British Journal of Nutrition (2021), 125, 1101–1110 doi:10.1017/S0007114520003505

Predictors of postprandial glycaemia, insulinaemia and insulin resistance in adolescents

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(Submitted 3 May 2020 – Final revision received 20 July 2020 – Accepted 25 August 2020 – First published online 7 September 2020)

Abstract

Postprandial glycaemia and insulinaemia are important risk factors for type 2 diabetes. The prevalence of insulin resistance in adolescents is increasing, but it is unknown how adolescent participant characteristics such as BMI, waist circumference, fitness and maturity offset may explain responses to a standard meal. The aim of the present study was to examine how such participant characteristics affect the postprandial glycaemic and insulinaemic responses to an ecologically valid mixed meal. Data from the control trials of three separate randomised, crossover experiments were pooled, resulting in a total of 108 participants (fifty-two boys, fifty-six girls; aged 12·5 (SD 0·6) years; BMI 19·05 (SD 2·66) kg/m^2). A fasting blood sample was taken for the calculation of fasting insulin resistance, using the homoeostatic model assessment of insulin resistance (HOMA-IR). Further capillary blood samples were taken before and 30, 60 and 120 min after a standardised lunch, providing 1·5 g/kg body mass of carbohydrate, for the quantification of blood glucose and plasma insulin total AUC (tAUC). Hierarchical multiple linear regression demonstrated significant predictors for plasma insulin tAUC were waist circumference, physical fitness and HOMA-IR ($F_{(3,98)} = 36{\cdot}78$, $P < 0{\cdot}001$, adjusted $R^2 = 0{\cdot}515$). The variance in blood glucose tAUC was not significantly explained by the predictors used ($F_{(7,94)} = 1{\cdot}44$, $P = 0{\cdot}198$). Significant predictors for HOMA-IR were BMI and maturity offset ($F_{(2,102)} = 14{\cdot}06$, $P < 0{\cdot}001$, adjusted $R^2 = 0{\cdot}021$). In summary, the key findings of the study are that waist circumference, followed by physical fitness, best explained the insulinaemic response to an ecologically valid standardised meal in adolescents. This has important behavioural consequences because these variables can be modified.

Key words: **Postprandial insulin: Postprandial glucose: Adolescents: Metabolism**

Insulin resistance and reduced glucose tolerance are typically implicated in the aetiology of type 2 diabetes[1], with an increasing degree of insulin resistance in young people[2]. Furthermore, the development of insulin resistance and type 2 diabetes in children and adolescents is associated with an increased risk of a number of co-morbidities, such as CVD, in later life[3,4]. Therefore, due to the potential concern for metabolic health across the lifespan, it is important to understand the factors that affect insulin resistance and glucose tolerance in young people. The postprandial response to an ecologically valid meal is an important marker of cardiometabolic health in young people and favoured over the more typically cited fasting markers[5–7]. However, the factors that affect the magnitude of the postprandial glycaemic and insulinaemic response in young people are not well understood.

There are many risk factors associated with the development of type 2 diabetes, some of which can be easily modified through lifestyle behaviour change[8]. One of the contributing factors to the stark increase in the prevalence of type 2 diabetes is weight status, particularly central adiposity. This can be assessed in various ways (such as waist circumference, sum of skinfolds and BMI) and is considered an important risk factors for the development of insulin resistance and, subsequently, type 2 diabetes[2,9,10]. Sex and pubertal status are also other risk factors during childhood (up to 11 years old) and adolescence (11–18 years old), given that there is a degree of pubertal insulin resistance, which may be of greater magnitude in females[11–13]; thus, it is particularly important to understand the association between risk factors of insulin resistance during adolescence, which has not been explored to date. Low physical activity and physical fitness are risk factors for the development of type 2 diabetes[14] in adults and are also linked with poor cardiometabolic health in children and adolescents[15].

Traditionally, fasting glucose and insulin concentrations are commonly used in models of insulin resistance, the most common being the homoeostatic model assessment of insulin resistance (HOMA-IR)[2]. However, it has been argued that the use of such measures do not appropriately screen for related conditions, like type 2 diabetes[5–7]. Furthermore, HOMA-IR typically reflects hepatic insulin sensitivity and does not account for

Abbreviations: HOMA-IR, homoeostatic model assessment of insulin resistance; OGTT, oral glucose tolerance test; tAUC, total AUC.

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peripheral insulin sensitivity[16,17]. Instead, the use of a dynamic assessment of postprandial glycaemia and insulinaemia has been suggested, as a more sensitive marker of cardiometabolic health given that young people spend most of the awake time in the postprandial state.

One such method of assessing the postprandial glycaemic and insulinaemic response is the oral glucose tolerance test (OGTT)[17], whereby glucose and insulin concentrations are determined at 0, 30, 36 and 120 min following a standard glucose load (75 g), which has been used in adolescents previously[18,19]. Recent work in adolescents has examined the responses to mixed meals[20–22], providing ecological insights about the responses to regularly consumed meals. Furthermore, assessment of postprandial insulinaemia is an applicable tool for identifying early insulin resistance in healthy, asymptomatic individuals[7].

Adiposity is a well-known risk factor for the development of insulin resistance and type 2 diabetes[2,9,10], but there is very little known about how adiposity affects postprandial responses in adolescents. A direct comparison of overweight/obese and normal-weight adolescents, using BMI, found that those who were overweight/obese had a larger insulinaemic response to a standardised meal[22]. This study, however, only considered BMI as a proxy of adiposity and did not consider the measure of waist circumference which is the preferred measure of adiposity when considering CVD risk[23]. Future work should consider the discriminatory capabilities of multiple makers of adiposity and how these affect postprandial responses.

It has been suggested that physical fitness and fasting insulin resistance are inversely related in adolescents[24–26]. In addition, physical fitness is also inversely related to blood lipids and low-grade chronic inflammation in adolescents[24,27] and metabolic syndrome incidence in adults[28]. It has been reported in one study that higher physical fitness in young people (aged 7–15 years), assessed by time taken to complete a 1·6 km run, is inversely related to insulin resistance (assessed via HOMA-IR) in adulthood[25]. It is worth noting, however, that this relationship was weaker when adjusting for childhood waist circumference, thus highlighting the importance of adiposity for metabolic health. However, no studies to date have examined whether physical fitness affects postprandial glycaemia and insulinaemia in adolescents, despite the importance of physical fitness for other risk factors for cardiometabolic health[24,27].

Therefore, the aim of the present study is to explore the factors affecting the postprandial glycaemic and insulinaemic responses in adolescents, including an examination of the interaction between factors known to affect these responses, such as sex and adiposity. In addition, the study will consider how physical fitness influences postprandial responses which is a completely a novel area of enquiry in adolescents.

Methods

Experimental design

Data from three separate studies[18,19] (Williams, Cooper, Dring, Hatch, Morris, Sunderland and Nevill, unpublished results), with identical designs, were pooled to examine the postprandial responses to lunch. Each of the involved studies conformed to the Declaration of Helsinki guidelines and were approved by the Nottingham Trent University Human Ethics Committee. Participants were recruited from secondary schools in the East Midlands area of the UK. Written parental consent and participant assent were obtained during recruitment. A health screen was completed by a parent/guardian of the participant and checked by a lead investigator to ensure that there were no medical conditions that would affect the child's participation. Participants were familiarised with all testing procedures at least 7 d in advance of the main experimental trial. Participants were instructed to refrain from eating or drinking from 21.00 hours the previous evening. Water was allowed *ad libitum*. Participants were also asked to refrain from physical activity in the 24 h preceding main trials. Participants reported to school at the beginning of the day (between 08.00 and 08.30 hours), and all procedures took place in a classroom at the school.

Participant characteristics

Anthropometric measurements. In total, the data set is composed of 108 participants (fifty-two boys) (Table 1). Participants underwent anthropometric measurements, consisting of stature (cm), body mass (kg) and sitting height (cm), which were used to calculate age at peak height velocity[29], which was subtracted from chronological age, in order to establish maturity offset. Height was measured with a Leicester Height Measure (Seca) accurate to 0·1 cm, and body mass was measured using a Seca 770 digital scale (Seca) accurate to 0·1 kg. For descriptive purposes, participants are classified as normal weight, overweight or obese based on age- and sex-specific cut points[30]. Waist circumference was measured at the narrowest abdominal point, between the lower margin of the lowest palpable rib and the iliac crest, to the nearest 0·1 cm[23]. Four skinfold sites were measured (triceps, subscapular, supraspinale and front thigh) as a surrogate of body composition. All measurements were repeated twice, on the right-hand side of the body, using the average of the two unless the measured differed by 5 % or more, in which case a third measure was taken and the median value used. The sum of the four skinfold thickness scores has been used as a marker of adiposity in previous research in this population[20,21].

Assessment of cardiorespiratory fitness. In each study, assessment of physical fitness was assessed using the multi-stage fitness test[31]. Briefly, the test required participants to complete progressive 20 m shuttle runs until volitional exhaustion. The multi-stage fitness test begins at a speed of 8·0 km/h (level 1), increases to 9·0 km/h (level 2) and then by 0·5 km/h for every subsequent level completed. To ensure maximum effort from the participants, participants were 'paced' by a member of the research team and investigators provided verbal encouragement and maximum heart rate was monitored continuously (Firstbeat Technologies Ltd). Performance on the test was determined by the total distance covered (m) (Table 1).

Experimental procedures

Standardised breakfast and lunch. On the morning of the trials (approximately 09.00 hours), a standardised breakfast was

Table 1. Participant characteristics and metabolic markers split into boys and girls (Mean values, standard deviations and ranges)

	Group					
	Boys (*n* 52)			Girls (*n* 56)		
Variable	Mean	SD	Range	Mean	SD	Range
Characteristics						
Age (years)	12·4	0·5	11·4–13·4	12·4	0·6	11·1–13·5
Height (m)	1·59	0·09	1·43–1·81	1·59	0·07	1·45–1·77
Body mass (kg)	48·4	10·7	31·9–78·1	48·2	9·0	32·6–74·3
BMI (kg/m^2)	19·0	2·7	14·0–24·9	19·1	2·7	14·1–28·3
BMI percentile	61·2	29·8	1·2–98·6	52·4	27·3	0·6–99·5
Maturity offset (years)	−1·0	0·6	−2·0–0·6	0·6	0·6	−0·8–2·1
Sum of skinfolds (mm)	48·0	21·8	14·1–102·5	52·4	21·9	24·0–127·0
Waist circumference (cm)	67·4	6·7	54·5–86·4	66·2	6·8	53·4–92·3
Multi-stage fitness test distance (m)	1240	420	420–2160	1080	340	360–1740
Metabolic markers						
Fasting blood glucose (mmol/l)	4·5	0·6	2·6–5·7	4·3	0·7	2·4–6·1
Fasting plasma insulin (pmol/l)	54·1	28·6	11·3–120·0	59·1	27·1	13·8–138·6
HOMA-IR (arbitrary units)	1·73	0·92	0·33–3·81	1·93	0·94	0·43–4·01
Insulin tAUC (pmol/l × 120 min)	27 590	16 419	9288–97 148	28 679	13 400	8240–73 224
Glucose tAUC (mmol/l × 120 min)	587	73	453–791	582	78	443–791

HOMA-IR, homoeostatic model assessment of insulin resistance; tAUC, total AUC.

Table 2. Example of the standard and vegetarian options for the test meal, with energy and macronutrient breakdown, based on a hypothetical 50 kg individual

	Meal option											
	Standard						Vegetarian					
	Amount	Energy		Carbohydrate	Fat	Protein	Amount	Energy		Carbohydrate	Fat	Protein
Ingredient	(g)	kJ	kcal	(g)	(g)	(g)	(g)	kJ	kcal	(g)	(g)	(g)
White bread*	70	690	165	32	1	6	70	690	165	32	1	6
Flora original†	8	134	32	0	4	0	8	134	32	0	4	0
Chicken‡	115	544	130	0	2	27						
Cheese§							34	556	133	0	11	9
Baked crisps‖	35	598	143	26	3	2	35	598	143	26	3	2
Apple¶	120	230	55	13	0	0	120	230	55	13	0	0
Total		2197	526	71	10	36		2209	529	71	19	17

* White bread (Kingsmill soft white thick slice).
† Margarine (Flora Original).
‡ Sainsbury's roast chicken slices (Sainsbury's Ltd).
§ Sainsbury's medium cheddar (Sainsbury's Ltd).
‖ Walkers ready salted baked crisps (Walkers).
¶ Braeburn apple.

provided, which provided 1·5 g/kg body mass of carbohydrate (cornflakes, milk, white toast and butter). The standardised lunch (the test meal) was provided 3 h post-breakfast (approximately 12.00 hours) and contained 1·5 g/kg body mass of carbohydrate (chicken sandwich, baked crisps and an apple, with a cheese alternative for vegetarians (*n* 2 participants had the cheese alternative)) (Table 2). Participants were given 15 min to consume breakfast and lunch. The postprandial period (2 h) started on the first mouthful of lunch[32].

Capillary blood samples. Capillary blood samples were preferred over venous samples due to ethical constraints in young people and have been used successfully previously in this population[20,21]. A fasting capillary blood sample was taken upon arrival at school. For the postprandial period, a baseline (pre-lunch) blood sample was taken at approximately 12.00 hours (always exactly 3 h post-breakfast), with additional blood samples at 30, 60 and 120 min post-lunch to represent the postprandial period.

In order to increase capillary blood flow, participants' hands were warmed via submersion in warm water prior to collection. A unistik single-use lancet (Unistik, Extra, 21G gauge, 2·0 mm depth, Owen Mumford Ltd) was used, and the blood was collected into a 300 µl EDTA-coated microvette (Sarstedt Ltd). A single 25 µl whole blood sample was also collected using a pre-calibrated glass pipette (Hawksley Ltd) and immediately deproteinised in 250 µl ice-cooled 2·5 % perchloric acid, in 1·5 ml plastic vials. Both samples were then centrifuged at 1000 ***g*** for 4 min, at 4°C (Eppendorph 5415C). Plasma was removed from the microvette and placed into 500 µl plastic vials for subsequent analysis. All samples were frozen immediately at –20°C and transferred to –80°C as soon as possible.

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Table 3. Correlation matrix for all independent variables
(*r* Values for correlations between independent variables)

	Sex	BM	BMI	MO	SumSF	WC	MSFT	HOMA-IR
Sex								
BM	0·01							
BMI	0·00	0·88**						
MO	−0·80**	0·38**	0·21					
SumSF	−0·09	0·64**	0·80**	0·18				
WC	0·09	0·85**	0·88**	0·20	0·76**			
MSFT	0·23	−0·31*	−0·45**	−0·14	−0·59**	−0·38**		
HOMA-IR	−0·05	0·41**	0·38**	0·21	0·26	0·35**	−0·17	

BM, body mass; MO, maturity offset; SumSF, sum of skinfolds; WC, waist circumference; MSFT, distance run on multi-stage fitness test; HOMA-IR, homoeostatic model assessment of insulin resistance.
Holm correction for multiple testing used. * $P < 0·01$, ** $P < 0·001$.

Blood glucose concentrations were measured in duplicate (GOD/PAP method, GL364, Randox), and plasma insulin concentrations were measured in singular (ELISA; Mercodia Ltd) determined using commercially available methods and according to the manufacturer's instructions. The intra-assay CV for the assays of blood glucose concentration and plasma insulin concentration were 2·3 and 3·2 %, respectively. Blood glucose and plasma insulin total AUC (tAUC) following the standardised lunch were calculated (GraphPad Prism 7, GraphPad Software), using methods described previously[33,34]. HOMA-IR was calculated as an index of insulin resistance[35]. For descriptive purposes, participants were classed as 'at risk' according to age- and sex-specific cut points[36].

Sample size justification

For multiple regression, it is recommended that sample size is a minimum of ten participants per predictor variable[37]. A maximum of eight predictors were available, which would dictate a minimum sample size of eighty for sufficient power.

Statistical analyses

All data were analysed using the open-source software RStudio version 1.2.1335 (RStudio Team., (2015), www.rstudio.com). A correlation matrix was created in order to evaluate multicollinearity between independent variables (sex, waist circumference, sum of skinfolds, body mass, BMI, maturity offset, multi-stage fitness test performance and HOMA-IR). Before analysis, waist circumference, sum of skinfolds, BMI and multi-stage fitness test performance were centred to the mean. Simple linear regression was initially conducted for each independent variable on each outcome variable (HOMA-IR, plasma insulin tAUC and blood glucose tAUC). Following this, stepwise hierarchical multiple regression – backwards elimination – was used to develop models for each outcome variable, using the 'lme4' package[38]. At each stage, the independent variable that provided the lowest contribution to the model (through evaluation of SE and *t*-statistic) was removed and then the model was re-run.

Results

A total of 80 (74·1 %) participants were considered normal weight, 18 (16·7 %) overweight and 10 (9·3 %) obese. Furthermore, 34 (31 %) participants were considered 'at risk' of insulin resistance, as calculated by HOMA-IR.

Multicollinearity between independent variables

Independent variables were assessed for multicollinearity prior to conducting the hierarchical multiple regression, the results of which are shown in Table 3. There was a strong correlation between BMI and body mass, which is not surprising given that body mass is used in the calculation of BMI. Therefore, these variables cannot be considered independent, and thus, body mass was excluded from subsequent analyses. All other variables did not demonstrate strong correlations ($r < 0·90$) and were thus included in the models.

Table 4. Summary of simple linear regression outputs for each variable predicting plasma insulin total AUC
(Standard errors and β-coefficients)

Predictor	β_0	β_1	SE	*t*	*P*	R^2	Adj. R^2
Sex	28 679	−1088	2886	−0·38	0·707	0·001	−0·008
WC	28 105	1364	169	8·07	<0·001***	0·383	0·377
SumSF	28 138	366	55	6·62	<0·001***	0·294	0·287
BMI	28 143	3226	442	7·29	<0·001***	0·336	0·330
MSFT	44 969	−14	3	−4·21	<0·001***	0·148	0·139
MO	28 524	2538	1431	1·77	0·079	0·029	0·020
HOMA-IR	12 268	8780	1324	6·63	<0·001***	0·299	0·292

β_0, Intercept; β_1, parameter estimate; Adj., adjusted; WC, waist circumference; SumSF, sum of skinfolds; MSFT, distance run on multi-stage fitness test; MO, maturity offset; HOMA-IR, homoeostatic model assessment of insulin resistance.
* $P < 0·05$, ** $P < 0·01$, *** $P < 0·001$.

Table 5. Summary of the hierarchical regression (backwards elimination) for variables predicting plasma insulin total AUC† (95 % confidence intervals and unstandardised coefficients; standard errors and β-coefficients)

						95 % CI		
Variable	B	SE	β	T	P	Lower	Upper	Adj. R^2
Step 1: (F(7,40) = 15·59, P < 0·001)								0·503
Intercept	22 269	4826						
Sex	−1855	4276	−0·06	−0·43	0·665	−10 346	6635	
WC	950	371	0·43	2·56	0·012*	214	1687	
SumSF	92	99	0·14	0·93	0·356	−105	290	
BMI	−582	948	−0·10	−0·61	0·541	−2466	1301	
MSFT	−4	3	−0·12	1·30	0·197	−11	2	
MO	−1329	2104	−0·09	−0·63	0·529	−5507	2849	
HOMA-IR	6428	1307	0·40	4·92	<0·001***	3831	9025	
Step 2: (F(6,54) = 18·32, P < 0·001)								0·507
Intercept	21 975	4757						
WC	883	335	0·40	2·63	0·009**	217	1550	
SumSF	101	92	0·15	1·04	0·299	−91	293	
BMI	−569	944	−0·10	−0·60	0·548	−2443	1305	
MSFT	−4	3	−0·13	−1·46	0·147	−11	1	
MO	−550	1095	−0·04	−0·50	0·616	−2725	1623	
HOMA-IR	6402	1300	0·39	4·92	<0·001***	3819	8985	
Step 3: (F(5,55) = 22·10, P < 0·001)								0·511
Intercept	22 259	4706						
WC	882	334	0·40	2·64	0·009**	218	1546	
SumSF	101	96	0·15	1·05	0·299	−90	292	
BMI	−585	940	−0·10	−0·62	0·535	−2451	1280	
MSFT	−4	3	−0·13	−1·45	0·149	−11	1	
HOMA-IR	6261	1265	0·38	4·95	<0·001***	3749	8773	
Step 4: (F(4,56) = 27·70, P < 0·001)								0·514
Intercept	22 479	4677						
WC	754	263	0·34	2·87	0·005**	231	1277	
SumSF	75	87	0·11	0·87	0·388	−98	249	
MSFT	−4	3	−0·13	−1·44	0·152	−11	1	
HOMA-IR	6113	1239	0·38	4·94	<0·001***	3654	8572	
Step 5: (F(3,39) = 36·78, P < 0·001)								0·515
Intercept	24 326	4158						
WC	921	180	0·41	5·12	<0·001***	564	1278	
MSFT	−6	3	−0·16	−2·19	0·031*	−12	0	
HOMA-IR	6046	1234	0·37	4·90	<0·001***	3595	8496	

B, regression coefficient; β, standardised coefficient; Adj., adjusted; WC, waist circumference; SumSF, sum of skinfolds; MSFT, distance run on multi-stage fitness test; MO, maturity offset; HOMA-IR, homoeostatic model assessment of insulin resistance.
* P < 0·05, ** P < 0·01, *** P < 0·001.
† 95 % CI are for unstandardised coefficients (B). ΔR^2: step 2 = 0·004, step 3 = 0·004, step 4 = 0·003, step 5 = 0·001.

Plasma insulin total AUC

Predictors individually. Simple linear regression models for insulin tAUC, with each independent variable separately, can be seen in Table 4. Waist circumference was the strongest individual predictor, explaining 37·7 % of the insulin tAUC variance (P < 0·001). BMI (P < 0·001, adjusted R^2 0·330), sum of skinfolds (P < 0·001, adjusted R^2 0·287), HOMA-IR (P < 0·001, adjusted R^2 0·292) and multi-stage fitness test performance (P < 0·001, adjusted R^2 0·139) were all significant individual predictors of plasma insulin tAUC. Sex (P = 0·707, adjusted R^2 −0·008) and maturity offset (P = 0·079, adjusted R^2 0·020) did not affect plasma insulin tAUC.

Final model development. The hierarchical regression (stepwise, backwards elimination) step-by-step process can be seen in Table 5. The final model (step 5) contained waist circumference, multi-stage fitness test performance and HOMA-IR as predictors, explaining 51·5 % of the variance in plasma insulin tAUC ($F_{(3,39)}$ = 36·78, P < 0·001, adjusted R^2 0·515). The model suggests that: for a 1 cm increase in waist circumference, insulin tAUC would increase by 921 pmol/l × 120 min (95 % CI 564, 1278); for a 20 m increase in distance ran during the multi-stage fitness test, insulin tAUC would decrease by 6 pmol/l × 120 min (95 % CI −12, −1) and for a 1 arbitrary unit (AU) increase in HOMA-IR, the model suggests that insulin tAUC would increase by 6046 pmol/l × 120 min (95 % CI 3595, 8497).

Blood glucose total AUC

Predictors individually. None of the available predictors provided a significant contribution to explaining the variance in blood glucose tAUC, individually (Table 6).

Final model development. The initial model (step 1) including all predictors did not provide sufficient explanation for the variance (3 %) in blood glucose tAUC (F(7,40) = 1·44, P = 0·198). As no predictors significantly explained any variance in blood glucose tAUC individually, or in the hierarchical model, the backwards elimination process was terminated at step 1.

Table 6. Summary of simple linear regression outputs for each variable predicting blood glucose total AUC (Standard errors and β-coefficients)

Predictor	β_0	β_1	SE	*T*	*P*	R^2	Adj. R^2
Sex	578	8·2	15·12	0·54	0·590	0·003	–0·007
WC	582	–0·1	1·13	–0·09	0·930	0·000	–0·009
SumSF	582	–0·2	0·34	–0·62	0·537	0·004	–0·006
BMI	582	0·5	2·86	0·17	0·862	0·000	–0·009
MSFT	605	–0·0	0·02	–1·04	0·299	0·011	0·010
MO	581	–6·6	7·58	–0·87	0·386	0·007	–0·002
HOMA-IR	558	13·9	8·26	1·68	0·097	0·027	0·018

β_0, Intercept; β_1, parameter estimate; Adj., adjusted; WC, waist circumference; SumSF, sum of skinfolds; MSFT, distance run on multi-stage fitness test; MO, maturity offset; HOMA-IR, homoeostatic model assessment of insulin resistance.

Table 7. Summary of simple linear regression outputs for each variable predicting homoeostatic model assessment of insulin resistance (Standard errors and β-coefficients)

Predictor	β_0	β_1	SE	*t*	*P*	R^2	Adj. R^2
Sex	2·02	–0·21	0·19	–1·08	0·284	0·011	0·002
WC	1·83	0·05	0·01	4·44	<0·001***	0·161	0·153
SumSF	1·31	0·01	0·00	2·71	0·008**	0·066	0·057
BMI	1·82	0·15	0·03	4·80	<0·001***	0·183	0·175
MSFT	2·48	–0·00	0·00	–2·16	0·033*	0·044	0·035
MO	1·95	0·28	0·09	2·93	0·004**	0·076	0·068

β_0, Intercept; β_1, parameter estimate; Adj., adjusted; WC, waist circumference; SumSF, sum of skinfolds; MSFT, distance run on multi-stage fitness test; MO, maturity offset.
* $P<0·05$, ** $P<0·01$, *** $P<0·001$.

Homoeostatic model assessment of insulin resistance

Predictors individually. Simple linear regression models for HOMA-IR, with each independent variable separately, can be seen in Table 7. BMI was the strongest predictor for HOMA-IR, explaining 17·5 % of the variance ($P<0·001$). Waist circumference ($P<0·001$, adjusted R^2 0·153), sum of skinfolds ($P=0·008$, adjusted R^2 0·057), multi-stage fitness test performance ($P=0·033$, adjusted R^2 0·035) and maturity offset ($P=0·004$, adjusted $R^2=0·068$) also provided a significant contribution to the variance in HOMA-IR. Sex did not significantly explain variance in HOMA-IR ($P=0·284$, adjusted R^2 0·002).

Final model development. The hierarchical regression (stepwise, backwards elimination) step-by-step process can be seen in Table 8. The final model containing BMI and maturity offset as independent variables (step 5; $F_{(2,41)}=14·06$, $P<0·001$, adjusted R^2 0·201) explained 20·1 % of the variance in HOMA-IR. Specifically, the model suggests that for each additional 1 kg/m^2 increase in BMI, HOMA-IR would increase by 0·14 AU; for each 1 year increase in maturity offset, HOMA-IR would increase by 0·17 AU.

Discussion

The main findings of the present study are that in adolescents: (i) the combination of waist circumference, performance on the multi-stage fitness test and HOMA-IR collectively explained 51·5 % of variance in the postprandial insulinaemic response to a standardised mixed meal; (ii) none of the independent variables (BMI, body mass, waist circumference, MSFT, sum of skinfolds, sex, maturity offset and HOMA-IR) explained the variance in the postprandial glycaemic response and (iii) BMI and maturity offset collectively explained 20·1 % of the variation in HOMA-IR. These findings highlight the importance of body composition, particularly central adiposity, in explaining the insulinaemic response to a standardised mixed meal in adolescents. Furthermore, the present study also highlights that physical fitness is an important explanatory variable when considering the postprandial insulinaemic response in adolescents.

The findings of the present study are novel because no study to date has investigated the factors affecting the postprandial glycaemic and insulinaemic responses in adolescents, which are recognised as important risk factors for cardiometabolic disease[5–7]. Furthermore, most waking hours are spent in a postprandial state; therefore, it seems logical to examine postprandial responses when evaluating an individual's metabolic function. Although glycaemia has potential clinical use for screening of disease prevalence and risk, there have been some arguments that more attention should be focused on postprandial insulinaemia[5,7]. Furthermore, we hypothesise that the changes in postprandial insulinaemic responses manifest earlier in the progression of cardiometabolic diseases than the postprandial glycaemic responses and should therefore be examined in young people. The present study provides novel evidence that waist circumference, physical fitness and HOMA-IR are key predictors of this postprandial insulinaemic response in adolescents. These novel findings provide further evidence that more consideration should be given to the assessment of postprandial insulinaemia, alongside glycaemia, as a risk factor for metabolic health[5–7], which highlights the utility of this marker for future research.

Out of all the explanatory variables, waist circumference provided the strongest individual explanation of the variance in the postprandial insulinaemic response and was also a strong predictor in the final model. These data are supported by a group

Table 8. Summary of the hierarchical regression (backwards elimination) for variables predicting homoeostatic model assessment of insulin resistance† (95 % confidence intervals and unstandardised coefficients; standard errors and *β*-coefficients)

						95 % CI		
Variable	B	SE	*β*	*t*	*P*	Lower	Upper	Adj. R^2
Step 1: ($F(6,54) = 4{\cdot}88$, $P < 0{\cdot}001$)								0·188
Intercept	1·94	0·32				1·45	2·10	
Sex	0·15	0·33	0·08	0·45	0·657	–0·52	0·82	
WC	0·02	0·03	0·17	0·82	0·413	–0·03	0·08	
SumSF	–0·01	0·01	–0·22	–1·18	0·242	–0·03	0·01	
BMI	0·13	0·07	0·37	1·75	0·083	–0·02	0·27	
MSFT	–0·00	0·00	–0·06	–0·50	0·616	0·00	0·00	
MO	0·25	0·16	0·27	1·49	0·139	–0·08	0·57	
Step 2: ($F(5,55) = 5{\cdot}87$, $P < 0{\cdot}001$)								0·194
Intercept	1·97	0·32				1·68	2·01	
WC	0·03	0·03	0·21	1·12	0·266	–0·02	0·08	
SumSF	–0·01	0·01	–0·24	–1·31	0·194	–0·03	0·01	
BMI	0·13	0·07	0·37	1·75	0·083	–0·02	0·27	
MSFT	–0·00	0·00	–0·05	–0·41	0·686	–0·00	0·00	
MO	0·18	0·08	0·20	2·16	0·033*	0·02	0·35	
Step 3: ($F(4,57) = 7{\cdot}59$, $P < 0{\cdot}001$)								0·202
Intercept	1·85	0·08				1·69	2·01	
WC	0·02	0·03	0·15	0·83	0·409	–0·03	0·07	
SumSF	–0·01	0·01	–0·21	–1·37	0·175	–0·02	0·00	
BMI	0·15	0·07	0·42	2·07	0·041*	0·01	0·29	
MO	0·17	0·08	0·19	2·06	0·042*	0·01	0·34	
Step 4: ($F(3,58) = 9{\cdot}92$, $P < 0{\cdot}001$)								0·204
Intercept	1·85	0·08				1·69	2·01	
SumSF	–0·08	0·01	–0·18	–1·22	0·224	–0·02	0·01	
BMI	0·19	0·05	0·53	3·61	<0·001***	0·08	0·29	
MO	0·17	0·08	0·19	2·09	0·039*	0·01	0·34	
Step 5: ($F(2,41) = 14{\cdot}06$, $P < 0{\cdot}001$)								0·201
Intercept	1·85	0·08				1·69	2·01	
BMI	0·14	0·03	0·39	4·34	<0·001***	0·07	0·20	
MO	0·17	0·08	0·19	2·09	0·039*	0·01	0·34	

B, regression coefficient; *β*, standardised coefficient; Adj., adjusted; WC, waist circumference; SumSF, sum of skinfolds; MSFT, distance run on multi-stage fitness test; MO, maturity offset.

* $P < 0{\cdot}05$, ** $P < 0{\cdot}01$, *** $P < 0{\cdot}001$.

† 95 % CI are for unstandardised coefficients (B). $\triangle R^2$: step 2 = 0·006, step 3 = 0·008, step 4 = 0·003, step 5 = –0·004.

comparison of postprandial insulinaemia whereby overweight/obese adolescents (aged 14–15 years) had a greater insulin AUC compared with normal-weight adolescents[22], as well as supporting the relationship between adiposity and insulin sensitivity over a 2-year period in children (aged 9–11 years)[39]. Whilst previous research has identified differences in postprandial insulinaemia between young people considered overweight and normal weight, the present study offers novel insights into the relationship of adiposity on postprandial responses in adolescents. Furthermore, waist circumference was superior compared with BMI and sum of skinfolds, which are also measures of body composition, therefore highlighting the importance and utility of this particular measure. Whilst central adiposity is of great importance for cardiometabolic disease risk, the direct measurement, via dual-energy x-ray absorptiometry, for example, requires an expensive and specialist radiological imaging equipment[40]. However, waist circumference is strongly advocated as a surrogate measure of central adiposity and has been associated with cardiometabolic disease risk[23,40]. This has important practical implications, given the low-cost and non-invasive nature of such a measuring waist circumference. Collectively, these results demonstrate the importance of adiposity – particularly central adiposity (as measured by waist circumference) – for cardiometabolic health in youth, which is pertinent given that central adiposity is linked to the development of insulin resistance[2,9,10].

Another novel finding of the present study was that physical fitness (assessed by distance covered on the multi-stage fitness test) was inversely related to plasma insulin tAUC. Physical fitness is known to be beneficial for many facets of cardiometabolic health[27]. However, to the authors' knowledge, no other studies have examined the relationship between physical fitness and postprandial insulinaemia. The closest comparison comes from evidence in children (aged 6–8 years) where physical fitness was inversely related to fasting insulin resistance[24]. Furthermore, there is evidence of improved beta-cell function in adults with a higher physical fitness[41], which lends support to the result of improved insulin sensitivity in participants with a higher physical fitness in the current data set. There is also a strong body of evidence that chronic exercise interventions improve insulin sensitivity in obese youth[42]. Whilst there has been suggestion that these improvements might be due to increased capillarisation of skeletal muscle[43] and increased GLUT4 translocation[43], others have suggested that the chronic improvements are largely mediated through weight loss[44]. Identifying a mechanism, through which physical fitness improves postprandial insulinaemia, was not in the scope of the present study. However, it is interesting that physical fitness

remained in the final model, even in the presence of adiposity. Nonetheless, it is important that future research investigates the mechanisms through which physical fitness leads to better postprandial insulinaemia, and whether this differs from those as a result of acute and chronic exercise. The present study is the first to show a beneficial relationship between physical fitness and postprandial insulinaemia in adolescents, suggesting that physical fitness may be a key predictor for this outcome even when considering the role of other predictors. This has important practical implications that highlight the need to promote physical fitness in youth, given the strong role it has in metabolic health.

The present study also demonstrates that HOMA-IR provides a significant explanation of the variance in postprandial insulinaemia. These data support and extend previous findings following a standardised breakfast[11] and an OGTT[45]. Previous work has shown that HOMA-IR is positively correlated (r 0·63) with insulin tAUC following an OGTT[45]. This is of similar magnitude to the present study (r 0·53); however, the previous association was only applicable to adolescent boys in response to an OGTT[45]. The present study extends this relationship to a sample of adolescent boys and girls, in response to an ecologically valid mixed meal. Although the meals provided between the present study and previous work[11] were different, they offered the same relative energy provision (1·5 g/kg body mass of carbohydrate). Collectively, these results suggest that basal metabolic function is important for determining the physiological response to test meals. The results from the present study also suggest that an increase in HOMA-IR (higher basal insulin resistance) will lead to greater postprandial insulinaemic responses, even when other strong predictors such as waist circumference and physical fitness are controlled for.

The present study suggests that when considering fasting metabolic status (using HOMA-IR), BMI and maturity offset were the most informative explanatory variables. Independently, BMI was the stronger explanatory variable which is consistent with previous work in this population stating that adiposity has a strong predictive role in fasting measures of insulin resistance[24,46,47], despite using different surrogate measures of adiposity. The current study advances previous work in obese adolescents[46] to demonstrate that BMI is strongly related to HOMA-IR in healthy, asymptomatic (from cardiometabolic health conditions) adolescents. Maturity offset was also positively related to HOMA-IR, which is consistent with previous literature stating that there is a degree of pubertal insulin resistance during adolescence[10–13], which is sometimes more profound in girls[11,12]. The role of maturity and sex, in the present study, seemed only to be reflected in the fasting proxy of insulin resistance, whereas previously it has been shown that girls are hyperinsulinaemic compared with boys, following the same standard meal[11]. This is an interesting observation which may be indicative of potentially differential insulin resistance development during puberty, where fasting hepatic insulin resistance occurs at the earlier stages, with postprandial peripheral insulin resistance developing in the latter stages. However, there are currently no data to support this suggestion which would require the measurement of postprandial insulinaemia in adolescents at different stages of puberty, or a longitudinal follow-up throughout the course of adolescence.

The results of the present study demonstrate that the use of low-cost, non-invasive measures of adiposity and physical fitness provides a much greater explanation of variance in postprandial insulinaemia than the traditional fasting marker of metabolic health, HOMA-IR. This has important practical implications, given the invasive and costly nature of HOMA-IR, and the potential use of these measurements (especially waist circumference) in predicting postprandial insulinaemia. However, there are still other characteristics that might provide additional information about the variance in postprandial insulinaemia. Habitual physical activity is known to attenuate the puberty-related insulin resistance seen in adolescence[48]. Furthermore, in adults matched for $\dot{V}O_{2max}$, those with greater levels of habitual physical activity were more insulin sensitive in response to an OGTT[49]. Given this evidence, it would be worthwhile including habitual physical activity as an explanatory variable in future work. In addition, this work could be extended by incorporating participants across the age of adolescence, which would help to identify if the relationships highlighted in the present study exist across different age groups and stages of pubertal development.

The present study has a number of limitations that need consideration. First, a mixed meal was consumed rather than a traditional OGTT. The OGTT is a valid test meal when examining postprandial responses, and the consumption of a solid mixed meal will have different gastric emptying rates compared with a drink solution; thus, comparisons may be limited[32]. However, examining the postprandial responses to a mixed meal has been favoured in recent paediatric research given that young people spend most of the awake time in the postprandial state. The present study also used maturity offset as a marker of maturation status[29], which is based on predictive modelling using anthropometric measurements. Despite being a prediction of maturation, maturity offset is often favoured in a non-clinical setting over traditional measures (such as the Tanner scale, which examines secondary sex characteristics), which are deemed invasive[50]. Whilst the present study included several relevant predictors of metabolic health, there were also a number of predictors not included (such as the habitual dietary intake and physical activity levels of participants, mode of transport to school and socio-economic status), which should be examined in future research. Furthermore, as the present study is cross-sectional, causality between the chosen predictors and postprandial responses cannot be inferred. Finally, it is important to consider that the participants in the current study are considered healthy and asymptomatic from cardiometabolic health conditions. Indeed, it might be more appropriate to study the relationships examined in the present study in populations with increased prevalence of risk factors for cardiometabolic diseases, given that they would be the target of future interventions. Nonetheless, identifying these relationships in healthy adolescents provides important information, given the role of postprandial hyperinsulinaemia in the pathophysiology of insulin resistance and related cardiometabolic health issues[5] and suggested early manifestation of such conditions[4].

In conclusion, the findings of the present study demonstrate that over half of the variance in postprandial insulinaemia in response to a standard mixed meal, in adolescents, can be explained by measurements that are frequently employed to

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characterise participants in paediatric exercise literature, waist circumference, multi-stage fitness test performance and HOMA-IR. Overall, measures of body composition (particularly waist circumference) were key when explaining the variance in metabolic health in this sample. These data extend previous work using different surrogates of body composition and fasting indices of insulin resistance, thus demonstrating that body composition (particularly waist circumference) is important for postprandial metabolic responses and cardiometabolic health. These findings have important practical implications, as the predictors identified are easily measurable in young people and considered modifiable. Future work should investigate additional variables that might help explain the variance in postprandial insulinaemia and glycaemia, such as habitual physical activity, and how the impact of these participant characteristics may change throughout the course of adolescence.

Acknowledgements

The authors would like to thank the participants and teachers at the secondary schools involved, for their time and effort with data collection.

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

The author contributions are as follows: R. W. contributed to the design of the study, the collection and analysis of the data and the writing of the manuscript. K. J. D. contributed to the design of the study and the collection and analysis of the data. S. B. C. contributed to the design of the study and the collection and analysis of the data. J. G. M. contributed to the design of the study and collection of the data. C. S. contributed to the design of the study and collection of the data. M. E. N. contributed to the design of the study and the collection of the data. R. W., K. J. D., S. B. C. and M. E. N. drafted the manuscript. All authors read and approved the final version of the manuscript.

The authors declare that there are no conflicts of interest.

References

1. Reaven G (2005) Insulin resistance, type 2 diabetes mellitus, and cardiovascular disease: the end of the beginning. *Circulation* **112**, 3030–3032.
2. Tagi VM, Giannini C & Chiarelli F (2019) Insulin resistance in children. *Front Endocrinol* **10**, 342.
3. Laitinen T, Laitinen TT, Pahkala K, *et al.* (2012) Ideal cardiovascular health in childhood and cardiometabolic outcomes in adulthood: the cardiovascular risk in young finns study. *Circulation* **125**, 1971–1978.
4. Steinberger J, Daniels SR, Eckel RH, *et al.* (2009) Progress and challenges in metabolic syndrome in children and adolescents. A scientific statement from the American Heart Association atherosclerosis, hypertension, and obesity in the young committee of the council on cardiovascular disease in the young. *Circulation* **119**, 628–647.
5. DiNicolantonio JJ, Bhutani J, OKeefe JH, *et al.* (2017) Postprandial insulin assay as the earliest biomarker for diagnosing pre-diabetes, type 2 diabetes and increased cardiovascular risk. *Open Heart* **4**, e000656.
6. Haffner SM (1998) The importance of hyperglycemia in the nonfasting state to the development of cardiovascular disease. *Endocr Rev* **19**, 583–592.
7. Lautt WW (2007) Postprandial insulin resistance as an early predictor of cardiovascular risk. *Ther Clin Risk Manag* **3**, 761–770.
8. Tuomilehto J, Lindström J, Eriksson JG, *et al.* (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* **344**, 1343–1350.
9. Arslanian SA (1996) Suprasongsin C insulin sensitivity, lipids and body composition in childhood: is "syndrome X" present? *J Clin Endocrinol Metab* **81**, 1058–1062.
10. Arslanian SA (2000) Type 2 diabetes mellitus in children: pathophysiology and risk factors. *J Pediatr Endocrinol Metab* **13**, 1385–1394.
11. Cooper SB, Dring KJ, Morris JG, *et al.* (2017) Sex differences in adolescents' glycaemic and insulinaemic responses to high and low glycaemic index breakfasts: a randomised control trial. *Br J Nutr* **117**, 541–547.
12. Kelsey MM & Zeitler PS (2016) Insulin resistance of puberty. *Curr Diab Rep* **16**, 64.
13. Reinehr T (2013) Type 2 diabetes mellitus in children and adolescents. *World J Diabetes* **4**, 270–281.
14. Aune D, Norat T, Leitzmann M, *et al.* (2015) Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *Eur J Epidemiol* **30**, 529–542.
15. Ekelund U, Luan JA, Sherar LB, *et al.* (2012) Moderate to vigorous physical activity and sedentary time and cardiometabolic risk factors in children and adolescents. *J Am Med Assoc* **307**, 704–712.
16. Abdul-Ghani MA, Matsuda M, Balas B, *et al.* (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. *Diabetes Care* **30**, 89–94.
17. Muniyappa R & Madan R (2000) Assessing insulin sensitivity, resistance in humans. In *NCBI Bookshelf Endotext* [KR Feingold, B Anawalt and A Boyce, editors]. South Dartmouth, MA: MDtext.com, Inc.
18. Cockcroft EJ, Williams CA, Tomlinson OW, *et al.* (2015) High intensity interval exercise is an effective alternative to moderate intensity exercise for improving glucose tolerance and insulin sensitivity in adolescent boys. *J Sci Med Sport* **18**, 720–724.
19. Cockcroft EJ, Williams CA, Weaver H, *et al.* (2017) Acute exercise and insulin sensitivity in boys: a time-course study. *Int J Sports Med* **38**, 967–974.
20. Dring KJ, Cooper SB, Morris JG, *et al.* (2019) Cytokine, glycemic, and insulinemic responses to an acute bout of games-based activity in adolescents. *Scand J Med Sci Sport* **29**, 597–605.
21. Dring KJ, Cooper SB, Williams RA, *et al.* (2020) Effect of exercise duration on postprandial glycaemic and insulinaemic responses in adolescents. *Nutrients* **12**, 754.
22. Short KR, Pratt LV & Teague AM (2018) A single exercise session increases insulin sensitivity in normal weight and overweight/obese adolescents. *Pediatr Diabetes* **19**, 1050–1057.
23. World Health Organisation (2008) *Waist Circumference and Waist–Hip Ratio*. Report of a WHO Expert Consultation. Geneva: WHO.
24. Dring KJ, Cooper SB, Morris JG, *et al.* (2019) Multi-stage fitness test performance, VO2 peak and adiposity: effect on risk factors for cardio-metabolic disease in adolescents. *Front Physiol* **10**, 629.
25. Fraser BJ, Blizzard L, Schmidt MD, *et al.* (2018) Childhood cardiorespiratory fitness, muscular fitness and adult measures of glucose homeostasis. *J Sci Med Sport* **21**, 935–940.
26. Haapala EA, Wiklund P, Lintu N, *et al.* (2019) Cardiorespiratory fitness, physical activity, and insulin resistance in children. *Med Sci Sports Exerc* **52**, 1144–1152.

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27. Zaqout M, Michels N, Bammann K, *et al.* (2016) Influence of physical fitness on cardio-metabolic risk factors in European children: the IDEFICS study. *Int J Obes* **40**, 1119–1125.
28. LaMonte MJ, Barlow CE, Jurca R, *et al.* (2005) Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome: a prospective study of men and women. *Circulation* **112**, 505–512.
29. Moore SA, McKay HA, Macdonald H, *et al.* (2015) Enhancing a somatic maturity prediction model. *Med Sci Sports Exerc* **47**, 1755–1764.
30. Cole TJ, Bellizzi MC, Flegal KM, *et al.* (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. *Br Med J* **320**, 1240–1243.
31. Ramsbottom R, Brewer J & Williams C (1988) A progressive shuttle run test to estimate maximal oxygen uptake. *Br J Sports Med* **22**, 141–144.
32. Brouns F, Bjorck I, Frayn KN, *et al.* (2005) Glycaemic index methodology. *Nutr Res Rev* **18**, 145–171.
33. Wolever TMS, Jenkins DJA, *et al.* (1991) The glycemic index: methodology and clinical implications. *Am J Clin Nutr* **54**, 846–54.
34. Wolever TM & Jenkins DJ (1986) The use of the glycemic index in predicting the blood glucose response to mixed meals. *Am J Clin Nutr* **43**, 167–172.
35. Matthews DR, Hosker JP, Rudenski AS, *et al.* (1985) Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* **28**, 412–419.
36. Shashaj B, Luciano R, Contoli B, *et al.* (2016) Reference ranges of HOMA-IR in normal-weight and obese young caucasians. *Acta Diabetol* **53**, 251–260.
37. VanVoorhis CW & Morgan BL (2007) Understanding power and rules of thumb for determining sample sizes. *Tutor Quant Methods Psychol* **3**, 43–50.
38. Bates D, Mächler M, Bolker B, *et al.* (2015) Fitting linear mixed-effects models using lme4. *J Stat Softw* **67**, 1–48.
39. Henderson M, Benedetti A, Barnett TA, *et al.* (2016) Influence of adiposity, physical activity, fitness, and screen time on insulin dynamics over 2 years in children. *JAMA Pediatr* **170**, 227–235.
40. Klein S, Allison DB, Heymsfield SB, *et al.* (2007) Waist circumference and cardiometabolic risk: a consensus statement from Shaping America's Health. *Diabetes Care* **30**, 1647–1652.
41. Ramos JS, Dalleck LC, Borrani F, *et al.* (2017) Cardiorespiratory fitness is positively associated with increased pancreatic beta cell function independent of fatness in individuals with the metabolic syndrome: fitness versus fatness. *J Sci Med Sport* **20**, 45–49.
42. Lee SJ & Kim YM (2013) Effects of exercise alone on insulin sensitivity and glucose tolerance in obese youth. *Diabetes Metab J* **37**, 225–232.
43. Bird SR & Hawley JA (2017) Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc Med* **2**, e000143.
44. Keshel T & Coker R (2015) Exercise training and insulin resistance: a current review. *J Obes Weight Loss Ther* **5**, S5–003.
45. Cockcroft EJ, Williams CA, Jackman SR, *et al.* (2017) Agreement and reliability of fasted and oral glucose tolerance test-derived indices of insulin sensitivity and beta cell function in boys. *Int J Sports Med* **38**, 411–417.
46. Barseem NF & Helwa MA (2015) Homeostatic model assessment of insulin resistance as a predictor of metabolic syndrome: consequences of obesity in children and adolescents. *Egypt Pediatr Assoc Gaz* **63**, 19–24.
47. Silva LR, Cavaglieri C, Lopes WA, *et al.* (2014) Endothelial wall thickness, cardiorespiratory fitness and inflammatory markers in obese and non-obese adolescents. *Brazilian J Phys Ther* **18**, 47–55.
48. Metcalf BS, Hosking J, Henley WE, *et al.* (2015) Physical activity attenuates the mid-adolescent peak in insulin resistance but by late adolescence the effect is lost: a longitudinal study with annual measures from 9–16 years (EarlyBird 66). *Diabetologia* **58**, 2699–2708.
49. Laye MJ, Nielsen MB, Hansen LS, *et al.* (2015) Physical activity enhances metabolic fitness independently of cardiorespiratory fitness in marathon runners. *Dis Markers* **2015**, 806418.
50. Mirwald RL, Baxter-Jones ADG, Bailey DA, *et al.* (2002) An assessment of maturity from anthropometric measurements. *Med Sci Sports Exerc* **34**, 689–694.