

1 **Fasting Plasma Glucose and 2-hour Postprandial Plasma Glucose Characteristics in a Large Multi-**
2 **ethnic Chinese Population**

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16 **Short title:** PPG less than FPG in China

17
18 **Highlights**

19 A quarter (26.04%) of participants in a Chinese population had plasma glucose levels following a
20 75g glucose load that were equal to or less than their fasting plasma glucose value.

21 Low Post Load was associated with a beneficial cardiometabolic profile with a lower BMI, lower
22 blood pressure, and favourable lipid profile.

23 IFG occurred more frequently in participants without hypoglycaemia (12.54% vs 1.25%, p=0.004).

24 The relationship between this phenomenon and high post load glucose and the progression to
25 prediabetes, diabetes and 'hard' cardiovascular outcomes in a Chinese population requires further
26 longitudinal investigation.

28 **Abstract**

29 Introduction

30 During an oral glucose tolerance test (OGTT), typically fasting plasma glucose is lower than 2-hour
31 postprandial plasma glucose (2-h). However, postprandial plasma glucose (PPG) levels lower than
32 fasting plasma glucose (FPG) levels may also occur. This study aims to describe the prevalence, clinical
33 characteristics, and contributing risk factors for $PPG \leq FPG$ in a large diverse Chinese population.

34

35 Materials and Methods

36 We conducted a cross-sectional analysis of baseline data from a nationwide cohort study
37 conducted in China. In addition to sociodemographic and anthropometric data collection, individuals
38 had OGTT, and blood chemistry tests. We determined the prevalence of $PPG \leq FPG$ ('Low Post Load'
39 group) and $PPG > FPG$ ('High Post Load' group) and used logistic regression to evaluate the association of
40 risk factors with the occurrence of Low Post Load .

41

42 Results

43 The prevalence of Low Post Load was 26.04% (n=3,773) and High Post Load was 73.96%
44 (n=10,714). Low Post Load was found to be related to younger age, male, lower BMI, lower blood
45 pressure, higher HDL cholesterol levels and lower triglycerides levels. Compared with participants in the
46 High Post Load group, participants in Low Post Load group had lower PPG (4.59 ± 0.83 mmol/L vs
47 7.15 ± 1.41 mmol/L) and HbA1c ($5.30 \pm 0.43\%$ vs $5.39 \pm 0.45\%$). People in Low Post Load group were more
48 likely to have hypoglycaemic episodes (2.12% vs 0.01%) and impaired fasting glucose (12.30% vs 4.81%)
49 compared with people with High Post Load, All $P < 0.001$.

50

51 Conclusions

52 We found a high prevalence of people with Low Post Load glucose (26.04%) in a Chinese
53 population cohort. The relationship between Low Post Load and the progression to or protection from

54 diabetes and related complications, and future incidence of cardiovascular disease needs further
55 exploration in longitudinal analyses.

56

57 **Keywords:** Fasting Plasma Glucose, Diabetes, OGTT, Glucose Tolerance, Cross-sectional Study

58 **Introduction**

59 The oral glucose tolerance test (OGTT) is a test commonly used to diagnose diabetes or
60 prediabetes, in which plasma glucose is tested after an overnight fast and again 2 hours following
61 ingestion of a 75-gram glucose solution. The 2-hour post glucose load plasma glucose measure
62 [hereafter referred to as postprandial plasma glucose (PPG)] is usually found to be higher than the
63 fasting plasma glucose levels(FPG). A PPG result higher than 7.8 mmol/l and less than 11.1 mmol/L
64 indicates impaired glucose tolerance (IGT), which is a well-established risk factor for type 2 diabetes(1).
65 The relationship between the PPG and FPG is thought to be related to the risk of developing type 2
66 diabetes as subjects whose PPG levels return to fasting levels more quickly have demonstrated a lower
67 risk for the development of type 2 diabetes(2).

68 PPG levels that are lower than or equal to FPG levels 2 hours after a glucose load has been described
69 in people with and without diabetes(3). Several factors have been associated with this phenomenon
70 including abnormal liver function, pancreatic dysfunction, late dumping syndrome and patients who have
71 had gastrectomy or bariatric surgery(4-10). In some cases, PPG levels can fall low enough to cause
72 hypoglycaemia, referred to as reactive hypoglycaemia. Plasma glucose levels are maintained within a
73 narrow normal range by the coordinated physiological responses of multiple organs(11). The liver
74 maintains plasma glucose level in the fasted state via activation of metabolic pathways like
75 gluconeogenesis and glycogenolysis, and the pancreas releases insulin to promote uptake of glucose into
76 the tissues (12-16). PPG lower than FPG has been observed in some patients with liver disease(17, 18)
77 and pancreatic dysfunction such as high insulin sensitivity, over-reaction of glucagon-like peptide 1, and
78 deficiencies of counter-regulatory hormones which can lead to PPG being lower than FPG (19-22). In
79 addition to antidiabetic medications, vigorous activity before sampling and insufficient food intake, late
80 dumping syndrome, related to a rapid rate of gastric emptying, results in the exposure of the distal gut to
81 more carbohydrates and leads to postprandial hyperglycaemia, which stimulates the pancreas resulting
82 in hyperinsulinaemia, leading to late hypoglycaemia or reactive hypoglycaemia(23, 24). Reactive
83 hypoglycaemia has been associated with a number of linked insulin resistance-related conditions such
84 type 2 diabetes, non-alcoholic fatty liver disease, polycystic ovarian syndrome and

85 hypertriglyceridaemia(17, 25). In fact, postprandial hyperinsulinemia which is a key physiological
86 mechanism in Low Post Load, and is reported to be independently associated with coronary artery
87 disease(26).

88 Although the relationship between PPG and FPG and the risks of developing diabetes have been
89 described in research settings, no studies have reported the population prevalence of $PPG \leq FPG$. In this
90 study, we used an FPG value and a PPG value measured 2-hours after a 75 grams OGTT to define 'Low
91 Post Load'($PPG \leq FPG$) and 'High Post Load'($PPG > FPG$) groups. We aimed to evaluate the population
92 prevalence of 'Low Post Load' and the clinical characteristics of people with 'Low Post Load'.

93

94 **Materials and methods**

95 Study population

96 All subjects were participants of the Study on Evaluation of Innovative Screening tools and
97 determination of optimal diagnostic cut-off points for type 2 diabetes in Chinese multi-ethnic
98 population (SENSIBLE) and SENSIBLE-Addition studies[The National Key R&D Program of China
99 (2016YFC1305700)](27, 28). It was conducted in 8 provinces from different regions of China across
100 several ethnic groups(27, 28). A multi-stage cluster and simple randomization method was used to
101 invite subjects aged 20 to 70 years who had been living in their residence for 5 years to participate.
102 Participants enrolled in the baseline study between November 2016 to June 2017. After providing
103 written informed consent participants completed a questionnaire, anthropometric examination and
104 laboratory evaluation. Individuals who refused to sign the informed consent, were pregnant, had a
105 significant psychiatric illness e.g. mild depression was not an exclusion or any other diseases that
106 cannot complete the investigation procedures were excluded from the study. In this paper, we use the
107 baseline data of the cohort to conduct a cross-sectional analysis.

108 A total of 17,629 participants were recruited into this study. We excluded participants with
109 missing data on sociodemographic information (e.g. age, gender, ethnicities, family history of diabetes)
110 and plasma glucose value (fasting plasma glucose and/or 2-hour plasma glucose), the outliers (>99.9
111 percentile or <0.1 percentile, including anthropometric examination characteristics ($BMI < 15.605 \text{ kg/m}^2$

112 or BMI>48.423 kg/m², waist<55cm or waist>126cm), and participants with self-reported diabetes or
113 who had been diagnosed with diabetes by the baseline OGTT.

114

115 Data collection

116 Eligible participants were invited to attend a study day and advised to maintain their usual
117 lifestyle/physical activity for at least 3 days prior and maintain an overnight fast of at least 10 hours. On
118 the study day the following assessments were conducted: 1. heart rate and blood pressure were
119 measured using electronic sphygmomanometers (YE680E, Jiangsu Yuyue Medical Equipment Inc.,
120 Nanjing, Jiangsu, China); 2. fasting plasma glucose; 3. blood chemistry tests and biochemistry
121 examination; 4. a standard 75-gram glucose solution for an oral glucose tolerance test (OGTT) was given
122 and plasma glucose measure taken 120 mins later; 5. completion of a face-to-face structured
123 questionnaire and anthropometric examination using standardized procedures(29).

124

125 Blood sample collection and analysis

126 All blood samples were centrifuged on-site within 30 min after collection. For the serum and the
127 whole blood samples, they were shipped at 4 °C by air to the central laboratory in Nanjing Adicon
128 Clinical Laboratories. All the blood specimens were analysed immediately after arrival using an
129 automatic chemistry analyser (Synchron LX-20, Beckman Coulter Inc., CA, USA). HbA1c was measured
130 with high-performance liquid chromatography (HPLC; D-10™ Haemoglobin Analyzer, Bio-Rad Inc., CA,
131 USA).

132

133 Questionnaire

134 The questionnaire was designed to collect demographic characteristics (age, gender, educational
135 level), lifestyle behaviour (smoking status, drinking status, regular physical activity) and health-related
136 characteristics. This standardized questionnaire was administered by trained interviewers to all
137 enrolled participants.

138 Occupations were categorized into two groups [Professional occupations including researcher,
139 doctor, teacher, administrative leader and office staff), and manual workers (including commerce or
140 service man, farmer, fisherman, soldier and workman) or student]. Lifestyle and behaviour questions,
141 i.e., smoking, alcohol, exercise, and diet information were categorical variables, scored on several
142 points scales or classified as 'yes' or 'no'.

143 Health-related characteristics were self-reported by participants, and included medical conditions
144 (the start time, control time or end time and severity level) and medication use (the start time and end
145 time).

146

147 Definitions of Diabetes and Type 2 Diabetes

148 Diabetes mellitus, impaired glucose tolerance(IGT), impaired fasting glucose(IFG), and normal
149 glucose tolerance(NGT) were defined using the Chinese Guideline 2020 edition (based on WHO 1999
150 diagnostic criteria)(30). The fasting plasma glucose (FPG) of normoglycaemia people has been set at
151 3.9–6.1 mmol/L and the 2h-postprandial plasma glucose at 7.8 mmol/L or less; impaired fasting
152 glucose(IFG) was defined as an FPG of greater than or equal to 6.1 mmol/L and less than 7.0 mmol/L,
153 and PPG at 120 min after oral glucose load less than 7.8 mmol/L; impaired glucose tolerance(IGT) was
154 defined as an FPG of less than 6.1 mmol/L, and PPG at 120 min after oral glucose loading of equal or
155 greater than 7.8 mmol/L and less than 11.1 mmol/L. Diabetes was defined as $FPG \geq 7.0$ mmol/L or 2h-
156 postprandial blood ≥ 11.1 mmol/L, the diagnostic criteria for hypoglycaemia were plasma glucose < 2.8
157 mmol/L.

158

159 Statistical analyses

160 Continuous variables were described as means (\pm SD) or median (interquartile range) and
161 categorical data are presented as number and percentage. Statistical differences in continuous data
162 were determined using Student's t-test and Welch's t-test. Categorical data were compared using the
163 chi-squared test or Fisher's exact test.

164 A multivariate logistic regression was used to identify factors associated with Low Post Load. All
165 variables with significant differences at univariate logistic regression analysis ($P < 0.05$) were included in
166 multivariate logistic regression analysis, and the odds ratio (OR) and 95%CI were calculated for each
167 factor. We further divided into those with and without hypoglycaemia and used logistic regression
168 model to compare respondent characteristics .

169 All statistical analyses were performed with SAS version 9.4 (SAS Institute Inc). Results were
170 considered significant when the P-value was less than 0.05 at two-sided test.

171

172 **Results**

173 In total, 17,629 people participated in the original study. A total of 14,487 participants (Figure 1)
174 were included in this analysis after exclusion of 93 subjects without FPG, 1281 subjects without PPG, 4
175 subjects without HbA1c, 49 subjects without sociodemographic information, 67 subjects without BMI
176 information, 17 outliers in BMI, 2 subjects lacking diet information and 68 subjects who self-reported
177 with diabetes and 1,561 subjects who were found to have diabetes in the OGTT.

178 Table 1 shows data on clinical, socio-economic, and behavioural characteristics of high and low
179 post load groups. The mean age of participants was 49.34 ± 11.92 years and 9,702 (66.97%) were female.
180 There were 3,773 participants (26.04%) in the Low Post Load group and 10,714 participants (73.96%) in
181 the High Post Load group. Participants in the Low Post Load group were significantly younger, were
182 more likely to be male, non-Han ethnicity, had lower BMI, heart rate less than 100 beats/min, higher
183 HDL, and lower TG levels, and were more likely to drink alcohol and exercise regularly compared with
184 participants in the High Post Load group.

185 Figure 2 shows Number of plasma values in Low Post Load group and High Post Load group.

186 Compared with participants in High Post Load group, participants in Low Post Load group had lower PPG
187 (4.59 ± 0.83 vs 7.15 ± 1.41) and HbA1c (5.30 ± 0.43 vs 5.39 ± 0.45), with higher hypoglycaemia incidence
188 (all $P < 0.001$). In the Low Post Load group, 87.70% ($n=3,309$) had normal glucose tolerance compared
189 with 66.18% ($n=7,090$) in the High Post Load group. There were no participants in the Low Post Load
190 group with IGT and 464(12.30%) participants had IFG. In the High Post Load group 515(4.81%)

191 participants had IFG, 2,313(21.59%) participants had IGT, and 796(7.43%) participants had both IFG and
192 IGT(P<0.001).

193 In Table 2, an adjusted logistic regression model indicated that most of the evaluated factors had
194 significant and independent positive or negative associations with Low Post Load. For the phenomenon
195 of Low Post Load, the significant factors were age<44 years; male; people of Uyghur or Zhuang
196 ethnicity; BMI<24kg/m²; normal blood pressure; heart rate<100 beats/min; status as never or former
197 drinker; HDL cholesterol≥1.55 mmol/L; triglycerides<1.70 mmol/L, all P<0.001.

198 Within the low post load group, a small number of participants (n=80/3,773; 2.12%) had
199 hypoglycaemia, defined as a blood glucose of <2.8 mmol/L in the OGTT.

200 As shown in Table 3, for participants in the Low Post Load group, the following variables had a
201 significant association with hypoglycaemia: age<44 years old, male, non-Han population, Manual-
202 worker, BMI<24kg/m² and cigarette smoking. Although participants with hypoglycaemia has lower FPG
203 (5.13±0.53 vs 5.44±0.56, p<0.001) and PPG(2.49±0.30 vs 4.64±0.78, p<0.001), there was no difference
204 in HbA1c compared with participants without hypoglycaemia.

205

206 Discussion

207 In this analysis we found a quarter (26.04%) of participants in a Chinese population had plasma
208 glucose levels following a 75g glucose load that were equal to or less than their fasting plasma glucose
209 values. Although this phenomenon that we have called Low post Load has been described in individuals
210 with specific clinical conditions, it can occur without any precipitating factors and until now there is a lack
211 of published data that provide estimates of the prevalence of this phenomenon in the general population.
212 This large cohort study now establishes the prevalence in a multi-ethnic Chinese population.

213 In our study, people with Low Post Load were more likely to be younger, have lower BMI, and to have
214 a number of characteristics such as lower triglycerides, LDL, blood pressure and higher HDL suggesting
215 that Low Post Load has a beneficial cardiometabolic profile. People with high post load were more likely
216 to have prediabetes. The Low post load group had a higher proportion of people with normal glucose
217 tolerance than the high post load group (87.7% vs 66.2%), 464 (11.93%) participants had IFG and no

218 participants had IGT, while in the High Post Load group, there was a lower proportion with IFG (4.21%),
219 higher proportions with IGT (18.92%) and both IFG and IGT(6.51%). Prediabetes is an intermediate
220 hyperglycaemic state between normal glucose tolerance and overt diabetes. Over a lifetime follow-up,
221 about 70% of people with prediabetes develop type 2 diabetes, with the risk of developing diabetes 2-
222 fold higher in those with IFG and IGT than those with isolated IFG or isolated IGT(31-33). IGT is associated
223 with more severe insulin resistance and beta-cell dysfunction(34-36). The San Antonio Heart Study
224 demonstrated that participants with normal glucose tolerance and High Post Load had 2.33-fold odds of
225 developing type 2 diabetes when compared with normal glucose tolerance participants with Low Post
226 Load, during 7 to 8 years of follow-up(2). In 20 years of follow up in the CARDIA (Coronary Artery Risk
227 Development in Young Adults) study normal glucose tolerance participants with Low Post Load had a
228 lower risk of developing type 2 diabetes(37).

229 We defined 'Low Post Load' as 2-hour post-load plasma glucose lower than fasting plasma glucose.
230 Using this definition, there are two sub-categories of people: 1) those with adequate insulin reserve who
231 are able to quickly normalise their plasma glucose after an oral load, and 2) those with over-correction of
232 their plasma glucose with post-load plasma glucose in the hypoglycaemic range, ie. reactive
233 hypoglycaemia. We found that IFG occurred less frequently in participants with hypoglycaemia (1.25% vs
234 12.54%, $p=0.004$). This might due to the higher insulin secretion or insulin response and a different
235 metabolic trajectory in participants with hypoglycaemia. We will follow these participants in subsequent
236 cohort studies to find if they are more prone to diabetes progression.

237 Smoking, caffeine intake, insufficient food intake, antidiabetic medications and heavy exercise have
238 been demonstrated as pre-analytical factors that affect plasma glucose levels(39, 40). We excluded
239 participants with diabetes (self-reported or diagnosed by OGTT). Use of glucose lowering agents could
240 affect glucose levels during OGTT. Also, people with diabetes have insulin resistance and relative insulin
241 insufficiency resulting in raised fasting and post-load glucose by definition. We found that current drinking
242 and vigorous exercise were related to hypoglycaemia after adjustment for age, gender and BMI in our
243 study.

244 The study has several limitations. About 70% of the study participants were women. This study was

245 conducted in areas where there is a lot of mobility of young men who travel to urban areas for work,
246 leaving predominantly women to be sampled in the study areas. In this study, there were 294(2.03%)
247 participants with liver disease, 3(0.02%) participants with pancreatic disease and 114(0.79%) participants
248 with upper digestive tract disease. These conditions have been associated with the occurrence of Low
249 post Load, however as the prevalence was limited and derived from self-reporting by subjects in
250 questionnaires, they may be underestimated, and we were not able to fully examine the contribution of
251 these conditions to the occurrence of Low Post Load. Fasting or postprandial insulin was not measured in
252 this study, and we could not investigate the association between insulin secretion, insulin resistance and
253 low or high post load. Additionally, there were missing data on waist-hip ratio, and we were unable to
254 examine the relationship between central obesity and this phenomenon.

255 In conclusion, we found a significant prevalence of people with Low Post Load glucose (26.04%) in
256 population-based baseline data of a cohort in China. Low Post Load was associated with a beneficial
257 cardiometabolic profile with a lower BMI, lower blood pressure, and favourable lipid profile. The
258 relationship between this phenomenon and high post load glucose and the progression to prediabetes,
259 diabetes and 'hard' cardiovascular outcomes in a Chinese population requires further longitudinal
260 investigation.

261

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266

267 **Disclosure**

268 The authors declare no conflict of interest.

269

270 **Approval of the research protocol**

271 The study was conducted in accordance with the Declaration of Helsinki, and this study protocol was

272 reviewed and approved by the Human Research Ethics Committee of Zhongda Hospital, Southeast
273 University, approval number: 2016ZDSYLL092-P01. The name of the institutions indicated in the Ethical
274 approval listed in the supplement.

275

276 **Informed Consent**

277 Written informed consent has been obtained from the patients to publish this paper.

278

279 **Approval date of Registry and the Registration No. of the study/trial:**

280 N/A

281

282 **Animal Studies**

283 N/A

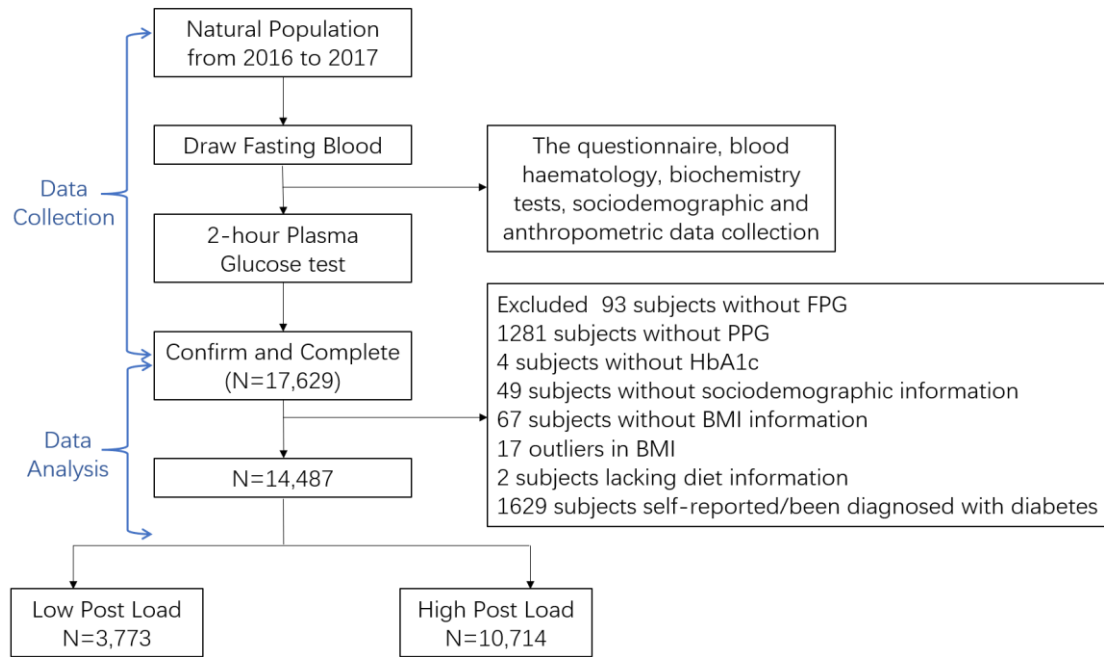
284

285 **Reference:**

- 286 1. Unwin N, Shaw J, Zimmet P, Alberti K. Impaired glucose tolerance and impaired fasting
287 glycaemia: the current status on definition and intervention. *Diabetic medicine: a journal of*
288 *the British Diabetic Association.* 2002;19(9):708-23.
- 289 2. Abdul-Ghani MA, Williams K, DeFronzo R, Stern M. Risk of progression to type 2
290 diabetes based on relationship between postload plasma glucose and fasting plasma glucose.
291 *Diabetes Care.* 2006;29(7):1613-8.
- 292 3. Pant V, Gautam K, Pradhan S. Postprandial Blood Glucose can be less than Fasting
293 Blood Glucose and this is not a Laboratory Error. *JNMA: Journal of the Nepal Medical*
294 *Association.* 2019;57(215):67.
- 295 4. Oki Y, Ono M, Hyogo H, Ochi T, Munekage K, Nozaki Y, et al. Evaluation of postprandial
296 hypoglycemia in patients with nonalcoholic fatty liver disease by oral glucose tolerance testing
297 and continuous glucose monitoring. *Eur J Gastroenterol Hepatol.* 2018;30(7):797-805.
- 298 5. Tamburrano G, Leonetti F, Sbraccia P, Giaccari A, Locuratolo N, Lala A. Increased
299 insulin sensitivity in patients with idiopathic reactive hypoglycemia. *J Clin Endocrinol Metab.*
300 1989;69(4):885-90.
- 301 6. Toft-Nielsen M, Madsbad S, Holst JJ. Exaggerated secretion of glucagon-like peptide-1
302 (GLP-1) could cause reactive hypoglycaemia. *Diabetologia.* 1998;41(10):1180-6.
- 303 7. Gebhard B, Holst JJ, Biegelmayer C, Miholic J. Postprandial GLP-1, norepinephrine, and
304 reactive hypoglycemia in dumping syndrome. *Dig Dis Sci.* 2001;46(9):1915-23.
- 305 8. Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL. Effects of weight loss on
306 regional fat distribution and insulin sensitivity in obesity. *Diabetes.* 1999;48(4):839-47.
- 307 9. Tack J, Arts J, Caenepeel P, De Wulf D, Bisschops R. Pathophysiology, diagnosis and
308 management of postoperative dumping syndrome. *Nat Rev Gastroenterol Hepatol.*
309 2009;6(10):583-90.

- 310 10. Nannipieri M, Belligoli A, Guarino D, Busetto L, Moriconi D, Fabris R, et al. Risk Factors
311 for Spontaneously Self-Reported Postprandial Hypoglycemia After Bariatric Surgery. *J Clin*
312 *Endocrinol Metab.* 2016;101(10):3600-7.
- 313 11. Abdul-Ghani MA, Tripathy D, DeFronzo RA. Contributions of β -cell dysfunction and
314 insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting
315 glucose. *Diabetes care.* 2006;29(5):1130-9.
- 316 12. Kim H, Zheng Z, Walker PD, Kapatos G, Zhang K. CREBH maintains circadian glucose
317 homeostasis by regulating hepatic glycogenolysis and gluconeogenesis. *Molecular and cellular*
318 *biology.* 2017;37(14):e00048-17.
- 319 13. Cherrington AD. Banting Lecture 1997. Control of glucose uptake and release by the
320 liver in vivo. *Diabetes.* 1999;48(5):1198-214.
- 321 14. Owen OE, Felig P, Morgan AP, Wahren J, Cahill GF. Liver and kidney metabolism
322 during prolonged starvation. *The Journal of clinical investigation.* 1969;48(3):574-83.
- 323 15. Exton J. Gluconeogenesis. *Metabolism.* 1972;21(10):945-90.
- 324 16. Dimitriadis GD, Maratou E, Kountouri A, Board M, Lambadiari V. Regulation of
325 postabsorptive and postprandial glucose metabolism by insulin-dependent and insulin-
326 independent mechanisms: an integrative approach. *Nutrients.* 2021;13(1):159.
- 327 17. Oki Y, Ono M, Hyogo H, Ochi T, Munekage K, Nozaki Y, et al. Evaluation of postprandial
328 hypoglycemia in patients with nonalcoholic fatty liver disease by oral glucose tolerance testing
329 and continuous glucose monitoring. *European journal of gastroenterology & hepatology.*
330 2018;30(7):797.
- 331 18. Nishida T. Diagnosis and clinical implications of diabetes in liver cirrhosis: a focus on
332 the oral glucose tolerance test. *Journal of the Endocrine Society.* 2017;1(7):886-96.
- 333 19. Gebhard B, Holst J, Biegelmayer C, Miholic J. Postprandial GLP-1, norepinephrine, and
334 reactive hypoglycemia in dumping syndrome. *Digestive diseases and sciences.*
335 2001;46(9):1915-23.
- 336 20. TAMBURRANO G, LEONETTI F, SBRACCIA P, GIACCARI A, LOCURATOLO N, LALA L.
337 Increased insulin sensitivity in patients with idiopathic reactive hypoglycemia. *The Journal of*
338 *Clinical Endocrinology & Metabolism.* 1989;69(4):885-90.
- 339 21. Toft-Nielsen M, Madsbad S, Holst J. Exaggerated secretion of glucagon-like peptide-1
340 (GLP-1) could cause reactive hypoglycaemia. *Diabetologia.* 1998;41(10):1180-6.
- 341 22. Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL. Effects of weight loss on
342 regional fat distribution and insulin sensitivity in obesity. *Diabetes.* 1999;48(4):839-47.
- 343 23. Tack J, Arts J, Caenepeel P, De Wulf D, Bisschops R. Pathophysiology, diagnosis and
344 management of postoperative dumping syndrome. *Nature reviews Gastroenterology &*
345 *hepatology.* 2009;6(10):583-90.
- 346 24. Nannipieri M, Belligoli A, Guarino D, Busetto L, Moriconi D, Fabris R, et al. Risk factors
347 for spontaneously self-reported postprandial hypoglycemia after bariatric surgery. *The Journal*
348 *of Clinical Endocrinology & Metabolism.* 2016;101(10):3600-7.
- 349 25. Mumm H, Altinok ML, Henriksen JE, Ravn P, Glintborg D, Andersen M. Prevalence and
350 possible mechanisms of reactive hypoglycemia in polycystic ovary syndrome. *Human*
351 *Reproduction.* 2016;31(5):1105-12.
- 352 26. Baltali M, Korkmaz ME, Kiziltan HT, Muderris IH, Ozin B, Anarat R. Association
353 between postprandial hyperinsulinemia and coronary artery disease among non-diabetic
354 women: a case control study. *International journal of cardiology.* 2003;88(2-3):215-21.
- 355 27. Li W, Xie B, Qiu S, Huang X, Chen J, Wang X, et al. Non-lab and semi-lab algorithms for
356 screening undiagnosed diabetes: a cross-sectional study. *EBioMedicine.* 2018;35:307-16.

- 357 28. Qiu S, Du Z, Li W, Chen J, Wu H, Liu J, et al. Exploration and validation of the
358 performance of hemoglobin A1c in detecting diabetes in community-dwellers with
359 hypertension. *Annals of Laboratory Medicine*. 2020;40(6):457-65.
- 360 29. Lim G, Bellemo V, Xie Y, Lee XQ, Yip MY, Ting DS. Different fundus imaging modalities
361 and technical factors in AI screening for diabetic retinopathy: a review. *Eye and Vision*.
362 2020;7(1):1-13.
- 363 30. Zhu D. Guideline for the prevention and treatment of type 2 diabetes mellitus in China
364 (2020 edition). *Chinese J Endocrinol Metab*. 2021.
- 365 31. Report of the Expert Committee on the Diagnosis and Classification of Diabetes
366 Mellitus. *Diabetes Care*. 1997;20(7):1183-97.
- 367 32. Abdul-Ghani MA, Abdul-Ghani T, Stern MP, Karavic J, Tuomi T, Bo I, et al. Two-step
368 approach for the prediction of future type 2 diabetes risk. *Diabetes Care*. 2011;34(9):2108-12.
- 369 33. Fiorentino TV, Marini MA, Andreozzi F, Arturi F, Succurro E, Perticone M, et al. One-
370 Hour Postload Hyperglycemia Is a Stronger Predictor of Type 2 Diabetes Than Impaired Fasting
371 Glucose. *J Clin Endocrinol Metab*. 2015;100(10):3744-51.
- 372 34. Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk
373 state for diabetes development. *The Lancet*. 2012;379(9833):2279-90.
- 374 35. van Haeften TW, Pimenta W, Mitrakou A, Korytkowski M, Jenssen T, Yki-Jarvinen H, et
375 al. Disturbances in β -cell function in impaired fasting glycemia. *Diabetes*.
376 2002;51(suppl_1):S265-S70.
- 377 36. Kanat M, Mari A, Norton L, Winnier D, DeFronzo RA, Jenkinson C, et al. Distinct β -cell
378 defects in impaired fasting glucose and impaired glucose tolerance. *Diabetes*. 2012;61(2):447-
379 53.
- 380 37. Vivek S, Carnethon MR, Prizment A, Carson AP, Bancks MP, Jacobs Jr DR, et al.
381 Association of the extent of return to fasting state 2-hours after a glucose challenge with
382 incident prediabetes and type 2 diabetes: The CARDIA study. *Diabetes Research and Clinical
383 Practice*. 2021;180:109004.
- 384 38. Si Y, Wang A, Yang Y, Liu H, Gu S, Mu Y, et al. Fasting blood glucose and 2-h
385 postprandial blood glucose predict hypertension: a report from the reaction study. *Diabetes
386 Therapy*. 2021;12(4):1117-28.
- 387 39. Janssen K, Delanghe J. Importance of the pre-analytical phase in blood glucose
388 analysis. *Acta Clinica Belgica*. 2010;65(5):311-8.
- 389 40. Bora K, Barman B, Ayubi AW. The curious case of postprandial glucose less than
390 fasting glucose: little things that matter much. *Clinical Chemistry and Laboratory Medicine
391 (CCLM)*. 2018;56(9):e223-e5.
- 392 41. Liu L-S, Wu Z, Wang J, Wang W, Bao Y, Cai J, et al. 2018 Chinese guidelines for
393 prevention and treatment of hypertension-A report of the revision committee of Chinese
394 guidelines for prevention and treatment of hypertension. *Journal of Geriatric Cardiology*.
395 2019;16(3):182-245.



397

398 **Figure 1. Flow chart of this research**

399

400 **Table 1. Baseline information of participants by Low/High Post Load**

	All N=14,487	Low Post Load N=3,773(26.04%)	High Post Load N=10,714(73.96%)	P- value
	Mean ± SD / N(%)	Mean ± SD / N(%)	Mean ± SD / N(%)	
Age(years)	49.34(11.92)	46.60(12.69)	50.31(11.48)	<0.001
Gender(Female)	9,702(66.97%)	2,136(56.61%)	7,566(70.62%)	<0.001
Ethnicity(Han)	7,056(48.71%)	1,590(42.14%)	5,466(51.02%)	<0.001
Education Levels(illiteracy)	1,415(9.77%)	274(7.26%)	1,141(10.65%)	<0.001
Occupation Type				<0.001
Professional	2,364(16.32%)	711(18.84%)	1,653(15.43%)	
Manual-worker	12,011(82.91%)	3,004(79.62%)	9,007(84.07%)	
Student	112(0.77%)	58(1.54%)	54(0.50%)	
Body mass index(kg/m²)	24.87(3.79)	24.17(3.65)	25.12(3.80)	<0.001
SBP (mmHg)	130.8(20.45)	128.0(19.87)	131.7(20.57)	<0.001
DBP (mmHg)	80.86(12.14)	79.47(12.05)	81.34(12.14)	<0.001
Heart rate (beats/min)	78.55(11.38)	77.27(11.18)	79.00(11.42)	<0.001
Total cholesterol(mmol/L)	5.03(1.09)	4.92(1.11)	5.06(1.08)	<0.001
HDL cholesterol(mmol/L)	1.57(0.39)	1.61(0.41)	1.55(1.54)	<0.001
LDL cholesterol(mmol/L)	2.84(0.81)	2.77(0.82)	2.87(0.80)	<0.001
Triglycerides(mmol/L)	1.55(1.53)	1.35(1.47)	1.62(1.54)	<0.001
Smoking				<0.001

Never	11,764(81.20%)	2,873(76.15%)	8,891(82.98%)	
Former	453(3.13%)	135(3.58%)	318(2.97%)	
Current	2,270(15.67%)	765(20.28%)	1,505(14.05%)	
Alcohol				<0.001
Never	10,991(75.87%)	2,721(72.12%)	8,270(77.19%)	
Former	534(3.69%)	168(4.45%)	366(3.42%)	
Current	2,962(20.45%)	884(23.43%)	2,078(19.40%)	
Vigorous Exercise	5,259(36.30%)	1,420(37.64%)	3,839(35.83%)	0.047
Regular meals	10,992(75.87%)	2,784(73.79%)	8,208(76.61%)	<0.001
Family History of diabetes	2,021(13.95%)	496(13.15%)	1,525(14.23%)	0.097
Hypoglycaemic drugs use	16(0.11%)	4(0.11%)	12(0.11%)	1.000
Self-report liver disease	294(2.03%)	65(1.72%)	229(2.14%)	0.120
Self-report pancreatic disease	3(0.02%)	1(0.03%)	2(0.02%)	1.000
Self-report upper digestive track disease	114(0.79%)	32(0.85%)	82(0.77%)	0.621
FPG(mmol/L)	5.43(0.57)	5.44(0.56)	5.43(0.58)	0.317
PPG(mmol/L)	6.49(1.71)	4.59(0.83)	7.15(1.41)	<0.001
Hypoglycaemia	81(0.56%)	80(2.12%)	1(0.01%)	<0.001
Difference(2hPPG-FPG)	1.06(1.59)	-0.85(0.70)	1.73(1.24)	<0.001
HbA1c(%)	5.37(0.45)	5.30(0.43)	5.39(0.45)	<0.001
Status (WHO1999)				<0.001
NGT	10,399(71.78%)	3,309(87.70%)	7,090(66.18%)	
IFG	979(6.76%)	464(12.30%)	515(4.81%)	
IGT	2,313(15.97%)	0(0.00%)	2,313(21.59%)	
IFG+IGT	796(5.49%)	0(0.00%)	796(7.43%)	

401 Data are presented as n, n(%), mean±SD or median(IQR).

402 Occupation type: Professional occupation: researcher, doctor, teacher, administrative leader and office

403 staff; manual worker: commerce or serviceman, farmer, fisherman, soldier and workman; student:

404 current student.

405 BMI: body mass index.

406 SBP: systolic blood pressure.

407 HDL: high-density lipoprotein.

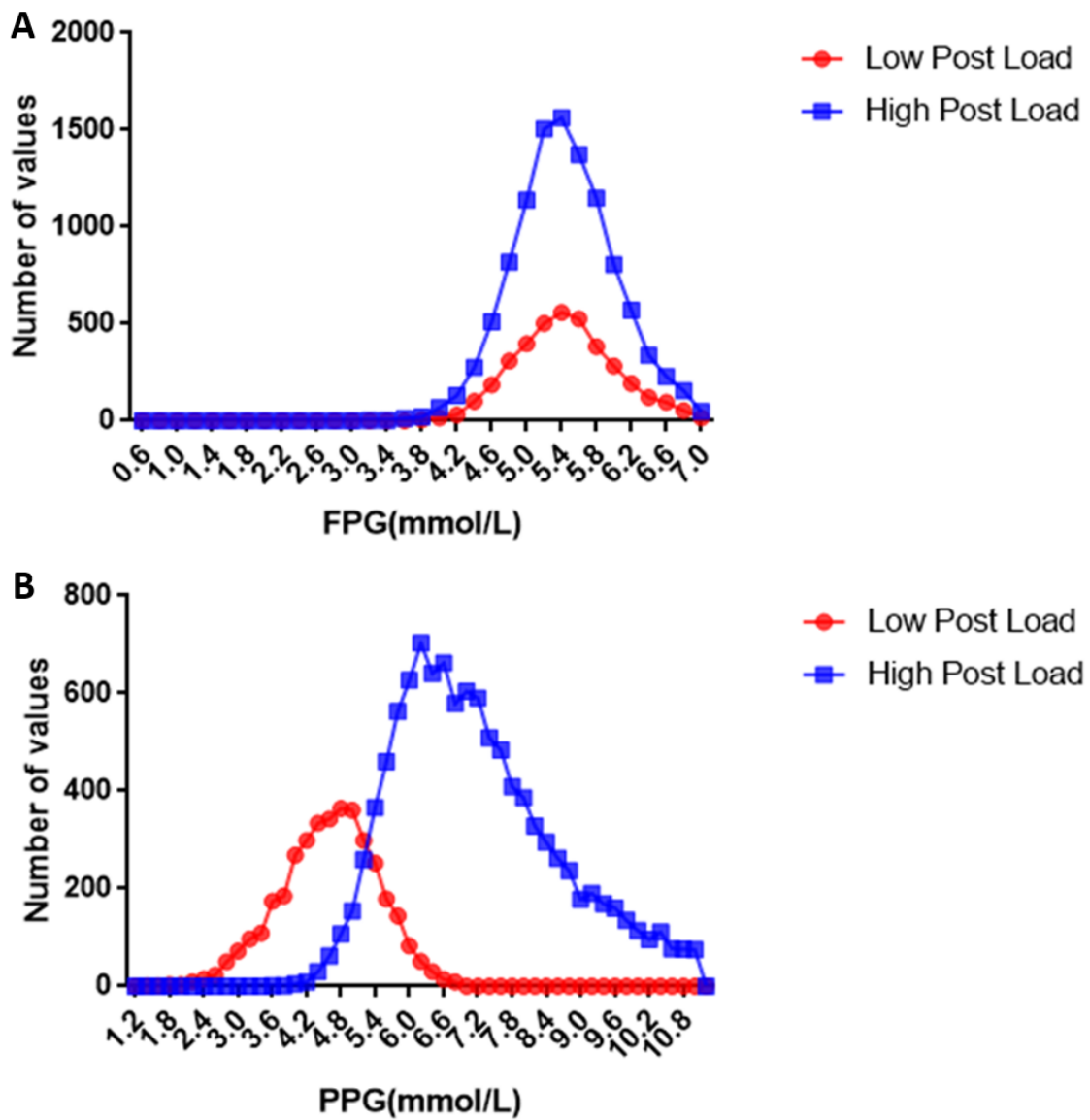
408 LDL: low-density lipoprotein.

409 FPG: fasting plasma glucose.

410 PPG: postprandial plasma glucose.

411 HbA1c: haemoglobin A1C.

412 Significance of differences at p-value < 0.05.



413

414 **Figure 2. Distribution of blood glucose values in Low Post Load group and High Post Load group**

415

416 **Table 2. Effects of respondent characteristics on Low Post Load in a sample of 14,487 Chinese**

417 **population**

Characteristics	OR (95%CI)	P-value
Age		
Young age (<44 years)	1.000	
Middle age (44-59 years)	0.629(0.567,0.697)	<0.001
Older adults (60-74 years)	0.478(0.420,0.545)	<0.001
Elderly (≥75 years)	0.225(0.073,0.697)	0.010
Gender		
Female	1.000	

Male	2.007(1.819,2.215)	<0.001
Ethnicity		
Han	1.000	
Dai	0.842(0.721,0.982)	0.029
Kazakh	1.136(0.921,1.401)	0.234
Korean	1.057(0.889,1.257)	0.528
Uyghur	1.900(1.639,2.203)	<0.001
Zhuang	1.655(1.436,1.906)	<0.001
Other	1.822(0.816,4.070)	0.144
Education levels		
Illiteracy	1.000	
Primary school	1.000(0.840,1.189)	0.996
Middle School	1.025(0.865,1.215)	0.774
High school	1.088(0.904,1.311)	0.372
Junior college, Undergraduate and above	1.228(1.018,1.482)	0.032
Occupation		
Professional occupation	1.000	
Manual-worker	0.825(0.727,0.935)	0.003
Student	1.494(0.915,2.442)	0.108
BMI		
Underweight (<18.5kg/m ²)	1.000	
Normal range (18.5-23.9kg/m ²)	0.826(0.620,1.102)	0.194
Overweight (24-27.9kg/m ²)	0.537(0.401,0.718)	<0.001
Obese(≥28kg/m ²)	0.425(0.314,0.576)	<0.001
Blood Pressure		
Normal	1.000	
High Normal	0.865(0.773,0.967)	0.011
Grade 1 Hypertension	0.898(0.789,1.022)	0.102
Grade 2 Hypertension	0.738(0.623,0.872)	<0.001
Grade 3 Hypertension	0.781(0.607,1.005)	0.054
Isolated systolic hypertension	0.940(0.825,1.072)	0.356
No Data	0.768(0.272,2.164)	0.617
Heart rate(beats/min)		
<60	1.000	
60-100	0.811(0.630,1.043)	0.102
>100	0.518(0.363,0.738)	<0.001
No Data	1.177(0.558,2.484)	0.668
Total cholesterol(mmol/L)		
<5.17	1.000	
5.17-6.46	0.981(0.892,1.078)	0.689
≥6.47	0.982(0.841,1.146)	0.815
HDL cholesterol(mmol/L)		
<0.91	1.000	
0.91-1.54	1.276(0.945,1.722)	0.112
≥1.55	1.694(1.251,2.292)	<0.001
LDL cholesterol(mmol/L)		
<3.37	1.000	

3.37-4.13	0.930(0.833,1.038)	0.196
≥4.14	1.018(0.863,1.202)	0.828
Triglycerides(mmol/L)		
<1.70	1.000	
1.70-2.25	0.667(0.584,0.762)	<0.001
≥2.26	0.552(0.483,0.630)	<0.001
Smoking		
Never	1.000	
Former	0.938(0.737,1.195)	0.605
Current	0.949(0.830,1.085)	0.444
Alcohol		
Never	1.000	
Former	1.031(0.801,1.327)	0.813
Current	0.839(0.733,0.959)	0.010
Vigorous Exercise‡	0.894(0.823,0.972)	0.009
Regular meals ‡	1.070(0.971,1.179)	0.171
Family history of diabetes ‡	1.117(0.982,1.271)	0.092

418 Occupation type: Professional occupation: researcher, doctor, teacher, administrative leader and office
419 staff; manual worker: commerce or serviceman, farmer, fisherman, soldier and workman; student:
420 current student.

421 BMI: body mass index.

422 Blood Pressure (mmHg): SBP: systolic blood pressure; DBP: diastolic blood pressure; Normal: SBP<130,

423 DBP<85; High Normal: 130≤SBP<140, 85≤DBP<90; Grade 1 Hypertension: 140≤SBP<160, 90≤DBP<100;

424 Grade 2 Hypertension: 160≤SBP<180, 100≤DBP<110; Grade 3 Hypertension: SBP≥180, DBP≥110;

425 Isolated systolic hypertension: SBP≥140, DBP<90(41).

426 HDL: high-density lipoprotein.

427 LDL: low-density lipoprotein.

428 ‡p-value for comparison between No Data or No VS Yes.

429 Adjusted by continuous age variable, gender and BMI, the significance of differences at p-value < 0.05.

430

431 **Table 3. Participants with/without hypoglycaemia in Low Post Load group**

	With hypoglycaemia N=80(2.12%)	Without hypoglycaemia N=3,693(97.88%)	P-value
	Mean ± SD / N(%)	Mean ± SD / N(%)	
Age(years)	42.68(14.42)	46.68(12.64)	0.016
Gender(Female)	27(33.75%)	2,109(57.11%)	<0.001
Ethnicity(Han)	11(13.75%)	1,579(42.76%)	<0.001

Education Levels(illiteracy)	3(3.75%)	271(7.34%)	0.315
Occupation Type			<0.001
Professional	3(3.75%)	708(19.17%)	
Manual-worker	73(91.25%)	2,931(79.37%)	
Student	4(5.00%)	54(1.46%)	
Body mass index(kg/m²)	23.47(3.04)	24.18(3.66)	0.041
SBP (mmHg)	125.8(17.75)	128.1(19.91)	0.304
DBP (mmHg)	76.49(11.56)	79.54(12.05)	0.025
Heart rate (beats/min)	76.43(12.15)	77.29(11.15)	0.492
Total cholesterol(mmol/L)	5.00(1.17)	4.92(1.11)	0.515
HDL cholesterol(mmol/L)	1.69(0.48)	1.61(0.40)	0.148
LDL cholesterol(mmol/L)	2.83(0.85)	2.76(0.82)	0.510
Triglycerides(mmol/L)	1.15(0.90)	1.35(1.48)	0.053
Smoking			0.009
Never	50(62.50%)	2,823(76.44%)	
Former	3(3.75%)	132(3.57%)	
Current	27(33.75%)	738(19.98%)	
Alcohol			0.200
Never	53(66.25%)	2,668(72.24%)	
Former	2(2.50%)	166(4.49%)	
Current	25(31.25%)	859(23.26%)	
Vigorous Exercise	34(42.50%)	1,386(37.53%)	0.364
Regular meals	60(75.00%)	2,724(73.76%)	0.803
Family History of diabetes	10(12.50%)	486(13.16%)	0.863
Hypoglycaemic drugs use	0(0.00%)	4(0.11%)	1.000
Self-report liver disease	1(1.25%)	64(1.73%)	1.000
Self-report pancreatic disease	0(0.00%)	1(0.03%)	1.000
Self-report upper digestive track disease	0(0.00%)	32(0.87%)	1.000
FPG(mmol/L)	5.13(0.53)	5.44(0.56)	<0.001
PPG(mmol/L)	2.49(0.30)	4.64(0.78)	<0.001
Difference(2hPPG-FPG)	-2.64(0.70)	-0.81(0.65)	<0.001
HbA1c(%)	5.22(0.54)	5.31(0.42)	0.171
Status (WHO1999)			0.004
NGT	79(98.75%)	3,230(87.46%)	
IFG	1(1.25%)	463(12.54%)	
IGT	0(0.00%)	0(0.00%)	
IFG+IGT	0(0.00%)	0(0.00%)	

432 Data are presented as n, n(%), mean±SD or median(IQR).

433 Occupation type: Professional occupation: researcher, doctor, teacher, administrative leader and office

434 staff; manual worker: commerce or serviceman, farmer, fisherman, soldier and workman; student:

435 current student.

436 BMI: body mass index.

437 SBP: systolic blood pressure.

- 438 HDL: high-density lipoprotein.
- 439 LDL: low-density lipoprotein.
- 440 FPG: fasting plasma glucose.
- 441 PPG: postprandial plasma glucose.
- 442 HbA1c: haemoglobin A1C.
- 443 Significance of differences at p-value < 0.05.