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1 A Slow-Digesting, Low-Glycaemic Load (SD-LGL) Nutritional Beverage
2 improves glucose tolerance in obese pregnant women without Gestational
3 Diabetes
4
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24
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27

28 Background: Obesity is a risk factor for gestational diabetes. Low glycaemic
29 index diets attenuate hyperglycaemia. We designed a study to determine
30 whether a slow-digesting low-glycaemic load (SD-LGI) beverage improves
31 glucose tolerance in obese pregnant women without gestational diabetes
32 (GDM).

33

34 Methods: This was a 3-arm comparison study comparing the effects of a SD-
35 LGL nutritional beverage (glycaemic load [GL] 730), an isocaloric control
36 beverage (GL 1124) and habitual diet on glycaemia in obese pregnant
37 women. Sixteen women (mean BMI 37kg/m^2) were recruited at 24-28 weeks'
38 to receive either the SD-LGL or eucaloric control beverage. This was
39 consumed with breakfast and as a mid-afternoon snack over 2 days with a
40 controlled diet. Following a 2-day washout period of habitual diet, women
41 completed 2 days on the alternative beverage with controlled diet. A 10h fast
42 preceded each intervention phase. 24h glucose was measured using
43 continuous glucose monitoring.

44

45 Results: Consumption of the lower glycaemic load beverage was associated
46 with improved measures of glycaemia, compared to the control beverage and
47 habitual diet at different time periods. Glucose estimates for control v SD-LGI
48 at 24h (0.23mmol/l [0.16 to 0.31], $p<0.001$), daytime (0.26mmol/l [0.18 to
49 0.34], $p<0.001$) and night time (0.05mmol/l [-0.01 to 0.11] ($p=0.09$). Post-

prandial glucose (PPG) was lower after breakfast but not after dinner, compared to the control beverage (0.09mmol/l [0.01 to 0.18], p=0.03).

Conclusion: A slow digesting low glycaemic nutritional beverage may facilitate improved glucose control in obese pregnant women. To address potential benefit for clinical outcomes, a randomised controlled trial is warranted.

75 Introduction

76

77 Obese women have a 2-4 fold increased risk of developing gestational
78 diabetes (GDM) [1] and maternal body mass index (BMI) is recognized as the
79 strongest potentially modifiable predictor of GDM [2]. Aberrant glucose
80 homeostasis is evident even amongst obese pregnant women who do not
81 meet the most rigorous of criteria for GDM diagnosis; in these, continuous
82 glucose monitoring (CGM) has revealed a delayed and greater post-prandial
83 peak glucose concentration (at 1h and 2h) [3, 4]. Fasting and post-prandial
84 glucose concentrations are also positively associated with greater fetal fat
85 mass in infants of obese women without GDM [5].

86

87 Rising rates of obesity combined with lower glucose thresholds for diagnosis
88 of GDM as recommended by the International Association of Diabetes
89 Pregnancy Study Groups (IADPSG), World Health Organisation (WHO) and
90 American Diabetes Association (ADA) has led to a tripling of incident cases [6,
91 7] necessitating a review of traditional therapeutic approaches to the
92 prevention and management of GDM.

93

94 Throughout pregnancy, obese women have greater concentrations of plasma
95 insulin, triglycerides (TGs) and free fatty acids (FFAs) compared to lean
96 controls, contributing to the multifactorial common pathway of insulin
97 resistance [5]. Thus dietary strategies designed to reduce these biomarkers and
98 postprandial hyperglycaemia from an early stage in obese pregnant women

99 provide a novel and logical approach to improve glucose control and avoid
100 adverse pregnancy outcomes.
101
102 Data from two systematic reviews are inconclusive to support universal
103 recommendation of low glycaemic index (LGI) diets to prevent or treat GDM
104 but have yielded important information regarding the safety of the approach [8,
105 9]. Overall, pregnancy outcomes in LGI dietary RCTs have been unchanged
106 but reported maternal benefits include reductions in gestational weight gain [10],
107 adiposity [11], plasma glucose concentration [10] and progression to insulin
108 therapy [12].
109
110 In this study, we undertook a proof of principle, 3-arm randomised comparison
111 study in obese pregnant women without GDM to evaluate the effects of a
112 slow-digesting low glycaemic load (SD-LGL) beverage on measures of
113 glycaemic control using continuous glucose monitoring (CGM) and selected
114 biomarkers implicated in the pathogenesis of insulin resistance. Comparison
115 was made to a control beverage composed of rapidly digesting carbohydrate
116 CHO and habitual diet.
117
118 RESEARCH DESIGN AND METHODS
119
120 Subjects and recruitment
121 Obese pregnant women (BMI≥30Kg/m^2) with a singleton pregnancy and no
122 history of GDM attending antenatal clinics at Guy's and St. Thomas' NHS
123 Foundation Trust, London, UK, were recruited at 24^{+0}-28^{+6} weeks' gestation,

124 prior to routine 75g oral glucose tolerance test (OGTT) at 28 weeks'.
125 Exclusions included any dietary intolerance, eating disorder and medical
126 conditions known to independently influence weight, body composition or
127 biochemistry. To exclude undiagnosed type 2 diabetes or impaired fasting
128 glycaemia (IFG) subjects were excluded if fasting plasma glucose was
129 ≥6.1mmol/l at first visit. Ethical approval was granted by the Riverside
130 Research Ethics Committee, London, UK (Integrated Research Applications
131 System [IRAS]: 12/LO/0307). An online database was designed and managed
132 by Medscinet® (www.medscinet.net).
133

134 A preliminary study was performed to examine the glycaemic effect
135 (determined by incremental area under the curve [iAUC]) and assess the
136 palatability of 2 SD-LGL beverages (71.6% of total CHO) compared to a
137 eucaloric control composed of rapid digesting CHO (100% of total CHO) in 4
138 categories of women (n=10 per group): lean non-pregnant (BMI ≥18.5-
139 ≤24.9kg/m^2), obese non-pregnant (BMI ≥30kg/m^2), lean pregnant (pre-
140 pregnancy BMI ≥18.5-≤24.9kg/m^2) and obese pregnant (pre-pregnancy BMI
141 ≥30kg/m^2). The beverage selected for this study achieved the lowest glucose
142 iAUC and greatest palatability scores across all groups of women (see
143 Appendix).
144

145 Pre-study visit and randomisation

146 Subjects were naïve to CGM technology thus a pre-study visit including a trial
147 wearing the sensor (Abbott FreeStyle® Navigator, Alameda, CA, USA) was
148 undertaken. Computerised randomisation, using the SQL Server

149 Randomisation function integrated in the online study database was adopted
150 and concealed until the study day.
151
152 Study Protocol
153 This was a 3-arm randomised comparison design. Study visits were held in a
154 clinical research facility (CRF) equipped with a metabolic kitchen, a research
155 dietician and physician. The study was performed over 6 consecutive days
156 divided into three 48h periods with CRF visits on days 1 and 5:

157 - Days 1- 2 test/control beverage
158 - Days 3-4 habitual diet
159 - Days 5-6 test/control beverage

160
161 Preparation instructions for test days included example menus for a 30-50g
162 CHO meal with overnight fast from 2200h.
163
164 All meals and snacks including the nutritional beverages (packaged in
165 standard drink cartons) for days 1-2 and 5-6 were provided. Women were
166 advised to consume their normal diet during the washout period with no
167 restriction to physical activity levels.
168
169 Empty food packets and drink cartons were returned and a food and physical
170 activity diary completed. This was reviewed with the dietician at each CRF
171 visit.
172

173 Day 1-2. Following CGM calibration and fasting venous blood sampling, the
174 prescribed breakfast and test/control beverage were consumed, and venous
175 sampling then carried out every 15 minutes for 3.5h. The importance of
176 adherence to the controlled diet until midnight on day 2 was reiterated.
177
178 Day 3-4. The habitual diet was adopted until 2200h on day 4, after which
179 participants fasted in preparation for day 5.
180 Day 5-6. The prescribed breakfast and the beverage (cross over: control if
181 previously test, test if previously control) were consumed with venous
182 sampling as above at the CRF. The controlled diet together with the
183 test/control beverage was consumed until midnight on day 6.
184
185 Subjects were excluded from data analysis if non-adherence to the controlled
186 diet was identified from CGM downloads (n=3).
187
188 Dietary Protocol
189 Macronutrient composition and caloric value were equivalent for the test and
190 control beverage (percentage total energy (%E) CHO 60.7%, fat 20.8%,
191 protein 18.5%; total energy and 303Kcal/8oz carton/24-h) (Table 1), in line
192 with dietary recommendations from the American Diabetes and Heart
193 Associations for prevention of diabetes and reduction of cardiovascular risk in
194 non-pregnant subjects [13, 14]. The concentration of CHO sub-groups, known to
195 affect absorption differed significantly, with the test product composed of more
196 slow-digesting, low-GL carbohydrates (SG-LGL) (72% v 0%), less rapid
197 digesting CHO (8.4% v 100%), resistant starch (16.3%) and indigestible fiber

198 (3.7%). The glycaemic load (GL) of the test and control beverages was 730
199 and 1124 respectively.
200
201 Beverages were provided in 8oz (237ml) cartons; 4oz consumed with
202 breakfast and 4oz as an afternoon snack (1500h). Addition of the nutritional
203 beverage to the controlled diet did not exceed recommended daily energy
204 requirements for the gestational age range of participants (24h total calorie
205 content 2014kcal inclusive of beverage) [15].
206
207 A standardised diet with a low residue and medium dietary GI reflecting the
208 "average UK diet" [16] was provided for the two 48 hour controlled periods (days
209 1-2 and day 5-6). On days 1 and 5, breakfast and lunch were provided in the
210 CRF with remaining food and study beverages measured out by research
211 staff. Women were advised to eat at similar times on each day.

212 Menu choices developed by the research dietician using standard food tables
213 and WISP® (Tinuviel) dietary software are supplied in the appendix.
214
215 Continuous Glucose Monitoring
216 The CGM sensor was inserted on day 1 (0800h) and replaced on day 5
217 (0800h). Mandatory calibrations (1, 2, 10, 24 and 72h) were performed using
218 the inbuilt capillary glucometer and interstitial glucose measured every 10
219 minutes for the duration of the study. For analysis of post-prandial glucose
220 (PPG) glucose response, subjects were required to enter all meal times into
221 the receiver, excluding the washout period when habitual data was recorded.
222 CGM data was downloaded using the CoPilot® Health Management System

223 (Abbott Diabetes Care, Alameda, CA USA) and checked by 2 diabetes
224 physicians.
225
226 Plasma analyses
227 Plasma insulin and C-peptide were measured at 15 time points (0-3.5h) and
228 analysed using manual ELISA kits (Mercodia, Uppsala, Sweden). Plasma
229 triglyceride and non-esterifed fatty acid (NEFA) concentrations were
230 measured in plasma samples (0, 60, 120, 180, 210 min) using a clinically
231 validated automated platform (Clinical Analyser ILab 650, Instrumentation
232 Laboratories, Warrington, UK) using IL Triglyceride and Randox (FA115) kits.
233
234 All standards, controls and samples were assayed in duplicate and quality
235 control (QC) was performed. The inter-assay coefficient of variation for all
236 assays was <5%. Analyses were performed on previously unthawed EDTA
237 and samples stored -80°C. Technical staff were blinded to the identity of the
238 samples.
239
240 Analysis and Statistical power
241 Linear mixed model regression method including trigonometric terms up to
242 order k=3 was employed in the CGM data analysis to take into account the
243 high intra-day variability and non-linear structure of CGM data. A linear mixed
244 model (LMM) assuming a normally distributed error term was fitted to the
245 data. Further addition of a random effect within the model to take into account
246 study period (hospital v home) and randomisation were assessed using the
247 likelihood ratio test. CGM data was analysed in clinically relevant time periods

248 for each 48h test phase as follows: 24h (0630h-0630h), daytime (0630h to
249 2350h), night-time (0000h to 0620h [one night only]), fasting blood glucose
250 (0600h to 0650h [one day only]) and post-prandial (1h, 2h and 3h after the
251 meal marker).

252

253 Logarithmic transformations were performed for insulin and C-peptide only,
254 following standard distributional checks.

255

256 All analyses were carried out at a 5% significance level using SPSS version
257 19 & Stata, version 11.2 (StataCorp, College Station, Texas) and 95%
258 confidence intervals were obtained for the estimates.

259

260 The study protocol recommended that 22 subjects be
261 randomised, conservatively assuming a correlation of no more than 0.3
262 between repeated measurements of glucose. However, as initial analyses
263 demonstrate a correlation of 0.7, a decision was made to recruit 16 subjects,
264 giving a power of 96% to detect a difference in glucose between test and
265 control beverage with 95% confidence ($p<0.05$).

266

267 Results

268 Analysis was performed with data from 16 subjects randomised to receive the
269 test or control beverage at the first visit [(BMI 37kg/m^2, range 31-46, SD 4.7)
270 (age 31 years, range 21-39, SD 4.8)]. Twelve were of Black ethnicity, 2 White
271 European and 2 of unclassified ethnicity. Three subjects were excluded from

272 analysis: 2 for non-adherence to the controlled diet (n=2) and 1 who was
273 unable to wear the sensor.
274
275 When considering the overall performance of the supplement throughout the
276 study period (2 days and one night), the glucose curve derived from the LMM
277 was lower than both habitual diet and control periods as shown in (Figure 1A).
278 Glucose estimates for habitual diet and control days were significantly greater
279 ($p<0.001$ for both) (Table 2).
280
281 Estimates of 24h mean glucose concentration for study day 1, 2 and 5 were
282 lower for the test beverage compared to the control. On the final day, day 6,
283 no difference was found (day 1: 4.56 v 4.68 mmol/l, $p<0.001$, day 2: 4.75mmol
284 v 4.84mmol/l, $p=0.001$, day 5: 4.47 v 4.73, $p<0.001$ and day 6: 4.72 v
285 4.78mmol/l, $p=0.51$).

286 Predicted mean blood glucose concentrations were consistently lower for the
287 test beverage throughout the day (Figure 1B), with the estimates for the
288 habitual diet (0.25mmol/l [0.19 to 0.31], $p<0.001$) and control beverage
289 (0.04mmol/l [0.18 to 0.34], $p<0.001$) being significantly greater than the test
290 beverage (Table 2). No difference was observed between glucose estimates
291 measured in the CRF versus home study days (-0.02mmol/l [-0.08 to 0.04],
292 $p=0.54$).
293
294 Review of CGM downloads in association with the food diaries indicated lack
295 of adherence to the protocol, with uncontrolled food consumption after
296 midnight on the 2nd night of each 48h test period. This data was excluded

297 and analysis of nocturnal data included the 1st night only (day 1 and day 5).
298 No difference was observed overnight between the test and control beverages
299 overnight (p=0.09) but glucose concentrations were significantly greater
300 during the habitual period compared to the test beverage overnight (p<0.001)
301 (Table 2) (Figure 1C).
302
303 Analysis of fasting glucose (0600-0650h) demonstrated a reduction in glucose
304 estimates until 0620h (before breakfast) for the test, control and habitual
305 phases, with a progressive rise thereafter (Figure 1D). Fasting CGM
306 concentrations recorded over this 50 minute period were significantly lower for
307 the test beverage compared to the habitual period (p<0.001) but no different
308 to the control (p=0.22) (Table 2).
309
310 Postprandial data (up to 3h) excluded the habitual washout period since
311 women were not requested to record meal markers. Glucose concentration
312 was significantly lower following consumption of the test beverage at
313 breakfast only (p=0.03) (Table 2). Postprandial glucose (PPG) concentrations
314 were generally lower on hospital days in the CRF compared to the second
315 day at home for all meals in both arms (breakfast p<0.001, lunch p=0.80 and
316 dinner p=0.43) (Table 2).
317
318 Linear regression analysis found no detectable effect of the test beverage
319 compared to control for concentrations of plasma insulin, C-peptide and TGs
320 (Table 3). A marginally higher concentration of plasma NEFA was observed

321 following the test supplement (difference in arithmetic means 0.05 [95%CI
322 0.00 to 0.10], p=0.049).
323
324 Conclusion
325
326 We tested two dietary beverages of identical macronutrient composition as
327 part of a calorie-controlled diet in obese pregnant women considered to be at
328 high risk of GDM. The supplements differed only by CHO composition (Table
329 1).
330
331 Using CGM, we demonstrated that consumption of a SD-LGL beverage,
332 specifically developed for use in pregnancy, significantly reduced glucose
333 concentration over a 24 hour period in addition to day and night periods when
334 examined separately, compared to habitual living (p<0.001 for all).
335
336 Numerous factors including meal composition, pre-meal glucose
337 concentration, physical activity, insulin secretion, gastric emptying and hepatic
338 glucose metabolism determine post-prandial glucose (PPG). Hence, the
339 reduction in PPG observed following traditional CHO restriction, may be
340 explicable only in part by the lower total CHO load. Since the rate of gastric
341 emptying is delayed by fat, the observed increase in percentage energy from
342 fat to approximately 45% following traditional dietary strategies recommended
343 by the American College of Obstetricians and Gynaecologists [17], will
344 undoubtedly influence PPG concentration [18]. We demonstrated improvements
345 in PPG concentrations without a reduction in CHO load or increase in

346 percentage of energy from fat, excluding this mechanism as a confounder and
347 thus supporting an independent role of CHO modification. Importantly in this
348 obese population, the addition of the nutritional supplement to the controlled
349 diet did not exceed recommended daily energy requirements for the
350 gestational age period studied [15].
351
352 Consensus methodology for the calculation of GI, requires the measurement
353 blood glucose 120 minutes after food consumption.[19] Recent use of CGM in
354 GI studies has revealed potential limitations of this long-standing approach.
355 Following the consumption of mixed meals, Chlup et al. confirmed changes in
356 glycemia exceeding 120 minutes with a prolonged return to baseline glucose
357 at 210 minutes and beyond [20]. In this study we evaluated the effect of the 2
358 beverages on PPG to 180minutes. With the advantage of this minimally
359 invasive approach, inclusion of CGM in future dietary studies may yield
360 important novel information on the impact of different food groups on PPG.
361
362 Post-prandial glucose was significantly lower following the test beverage
363 compared to the control and habitual diet at breakfast. Clinically, this presents
364 the most challenging period to achieve adequate glycaemic control for women
365 with diabetes in pregnancy due to the physiological secretion of insulin
366 counter-regulatory hormones coupled with high concentrations of processed
367 CHO contained in breakfast foods [21]. This often results in the use of higher
368 insulin doses, associated with greater risks of hypoglycaemia or the practice
369 of excluding CHO from the meal entirely, a potentially challenging option
370 typically resulting in greater fat consumption. Increased concentrations of

371 maternal TGs and NEFA, correlated with dietary intake, are strong predictors
372 of excess fetal fat accretion [5, 22], therefore therapeutic interventions utilising
373 resistant or LGL CHO to attenuate postprandial hyperglycaemia, which also
374 limit dietary fat, may have a role not only in the management of diabetes in
375 pregnancy but also in obese non-diabetic pregnant women who have a 2-5
376 fold increased risk of delivering a large for gestational age (LGA) infant [23].
377
378 Obese pregnant women are at increased risk of lipotoxicity and its metabolic
379 sequelae. This occurs as a consequence of increased hydrolysis of dietary
380 TGs and expanded adipose depots generating FFAs, contributing to insulin
381 resistance [24, 25]. Low GI and GL diets may therefore be more effective in
382 obese compared to lean women as they are likely to be more insulin resistant
383 [26, 27].
384
385 Most adequately powered studies comparing responses to dietary advice,
386 designed to increase the consumption of low GI foods in women with [28-31] and
387 without GDM [10, 29], have been carried out in women with BMI 24-27kg/m^2 with
388 equivocal results. Moses et al., reported improved obstetric outcomes (birth
389 weight, ponderal index and incidence of LGA) comparing LGI to a “high-fibre
390 moderate-to-high GI (HGI)” diet in healthy women without GDM (n=62, mean
391 BMI 25.5kg/m^2, mean GI 51 v 58 for LGI and HGI respectively) but did not
392 replicate these findings in a larger RCT (mean BMI 24.5kg/m^2) [29, 32]. In both
393 studies a relatively small albeit significant reduction in GI was achieved in the
394 intervention arm compared to the control with a greater GI point difference
395 reported in the former [29, 32].

396

397 Of those dietary advice intervention studies undertaken in women of a higher
398 BMI, the ROLO study (Low glycaemic index diet in pregnancy to prevent
399 macrosomia RCT) (mean BMI 26.8kg/m^2) reported a reduction in GL and 1h
400 glucose following a 50g glucose challenge test [10]. In the heterogeneous
401 overweight and obese population of the LIMIT trial (n=2212) (The effects of
402 antenatal dietary and lifestyle advice for women who are overweight or obese
403 on maternal diet and physical activity), a lifestyle intervention designed to
404 reduce LGA infants in overweight and obese women, general dietary advice
405 led to a small reduction in the GL but no change in the primary outcome or
406 GDM, although the number of infants with macrosomia was reduced [33]. A
407 reduction in GDM, the primary outcome, was also not met in the exclusively
408 obese UPBEAT study (mean BMI 36.3kg/m^2) but, GI and GL were reduced in
409 the intervention group as was consumption of CHO, total fat, saturated fat and
410 total energy. Daily intake of fibre and protein was increased, and gestational
411 weight gain and maternal adiposity were significantly less at the time of the
412 oral glucose tolerance test and over the entire pregnancy [11].

413 Considering the potential therapeutic benefits of low GI and GL diets in
414 pregnancy, improving glycaemic control using a low GI beverage in high-risk
415 obese women to attenuate glucose intolerance warrants further exploration.
416 Current UK National Institute for Health and Care Excellence (NICE)
417 recommendations include general dietary advice for all obese pregnant
418 women at the 1st clinical consultation (nice.org.uk/guidance/ph27) and the
419 most recent economic evaluation of non-pharmacological approaches to
420 weight management outside of pregnancy reported lower costs associated

421 with dietary compared to physical interventions [34]. This advice is generalised
422 and at present not adopted across the UK; pragmatically, therefore, we would
423 recommend habitual diet and activity as the control in future studies of LGI
424 diets in pregnancy as opposed to specific dietary recommendations for
425 'healthy eating'.

426 Using a similar design as in the present investigation, Hernandez et al.
427 conducted a study to determine whether reducing the fat content of a complex
428 carbohydrate traditional 'GDM' diet in obese pregnant women with GDM
429 would improve glucose control, using CGM in controlled and free living
430 environments [35]. No difference in mean glucose between the lower and
431 control higher fat diets were observed but the glucose AUC was significantly
432 greater in those on the lower fat diet for daytime and 24-hour periods. The
433 clinical relevance of the increase in glucose exposure reported, together with
434 the modest reductions observed in our study on pregnancy outcomes,
435 requires assessment. We found no difference following the SD-LGL beverage
436 in the concentration of relevant biomarkers (plasma insulin, C-peptide and
437 TGs) but a small increase in NEFA. It would be of interest in future studies to
438 determine whether glucose-independent pathways contributing to insulin
439 resistance, as assessed by a targeted metabolome are influenced by this
440 dietary intervention [36].

441 Limitations of the study include the small sample size and short duration. This
442 was a proof of concept study and we would recommend future studies of the
443 SD-LGI beverage extend until delivery and include evaluation of neonatal
444 outcomes. It is unclear whether the small reduction in glucose estimates

445 observed, would correspond to a clinically significant reduction in HbA1c or
446 adverse neonatal outcomes including macrosomia but analysis of alternative
447 measures of glycaemia utilising CGM is warranted.
448
449 We recruited a high number of women from Black ethnic minorities who are
450 recognised to have a significantly greater risk of GDM and type 2 diabetes
451 compared to White European women of equivalent BMI [37]. It is possible that
452 reductions in glucose observed may not be as pronounced in a Caucasian
453 population. Conversely, the results indicate that those at greatest risk of GDM
454 may stand to gain the greatest benefit, as suggested by Louie et al. [30]. OGTT
455 was not performed at recruitment therefore in the absence of biochemical
456 evidence of glucose intolerance, "high risk for GDM" was defined by BMI on
457 entry in keeping with similar LGI studies in pregnancy.

458 Participation in dietary studies may introduce a degree of bias or confounding
459 as a consequence of the "observer" or "Hawthorn effect," when individual
460 behaviours are modified in response to an awareness of being observed. In
461 this study however, the greatest differences in glycaemia were observed
462 between the test beverage with controlled diet and habitual diet for all time
463 periods examined suggesting that diet was not specifically modified on the
464 habitual days.

465 The CONCEPTT study demonstrated improvements in maternal glycaemia
466 and neonatal outcomes in women with T1DM who used CGM [38]. It is possible
467 that CGM plus dietary advice in this high risk obese population may improve

468 maternal glycaemia or reduce progression to GDM but to the best of our
469 knowledge there are no studies specifically examining this.

470 Glucose concentrations were generally lower on the 1st day compared to the
471 2nd of each 48h test period for both beverages. Visits on these days were
472 conducted in the CRF, a highly controlled environment, with limited ability to
473 exercise. This could indicate issues with non-adherence to the prescribed
474 diet on "home" days or could reflect a chance finding although several
475 methods to improve compliance were adopted: participants being requested
476 to return all empty food packets/drink cartons and complete a food and
477 exercise diary.

478 In conclusion, we have demonstrated in obese women at high risk of GDM
479 that consumption of a SD-LGL beverage when compared to habitual diet
480 reduces glucose concentration over a 24-hour period, and that this includes
481 differences during both day and night time. In contrast to previously reported
482 low GI diets in obese pregnant women, the beverage comprised both a low GI
483 CHO and slow digesting CHO, which could have additive clinical benefit. A
484 reduction in post-prandial glucose at breakfast is also of particular clinical
485 relevance. Evaluation of this dietary approach in a RCT to reduce incidence of
486 GDM in high-risk obese women is justified.

487

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Duality of Interest

B.M, C.S., J.M.L.P and R.R. are employed by Abbott Nutrition.

Author Contributions

R.M. researched data, wrote the manuscript and edited the final version. N.P., C.S., B.M, J.M.L.P., H.M., R.R. and L.P. edited and contributed to the manuscript. R.M. and S.B. designed the study protocol. P.S. and L.G.F. provided statistical analysis of the data and review of the manuscript.

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