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Authors

Analise Nicholl, Mary Du Heaume, Trevor A. Mori, Lawrence J. Beilin, Wendy H. Oddy, Alexandra P. Bremner, and Therese A. O'Sullivan

1 **Higher breakfast glyceic load is associated with increased metabolic syndrome risk,**
2 **including lower HDL-cholesterol and increased triglycerides, in adolescent girls**

3 **ABSTRACT**

4 Almost all previous studies examining associations between glyceic load (GL) and
5 metabolic risk have used a daily GL value. The daily value does not distinguish between
6 peaks of GL intake over the day, which may be more closely associated with metabolic risk.
7 We aimed to investigate cross-sectional associations between daily and mealtime measures of
8 GL and metabolic syndrome risk, including metabolic syndrome components, in adolescents.
9 Three-day food records and metabolic assessments were completed by adolescents
10 participating in the 14-year follow-up of the Western Australian Pregnancy Cohort (Raine)
11 Study. Breakfast GL, lunch GL, dinner GL and a score representing meal GL peaks over the
12 day were determined in 516 adolescents. Logistic regression models investigated whether GL
13 variables were independent predictors of metabolic syndrome in this population based cohort
14 (3.5% prevalence of metabolic syndrome). Breakfast GL was predictive of metabolic
15 syndrome in girls (OR = 1.15; 95% CI = 1.04,1.27; P<0.01) but not in boys. Other meal GL
16 values and daily GL were not significant predictors of metabolic syndrome. When breakfast
17 GL was examined in relation to each of the metabolic syndrome components in girls, it was
18 negatively associated with fasting HDL cholesterol (P=0.037; β =-0.004; 95% CI= -0.008, -
19 0.002) and positively associated with fasting triglycerides (P=0.008; $\exp(\beta)$ =1.002; 95%
20 CI=1.001, 1.004). Our results suggest that there may be a link between breakfast composition
21 and metabolic syndrome components in adolescent girls. These findings support further
22 investigation into including lower GL foods as part of a healthy breakfast in adolescence,
23 particularly for girls.

24

25 **INTRODUCTION**

26 The metabolic syndrome is a cluster of metabolic disturbances that increases the risk of
27 developing type 2 diabetes and cardiovascular disease ^(1; 2). In Australia, prevalence of
28 metabolic syndrome in adolescents has been previously reported at 3.6% using International
29 Diabetes Federation (IDF) paediatric diagnostic criteria ⁽³⁾, increasing to 22.1% in adulthood
30 (adult IDF criteria) ⁽⁴⁾. Diet is one of the factors that may have the ability to influence this
31 progression from adolescence to adulthood.

32

33 The glycemic index (GI) was developed 30 years ago with the aim of improving postprandial
34 glycemia in the diabetic population ⁽⁵⁾. The GI ranks foods or beverages on their ability to
35 raise blood glucose levels compared to ingestion of the same quantity of carbohydrate,
36 expressed as a percentage. A high GI food consumed in a small amount can have a minimal
37 impact on blood glucose concentrations, and conversely a low GI food consumed in a large
38 amount can have a major impact on blood glucose concentrations. The glycemic load (GL) is
39 a product of the quantity of carbohydrate present in food and the GI; by taking the
40 carbohydrate into consideration, it represents the total impact of the food on blood glucose
41 concentrations ⁽⁶⁾. Hence, the GL is better able to distinguish impact on postprandial glycemia
42 compared with the GI.

43

44 Habitual dietary intake of a diet with high postprandial glycemia may lead to
45 hyperinsulinemia and disturbed lipid metabolism ⁽⁷⁾, with increased risk of developing
46 metabolic syndrome ^(8; 9). Diets lower in GI/GL have been associated with improved health
47 outcomes for various metabolic risk factors and chronic diseases in studies and meta-analyses
48 ^(10; 11; 12). Other studies have not found significant associations between low GI/GL diets and
49 reduced risk of diabetes ^(13; 14), perhaps in part because the use of daily values has some
50 limitations in representing metabolic processes resulting from habitual dietary carbohydrate
51 intake over the course of the day ⁽¹³⁾. Studies investigating associations with dietary GI and
52 GL often use food frequency questionnaires, which can estimate daily GI/GL but not
53 individual meal values. We identified two studies which were able to assess meal values
54 using either a food record (Hong Kong children aged 6-7 years ⁽¹⁵⁾) or diet history (older
55 Australian women ⁽¹⁶⁾). The latter considered a new measure of high glycemic carbohydrate
56 impact, the GL peak score, based on the summation of individual mealtime GLs that scored a
57 peak above the daily GL mean ⁽¹⁶⁾. To date, no published adolescent studies appear to have

58 examined mealtime patterns of glycemic impact, including investigation of periods when GL
59 intake may peak substantially.

60

61 Determining patterns of carbohydrate intake may provide insight into potential glycemic
62 impacts for adolescents, who are also undergoing the stresses of growth, and metabolic and
63 hormonal changes. In this explorative study, we aimed to investigate mealtime measures of
64 GL intake in relation to metabolic syndrome risk, as well as components of the metabolic
65 syndrome, in the 14-year follow-up of the Western Australian Pregnancy Cohort (Raine)
66 Study in Perth, Western Australia. We hypothesised that individual meal GL values and a
67 score representing peaks in meal GL would be better predictors of metabolic syndrome risk
68 than a daily GL value.

69

70 **RESEARCH DESIGN AND METHODS**

71 **Study population**

72 This study is a cross-sectional analysis of adolescents who participated in the 14-year follow-
73 up of the Raine Study. As previously described ⁽¹⁷⁾, 2900 pregnant women were enrolled in a
74 controlled trial from public and private antenatal clinics at or near King Edward Memorial
75 Hospital in Perth, Western Australia between May 1989 and November 1991. The resulting
76 2868 children were recruited for cohort follow-up. The 14-year follow-up (mean age 14.0 ±
77 0.2 years, age range 13.0–15.0 years) occurred from 2003 to 2005, and was the first to collect
78 comprehensive dietary data allowing nutrient analysis of individual meals in habitual diet.
79 Adolescents with type 1 or type 2 diabetes mellitus or implausible energy intakes (< 3000 or
80 > 20 000 kJ/day, as previously used in studies of adolescents ^(18; 19)) were excluded from the
81 study. Informed written consent for the 14-year follow-up procedures was provided by study
82 participants and a parent/guardian, and approval was obtained from the ethics committees of
83 King Edward Memorial Hospital and Princess Margaret Hospital for Children.

84

85

86 **Dietary glycemic intake assessment**

87 Three-day food records were completed by the adolescents, with parental support if
88 requested. Intakes were recorded in household measures. Subjects were provided with written
89 and verbal instructions, as well as metric measuring cups and spoons. Consumption away
90 from home was recorded in relation to serve size (for example, two slices of a large pizza or
91 one Whopper hamburger) or estimated in household measures. A checklist ascertained
92 whether each of the three days recorded was typical of the subject's usual intake, and only
93 those records completed and classified as representative were used. A dietitian checked each
94 food diary as it was returned and sought clarification via follow-up telephone calls ⁽²⁰⁾. Food
95 record data were entered into FoodWorks dietary analysis software (Professional Version
96 4.00, Xyris Software, Brisbane, Queensland, Australia). Food composition data that were not
97 available through FoodWorks were obtained from a Australian nutrition website with a
98 customized GI database ⁽²¹⁾. Where GI values for a specific product were not available, the GI
99 value was imputed from a product or subgroup of products that was assessed by the
100 researchers to be sufficiently similar in terms of type of starch, molecular monosaccharide
101 components, ingredients, including amounts of protein and fat, amount of dietary fibre
102 present, and degree of cooking or processing. If a product was too specialised to be a good

103 match, (for example, a specific type of body building powder) no GI value was given. GI
104 values for mixed foods and recipes were estimated from component foods, for example, the
105 GI for trifle was based on a weighted GI calculation of the carbohydrate containing
106 ingredients (sponge, jelly and custard). The formula used to calculate the composite GI of
107 meals based on relative weighting of carbohydrate content does not take into account the
108 effect of the whole dish, and there is likely to be a variable loss of discrimination of
109 individual GI values in composite foods.

110

111 To ensure that food records were representative, 80% or more of the total daily dietary
112 carbohydrate required an assigned GI value for the record to be included. GL values for
113 individual meals comprised the sum of GL values for all foods and beverages in that meal.
114 Meal GL values were obtained by averaging the values for each particular meal over the three
115 days recorded, to produce daily breakfast, morning tea, lunch, afternoon tea, dinner and
116 supper GL values for each subject. Limited availability of GI values may affect the results of
117 studies examining associations between GI/ GL and chronic disease, particularly when local/
118 traditional foods are involved. In our cohort, GI values were able to be assigned to 92% of all
119 carbohydrate foods and beverages ⁽³⁾. This meant that for some subjects, carbohydrate foods
120 or beverages in a meal were not able to be allocated a GI value. Non-allocation of a GI
121 meant the contribution of these foods or beverages to the GL for the meal was unable to be
122 calculated (despite having a likely effect on blood glucose levels). To ensure that the GL
123 values we were using were as representative as possible of the food being consumed, we
124 decided that 80% or more of the dietary carbohydrate per meal should be assigned a GI value
125 in order for the meal GL to be used in the study. This was based on methods used in previous
126 research and professional opinion of clinical relevance, whereby a value of lower than 80%
127 was thought to potentially compromise the validity of the data ⁽³⁾. Subjects were excluded if
128 this meant that two or more meals of the same type (eg breakfast) out of the three-day record
129 period did not have usable GL values.

130

131 Mean breakfast GL, morning tea GL, lunch GL, afternoon tea GL, dinner GL and supper GL
132 values were calculated for each subject where possible. Together with the mean meal GL (the
133 mean of the above six meal GLs), these were used to produce the peak score GL. Meal peak
134 GL values were calculated for each subject by subtracting the mean meal GL from each meal
135 GL value, and are represented graphically as a set of positive and negative peaks with the

136 mean set to zero. Peak score GL was calculated by adding all the positive meal peak values
137 ⁽¹⁶⁾ (see **Figure 1**). For the purposes of this study, we investigated five GL variables: 1)
138 breakfast GL, 2) lunch GL, 3) dinner GL, 4) peak score GL, 5) daily GL.

139

140 **Metabolic syndrome definition**

141 Prevalence of metabolic syndrome in this adolescent cohort at the 14-year follow-up has
142 previously been reported as 3.6% or 4.0% ⁽³⁾, using age-specific adolescent definitions from
143 the IDF and the National Cholesterol Education Program Adult Treatment Panel III
144 respectively ⁽²²⁾. While no consistent adolescent definition for the metabolic syndrome exists,
145 the American Heart Association recommends using the IDF paediatric definition for
146 adolescents ⁽²³⁾, and this has been used in the current study. The IDF metabolic syndrome
147 definition requires the presence of a high waist circumference in addition to two or more of
148 the following: high systolic or diastolic blood pressure; high fasting serum triglycerides; low
149 fasting serum high-density lipoprotein (HDL) cholesterol; or high fasting plasma glucose
150 concentrations. Cut points for categorization of these high and low subgroups vary by gender
151 and age, as published previously ⁽²²⁾. A research nurse took at waist measurements at the level
152 of the umbilicus from adolescents standing in the anatomical position, to the nearest 0.1 cm
153 until two readings were within a centimetre of each other. Phlebotomists visited adolescents
154 at their homes to obtain fasting blood samples. Serum glucose was measured using an
155 automated Technicon Axon Analyzer (Bayer Diagnostics, Sydney, NSW, Australia),
156 triglycerides were measured using the Cobas MIRA analyser (Roche Diagnostics, Basel,
157 Switzerland), and HDL-C was determined on a heparin–manganese supernatant. PathWest
158 Laboratories at Royal Perth Hospital conducted the biochemistry assays. Six measurements
159 seated blood pressure readings were taken at rest over a 10-minute period using a Dinamap
160 ProCare 100 automatic oscillometric recorder (GE Healthcare Technologies, Rydalmere,
161 NSW, Australia). The first measurement was disregarded, and the mean of the next five
162 measurements was calculated to give diastolic and systolic blood pressure values.

163

164 **Potential confounding variables**

165 Information regarding potential confounding variables was collected from adolescents
166 themselves and their parents/guardians ⁽³⁾. Information on physical and sedentary activity was
167 assessed by time spent outside school hours participating in physical activity that caused

168 breathlessness or sweating (categorized as less than once a week = low exercise, once to three
169 times a week = moderate exercise, or four times or more per week = high exercise), and time
170 spent watching television/videos and using computers for school, work and recreation
171 (categorized as less than two hours per day = low screen use, two to four hours per day =
172 moderate screen use, or over four hours per day = high screen use). These variables were
173 combined into a five category summary variable, which ranged from low screen use with
174 high exercise to high screen use with low exercise. Family characteristics including family
175 structure, family income, maternal age, maternal education and family history of diabetes and
176 cardiovascular disease were supplied by parental report. The Tanner stages of pubic hair
177 development was used to assess puberty status in the cohort ^(24; 25). Adolescents were asked to
178 select their corresponding developmental stage from a set of standard drawings depicting
179 Tanner stages two (sparse) to five (adult), in a privately completed questionnaire. Stage one
180 was omitted as an option as this corresponds to a pre-pubescent period (<10 years of age).
181 Dietary variables considered as potential confounding factors in the models included average
182 daily intakes of total energy, total fat, saturated fat, and protein. Body mass index (BMI),
183 calculated as weight in kilograms divided by height in meters squared, was also considered.
184 Trained researchers measured weight to the nearest 100 g using a Wedderburn Digital Chair
185 Scale, and height to the nearest 0.1 cm with a Holtain Stadiometer. Due to the narrow age
186 range in the 14-year follow-up, age was not considered as a confounding factor.

187

188 **Statistical analysis**

189 Nutrient intakes, including GL measures, were adjusted for total energy using the residuals
190 method to control for confounding and reduce extraneous variation ⁽²⁶⁾. Continuous measures
191 were expressed as mean \pm standard deviation. Student's independent sample t-tests, Mann-
192 Whitney U-tests and Chi-square tests were used to compare subject characteristics between
193 included and excluded adolescent populations. Logistic regression models were used to
194 analyse the relationship between mealtime GL measures and metabolic syndrome, adjusted
195 for potential confounding variables and split by gender (due to significant interaction effects
196 between sex and GL measures). Potential confounding variables were tested in the models.
197 Nagelkerke R² values were compared between models, with increasing values indicating
198 better fit ⁽²⁷⁾. Variables were retained as confounders in the model if they were significant or
199 improved the fit of the model. Models were fitted with and without BMI to allow

200 comparisons, because BMI is associated with the metabolic syndrome - the definition of
201 metabolic syndrome includes waist circumference. Odds ratios (ORs) and 95% confidence
202 intervals (CIs) were obtained for all variables. Where GL measures were found to be
203 significant predictors of metabolic syndrome, regression models were used to examine
204 associations with continuous measures of metabolic syndrome components (waist
205 circumference, blood pressure, fasting serum triglycerides, fasting HDL-cholesterol and
206 fasting plasma glucose). Components were logged as required to normalise data. BMI was
207 included in each of these analyses, with the exception of waist circumference. No
208 mathematical correction was made for multiple comparisons. Statistical analyses were
209 performed using the Statistical Package for Social Sciences (SPSS Statistics for Windows,
210 version 19.0, IBM corp, New York, USA) and tests used a significance level of 0.05.
211

212 **RESULTS**

213 **Study population**

214 From the original cohort of 2868 at birth, 1286 adolescents in the 14-year follow-up agreed to
215 complete the 3-day food record. Adolescents who completed the 3-day food record were
216 more likely to have older mothers, a higher family income and a lower BMI compared with
217 other adolescents in the follow-up who did not complete a food record ⁽²⁸⁾. Completed records
218 were returned by 962 subjects ⁽³⁾. Of these, 822 were considered complete and representative
219 of usual diet. Five subjects were excluded as they had diagnosed diabetes, no subjects were
220 excluded for implausible energy intakes. A total of 516 non-diabetic adolescents provided
221 records where all six meals had at least two GL values to average, and this “two-meal valid”
222 group was used in the statistical models. **Table 1** shows a comparison of subject
223 characteristics for the adolescents between the included (n=516) and excluded (n=306)
224 groups, from the total of 822 adolescents with food dairies that were considered complete and
225 representative of usual diet. Daily dietary carbohydrate intake was found to be significantly
226 higher in the excluded subject group (P=0.028).

227

228 **Mealtime glycemic carbohydrate intake**

229 Meal GL values are described in **Table 2**. Dinner was the meal with the highest GL value
230 (mean \pm SD, 44.9 \pm 20.1), followed by lunch (31.6 \pm 16.5), breakfast (30.9 \pm 14.9), afternoon
231 tea (23.9 \pm 18.6), morning tea (15.5 \pm 13.2) and supper (10.7 \pm 11.5). **Table 2** also provides a
232 breakdown of dietary intake and metabolic syndrome by mean meal GL tertile for boys and
233 girls. Boys and girls with higher mean meal GL values were more likely to have higher
234 energy adjusted carbohydrate intakes and lower protein and fat intakes when compared with
235 boys and girls with lower mean meal GL values (P<0.05). From the group of 516
236 adolescents, 480 had data available to assess metabolic syndrome, which was identified in 17
237 subjects out of 480 (3.5%). Increasing risk of metabolic syndrome with increasing mean meal
238 GL tertiles was observed in boys but not girls (**Table 2**).

239

240 **Associations with metabolic syndrome**

241 Final logistic regression models included BMI, single parent family, physical activity and
242 daily protein intake as confounding variables. The other factors investigated did not
243 contribute significantly to the fit of the models, so were not included as confounders. Results
244 of the logistic regression analyses are shown in **Table 3**; there was little difference in odds
245 ratios and significance when BMI was included or excluded as a confounder in these models.
246 Daily GL was not a significant predictor of metabolic syndrome. Breakfast GL was
247 associated with increased risk of metabolic syndrome (OR=1.15; 95% CI=1.04-1.27; P<0.01)
248 in girls. That is, for each unit increase in breakfast GL, the odds of metabolic syndrome
249 increased by a factor of 1.15 (or equivalently, by 15%). With BMI removed from the model,
250 breakfast GL was still a significant predictor (OR=1.06; 95% CI=1.00-1.12; P=0.04).
251 Breakfast GL was not a significant predictor of metabolic syndrome in boys (P=0.15). No
252 other GL values were significant predictors of metabolic syndrome. When breakfast GL was
253 examined in relation to each of the components of the metabolic syndrome in girls, it was
254 negatively associated with fasting HDL cholesterol (P=0.037; β =-0.004; 95% CI= -0.008, -
255 0.002) and positively associated with fasting triglycerides (P=0.008; β =0.002 for logged
256 triglyceride values; $\exp(\beta)$ =1.002; 95% CI=1.001-1.004). That is, for each unit increase in
257 breakfast GL there was a mean decrease in HDL cholesterol of 0.004 mmol/L and a 0.2%
258 increase in the geometric mean fasting triglyceride level.

259

260

261

262 **DISCUSSION**

263 In this study we aimed to explore mealtime measures of GL intake in relation to metabolic
264 syndrome risk as well as components of the metabolic syndrome, in 14-year old adolescents.

265 We hypothesised that meal based GL values would be better predictors of metabolic
266 syndrome risk than a daily GL value. In our group of 516 adolescents, no significant
267 association was found with daily GL values and metabolic syndrome. However, breakfast GL
268 was a significant independent predictor of metabolic syndrome in the same group. As we
269 were comparing GL values on a meal basis, we excluded adolescents where it was not
270 possible to accurately and consistently allocate meal GL values. In a previously published
271 study of the larger Raine Study cohort, a significant association was found with daily GL and
272 metabolic syndrome ⁽³⁾. It is likely that a reduced sample size meant we were no longer able
273 to detect a significant association with daily GL. We would expect a low prevalence from a
274 paediatric population cohort study rather than a clinical group, and caution must be taken
275 when interpreting the results due to low statistical power to find associations with dietary
276 components ⁽²⁹⁾. However, our current findings suggest that breakfast GL may be a more
277 sensitive predictor than daily GL in our adolescent group.

278 Breakfast GL was found to be significantly associated with odds of metabolic syndrome in
279 girls, but not in boys. This association was seen independently and dependently of BMI, so
280 BMI does not appear to mediate the observed association. To put these associations into
281 perspective, our results suggest that if an additional slice of white bread (GL = 12) were
282 added on top of the girls' existing breakfast, the theoretical associated odds of metabolic
283 syndrome would be 5.35 times greater, with an associated 95% CI of 1.60-17.6 times. It must
284 be noted that the confidence interval here is large, due in part to the low prevalence of
285 metabolic syndrome in the study group (n = 17 adolescents; n = 9 girls). Breakfast GL was
286 also found to be significantly associated with two components of the metabolic syndrome,
287 decreased fasting HDL cholesterol and increased fasting triglycerides.

288

289 Almost all previous studies using daily GI/GL values have not been able to distinguish
290 between different mealtime effects on glucose and insulin responses, and this may have
291 contributed to conflicting results on whether dietary glycemic carbohydrate intake is a useful

292 predictor of chronic disease risk^(9; 11; 12; 13; 14; 30; 31; 32; 33; 34). Our findings suggest that breakfast
293 GL may be particularly important. Blood glucose and insulin responses have been shown to
294 be proportional to breakfast GL in clinical trials^(31; 32). Bao et al.⁽³¹⁾ suggest that breakfast
295 metabolic responses may not necessarily reflect responses to other meals. In adolescents,
296 clinical trials have shown the benefits of consumption of low-GI carbohydrate at breakfast
297⁽³⁵⁾, with increased satiety and reduced consumption at an *ad libitum* lunch, while breakfasts
298 with sufficiently low-GI, multi-grain cereals may produce second meal effects that can last
299 through to lunch or beyond⁽³⁶⁾. It is possible that a low-GL breakfast may have the benefit of
300 decreasing the amount eaten at lunch (and potentially the lunch GL), thus reducing the
301 metabolic risk associated with both meals. Effects may differ by age - in older women,
302 O'Sullivan et al.⁽¹⁶⁾ showed that increasing lunch GL was significantly associated with
303 increased risk of insulin resistance, along with peak score GL.

304 We found that two components of the metabolic syndrome, decreased fasting HDL
305 cholesterol and increased fasting triglycerides, were significantly associated with increasing
306 breakfast GL. Other studies in both youth and adults have also found similar associations
307 with GL. In a randomised controlled trial involving 32 healthy 11 to 25 year olds, higher GL
308 diets were associated with lower HDL cholesterol⁽³⁷⁾. In adults, a systematic review and
309 meta-analysis⁽¹⁰⁾ concluded that reduced fasting plasma triglycerides were associated with
310 lower GL diets in adults. In an adult male population, fasting triglycerides were found to
311 increase with increasing dietary GI but not GL, while HDL cholesterol decreased with
312 increasing GL⁽³⁸⁾. Risk of developing metabolic syndrome was related to daily GI and GL in
313 Korean women (but not men), with high triglyceride and low HDL cholesterol the
314 components that were associated with high intakes. Although more research is needed to
315 expand on our findings, there are potential mechanisms to explain our results. Habitual
316 intake of high meal GLs can result in hyperglycemia, hyperinsulinemia and disturbed lipid
317 metabolism⁽⁷⁾, which have been linked to the development of chronic diseases such as
318 metabolic syndrome and consequent type 2 diabetes and heart disease^(31; 39; 40; 41). Following
319 a high peak in glucose and subsequently insulin, post-prandial hypoglycaemia is common
320 four to six hours after a high GL meal. This can stimulate counter-regulatory hormone
321 secretions that raise glucose and free fatty acids levels⁽⁷⁾. This is linked to increased levels of
322 inflammatory mediators and triglycerides, and decreased HDL cholesterol⁽⁴²⁾.

323

324 In our study we found significant associations in girls, but not in boys. Higher GL diets have
325 been previously associated with a greater risk of the metabolic syndrome in women, but not
326 men⁽⁴³⁾. Females may be more innately insulin-resistant than males due to specific sex-linked
327 gene expression, leading to changes in receptor and signalling pathways⁽⁴⁴⁾. In puberty, there
328 is a natural tendency for girls to have more fat gain relative to boys^(44; 45). Hormones in girls
329 such as oestradiol favour fat deposition while those of boys favour muscle tissue
330 accumulation⁽⁴⁵⁾. Increased oestradiol is associated with an increased subcutaneous fat
331 deposition and insulin response, and decreases fatty acid oxidation⁽⁴⁶⁾. Higher fat stores and
332 insulin levels in turn increase secretion of leptin; increased leptin leads to increased oestradiol
333 and subsequent IGF-1 (insulin-like growth factor 1), further increasing insulin secretion and
334 fat storage⁽⁴⁵⁾. Although highly speculative, the effect of hormonal surges at a key stage in
335 puberty is a possible reason for an increased sensitivity to GL in relation to metabolic risk at
336 this time.

337

338 Daily dietary protein intake was noted as an important confounding factor in the association
339 of breakfast GL with metabolic syndrome in girls. The adolescents in our study were
340 observed to consume breakfasts with a relatively high GL but low protein content when
341 compared to lunch and dinner. Increasing protein consumption at meals lowers the glycemic
342 response by delaying gastric emptying⁽⁴⁷⁾. A high-protein, low-GI diet produced a combined
343 beneficial effect attributed to reduced insulin response, increased satiety and decreased
344 energy intake in children (5 to 18 years) in the DiOGenes dietary study⁽⁴⁸⁾, while higher
345 versus lower protein intake was associated with lower waist circumference and lower LDL
346 cholesterol levels in another paediatric subset of this study⁽⁴⁹⁾. Higher protein breakfasts may
347 have the ability to attenuate high-GL responses sufficiently to reduce metabolic syndrome
348 risk. Quality protein for breakfast may lower the meal GL by promoting satiety and by
349 displacing carbohydrate. Further research is required to test this concept

350

351 **Strengths and limitations**

352 Strengths of this study include the use of three-day food records, which enabled investigation
353 of GL at a mealtime level. Our study also allowed for gender-specific analysis of the group.
354 Limitations of this study include the inability to generalise to other Western adolescent

355 populations, with the adolescents completing food records in our study more likely to have
356 lower BMIs and older mothers, and come from households with a higher annual income. In
357 reducing the sample size to 480 adolescents to ensure accurate and consistent GL meal data
358 across the three-day record, 17 remained with diagnosed metabolic syndrome, of which nine
359 were female. Subjects excluded had significantly higher intakes of carbohydrates (**Table 1**),
360 and this may have meant that some associations with higher intakes went undetected. The
361 bulk of published GI values come from Australia and the USA ⁽⁵⁰⁾, and despite the high
362 representation of Australian foods, there is a need for a larger GI database of carbohydrate
363 foods commonly consumed by younger populations, such as fast foods and snack bars.
364 Consumption of foods that did not have GI values often occurred at the same mealtime on
365 two consecutive days, which effectively removed a subject from the study each time (via the
366 previously-determined exclusion criterion requiring at least two GL values to average for any
367 one meal). Although many adolescents were removed due to our strict criteria, this method
368 helped to maintain accuracy of the data by ensuring the meal GL values represented a true
369 reflection of the foods reported. Although we attempted to minimise under- and over-
370 reporting through the use of cut-offs previously used in adolescent studies, this method is
371 imprecise and it is possible that we included adolescents in our study who were misreporting
372 their intake. It has been suggested that adolescents with higher BMIs (and therefore at higher
373 risk of metabolic syndrome) are more likely to misreport dietary intake ⁽¹⁸⁾ and this could
374 affect the associations observed. In addition, this study is a cross-sectional snapshot of the
375 prospective cohort, and as such causality cannot be established.

376

377 **Implications**

378 In this study we hypothesised that meal based GL values would be better predictors of
379 metabolic syndrome risk than a daily GL value; breakfast GL did appear to have a more
380 sensitive association. Adolescence is an important time for establishing dietary patterns into
381 adulthood, and insight into their impact on disease processes may provide meaningful data to
382 formulate dietary advice. Although we cannot determine causality from our study, it is
383 possible that the addition of low GL foods to breakfast may be beneficial for girls. Our
384 findings support previous recommendations made in this regard around consumption of a low
385 GL breakfast ^{(51) (52)}.

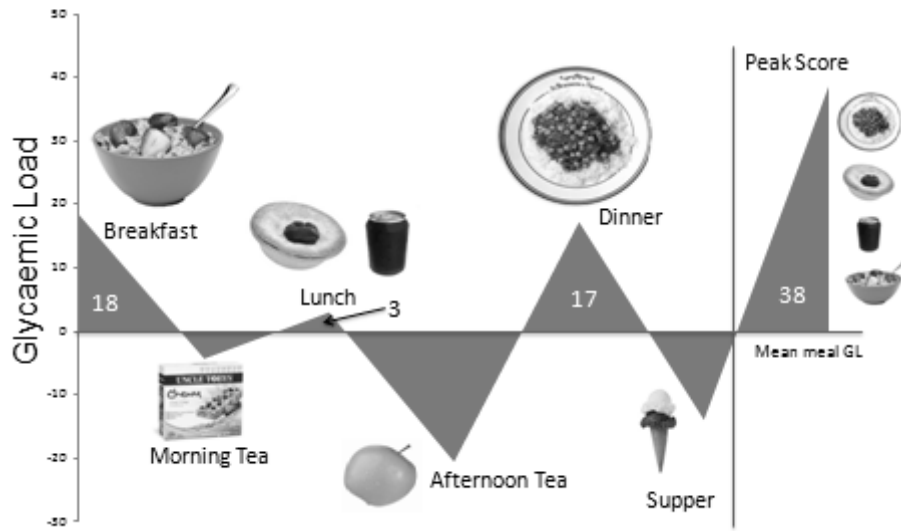
386

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400 WO, LB and TM were involved in data collection, TO'S conceptualised and supervised the
401 research, AN, MD, AB and TO'S were involved in data analysis and drafting the manuscript,
402 all authors were involved in review of the manuscript.



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406 **Figure 1.** Glycaemic load (GL) variables and food intake for a sample subject in the
407 Raine study (chosen for illustrative purposes only). The mean meal GL was set to
408 zero, producing both positive and negative peaks. For this subject, positive peaks are
409 seen at breakfast (18), lunch (3) and dinner (17). These are summed to create the peak
410 GL score, which is 38 (sum of positive peaks).

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424 **Table 1.** A comparison of adolescent subject characteristics between the populations included (minimum of
 425 two-meals with valid GL) and excluded (due to >20% dietary carbohydrate not assigned a GI, insufficient valid
 426 meal GL values, or diabetes) from the study, out of the group that returned complete and representative food
 427 diaries (n = 822)

Subject characteristics	Two-meal valid population n = 516	Excluded population n = 306	P value ^a
Characteristics			
Gender (female - n; %)	252; 48.8 %	149; 48.7 %	0.968
Weight categories ^b (n; %)			
Underweight	30; 5.8%	25; 8.2%	
Normal weight	352; 68.5%	225; 73.8%	0.053
Overweight	102; 19.9%	45; 14.7%	
Obese	30; 5.8%	10; 3.3%	
Physical activity participation (n; %)			
4+ times/week	179; 34.8 %	108; 35.4 %	
1-3 times/week	288; 56.0 %	170; 55.7 %	0.980
≤ 1 time/month	47; 9.1 %	27; 8.8 %	
Screen time – computers, TV, video (n; %)			
4+ hours/day	159; 31.2 %	94; 31.1 %	
2-4 hours/day	201; 39.5 %	126; 41.7 %	0.766
< 2 hours/day	149; 29.3 %	82; 27.2 %	
Single parent family (n; %)	97; 19.0 %	47; 15.5 %	0.210
Annual family income (pa, \$AUD) (n; %)			
< \$35 000	106; 20.9 %	63; 20.9 %	
\$35 001 - \$70 000	180; 35.6%	110; 36.5 %	0.956
> \$70 001	220; 43.5 %	128; 42.5 %	
Maternal education (n; %)			
< Year 12	240; 46.6 %	146; 47.7 %	0.758
≥ Year 12	275; 53.4 %	160; 52.3 %	
Dietary variables			
Energy (kcal/d)	2225 ± 579	2303 ± 584	0.067
Carbohydrate (g/day)	277 ± 79	291 ± 87	0.028
Protein (g/day)	88.4 ± 26.1	89.6 ± 26.5	0.529
Total fat (g/day)	80.7 ± 24.7	82.7 ± 23.8	0.249
Saturated fat (g/day)	34.3 ± 12.3	35.4 ± 11.6	0.231

428 *a: All comparison of means for normally-distributed scale variables used Student's t-test for independent*
 429 *samples; Mann-Whitney U tests were used where scale variables were not normally distributed. The Chi-*
 430 *square test of contingencies was used to compare categorical variables between the two populations. P (2-*
 431 *tailed) <0.05 in all cases. b: Standard adolescent criteria were used to classify participants into BMI categories*
 432 *of underweight, normal weight, overweight, and obese ^(53; 54)*

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435 **Table 2.** *GL variables and prevalence of the metabolic syndrome in Raine Study adolescents arranged according*
 436 *to tertiles of mean meal GL*

Variable	Total group n = 516	BOYS			GIRLS		
		Low meal GL ^b n = 88	Medium meal GL ^b n = 82	High meal GL ^{b,c} n = 94	Low meal GL ^b n = 95	Medium meal GL ^b n = 94	High meal GL ^{b,c} n = 78
Daily nutrient intakes^a							
Energy (kcal)	2225±579	2533±609	2430±637	2497±541	1892±378	1910±435	2057±398*
Carbohydrate (g)	277±79	249±28	277±20	304±22 *	253±20	278±17	303±25 *
Protein (g)	88.4±26.1	97.8±17.5	91.0±13.9	84.2±14.7 *	93.9±11.2	85.4±11.1	78.4±12.7 *
Total fat (g)	80.7±24.7	89.3±11.2	79.7±9.0	71.2±9.4 *	88.8±8.7	81.9±8.4	73.9±9.8 *
Saturated fat (g)	34.3±12.3	38.7±7.7	34.5±5.8	29.6±6.0 *	36.8±5.4	35.1±5.7	31.2±5.8 *
Daily GI (%)	54.6±4.9	51.3±4.1	55.0±3.5	57.5±4.2 *	51.6±4.9	54.3±3.8	58.1±4.5 *
Daily GL	152±45	126±16	152±10	175±15 *	131±13	150±9	175±16 *
GL variables^a							
Breakfast GL	30.9±14.9	26.5±11.8	34.6±14.8	35.2±16.5 *	25.9±9.0	30.1±10.5	32.6±12.6 *
Morning Tea GL	15.5±13.2	10.7±11.4	13.5±11.1	17.6±13.7 *	13.5±9.4	15.8±10.6	21.9±15.2 *
Lunch GL	31.6±16.5	29.8±16.8	27.5±14.7	38.9±15.6 *	26.7±11.8	32.2±12.1	33.6±14.4 *
Afternoon tea GL	23.9±18.6	17.2±15.1	25.3±15.9	26.6±20.8 *	20.0±10.6	22.6±11.9	32.1±19.4 *
Dinner GL	44.9±20.1	37.3±14.0	42.6±16.2	53.9±24.0 *	39.1±13.2	44.1±13.9	51.8±18.8 *
Supper GL	10.7±11.5	7.7±8.9	11.8±12.8	11.8±14.7 *	9.0±6.1	11.4±8.4	12.4±9.2 *
Peak score GL	42.3±15.6	38.5±14.5	41.7±15.6	50.7±19.5 *	36.4±10.2	40.3±1.6	46.2±16.0 *
Metabolic Syndrome^d (n; %)							
Yes	17; 3.5 %	2; 2.4 %	0; 0.0 %	6; 6.8 % *	2; 2.6 %	5; 5.7 %	2; 2.8 %
No	463; 96.5%	81; 97.6%	73; 100 %	82; 93.2 %	74; 97.4 %	83; 94.3 %	70; 97.2 %

437 Abbreviations:- *GI: glycemic index; GL: glycemic load*

438 *a: Daily intakes adjusted for energy*

439 *b: Arranged into tertiles of mean meal GL, where mean meal GL = $\Sigma(\text{Breakfast GL} + \text{Morning tea GL} + \text{Lunch}$*

440 *GL + Afternoon tea GL + Dinner GL + Supper GL)/6*

441 *c: Comparison between highest and lowest tertiles; all comparison of means for normally-distributed scale*

442 *variables used Student's t-test for independent samples; Mann-Whitney U tests were used where scale variables*

443 *were not normally distributed. The Chi-square test of contingencies was used to compare categorical variables*

444 *between the two populations. P (2-tailed) <0.05 in all cases, with significance indicated by an asterisk (*)*

445 *d: International Diabetes Foundation definition of metabolic syndrome i.e. high waist circumference and any 2 or*

446 *more of the following: high systolic or diastolic blood pressure; high fasting serum triglycerides; low serum*

447 *high-density lipoprotein cholesterol, or high plasma glucose concentrations; cut points for categorization of*

448 *these high and low subgroups vary by gender and age, as published previously⁽²²⁾*

449 **Table 3.** Meal, peak score and daily GL^a variables and risk of metabolic syndrome^b in Raine Study
 450 adolescents (n = 516) in unadjusted and adjusted logistic regression models (with and without BMI)^c
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Meal GL Variable (BMI excluded/included) ^c	GIRLS (n=252)		BOYS (n=264)	
	OR (95% CI)	P	OR (95% CI)	P
Breakfast GL				
Unadjusted	1.05 (0.99 – 1.11)	0.07	1.01 (0.97 – 1.06)	0.51
Adjusted, BMI excluded	1.06 (1.00 – 1.12)	0.04	1.04 (0.98 – 1.09)	0.18
Adjusted, BMI included	1.15 (1.04 – 1.27)	< 0.01	0.83 (0.64 – 1.07)	0.15
Lunch GL				
Unadjusted	1.04 (0.99 – 1.09)	0.06	1.03 (0.99 – 1.07)	0.09
Adjusted, BMI excluded	1.04 (0.99 – 1.08)	0.15	1.04 (1.00 – 1.09)	0.06
Adjusted, BMI included	1.04 (0.99 – 1.10)	0.14	1.05 (0.97 – 1.15)	0.24
Dinner GL				
Unadjusted	1.00 (0.95 – 1.04)	0.84	0.99 (0.95 – 1.03)	0.56
Adjusted, BMI excluded	0.98 (0.94 – 1.03)	0.44	0.97 (0.93 – 1.01)	0.14
Adjusted, BMI included	0.97 (0.91 – 1.04)	0.43	0.96 (0.89 – 1.02)	0.19
Peak Score GL				
Unadjusted	1.01 (0.97 – 1.07)	0.58	1.01 (0.97 – 1.05)	0.70
Adjusted, BMI excluded	1.00 (0.94 – 1.05)	0.94	0.99 (0.95 – 1.04)	0.78
Adjusted, BMI included	1.01 (0.95 – 1.08)	0.71	0.95 (0.86 – 1.04)	0.24
Daily GL				
Unadjusted	1.00 (0.98 – 1.02)	0.77	1.01 (0.99 – 1.02)	0.48
Adjusted, BMI excluded	1.00 (0.98 – 1.02)	0.90	1.00 (0.99 – 1.02)	0.64
Adjusted, BMI included	1.01 (0.99 – 1.04)	0.44	1.03 (0.99 – 1.06)	0.19

452 *Abbreviations:- GL: glycemic load; OR: odds ratio; 95% CI: 95% confidence interval*

453 *a: All GL variables were adjusted for energy*

454 *b: Using the age-specific International Diabetes Foundation definition of metabolic syndrome⁽²²⁾*

455 *c: Logistic regression models were adjusted for single parent family, physical activity and energy-adjusted*
 456 *daily protein intake, with BMI excluded or included as an additional confounder*
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