* Title Page and Abstract

Six-year change in youth physical activity & effect on fasting insulin & HOMA

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ABSTRACT

Background: There is a shortage of longitudinal data analyzing associations between physical activity and indicators of insulin resistance among children and adolescents after accounting for adiposity change. To guide future prevention efforts we used data from the Danish arm of the European Youth Heart Study (EYHS) to examine these issues.

Methods: Participants were 384, 9th grade students (15 years of age) from the Municipality of Odense (Denmark) who participated in surveys in 1997 and 2003. Physical activity was monitored for at least 3 days by accelerometer and mean counts per minute (CPM) and minutes > 3000 counts per minute (minutes > 3000 CPM) per day obtained. Blood samples were collected and fasting insulin, glucose, and homeostatic level of insulin resistance (HOMA-IR) obtained. Data were analysed in 2008.

Results: Physical activity declined from 45 minutes > 3000 CPM in 1997 to 35 minutes in 2003. Longitudinal regression analyses showed that change in minutes >3000 CPM was negatively associated with fasting insulin levels ($z = -2.47$, $p = 0.014$) and HOMA-IR ($z = -2.31$, $p = 0.021$) in 2003. Similar findings were found when CPM was used as the physical activity variable. Results demonstrated that six-year decline physical activity was associated with higher insulin and HOMA-IR levels.

Conclusions: Six-year change in the volume of physical activity in which 15 year old adolescents engaged were negatively associated with fasting insulin and HOMA-IR. Preventing the age-related decline in physical activity may be an effective means of preventing youth insulin resistance.

Key words: Glucose, waist circumference, cohort, children, Type 2 diabetes, prevention

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Methods: Participants were 384, 9th grade students (15 years of age) from the Municipality of Odense (Denmark) who participated in surveys in 1997 and 2003. Physical activity was monitored for at least 3 days by accelerometer and mean counts per minute (CPM) and minutes > 3000 counts per minute (minutes > 3000 CPM) per day obtained. Blood samples were collected and fasting insulin, glucose, and homeostatic level of insulin resistance (HOMA-IR) obtained. Data were analysed in 2008.

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Conclusions: Six-year change in the volume of physical activity in which 15 year old adolescents engaged were negatively associated with fasting insulin and HOMA-IR. Preventing the age-related decline in physical activity may be an effective means of preventing youth insulin resistance.

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BACKGROUND

It has been estimated that in 2006, 22 million children in the European Union (EU) were overweight and of these 5 million children were obese. [1] It is also estimated that over 27,000 European children have type 2 diabetes and over 400,000 have impaired glucose levels. [2] As the prevalence of childhood obesity within the EU is expected to rise by over a million cases per year [1], the number of insulin resistant youths is also likely to increase. To prevent future type 2 diabetes we need to develop effective means of limiting the number of youths who become insulin resistant.

Physical activity is important in the prevention of insulin resistance because it burns calories, leading to decreased body weight and increasing metabolic rate.[3-5] Physical activity also impacts directly on insulin resistance by leading to short term activation of the GLUT-4 receptors to improve glucose uptake and stimulating the alpha-adrenergic receptors of the beta cells, which leads to a decrease in circulating insulin levels.[6-9]

In previous research physical activity has been cross-sectionally associated with adiposity and insulin resistance (IR) among both children and adolescents, thereby supporting physical activity as a means of preventing the development of insulin resistance.[10, 11] However, the cross-sectional design of these studies prevents an examination of whether associations change as youth age. Moreover, although adiposity has been associated with IR, current research has not examined if the associations between activity and IR are maintained after controlling for the potential confounding effect of a change in adiposity. Finally, current research provides few clues on whether it is the volume or intensity of physical activity that is important for the prevention of IR. This information is needed to provide better guidance on the type of activity that future intervention programs should promote. This paper uses data from a cohort of Danish adolescents, who were first studied at age nine and then again at fifteen, to examine the extent to which physical activity is associated with indicators of insulin resistance after accounting for adiposity.

METHODS

Participants

Data are from the Danish arm of the European Youth Heart Study (EYHS). The sampling frame has been discussed in detail elsewhere, but in 1997 3rd grade students were recruited from a sample of schools in the Municipality of Odense.[12, 13] The sample was stratified by the socio-economic status of the area. Data were initially collected on 590, 3rd grade students (310 female) in 1997. In 2003, a second survey was completed in which all of the original participants, now 9th grade students, were invited to participate in the study again. Data were analysed in 2008. As the baseline results have been reported in detail elsewhere, the sample for this paper was limited to the 384 participants (214 female) who took part in both assessments.[11, 13, 14] A Chi-square test indicated no significant difference in the household education of participants who took part in both surveys when compared with those who only took part in 2003 ($p>.05$). Analysis of variance indicated no significant difference in the fasting insulin, glucose or waist circumference of the two groups, but the mean BMI (1997) of participants who took part in both surveys was significantly lower ($f=4.42$, $p =.038$) than that of the participants who took just took part in the 1997 survey (17.15 vs. 17.59 kg/m^2). For the 384 participants with data at both time-points, we report cross-sectional associations at the 9th grade as well as longitudinal changes from 3rd to 9th grade. The study was approved by the ethics committee of Vejle and Funen. Written parental and verbal child consent was obtained for all participants.

Physical activity assessment

Physical activity assessment has been reported elsewhere.[15, 16] Briefly, participants wore an accelerometer (Actigraph model 7164, Manufacturing Technologies Inc) programmed to record physical activity in one minute epochs for at least 4 days (including two weekend days), except when swimming or bathing, on their hip. As there is no standard criteria for defining when monitors were not worn, we applied the previously published EYHS criteria whereby periods in which 10 or more minutes of zero counts were obtained were interpreted as time that the monitor was not worn and these periods were removed from the analysis.[17] Each day of accelerometer data was considered valid if data were obtained for at least 600 minutes. Participants were included in the cross-sectional analyses if they possessed 3 days of valid data in 2003. Participants were included in the longitudinal analyses if they possessed 3 days of valid data in 1997 and 2003. Mean counts per minute (CPM), an indication of the volume of activity in which participants engaged, was averaged across valid days. The mean number of minutes engaged in activity that resulted in greater than 3000 CPM was obtained for each participant and treated as minutes of moderate to vigorous physical activity (MVPA) per day.[18] While there is controversy over accelerometer cutpoints, the 3000 CPM is based on a field validation among adolescents [18] and is comparable to the 3200 CPM value obtained from laboratory calorimetery among 6 to 16 year old US youth, thereby providing a value that is appropriate for our participants.[19]

Insulin resistance (IR) and blood samples

We used three indicators of insulin resistance: fasting insulin, fasting glucose, and the homeostatis model of assessment of insulin resistance (HOMA-IR). HOMA-IR is a simple method of assessing insulin resistance based on fasting insulin and glucose levels.[20, 21] A recent study highlighted that HOMA-IR provided a better indication of clustered cardiovascular risk factors among young adults than an oral glucose tolerance test, indicating that HOMA-IR is likely to provide a better indication of insulin resistance until beta cell function is reduced.[22]

Fasting intravenous blood samples were taken in the morning from the antecubital vein of children who did not have a current diagnosis of diabetes one hour after the application of an anesthetic cream (lidocaine/prilocaine – EMLA cream, Astra). Blood samples were aliquoted and separated within 30 minutes of veni-puncture and stored at -80°C until transported to a WHO certified lab for analysis. In 1997, blood samples were measured at the University of Bristol. Glucose was measured by the hexokinase method on an Olympus AU600 autoanalyser (Olympus Diagnostica, Hamburg, Germany). Insulin was measured by enzyme immunoassay (microtitre plate format – Dako Diagnostics Ltd, Ely, England). In 2003, blood samples were analysed at the University of Cambridge. Plasma specific insulin was determined by two-site immunometric assays with either 125I or alkaline phosphatase labels. Between laboratories correlations for 30 randomly selected samples analyzed at Cambridge and Bristol were 0.94 to 0.98. HOMA-IR was computed (Glucose*Insulin / 22.5).[20, 23] Self-reported non-fasting participants were excluded from analyses.

Body composition assessment

Height was assessed to the nearest 0.5cm using a Harpenden stadiometer. Weight was assessed to the nearest 0.1kg using a Seca beam scale. Body mass index (BMI = kg/m^2) was calculated and converted into representative Danish age and gender specific BMI z-scores that were previously developed using the Cole LMS method.[24] Waist circumference was measured midway between the lower rib and iliac crest after gentle expiration. Puberty was assessed using Tanner Scales.[25]

Statistics

Descriptive statistics were calculated for all variables for each assessment period, histograms plotted and the skewness (<2.0) and kurtosis (<5.0) checked to ensure that the data approximated normality. All variables except the physical activity variables, which were positively skewed, approximated normality. Independent sample t-test's were used to examine whether there were any gender differences in the participants' BMI, waist circumference, insulin, glucose, HOMA-IR, and both indicators of physical activity. As there was a significant drop in physical activity between 1997 and 2003 (Table 1) and we hypothesised that the change in physical activity was likely to be an important predictor of insulin resistance, physical activity change variables (2003 – 1997) were computed for CPM and minutes above 3000 CPM.

All analyses used linear regression models. As participants were recruited from schools, models employed a hierarchical design in which participants were nested within schools using the ***xtreg*** procedure in STATA (Version 9, College Station TX). In light of the clustered nature of the data and the skewed physical activity variables, we also used robust standard errors for all models. Robust standard errors apply a sandwich estimate of the variance structure of the data that makes no assumptions about the variance structure of the data (normal or otherwise).[26]

Cross-sectional models were run to examine the extent to which fasting insulin, glucose and HOMA-IR values were predicted by physical activity when the participants were in the 9th

grade. Fasting insulin, glucose, and HOMA-IR values were the dependent variables with gender, parental education, BMI, waist circumference, and either mean minutes above 3000CPM or mean CPM as independent variables.

Longitudinal models examined whether change (2003 – 1997) in physical activity predicted 2003 insulin, glucose, and HOMA-IR after controlling for gender and parental education. To account for the possibility that change in activity could be influenced by change in adiposity indicators, the models also controlled for change in BMI and waist circumference and the relevant 1997 indicator of IR. Tanner stage data indicated that 82.6% of participants were Tanner stage 1 or 2 in 1997 and 94.0% were Tanner stage 4 or 5 in 2003 and therefore given the lack of variability in these values, Tanner stage was not included in the models. The within school R^2 and the overall R^2 (analogous to a traditional R^2) were obtained for all models. Alpha was set 0.05.

RESULTS

Participant characteristics are shown in Table 1. There were 384 participants and of these 216 (56.3%) lived in a household with a university graduate. The mean BMI increased from 17.2 kg/m^2 in 1997 to 21.2 kg/m^2 in 2003. Mean minutes above 3000 CPM were 45.6 minutes in 1997 and 35.1minutes in 2003. Independent sample t-tests indicated larger 2003 waist circumferences among males (75.94 cm vs. 72.96 cm, t = -3.84, p <0.001), higher 2003 glucose levels among males (5.16 mmol/l vs. 4.89 mmol/l, t = -6.67, p <0.001), higher activity among males with more minutes >3000 cpm (42.73 vs 28.9, t = -5.69, p <0.001), and more CPM (492.2 vs 397.9, t = -5.14, p <0.001). The mean accelerometer counts for 9th grade males and females in 2003 were 496 and 397 counts per minute (CPM) respectively, which is similar to the 501 and 440 CPM that was previously reported for 9th grade adolescents from the same schools in 1997 when our participants were in the 3rd grade.[16]

Waist circumference was crossectionally associated with fasting insulin levels (z = 2.05, p = 0.040), while minutes of activity >3000 CPM was negatively associated (z = -3.17 p = 0.002). The same pattern was evident when mean CPM were used as the physical activity variables. Gender was associated with fasting glucose (z = 3.76, p = 0.001) and this was largely unchanged when CPM was the physical activity variable. Minutes >3000 CPM was negatively associated with HOMA-IR (z = 2.69, p = 0.007). When the model was re-run using CPM , physical activity was negatively associated with HOMA-IR (z = -2.57, p = 0.010) while BMI Z score was positively associated (z = 2.02, p = 0.043), (Table 2).

Insulin in 1997 (z = 2.79, p = 0.005) and change in waist circumference (z =3.16, p = 0.002) were positively associated with insulin in 2003, while change in minutes >3000 CPM was negatively associated (z =-2.47, p = 0.014). Patterns were similar when counts per minute were used as the physical activity variable. Models accounted for 22-23% of the variance within schools and 24% of the overall variance (Table 3). Inspection of the beta coefficients indicated that if all other variables were held constant, the fasting insulin levels of participants whose physical activity level declined by around 22 minutes >3000 CPM per day, or 198 counts per minute, between 1997 and 2003 would be 0.5 mmol/l higher than those whose activity level did not decline.

Glucose from 1997 (z = 3.55, p<0.001) and gender (z = 3.17, p = 0.002) were significant predictors of glucose in 2003, indicating that glucose was higher among males. A comparable pattern was evident when CPM was used in the model. HOMA-IR from 1997 was positively associated with HOMA-IR in 2003 (z = 2.74, P = 0.006) with change in waist circumference also associated with higher HOMA-IR levels (z = 3.39, p = 0.001), while change in minutes

>3000CPM was negatively associated (z = -2.31, p = 0.021). When change in counts per minute was the physical activity variable all three variables remained significant. Beta values indicated that after holding all other variables constant, a 20.6 minutes >3000 CPM per day decline or a 171 count per minute decline in physical activity between 1997 and 2003 was associated with HOMA-IR values that were on average 0.1 units higher. The variance accounted for within schools was 21-22% with the overall variance explained 23%.

DISCUSSION

The physical activity levels of Danish adolescents declined from nine to fifteen years of age and this decline was associated with the participants' fasting insulin and HOMA-IR levels at age fifteen. Estimations based on our data indicate that if mean accelerometer counts declined by about 171 counts per minute or 20.6 minutes >3000CPM between 1997 and 2003, the HOMA-IR levels of participants would be 0.1 units higher than those whose activity did not decline. Similarly, the fasting insulin levels of participants whose physical activity declined by about 22 minutes >3000CPM per day, or 198 accelerometer counts per minute, between 1997 and 2003 would be 0.5 mmol/l higher than the insulin levels of participants whose activity levels did not decline. Cross-sectional analyses also indicated that physical activity was consistently associated with fasting insulin and HOMA-IR levels at age fifteen. These findings buttress previous studies among children and adolescents which have reported cross-sectional associations between physical activity and indicators of insulin resistance by demonstrating that associations are maintained through childhood into adolescence.[11, 27] Findings therefore provide new longitudinal, support for the promotion of physical activity among youth, as a means of maintaining desirable metabolic health.

Physical activity levels were lower at age 15 than at age nine. Comparison of the 9th grade participants in this study with previously published data that was obtained from the same schools in 1997 provided little evidence of the difference between the two groups. The decline in activity from age 9 to 15 is therefore unlikely to be a function of a cultural shift in physical activity. Findings are consistent with previous self-reported age related declines in physical activity and cross-sectional studies reporting lower levels of physical activity among older youth.[28-30] The age related decline is important because youth physical activity interventions have had limited, short-term effects.[31-35] The central premise of all youth interventions has been the addition of physical activity into the participant's day and this increase has required behaviour change.[32] Given the low success of these programs, investigators should consider re-examining the design of youth interventions as longitudinal programs that focus on stemming age-related declines in physical activity may be more effective for protection against insulin resistance.

There has been some debate as to whether the volume of physical activity (as indicated by CPM) or the time spent in activity of a sufficient intensity (minutes > 3000 CPM) is of most benefit for health enhancement.[36, 37] It has been suggested that the overall volume of physical activity could be important for metabolic health, [38] but bursts of moderate to vigorous physical activity could be more important for cardiovascular health.[39, 40] Our data suggests that both the volume and intensity of physical activity are important for the prevention of insulin resistance among adolescents. Therefore, strategies need to be encouraged to promote all kinds of physical activity among youth.

Waist circumference was a significant predictor of insulin and HOMA-IR in both the cross-sectional and longitudinal regression models. This finding is consistent with the data from the

US National Heart, Lung, and Blood Institute's Growth and Health Study which reported that among girls waist circumference at age 10 was a strong independent predictor of developing the metabolic syndrome at age 18.[41] The same study also showed that the tracking coefficient for waist circumference was 0.83, indicating that girls with a large waist circumference at age 10 were likely to still have a large waist circumference at age 18.[41] Collectively the findings of this study and others suggest that routine waist circumference screening, either instead of or as well as BMI, could be particularly important in identifying youth at risk of developing insulin resistance.

Strengths and limitations

The major strength of this study is the physical activity and insulin resistance risk factor information on a cohort of children and adolescents that was assessed at two time points six years apart. The study is limited by the relatively small number of participants with complete physical activity, body composition, blood, and parental education information at both time points, which limited our power to detect relationships. Over 56% of participants resided in homes where a parent was degree educated, which limits our ability to relate the findings to wider socioeconomic groups. It is also important to acknowledge that accelerometers provide poor assessments of cycling and, as they are not worn in water, cannot capture the physical activity associated with swimming.

CONCLUSIONS

This paper has provided further cross-sectional and new longitudinal data on the association between physical activity and indicators of insulin resistance among fifteen year old Danish adolescents. Reductions in physical activity between nine and fifteen years of age were associated with higher fasting insulin levels and HOMA-IR levels. New programs that focus on stemming the age related decline in physical activity are likely to be an effective means of preventing insulin resistance.

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Tables

Table 1: Participant characteristics

Table 2: Cross-sectional regression models predicting indicators of insulin resistance by demographics, waist circumference and physical activity when participants were in the 9^{th} grade (2003)

Table 3: Regression models predicting follow-up indicators of insulin resistance by demographics, change in physical activity, BMI and waist circumference and baseline Insulin Resistance (IR) variables

Table 1: Participant characteristics

	1997 – Participants in 3rd Grade		2003 – Participants in 9th Grade	
Gender	**N**	**(%)**	**N**	**(%)**
Female	214	55.7	214	55.7
Male	170	44.3	170	44.3
Highest education in household				
High School	79	20.6	79	20.6
High school & some University	86	22.4	86	22.4
University graduate & higher	216	56.3	216	56.3
Puberty (3 groups)				
1	317	82.6	0	0
2 (Tanner group 2 and 3)	62	16.1	23	6.0
3 (Tanner 4 and 5)	0	0	361	94.0
Missing	5	1.3	0	0
	N	**Mean (SD)**	**N**	**Mean (SD)**
Age (yrs)	383	9.65 (0.43)	384	15.72 (0.35)
BMI (kg/m^2)	384	17.15 (2.25)	384	21.23 (2.99)
Waist circumference (cm)	379	58.16 (5.41)	383	74.28 (7.68)
Insulin (micro iu/ml)	340	7.95 (4.06)	359	8.75 (3.84)
Glucose (mmol/l)	345	5.11 (0.37)	359	5.02 (0.41)
HOMA-IR	340	1.83 (0.98)	359	1.97 (0.93)
Physical activity data				
Mean days of valid accelerometer data	266	4.22 (1.26)	301	4.42 (0.84)
Mean mins accelerometer data per day	266	777.41 (43.96)	301	817.01 (160.71)
Mean min > 3000 CPM	266	45.64 (29.05)	301	35.08 (21.97)
Mean CPM	266	655.10 (234.43)	301	440.00 (164.55)

Table 2: Cross-sectional regression models predicting indicators of insulin resistance by demographics, waist circumference and physical activity when participants were in the 9th grade (2003)

Dependent Variable = Insulin 2003							
Ind. V (n = 235)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 235)**	**Beta (95% CI)**	**z**	**Sig**
Gender	-0.96 (-1.96; 0.05)	-1.87	0.062	Gender	-1.00 (-2.00; -0.00)	-1.96	0.050
High school*	0.36 (-0.85; 1.56)	0.58	0.563	High school*	0.39 (-0.81; 1.60)	0.65	0.517
Some University*	0.16 (-0.75; 1.07)	0.35	0.729	Some University*	0.29 (-0.64; 1.23)	0.61	0.540
BMI Z Score	0.79 (-0.07; 1.64)	1.80	0.071	BMI Z Score	0.88 (-0.00; 1.77)	1.96	0.050
WC (cm)	0.11 (0.00; 0.22)	2.05	**0.040**	WC (cm)	0.12 (0.01; 0.22)	2.09	**0.036**
Min > 3000	-0.03 (-0.05; 0.01)	-3.17	**0.002**	Mean CPM	-0.00 (-0.01; -0.00)	-2.91	**0.004**
Within R^2 = 0.194 Overall R^2 = 0.224				Within R^2 = 0.206 Overall R^2 = 0.235			
Dependent Variable = Glucose 2003							
Ind. V (n = 235)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 2235)**	**Beta (95% CI)**	**z**	**Sig**
Gender	0.22 (0.11; 0.34)	3.76	**<0.001**	Gender	0.23 (0.11; 0.34)	3.82	**<0.001**
High school*	0.09 (-0.05; 0.22)	1.22	0.224	High school*	0.09 (-0.05; 0.23)	1.27	0.203
Some University*	0.07 (-0.06; 0.19)	1.02	0.308	Some University*	0.09 (-0.04; 0.21)	1.34	0.181
BMI Z Score	0.03 (-.07; 0.12)	0.61	0.541	BMI Z Score	0.03 (-0.06; 0.13)	0.67	0.503
WC (cm)	-0.00 (-0.01; 0.01)	-0.11	0.915	WC (cm)	-0.00 (-0.01; 0.01)	-0.25	0.805
Min > 3000	-0.00 (-0.00, 0.00)	-0.32	0.747	Mean CPM	-0.00 (-0.00; 0.00)	-0.66	0.511
Within R^2 = 0.094 Overall R^2 = 0.110				Within R^2 = 0.098 = Overall R^2 = 0.111			
Dependent Variable = HOMA-IR 2003							
Ind. V (n = 235)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 235)**	**Beta (95% CI)**	**z**	**Sig**
Gender	-0.10 (-0.37; 0.16)	-0.77	0.440	Gender	-0.11 (0.38; 0.15)	-0.83	0.405
High school*	0.13 (-0.19; 0.44)	0.81	0.418	High school*	0.14 (-0.17; 0.46)	0.89	0.375
Some University*	0.05 (-0.17; 0.26)	0.45	0.654	Some University*	0.09 (-0.13; 0.31)	0.77	0.441
BMI Z Score	0.21 (-0.01; 0.42)	1.89	0.059	BMI Z Score	0.23 (0.01; 0.45)	2.02	**0.043**
WC (cm)	0.02 (-0.01; 0.05)	1.87	0.062	WC (cm)	0.02 (-0.00; 0.05)	1.91	0.057
Min > 3000	-0.01 (-0.01; -0.00)	-2.69	**0.007**	Mean CPM	-0.00 (-0.00; -0.00)	-2.57	**0.010**
Within R^2 = 0.179 Overall R^2 = 0.202				Within R^2 = 0.191 Overall R^2 = 0.211			

* University educated is reference group WC = Waist Circumference CPM = Counts per minute

Table 3: Regression models predicting follow-up indicators of insulin resistance by demographics, change in physical activity, BMI and waist circumference and baseline Insulin Resistance (IR) variables

Dependent Variable = Insulin 2003							
Ind. V (n = 147)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 147)**	**Beta (95% CI)**	**z**	**Sig**
Gender	-0.76 (-1.77; 0.26)	-1.47	0.143	Gender	-0.72 (-1.76; 0.32)	-1.35	0.177
High school*	0.63 (-1.02; 2.29)	0.75	0.453	High school*	0.68 (-0.97; 2.33)	0.81	0.417
Some University*	-0.18 (-1.26; 0.90)	-0.32	0.749	Some University*	0.01 (-1.14; 1.18)	0.02	0.981
Δ BMI Z score	0.67 (-0.32; 1.65)	1.33	0.184	Δ BMI Z score	0.68 (-0.32; 1.68)	1.34	0.181
1997 insulin (mmol/l)	0.17 (0.05; 0.29)	2.79	**0.005**	1997 insulin (mmol/l)	0.17 (0.04; 0.29)	2.59	**0.010**
Δ WC (cm)	0.18 (0.07; 0.30)	3.16	**0.002**	Δ WC (cm)	0.20 (0.08; 0.32)	3.30	**0.001**
Δ Min > 3000	-0.02 (-0.04; -0.00)	-2.47	**0.014**	Δ Mean CPM	-0.00 (-0.00; -0.00)	-2.18	**0.029**
Within R^2 = 0.220		Overall R^2 = 0.241		Within R^2 = 0.234		Overall R^2 = 0.241	
Dependent Variable = Glucose 2003							
Ind. V (n = 149)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 149)**	**Beta (95% CI)**	**z**	**Sig**
Gender	0.21 (0.08; 0.34)	3.17	**0.002**	Gender	0.21 (0.08; 0.38)	3.14	**0.002**
High school*	0.08 (-0.10; 0.25)	0.87	0.384	High school*	0.08 (-0.09; 0.26)	0.92	0.359
Some University*	0.02 (-0.15; 0.18)	0.18	0.856	Some University*	0.03 (-0.14; 0.19)	0.30	0.765
Δ BMI Z score	0.02 (-0.09; 0.13)	0.42	0.675	Δ BMI Z score	0.02 (-0.09; 0.13)	0.37	0.712
1997 Glucose (mmol/l)	0.36 (0.16; 0.55)	3.55	**<0.001**	1997 Glucose (mmol/l)	0.36 (0.16; 0.56)	3.55	**<0.001**
Δ WC (cm)	0.01 (-0.00; 0.02)	1.19	0.234	Δ WC (cm)	0.01 (-0.01; 0.02)	0.99	0.321
Δ Min > 3000	-0.00 (-0.00; 0.00)	-0.77	0.443	Δ Mean CPM	-0.00 (-0.00; 0.00)	-1.55	0.121
Within R^2 = 0.244		Overall R^2 = 0.206		Within R^2 = 0.239		Overall R^2 = 0.206	
Dependent Variable = HOMA-IR 2003							
Ind. V (n = 147)	**Beta (95% CI)**	**z**	**Sig**	**Ind. V (n = 174)**	**Beta (95% CI)**	**z**	**Sig**
Gender	-0.05 (-0.30; 0.20)	-0.41	0.683	Gender	-0.04 (-0.29; 0.21)	-0.33	0.745
High school*	0.21 (-0.25; 0.67)	0.91	0.363	High school*	0.23 (-0.23; 0.69)	0.96	0.336
Some University*	-0.04 (-0.30; 0.21)	-0.32	0.749	Some University*	0.00 (-0.27; 0.27)	0.01	0.995
Δ BMI Z score	0.17 (-0.09; 0.42)	1.26	0.206	Δ BMI Z score	0.17 (-0.09; 0.43)	1.28	0.200
1997 HOMA-IR	0.17 (0.05; 0.29)	2.74	**0.006**	1997 HOMA-IR	0.17 (-0.04; 0.30)	2.60	**0.009**
Δ WC (cm)	0.05 (0.02; 0.07)	3.39	**0.001**	Δ WC (cm)	0.05 (0.02; 0.08)	3.54	**<0.001**
Δ Min > 3000	-0.00 (-0.01; -0.00)	-2.31	**0.021**	Δ Mean CPM	-0.00 (-0.00; -0.00)	-2.09	**0.037**
Within R^2 = 0.214		Overall R^2 = 0.231		Within R^2 = 0.228		Overall R^2 = 0.235	

* University educated is reference group WC = Waist Circumference CPM = Counts per minute