour postload plasma glucose levels are associated with kidney dysfunction. Clin J Am Soc Nephrol 2010;5(11):1922–7.
[85] Cassano V, Pelaia C, Armentaro G, Miceli S, Tallarico V, Perini DD, et al. New potential biomarkers for early chronic kidney disease diagnosis in patients with different glucose tolerance status. Front Endocrinol 2023;14:1206336.
[86] Saunajoki A, Auvinen J, Bloigu A, Saramies J, Tuomilehto J, Uusitalo H, et al. Elevated one-hour post-load glucose is independently associated with albuminuria: a cross-sectional population study. J Clin Med 2022;11(14):4124.
[87] Lind M, Tuomilehto J, Uusitupa M, Nerman O, Eriksson J, LlanneParikka P, et al. The association between Hba1c, fasting glucose, 1-hour glucose and 2-hour glucose during an oral glucose tolerance test and cardiovascular disease in individuals with elevated risk for diabetes. PLoS One 2014;9(10):e109506.
[88] Abdul-Ghani MA, Lyssenko V, Tuomi T, DeFronzo RA, Groop L. Fasting versus postload plasma glucose concentration and the risk for future type 2 diabetes: results from the botnia study. Diabetes Care 2009;32(2):281–6.
[89] Nakagomi A, Sunami Y, Okada S, Ohno Y, Shoji T, Fujisawa T, et al. Association between 1-h post-load plasma glucose levels and arterial stiffness in normotensive subjects with normal glucose tolerance. Diab Vasc Dis Res 2018;15(1):39–45.
[90] Fiorentino TV, Sesti F, Andreozzi F, Pedace E, Succurro E, Sciacqua A, et al. Frequency of 1-h post-load glucose ≥155 mg/dl among individuals with different glucose tolerance conditions. Nutr Metab Cardiovasc Dis 2016;26(5):439–41.
[91] Bardini G, Dicembrini I, Cresci B, Rotella CM. Inflammation markers and metabolic characteristics of subjects with 1-h plasma glucose levels. Diabetes Care 2010;33(2):411–3.
[92] Bianchi C, Miccoli R, Trombetta M, Giorgino F, Frontoni S, Faloia E, et al. Elevated 1-hour postload plasma glucose levels identify subjects with normal glucose tolerance but impaired β-cell function, insulin resistance, and worse cardiovascular risk profile: the GENFIEV study. J Clin Endocrinol Metab 2013;98 (5):2100–5.
[93] Kim JY, Goran MI, Toledo-Corral CM, Weigensberg MJ, Choi M, Shaibi GQ. One-hour glucose during an Oral glucose challenge prospectively predicts β-cell deterioration and prediabetes in obese hispanic youth. Diabetes Care 2013;36(6): 1681–6.
[94] Fintini D, Cappa M, Brufani C, Bernardini S, Barbetti F. Prevalence of elevated 1-h plasma glucose and its associations in obese youth. Diabetes Res Clin Pract 2016; 116:202–4.
[95] Ha J, Chung ST, Bogardus C, Jagannathan R, Bergman M, Sherman AS. One-hour glucose is an earlier marker of dysglycemia than two-hour glucose. Diabetes Res Clin Pract 2023;203:110839.
[96] Ahuja V, Aronen P, Pramodkumar TA, Looker H, Chetrit A, Bloigu AH, et al. Accuracy of 1-hour plasma glucose during the Oral glucose tolerance test in diagnosis of type 2 diabetes in adults: a meta-analysis. Diabetes Care 2021;44(4): 1062–9.
[97] Tabák AG, Jokela M, Akbaraly TN, Brunner EJ, Kivimäki M, Witte DR. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet 2009; 373(9682):2215–21.
[98] Ferrannini E, Gastaldelli A, Miyazaki Y, Matsuda M, Mari A, DeFronzo RA. β-Cell function in subjects spanning the range from Normal glucose tolerance to overt diabetes: a new analysis. J Clin Endocrinol Metab 2005;90(1):493–500.
[99] Chow EYK, Chan JCN. Insulin resistance versus β-cell dysfunction in type 2 diabetes: where public and personalised health meet. Lancet Diabetes Endocrinol 2020;8(2):92–3.
[100] Yabe D, Seino Y. Type 2 diabetes via β-cell dysfunction in east Asian people. Lancet Diabetes Endocrinol 2016;4(1):2–3.
[101] Staimez LR, Weber MB, Ranjani H, Ali MK, Echouffo-Tcheugui JB, Phillips LS, et al. Evidence of reduced β-cell function in Asian Indians with mild dysglycemia. Diabetes Care 2013;36(9):2772–8.
[102] Tura A, Grespan E, Göobl CS, Koivula RW, Franks PW, Pearson ER, et al. Profiles of glucose metabolism in different prediabetes phenotypes, classified by fasting glycemia, 2-hour OGTT, glycated haemoglobin, and 1-hour OGTT: an IMI DIRECT study. Diabetes 2021;70(9):2092–106.
[103] Sato M, Tamura Y, Someya Y, Takeno K, Kaga H, Kadowaki S, et al. Characteristics associated with elevated 1-h plasma glucose levels during a 75-g oral glucose tolerance test in non-obese Japanese men. J Diabetes Investig 2020; 11(6):1520–3.
[104] Jalleh RJ, Marathe CS, Trahair LG, Jones KL, Horowitz M. A biphasic glucose response during an oral glucose tolerance test is associated with greater plasma insulin and GLP-1 responses and a reduction in 1-hour glucose but does not relate to the rate of gastric emptying in healthy, older adults. Nutrients 2023;15(18): 3889.
[105] Mann BK, Bhandohal JS, Hong J. An overall glance of evidence supportive of one-hour and two-hour postload plasma glucose levels as predictors of long-term cardiovascular events. Int J Endocrinol 2019;2019:6048954.
[106] Ceriello A. Targeting one-hour postmeal glucose: is it time for a paradigm switch in diabetes management? Diabetes Technol Ther 2017;19(9):493–7.
[107] Guerreiro V, Maia I, Neves JS, Salazar D, Ferreira MJ, Mendonça F, et al. Oral glucose tolerance testing at 1 h and 2 h: relationship with glucose and cardiometabolic parameters and agreement for pre-diabetes diagnosis in patients with morbid obesity. Diabetol Metab Syndr 2022;14(1):91.
[108] Marini MA, Succurro E, Frontoni S, Mastroianni S, Arturi F, Sciacqua A, et al. Insulin sensitivity, β-cell function, and incretin effect in individuals with elevated 1-hour postload plasma glucose levels. Diabetes Care 2012;35(4):868–72.
[109] Succurro E, Arturi F, Grembiale A, Iorio F, Fiorentino TV, Andreozzi F, et al. One-hour post-load plasma glucose levels are associated with elevated liver enzymes. Nutr Metab Cardiovasc Dis 2011;21(9):713–8.
[110] Sesti G, Hribal ML, Fiorentino TV, Sciacqua A, Perticone F. Elevated 1 h postload plasma glucose levels identify adults with normal glucose tolerance but increased risk of non-alcoholic fatty liver disease. BMJ Open Diabetes Res Care 2014;2(1): e000016.
[111] Haverals L, Van Dessel K, Verrijken A, Dirinck E, Peiffer F, Verhaegen A, et al. Cardiometabolic importance of 1-h plasma glucose in obese subjects. Nutr Diabetes 2019;9(1):16.

[112] Pramodkumar T, Priya M, Jebarani S, Anjana R, Mohan V, Pradeepa R. Metabolic profile of normal glucose-tolerant subjects with elevated 1-h plasma glucose values. Indian J Endocrinol Metab 2016;20(5):612–8.
[113] Park SK, Ryoo JH, Oh CM, Choi JM, Jung JY. 1-hour and 2-hour postload glucose level on oral glucose tolerance test and the risk of incident metabolic syndrome. J Clin Endocrinol Metab 2019;104(2):539–49.
[114] Andreozzi F, Mannino GC, Perticone M, Perticone F, Sesti G. Elevated 1-h post-load plasma glucose levels in subjects with normal glucose tolerance are associated with a pro-atherogenic lipid profile. Atherosclerosis 2017;256:15–20.
[115] Abbasi F, Tern PJ, Reaven GM. Plasma glucose concentration 60 min post oral glucose load and risk of type 2 diabetes and cardiovascular disease: pathophysiological implications. Diab Vasc Dis Res 2019;16(4):337–43.
[116] Perticone F, Sciacqua A, Perticone M, Arturi F, Scarpino PE, Quero M, et al. Serum uric acid and 1-h postload glucose in essential hypertension. Diabetes Care 2012; 35(1):153–7.
[117] Marini MA, Fiorentino TV, Andreozzi F, Mannino GC, Perticone M, Sciacqua A, et al. Elevated 1-h post-challenge plasma glucose levels in subjects with normal glucose tolerance or impaired glucose tolerance are associated with whole blood viscosity. Acta Diabetol 2017;54(8):775–84.
[118] Sciacqua A, Perticone M, Grillo N, Falbo T, Bencardino G, Angotti E, et al. Vitamin D and 1-hour post-load plasma glucose in hypertensive patients. Cardiovasc Diabetol 2014;13:48.
[119] Sesti G, Fiorentino TV, Succurro E, Perticone M, Arturi F, Sciacqua A, et al. Elevated 1-h post-load plasma glucose levels in subjects with normal glucose tolerance are associated with unfavorable inflammatory profile. Acta Diabetol 2014;51(6):927–32.
[120] Perticone M, Maio R, Gigliotti S, Arturi F, Succurro E, Sciacqua A, et al. Immuno-mediated inflammation in hypertensive patients with 1-h post-load hyperglycemia. Int J Mol Sci 2022;23(18):10891.
[121] Cassano V, Miceli S, Armentaro G, Mannino GC, Fiorentino VT, Perticone M, et al. Oxidative stress and left ventricular performance in patients with different glycometabolic phenotypes. Nutrients 2022;14(6):1299.
[122] Perticone F, Sciacqua A, Tassone EJ, Miceli S, Maio R, Addesi D, et al. One-hour post-load plasma glucose and IGF-1 in hypertensive patients. Eur J Clin Invest 2012;42(12):1325–31.
[123] La Sala L, Tagliabue E, de Candia P, Prattichizzo F, Ceriello A. One-hour plasma glucose combined with skin autofluorescence identifies subjects with pre-diabetes: the DIAPASON study. BMJ Open Diabetes Res Care 2020;8(1).
[124] Di Pino A, Urbano F, Scicali R, Di Mauro S, Filippello A, Scamporrino A, et al. 1 h postload glycemia is associated with low endogenous secretory receptor for advanced glycation end product levels and early markers of cardiovascular disease. Cells 2019;8(8).
[125] Succurro E, Marini MA, Arturi F, Grembiale A, Lugarà M, Andreozzi F, et al. Elevated one-hour post-load plasma glucose levels identifies subjects with normal glucose tolerance but early carotid atherosclerosis. Atherosclerosis 2009;207(1): 245–9.
[126] Tanaka K, Kanazawa I, Yamaguchi T, Sugimoto T. One-hour post-load hyperglycemia by 75g oral glucose tolerance test as a novel risk factor of atherosclerosis. Endocr J 2014;61(4):329–34.
[127] Fiorentino TV, Sesti F, Andreozzi F, Pedace E, Sciacqua A, Hribal ML, et al. One-hour post-load hyperglycemia combined with HbA1c identifies pre-diabetic individuals with a higher cardio-metabolic risk burden. Atherosclerosis 2016;253: 61–9.
[128] Sciacqua A, Maio R, Miceli S, Pascale A, Carullo G, Grillo N, et al. Association between one-hour post-load plasma glucose levels and vascular stiffness in essential hypertension. PLoS One 2012;7(9):e44470.
[129] Nakagomi A, Sunami Y, Okada S, Fujisawa T, Kobayashi Y. Synergistic effects of 1 h post-load plasma glucose and smoking on arterial stiffness in apparently healthy men: a cross-sectional study. J Atheroscler Thromb 2019;26(6):505–12.
[130] Sciacqua A, Miceli S, Carullo G, Greco L, Succurro E, Arturi F, et al. One-hour postload plasma glucose levels and left ventricular mass in hypertensive patients. Diabetes Care 2011;34(6):1406–11.
[131] Sciacqua A, Miceli S, Greco L, Arturi F, Naccarato P, Mazzaferro D, et al. One-hour postload plasma glucose levels and diastolic function in hypertensive patients. Diabetes Care 2011;34(10):2291–6.
[132] Sciacqua A, Perticone M, Miceli S, Pinto A, Cassano V, Succurro E, et al. Elevated 1-h post-load plasma glucose is associated with right ventricular morphofunctional parameters in hypertensive patients. Endocrine 2019;64(3): 525–35.
[133] Miceli S, Cassano V, Clausi E, Armentaro G, Tallarico V, Dallimonti Perini D, et al. One-hour post-load glucose and subclinical left atrial myocardial dysfunction in hypertensive patients. Eur J Clin Invest 2023;53(9):e14009.
[134] Succurro E, Pedace E, Andreozzi F, Papa A, Vizza P, Fiorentino TV, et al. Reduction in global myocardial glucose metabolism in subjects with 1-hour postload hyperglycemia and impaired glucose tolerance. Diabetes Care 2020;43 (3):669–76.
[135] Fiorentino TV, Miceli S, Succurro E, Sciacqua A, Andreozzi F, Sesti G. Depressed myocardial mechano-energetic efficiency in subjects with dysglycemia. Diabetes Res Clin Pract 2021;177:108883.
[136] Perticone M, Di Lorenzo C, Arabia G, Arturi F, Caroleo B, Tassone B, et al. One hour-post-load plasma glucose ≥155 mg/dl in healthy glucose normotolerant subjects is associated with subcortical brain MRI alterations and impaired cognition: a pilot study. Front Aging Neurosci 2021;13:608736.
[137] Fiorentino TV, De Vito F, Suraci E, Marasco R, Catalano F, Andreozzi F, et al. Augmented duodenal levels of sodium/glucose co-transporter 1 are associated with higher risk of nonalcoholic fatty liver disease and noninvasive index of liver fibrosis. Diabetes Res Clin Pract 2022;185:109789.
[138] Fiorentino TV, Andreozzi F, Mannino GC, Pedace E, Perticone M, Sciacqua A, et al. One-hour postload hyperglycemia confers higher risk of hepatic steatosis to HbA1c-defined IH subjects. J Clin Endocrinol Metab 2016;101(11):4030–8.
[139] Jagannathan R, Fiorentino TV, Marini MA, Sesti G, Bergman M. One-hour post-load glucose is associated with severity of hepatic fibrosis risk. Diabetes Res Clin Pract 2022;189:109977.
[140] Brodsky J, Dougherty S, Makani R, Rubenstein RC, Kelly A. Elevation of 1-hour plasma glucose during oral glucose tolerance testing is associated with worse pulmonary function in cystic fibrosis. Diabetes Care 2011;34(2):292–5.
[141] Lorenz AN, Pyle L, Ha J, Sherman A, Cree-Green M, Sagel SD, et al. Predictive value of 1-hour glucose elevations during oral glucose tolerance testing for cystic fibrosis-related diabetes. Pediatr Diabetes 2023;2023:4395556.
[142] Nyirjesy SC, Sheikh S, Hadjiliadis D, De Leon DD, Peleckis AJ, Eiel JN, et al. β-Cell secretory defects are present in pancreatic insufficient cystic fibrosis with 1-hour oral glucose tolerance test glucose ≥155 mg/dL. Pediatr Diabetes 2018;19(7): 1173–82.
[143] Schmid K, Fink K, Holl RW, Hebestreit H, Ballmann M. Predictors for future cystic fibrosis-related diabetes by oral glucose tolerance test. J Cyst Fibros 2014;13(1): 80–5.
[144] Sheikh S, Putt ME, Forde KA, Rubenstein RC, Kelly A. Elevation of one hour plasma glucose during oral glucose tolerance testing. Pediatr Pulmonol 2015;50 (10):963–9.
[145] Tommerdahl KL, Brinton JT, Vigers T, Cree-Green M, Zeitler PS, Nadeau KJ, et al. Delayed glucose peak and elevated 1-hour glucose on the oral glucose tolerance test identify youth with cystic fibrosis with lower oral disposition index. J Cyst Fibros 2021;20(2):339–45.
[146] Orencia AJ, Daviglus ML, Dyer AR, Walsh M, Greenland P, Stamler J. One-hour postload plasma glucose and risks of fatal coronary heart disease and stroke among nondiabetic men and women: the Chicago heart association detection project in industry (CHA) study. J Clin Epidemiol 1997;50(12):1369–76.
[147] Donahue RP, Abbott RD, Reed DM, Yano K. Postchallenge glucose concentration and coronary heart disease in men of Japanese ancestry. Honolulu Heart Program Diabetes 1987;36(6):689–92.
[148] Cao L, Wang P, Luan H, Chen H, Luo C, Zhu D, et al. Elevated 1-h postload plasma glucose levels identify coronary heart disease patients with greater severity of coronary artery lesions and higher risk of 1-year re-admission. Diab Vasc Dis Res 2020;17(1):1479164119896978.
[149] Fiorentino TV, Succurro E, Andreozzi F, Sciacqua A, Perticone F, Sesti G. One-hour post-load hyperglycemia combined with HbA1c identifies individuals with higher risk of cardiovascular diseases: cross-sectional data from the CATAMERI study. Diabetes Metab Res Rev 2019;35(2):e3096.
[150] Saunajoki A, Auvinen J, Bloigu A, Ukkola O, Keinänen-Kiukaanniemi S, Timonen M. One-hour post-load glucose improves the prediction of cardiovascular events in the OPERA study. Ann Med 2021;53(1):478–84.
[151] Rong L, Cheng X, Yang Z, Gong Y, Li C, Yan S, et al. One-hour plasma glucose as a long-term predictor of cardiovascular events and all-cause mortality in a chinese older male population without diabetes: a 20-year retrospective and prospective study. Front Cardiovasc Med 2022;9:947292.
[152] Zywicki V, Capozza P, Caravelli P, Del Prato S, De Caterina R. Glucose tolerance and markers of myocardial injury after an acute coronary syndrome: predictive role of the 1-h plus 2-h plasma glucose at the oral glucose tolerance test. Cardiovasc Diabetol 2022;21(1):152.
[153] Meisinger C, Wölke G, Brasche S, Strube G, Heinrich J. Postload plasma glucose and 30-year mortality among nondiabetic middle-aged men from the general population: the ERFORT study. Ann Epidemiol 2006;16(7):534–9.
[154] Bergman M, Chetrit A, Roth J, Dankner R. One-hour post-load plasma glucose level during the OGTT predicts mortality: observations from the Israel study of glucose intolerance. Obesity and Hypertension Diabet Med 2016;33(8):1060–8.
[155] Nielsen ML, Pareek M, Leósdóttir M, Eriksson KF, Nilsson PM, Olsen MH. One-hour glucose value as a long-term predictor of cardiovascular morbidity and mortality: the Malmö preventive project. Eur J Endocrinol 2018;178(3):225–36.
[156] Li N, Fan Y, Zhou JP, Maimba OD, Zhang L, Li QY. Obstructive sleep apnea exacerbates glucose dysmetabolism and pancreatic β-cell dysfunction in overweight and obese nondiabetic young adults. Diabetes Metab Syndr Obes 2020;13:2465–76.
[157] Pamidi S, Benedetti A, Tasali E. One hour post-load glucose levels among patients with obstructive sleep apnea and normal glucose tolerance. J Diabetes Complications 2023;37(8):108551.
[158] Umano GR, Galderisi A, Aiello F, Martino M, Camponesco O, Di Sessa A, et al. Obstructive sleep apnea (OSA) is associated with the impairment of beta-cell response to glucose in children and adolescents with obesity. Int J Obes (Lond) 2023;47(4):257–62.
[159] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64(1):73–84.
[160] Adams LA, Anstee QM, Tilg H, Targher G. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut 2017;66(6):1138–53.
[161] Andreozzi F, Mancuso E, Mazza E, Mannino GC, Fiorentino TV, Arturi F, et al. One-hour post-load glucose levels are associated with hepatic steatosis assessed by transient elastography. Diabetes Obes Metab 2023;26(2):682–9.
[162] Lebeaupin C, Vallée D, Hazari Y, Hetz C, Chevet E, Bailly-Maitre B. Endoplasmic reticulum stress signalling and the pathogenesis of non-alcoholic fatty liver disease. J Hepatol 2018;69(4):927–47.

[163] Jesrani G, Gupta M, Kaur J, Kaur N, Lehl S, Singh R. One-hour postload plasma glucose in obese indian adults with nonalcoholic fatty liver disease: an observational study from North India. Indian J Endocrinol Metab 2021;25(5):450–5.
[164] Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346(6):393–403.
[165] Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75.
[166] Golovaty I, Ritchie ND, Tuomilehto J, Mohan V, Ali MK, Gregg EW, et al. Two decades of diabetes prevention efforts: a call to innovate and revitalize our approach to lifestyle change. Diabetes Res Clin Pract 2023;198:110195.
[167] Molitch ME, Fujimoto W, Hamman RF, Knowler WC. The diabetes prevention program and its global implications. J Am Soc Nephrol 2003;14(7 Suppl 2):S103–7.
[168] Tuomilehto J, Uusitupa M, Gregg EW, Lindström J. Type 2 diabetes prevention programs—from proof-of-concept trials to national intervention and beyond. J Clin Med 2023;12(5):1876.
[169] Armato JP, DeFronzo RA, Abdul-Ghani M, Ruby RJ. Successful treatment of prediabetes in clinical practice using physiological assessment (STOP DIABETES). Lancet Diabetes Endocrinol 2018;6(10):781–9.
[170] Andellini M, Manco M, Esposito MT, Tozzi AE, Bergman M, Ritrovato M. A simulation model estimates lifetime health and economic outcomes of screening prediabetes using the 1-h plasma glucose. Acta Diabetol 2023;60(1):9–17.
[171] Perreault L, Kahn SE, Christophi CA, Knowler WC, Hamman RF. Regression from pre-diabetes to normal glucose regulation in the diabetes prevention program. Diabetes Care 2009;32(9):1583–8.
[172] American Diabetes Association Professional Practice Committee. 14. Children and adolescents: standards of medical care in diabetes—2022. Diabetes Care. 2022;45 (Supplement_1):S208-S31.
[173] Brufani C, Tura A, Bedogni G, Luciano R, Sbrignadello S, Fintini D, et al. Inside out the ragbag of glucose intolerance in obese adolescents. Horm Res Paediatr 2017;87(5):287–94.
[174] Galderisi A, Giannini C, Weiss R, Kim G, Shabanova V, Santoro N, et al. Trajectories of changes in glucose tolerance in a multiethnic cohort of obese youths: an observational prospective analysis. Lancet Child Adolesc Health 2018;2(10):726–35.
[175] Savoye M, Caprio S, Dziura J, Camp A, Germain G, Summers C, et al. Reversal of early abnormalities in glucose metabolism in obese youth: Results of an intensive lifestyle randomized controlled trial. Diabetes Care 2014;37(2):317–24.
[176] Pedicelli S, Fintini D, Ravà L, Inzaghi E, Deodati A, Spreghini MR, et al. Prevalence of prediabetes in children and adolescents by class of obesity. Pediatr Obes 2022;17(7):e12900.
[177] Ravà L, Fintini D, Mariani M, Deodati A, Inzaghi E, Pedicelli S, et al. High 1-h glucose in youths with obesity as marker of prediabetes and cardiovascular risk. J Endocrinol Invest 2023;46(12):2555–62.
[178] Manco M, Miraglia Del Giudice E, Spreghini MR, Cappa M, Perrone L, Brufani C, et al. 1-hour plasma glucose in obese youth. Acta Diabetol 2012;49(6):435–43.
[179] Mengen E, Uçaktürk SA. Evaluation of the relationship between the one-hour plasma glucose concentration and beta-cell functions and cardiometabolic parameters during oral glucose tolerance test in obese children and adolescents. J Pediatr Endrocrinol Metab 2020;33(6):767–75.
[180] Tfayli H, Jung Lee S, Bacha F, Arslanian S. One-hour plasma glucose concentration during the OGTT: what does it tell about β-cell function relative to insulin sensitivity in overweight/obese children? Pediatr Diabetes 2011;12(6):572–9.
[181] Tricò D, Galderisi A, Mari A, Santoro N, Caprio S. One-hour post-load plasma glucose predicts progression to prediabetes in a multi-ethnic cohort of obese youths. Diabetes Obes Metab 2019;21(5):1191–8.
[182] Brar PC, Mehta S, Brar A, Pierce KA, Albano A, Bergman M. Value of 1-hour plasma glucose during an Oral glucose tolerance test in a multiethnic cohort of obese children and adolescents. Clin Med Insights Endocrinol Diabetes 2023;16:11795514231177206.
[183] The DECODE Study Group. Age- and sex-specific prevalences of diabetes and impaired glucose regulation in 13 European cohorts. Diabetes Care 2003;26(1):61–9.
[184] The DECODA Study Group. Age- and sex-specific prevalence of diabetes and impaired glucose regulation in 11 Asian cohorts. Diabetes Care 2003;26(6):1770–80.
[185] Wahl PW, Savage PJ, Psaty BM, Orchard TJ, Robbins JA, Tracy RP. Diabetes in older adults: comparison of 1997 American Diabetes Association classification of diabetes mellitus with 1985 WHO classification. Lancet 1998;352(9133):1012–5.
[186] Barrett-Connor E, Ferrara A. Isolated postchallenge hyperglycemia and the risk of fatal cardiovascular disease in older women and men: the rancho bernardo study. Diabetes Care 1998;21(8):1236–9.
[187] Joung KH, Ju SH, Kim JM, Choung S, Lee JM, Park KS, et al. Clinical implications of using post-challenge plasma glucose levels for early diagnosis of type 2 diabetes mellitus in older individuals. Diabetes Metab J 2018;42(2):147–54.
[188] Saramies J, Koiranen M, Auvinen J, Uusitalo H, Hussi E, Cederberg H, et al. 22-year trends in dysglycemia and body mass index: a population-based cohort study in savitaipale. Finland Prim Care Diabetes 2021;15(6):977–84.
[189] Schwarz P, Li J, Lindstrom J, Tuomilehto J. Tools for predicting the risk of type 2 diabetes in daily practice. Horm Metab Res 2009;41(02):86–97.
[190] 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.
[191] Saaristo T, Peltonen M, Lindström J, Saarikoski L, Sundvall J, Eriksson JG, 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. Diab Vasc Dis Res 2005;2(2):67–72.
[192] Bahijri S, Al-Raddadi R, Ajabnoor G, Jambi H, Al Ahmadi J, Borai A, et al. Dysglycemia risk score in Saudi Arabia: a tool to identify people at high future risk of developing type 2 diabetes. J Diabetes Investig 2020;11(4):844–55.
[193] Campos MAA, Reichelt AAJ, Façanha C, Forti AC, Schmidt MI. Evaluation of a 1-h 75-g oral glucose tolerance test in the diagnosis of gestational diabetes. Braz J Med Biol Res 2008;41(8):684–8.
[194] Barbosa M, Moreira Gomes P, Monteiro AM, Matos C, Lopes Pereira M, Fernandes V. Postpartum reclassification test in gestational diabetes: can the test be reduced to 1 hour? Hormones 2022;21(2):287–93.
[195] de Sanctis V, Soliman A, Tzoulis P, Daar S, Pozzobon GC, Kattamis C. A study of isolated hyperglycemia (Blood glucose ≥155 mg/dl) at 1-hour of oral glucose tolerance test (OGTT) in patients with β-transfusion dependent thalassemia (β-TDT) followed for 12 years. Acta Biomed. 2021;92(4):e2021322 [This retrospective study demonstrated that an isolated high 1-hour post-load glucose level (≥155 mg/dL; H-NGT) during the OGTT may serve as a simple biomarker to detect high-risk patients, with chronic liver disease and/or iron overload, who need periodic glycemic surveillance].
[196] Di Bonito P, Valerio G, Licenziati MR, Corica D, Wasniewska M, Di Sessa A, et al. One-Hour Post-Load Plasma Glucose and Altered Glucometabolic Profile in Youths with Overweight or Obesity. Int J Environ Res Public Health. 2023;20(11):5961 [The results confirmed and extended the findings of previous studies about the use of one-hour post-load glucose in identifying children and adolescents with isolated IGT and metabolic abnormalities. An elevated one-hour post-load plasma glucose level, not measured with current diagnostic standards, may provide an opportunity for the early identification of a large population despite normal levels of fasting glucose and HbA1c. The finding of an elevated one-hour post-load plasma glucose level can allow lifestyle intervention that has the greatest benefit for preserving or reversing β-cell function and preventing further progression to prediabetes and diabetes].
[197] Jagannathan R, Stefanovski D, Smiley DD, Oladejo O, Cotten LF, Umpierrez G, et al. 1-h Glucose During Oral Glucose Tolerance Test Predicts Hyperglycemia Relapse-Free Survival in Obese Black Patients With Hyperglycemic Crises. Front Endocrinol. 2022;13:871965 [One-hour PG at the time of remission is a better predictor of hyperglycemia relapse than traditional glycemic markers among obese Black patients presenting with DKA/severe hyperglycemia. Testing 1-h PG at insulin discontinuation identifies individuals at high risk of developing hyperglycemia relapse].
[198] Jalleh RJ, Xie C, Deane AM, Plummer MP, Jones KL, Horowitz M, et al. One-hour plasma glucose level after a 75 g oral glucose load and its relationship to gastric emptying in survivors of critical illness and stress hyperglycaemia. Crit Care Resusc. 2022;24(3):268–71 [Glucose intolerance, when defined as 1-hour glucose level ≥ 8.6 mmol/L following a 75 g oral glucose load, persists at 3 months in most survivors of stress hyperglycaemia and is dependent on the rate of gastric emptying. Longitudinal studies to characterise mechanisms underlying dysglycaemia and progression to diabetes in individuals with stress hyperglycaemia are indicated].
[199] Kılınç S, Demirbaş T, Atay E, Ceran Ö, Atay Z. Elevated 1-h post-load plasma glucose levels in normal glucose tolerance children with obesity is associated with early carotid atherosclerosis. Obes Res Clin Pract. 2020;14(2):136–41 [As compared with NGT individuals with a 1-h PG <155mg/dL, NGT individuals with a 1-h PG ≥155mg/dL exhibited higher carotid IMT (0.75±0.15mm vs. 0.68 ±0.15mm; p<0.05). No significant differences were observed in carotid IMT between IGT and NGT subjects with a 1-h PG ≥155mg/dL (0.75±0.18mm vs 0.75 ±0.15mm; p>0.05). Of the three glycemic parameters, 1-h and 2-h PG, but not fasting glucose, were significantly correlated with carotid IMT. There were no significant differences for increased risk of having NAFLD between the three groups. These data suggest that a value of 1-h PG ≥155mg/dL in children and adolescents with obesity is as important as IGT with respect to cardiovascular risk].
[200] Massimino M, Monea G, Marinaro G, Rubino M, Mancuso E, Mannino GC, et al. The Triglycerides and Glucose (TyG) Index Is Associated with 1-Hour Glucose Levels during an OGTT. Int J Environ Res Public Health. 2023;20(1):787 [The study demonstrated that the TyG index, an efficient and cost-effective marker of insulin resistance, is associated with the variability of early post-challenge glucose levels and is an independent marker of being NGT-1h-high].
[201] Mogoi M, Pop LL, Dediu M, Ciuca IM. Oral glucose tolerance test in patients with cystic fibrosis compared to the overweight and obese: a different approach in understanding the results. Children. 2022;9(4):533 [Late peak glucose and 1 h glucose level ≥ 155 mg/dL during OGTT can be used for diagnosing the early glucose metabolism alteration in children with CF].
[202] Ozgu-Erdinc AS, Iskender C, Uygur D, Oksuzoglu A, Seckin KD, Yeral MI, et al. One-hour versus two-hour postprandial blood glucose measurement in women with gestational diabetes mellitus: which is more predictive? Endocrine. 2016;52(3):561–70 [Postprandial 1-h and postprandial 2-h plasma glucose measurements were not superior to each other in predicting fetal macrosomia or perinatal complications. Based on our findings, it can be concluded that both methods may be suitable for follow-up as there are no clear advantages of one measurement over the other].

[203] Poon SW-Y, Tung JY-L. Thirty-minute post-load glucose could be a useful screening measure for abnormal oral glucose tolerance test response in adolescents with obesity. J Obes Metab Syndr. 2022;31(3):272–6 [Addition of 30-minute PG to non-fasting parameters improved the clinical utility in identifying high-risk individuals for abnormal OGTT response].

[204] Popovic DS, Papanas N. 1 h post-load plasma glucose: Should it be re-examined as a diagnostic criterion of diabetes? Prim Care Diabetes. 2021;15(3):622 [According to the current American Diabetes Association guidelines, diagnosis of both prediabetes and diabetes in asymptomatic individuals is based on the measurements of fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG) during a 75-g oral glucose tolerance test (OGTT), and glycated haemoglobin (HbA1c) [1]. Pre-diabetes is intermediate glucose metabolism abnormality, encompassing impaired fasting glucose (IFG), impaired glucose tolerance, and borderline HbA1c. Moreover, 1-h plasma glucose (1-h PG) during OGTT is used exclusively for diagnosing gestational diabetes. Forty years ago, 1-h PG was abandoned as diagnostic criterion for dysglycemia, primarily due to fact that it has been proven as a less sensitive and specific indicator of diabetes presence in comparison to 2-h PG. However, at that time, the election between these two criteria was not based on their ability to predict the risk of diabetic complications, which was scrutinised in the study demonstrating that 1-h PG is equally useful to 2-h PG in the prediction of retinopathy risk. Nevertheless, accumulating evidence indicates that 1-h PG $\geq$ 8.6 mmol/l in individuals with normal glucose tolerance (NGT) is highly predictive of progression to type 2 diabetes, microvascular and macrovascular complications, and mortality. Hence, a group of experts have united in advocating replacement of current OGTT criteria for pre-diabetes. The repercussion of this initiative is more frequent sampling of 1-h PG during the assessment of glucose tolerance. However, this trend raises one important practical question: How shall we correctly interpret the significantly elevated 1-h PG (e.g. $\geq$11.1 mmol/l) in individuals not diagnosed with diabetes, especially among those classified as having prediabetes defined by the presence of IFG and/or borderline HbA1c, or among those characterised as having NGT?. Available data on the potential specific cut-off value of 1-h PG for diagnosing diabetes is sparse. The aforementioned study has reported that 1-h PG $\geq$ 12.8 mmol/l may be a threshold for diabetes diagnosis, given that it has almost identical sensitivity and specificity for retinopathy as 2-h PG $\geq$ 11.1 mmol/l. Furthermore, in the EUROASPIRE IV trial including coronary artery disease patients without previous history of diabetes, the cut-off value of 1 h-PG $\geq$12.0 mmol/l has demonstrated balanced sensitivity and specificity for detecting diabetes. Obviously, future studies re-examining the utility of 1-h PG in the timely diagnosis of diabetes, potentially contributing to the reduction of chronic complications, are highly desirable].

[205] Sasaki N, Maeda R, Ozono R, Nakano Y, Higashi Y. Diversity in the risk of type 2 diabetes associated with age, sex, and 1-h post-load plasma glucose levels in the Japanese population with prediabetes. Diabetes Res Clin Pract. 2021;175:108780 [The assessment of age and sex-differences and subdivided prediabetes categories based on FPG and 1-h post-load glucose levels may effectively evaluate the risk of type 2 diabetes, which displays marked diversity].

[206] Wang R, Liu XL, Jia XJ, Liu Y, Lu Q. one-hour post-load plasma glucose levels are associated with early arterial stiffness in subjects with different glucose tolerance. Diabetes Metab Syndr Obes. 2022;15:1537–42 [The present study demonstrated the presence of early arterial stiffness in diabetes. Elevated 1-hour post-load plasma glucose level is closely related to the change of arterial elasticity in diabetes].

[207] Xiong T, Zhong C, Sun G, Zhou X, Chen R, Li Q, et al. Early maternal circulating alkaline phosphatase with subsequent gestational diabetes mellitus and glucose regulation: a prospective cohort study in China. Endocrine. 2019;65(2):295–303 [Each additional 10 U/L ALP level was associated with a 2% higher FBG (p = 0.043) and a 12% higher 1-h PBG (p = 0.004)].

Glossary

1-h PG: 1-hour plasma glucose
2-h PG: 2-hour plasma glucose
ADA: American Diabetes Association
AHI: Apnoea-hypopnoea index
AUC_{ROC}: Area under the receiver-operating characteristic curve
BMI: Body mass index
CATAMERI: CATAnzaro Metabolic Risk factors
CFRD: Cystic fibrosis-related diabetes mellitus
CI: Confidence interval
C-index: Concordance index
CVD: Cardiovascular disease
DI: Disposition Index
DPPOS: DPP Outcomes Study
eGFR: Estimated glomerular filtration rate
EUGENE2: European Network on Functional Genomics of T2D
FINDRISC: Finnish Diabetes Risk Calculator
FPG: Fasting plasma glucose
GDM: Gestational diabetes mellitus
GENFIEV: Genetic, Physiopathology and Evolution of Type 2 Diabetes
HbA_{1c}: Glycated haemoglobin
GOH: Israel Study of Glucose Intolerance, Obesity and Hypertension
HOMA-β: Homeostatic model assessment β-cell function
HOMA-IR: Homeostatic model assessment Insulin resistance
HR: Hazard ratio
IDF: International Diabetes Federation
IEC: International Expert Committee
IFG: Impaired fasting glucose
IGT: Impaired glucose tolerance
IH: Intermediate Hyperglycaemia
KoGES: Korean Genome and Epidemiology Study
MASLD: Metabolic dysfunction-associated steatotic liver disease
MMP: Malmö Preventive Project
NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III
NDDG: National Diabetes Data Group
NGT: Normal glucose tolerance
NHANES III: National Health and Nutrition Examination Survey III
OGTT: Oral glucose tolerance test
OSA: Obstructive sleep apnoea
OR: Odds ratio
PPV: Positive predictive value
RISC: Relationship between Insulin Sensitivity and Cardiovascular Risk
SADPM: San Antonio Diabetes Prediction Model
SAHS: San Antonio Heart Study
SOLAR: Study of Latino Adolescents at Risk of Type 2 Diabetes
SWNA: Southwestern Native American
T2D: Type 2 diabetes
UKPDS: United Kingdom Prospective Diabetes Study
WHO: World Health Organization