Title: Relationships between a walk test, body size and metabolic risk among a New Zealand Māori Community

Running head: Walk test and metabolic risk

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ABSTRACT

Aims Programmes to prevent or delay chronic disease incorporate promotion of physical activity particularly walking. The objective of this study was to test the associations of the ability to walk quickly with measures of adiposity and metabolic risk including dysglycaemia.

Subjects and methods Participants (3209), without known diabetes, in a lifestyle trial undertook a 4 minute walk test (4MWT) following measurements of fasting lipids, 75g oral glucose tolerance test, anthropometry and blood pressure. Lower socioeconomic status was defined by possession of a "community services card" (CSC). Dysglycemia (diabetes, impaired glucose tolerance and impaired fasting glucose) and metabolic syndrome (MS) were defined by WHO and ATPIII criteria respectively.

Results Controlling for age, length of the walk-course and height; distance walked during the 4MWT decreased linearly (P<0.001) with increasing waist, body mass index, %fat mass and MS risk. On average those with dysglycemia walked 15.2(95%CI 9.3,20.8)m less than "normal" participants independent of gender. In the best-fit regression model, distance walked was associated with reduced distances walked 1.3(1.2,1.5)m/year of age, 0.9(0.8,1.1)m/kg fat, 15.7(11.2,19.5)m with a CSC and 8.0(5.8,10.2)m if currently smoking. Each additional MS factor was associated with a reduction of the distance walked by 6.6(4.6, 8.6)m.

Conclusion Increasing numbers of MS components are associated with slower walking. The 4MWT is an easy assessment of functional limitation, which may have use in guiding intervention.

KEYWORDS: walk test, diabetes, obesity, metabolic syndrome X, Māori.

Abbreviations: 4 MWT 4 minute walk test, ATP adult treatment panel, ANCOVA analysis of covariance, BMI body mass index, CI confidence interval, CSC community services card, DHB district health board, HDL-C high density lipoprotein cholesterol, IFG impaired fasting glucose, IGT impaired glucose tolerance, LDL-C low density lipoprotein cholesterol, OGTT oral glucose tolerance test, WHO world Health Organisation,

INTRODUCTION

Inadequate physical activity is an important risk factor for diabetes and the metabolic syndrome.(Hamilton et al. 2007) Walking is the most common physical activity that contributes to mobility, energy expenditure (Bassuk & Manson 2005), physical fitness and health (Warburton et al. 2006) and is a major determinant of quality of life.(Guyatt et al. 1993) The muscles involved in walking involve up to 20% of body mass (Janssen et al. 2000) and have a major role in both glucose disposal and storage.(Moore et al. 2003) Mass and quality of skeletal muscle are very important mediators of glucose disposal (Goodpaster et al. 1997; Juel 2006), lipid homeostasis and insulin resistance.(Janssen & Ross 2005)

Current methods to assess physical activity include self-report questionnaires, which can be significantly and subjectively biased (Neilson et al. 2008), and using expensive equipment such as accelerometers and pedometers (Corder et al. 2007). Functional status measurements such as the ability to walk may be difficult to interpret because small differences may not be clinically significant or below the threshold at which a difference in function is noticed by the individual.(Redelmeier et al. 1997; Norman et al. 2003) A robust assessment of physical function could be useful in epidemiological surveys, patient management and in the evaluation of interventions. A six minute walk test is currently used in chronic disease to assess function.(Enright 2003) In large epidemiological surveys and in the clinical setting the time taken to complete the exercise, with the subsequent rest period required, may be too long for some individuals and reduce the number able to undergo the test.

Te Wai o Rona: Diabetes Prevention Strategy was a large trial of intensive lifestyle intervention among Maori without known diabetes in New Zealand.(Lim et al. 2008) A shorter (four minute) walk test was devised to reduce the respondent and research assistant burden, to maximise the number of people that could be measured on any one day, and allow

the test to be administered in a variety of venues and conditions. The purpose of this analysis was to assess the associations of body composition, metabolic risk factors (including dysglycemia and smoking status) with the distance covered in the four minute walk test (4MWT). We hypothesised that the distance walked in four minutes would be reduced by adiposity, and measures of metabolic risk including glycemic status and smoking.

METHODS

Participants.

Those invited were self-identified Maori and other household members aged ≥28 years on 30/9/2004, without known diabetes and resident within the boundaries of the Waikato District Health Board (DHB), and the tribal area of Ngati Tuwharetoa in the neighbouring Lakes DHB. Younger Maori with past gestational diabetes mellitus or with 2 parents with known diabetes were eligible. Exclusion criteria included terminal illness and those unfit to sign the consent form. Recruitment (5/2004-3/2006) occurred through a variety of health, community and media channels. The study was approved by the Northern Y Regional Ethics Committee and written signed informed consent was obtained from all subjects. The trial was registered with the Australasian Controlled Trials Registry (ACTRN012605000622606).

Procedures.

Participants were asked to fast overnight and transport to the screening venue was provided. At the screening venue, signed informed consent was obtained and fasting status (number of hours since last ate) was ascertained. Before consuming 75g glucose for the glucose tolerance test, a fasting sample was obtained by venepuncture for glucose and lipids. Two hours after consuming the glucose a further venepuncture sample was taken. Less than 30 minutes after each sampling point the blood was centrifuged (4000 rpm for 10 minutes) and refrigerated at 4 C for transport to the laboratory for analysis the same day as sampling.

Glucose was determined by a hexokinase method and total cholesterol, high density lipoprotein cholesterol (HDL-C) and triglyceride by enzymatic colorimetric methods using a Roche modular P800 instrument. (Roche Diagnostics, Mt Wellington, Auckland). Low density lipoprotein cholesterol (LDL-C) was then derived using the formula: LDL-C= [total cholesterol - (triglyceride/2.2) – HDL-C]. All assays were within target limits specified by the Royal College of Pathologists of Australasia Quality Assurance Program. These assays were carried out by the Waikato District Health Board Laboratory which has International Accreditation New Zealand ISO9002 accreditation. WHO criteria (World Health Organization & International Diabetes Federation 2006) were applied to the two glucose measurements to define dysglycemia (impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or diabetes). IFG when fasting glucose was ≥6.1 and <7.0 mmol/L, IGT when fasting glucose was <7.0 and two hour was ≥7.8 and <11.1 mmol/L and Diabetes when fasting was ≥7.0 and/or two hour was ≥11.1 mmol/L.

During the OGTT, other measurements included resting (at least 10 minutes) blood pressure (Auto Blood Pressure Monitor T8; Omron Corporation, Tokyo), height±0.5cm without shoes (portable height scale PE087; Mentone Education Centre, Victoria, Australia) and weight±0.1kg in light clothing (Wedderburn TI-TH316 or Wedderburn TI-BWB800 Personal scales (up to 200kg) for oversize participants). Waist±0.5cm at the lateral mid point between the lower rib and iliac crest was measured with the participant standing, Resistance was assessed by single frequency 50 Hz, hand-to-foot bioimpedance (IMP5, Impedimed, Queensland) and body fat determined using a previously validated equation.(Swinburn et al. 1999)

Given the number to be screened the walk test was amended to 4 minutes rather than the conventional 6 minutes (American Thoracic Society 2002) and the course length adjusted to fit the available environment. The 4MWT was conducted according to standardised

protocols (American Thoracic Society 2002) after completion of the OGTT and before breakfast. Participants were told that "the purpose of this test is to see how far you can walk in four minutes". They were shown how to walk and turn quickly at the ends of the course, which was marked with cones at the start and finish lines. They were told they were allowed to stop and rest during the test if necessary. Each participant received standardised individual encouragement throughout. Laps were recorded with a lap counter, and partial lap distance estimated from cones which were placed along the course at 5m intervals. Duration of the test was timed with a stopwatch. Pedometers were worn by participants and the number of steps noted as a quality control check of the distance recorded. At the end of the test they were asked if they had experienced any symptoms such as chest pain, dizziness or lower limb pain. The number of testing occasions was 245, at 90 venues, with between 1 and 112 tested (median of 5). Course length varied between 20m and 40m (median 40)m.

Criteria for exclusion from the walk test included: measured resting systolic blood pressure >200mmHg, diastolic blood pressure >130 mmHg, resting pulse >110bpm, or if in the responses to the Physical Activity Readiness Questionnaire (Cardinal et al. 1996) there was (a) an existing heart condition and physical activity was not recommended by a doctor, (b) chest pain with activity or (c) chest pain when not doing physical activity and aged ≥40 years.

In another study approved by the Auckland University of Technology Ethics Committee a convenience sample of twelve healthy subjects aged 62-81y (8 women, 4 men) attending a fitness programme repeated the four minute walk test protocol on 3 different days three days apart. There was no difference within subject of distance walked (392±52m, P=0.99) between test occasions. The intra-individual coefficient of variation was 7.6%. This compares with a 4.2% intra-individual variation for 29 older adults (426±143m), in a 6 minute walk test repeated after a week (Eaton et al. 2005). The sample size necessary to

detect a difference in distance travelled of 10m (SD 52 and a 2.5% difference in distance travelled) with a power of 80% and an alpha of 0.05 was 426.

Of the 5309 participants aged 19 to 85y, enrolled in Te Wai o Rona Diabetes Prevention Strategy pregnant women (n=50) and those subsequently found to have pre-existing diabetes (n=19) were excluded from this analysis. Overall, 3203 participants (Figure 1) completed the walk test, and of these 87.5% self identified as Māori descent, 6.0% as European and 6.5% as other (mainly Pacific Island). Of those with walk test and anthropometric data, 89.9% (2878/3203) reported after an overnight fast and completed the OGTT. In these subjects metabolic syndrome (MS) risk factors were defined by ATPIII criteria (National Cholesterol Education Program Expert Panel 2001). Waist measurement was not used as a risk factor because, at present, there is not a defined waist cutpoint for Polynesians for metabolic syndrome. The 328 who did not have complete MS criteria measured, and were excluded, did not differ in proportion of men and women, but were 4 years younger and had a waist measurement 3cm less than those who underwent an OGTT. 95% of the cohort answered "yes" or "no" to the question concerning possession of a community services card (CSC), issued by the Ministry of Social Development dependent on income, family status and accommodation criteria. Possession of this card is representative of low socioeconomic status. Smoking status was not recorded by 1.0%. Only for analyses that included CSC or smoking status were the participants without this information excluded.

Statistics

The study population was characterised separately by sex using frequency for categorical variables and mean and standard deviation for normally distributed variables. Differences between males and females were determined by chi-squared tests for categorical data and by unpaired Student's t test for normally distributed data. Multiple linear regression with adjustment for sex (female 0, male 1), age, height (a surrogate for leg/step length) and course

length were used to explore the effect of BMI, waist, fat mass and body fat percent on the distance walked. The extent of collinearity in the multiple linear regression model was investigated using the variance inflation factor. Analysis of covariance (ANCOVA) with adjustment for height (a surrogate for leg/step length), age and course length was used to examine the trends related to walk distance and categorical variables including socioeconomic and smoking status and number of MS risk factors. Comparisons between subgroups were made using the Tukey HSD test to reduce the chance making a type I error. Stepwise multiple linear regression analysis determined the best potential predictors of total distance walked and their partial correlation within the model. All comparisons were two sided and $P < 0.05$ taken as significant.

RESULTS

Men were taller, heavier, had less body fat and higher systolic and diastolic blood pressure, and walked further in 4 minutes than women, Table I. Smoking prevalence was high: 38.6% of women and 47.7% of men had never smoked (Table I) . More women than men were currently smoking. Men had a higher prevalence of at least one MS component and dysglycemia ($P < 0.0001$). 57.4% of participants had a CSC.

Insert Figure 1 and Table I here

The relationships between distance walked and anthropometric variables BMI, waist, fat mass and body fat percentage were investigated with explanatory variables height, course length, sex and age. All models accounted for about 18% of the variance in the relationship, which is shown in detail for waist and body fat percentage only, in Table II. BMI and fat mass are not shown in this table as their association follows the same pattern as waist and body fat percentage. Distance walked decreased with increasing age, BMI, waist, fat mass and body fat%. A longer course length and longer legs were associated with increased walk distance. Compared with women, being male was associated with increased distance walked

for the BMI and waist models. However, for the same body fat percentage, age and height males would walk 13 metres less than women.

Insert Table II here

One to four MS risk factors were present in 75.4% of women and 87.8% of men. As number of MS risk factors (MS count) increased, the distance completed decreased (women P =0.001, men P =0.05) (Figure 2). Those with dysglycemia walked 15.2(95%CI 9.3-20.8) m less than "normal" participants (P<0.0001) independent of gender (dysglycemia 350.5(345.3, 355.7)m vs normal 365.7(363.5-367.8)m P<0.001). These patterns of relationship of distance walked with MS count and dysglycaemia remained after adjustment for fat mass and body mass (data not shown). The relationship between BMI, fat mass and ethnicity (Māori vs European) was explored and we were not able to see any difference by ethnicity. Smoking status explained the biggest difference in 4MWT distance. The 42% currently smoking walked 357(368, 374)m (adjusted mean) less than the 21% former regular smokers (362(358, 367)m), and the 37% who had never smoked or never smoked regularly (371(368-374)m) independent of sex (P=<0.0001).

Insert Figure 2 here

Stepwise, forward and backward multiple regression using all the risk factors were used to predict factors affecting distance walked. In the best model each year of age, kg of fat mass, CSC (1 yes, 0 no) and smoking (1 yes 0 not now but heavy smoker previously, -1 never smoked) reduced the distance walked by 1.3(CI -1.5, -1.2), 0.9 (-1.1, -0.76), -15.7(-19.5, -11.2) and 8.0(-10.2, -5.8)m respectively. Each metre of course length and centimetre of height increased the distance walked by 2.3(2.0, 2.6) and 1.1(0.7, 1.4) m respectively, R^2=0.21, SEE 53m. None of sex, waist, glycemic status, lipids or blood pressure were predictors. The generalised equation for distance completed in the 4MWT is represented in Table III in order of best fit and showing partial correlations. More people with a CSC

smoked, but after controlling for CSC, smoking past and present still reduced the distance walked. When number of MS factors were included in the model (adjusted for height, age and course length) each additional MS factor reduced the distance walked by 6.6(4.6, 8.6)m adjusted R^2=0.16, SEE 54m.

DISCUSSION

Our study validates a new, easy, safe and objective measure of functional physical activity behaviour for use in population studies, clinical service delivery and even community groups. Unfortunately, due to funding issues we were not able to follow-up in this cohort any change in walk test distance after the lifestyle intervention.(Simmons et al. 2008) The linear downward trend between the distance covered in the 4MWT and number of MS factors in both sexes, further validates its use in similar populations. It is worthwhile noting that only 86/3723 (2.3%) paused or stopped during the walk test with reasons that included chest pain, breathlessness and hip and calf pain. While we were not able to test the validity of the test others have shown that six minute(Enright 2003) and the two minute(Leung et al. 2006) walk tests are valid measures of exercise capacity, we believe that 4 minutes should also be a valid measure.

Distance walked in four minutes was most strongly and negatively related to four factors -age, fat mass, lower socioeconomic status and smoking, and also with increasing numbers of components of the metabolic syndrome. Our measure of socioeconomic status reflects multifactorial individual and environmental confounders which have complex interrelationships with health and function. One long term, environmental change possible would be to improve neighbourhood walkability in lower socioeconomic areas (Rundle et al. 2008).

In children (Grund et al. 2000) and the elderly (Sternfeld et al. 2002) increased fat mass has been associated with a reduction in physical performance. Our results also indicate

that increased central adiposity (as reflected by waist adjusted for height) has an influence alongside total fat mass. The relationships between the distance walked in the 4 minute walk test, metabolic syndrome count and dysglycaemia were confounded by fat mass and total body mass but the relationships shown in Figure 2 still held after these adjustments. Smoking had a profound effect on physical performance (Fagerstrom 2002) – equivalent in our study to an age related decline of 10 years. This impairment of performance is similar to the report for elderly women (Rapuri et al. 2007). While in general those with a smaller waist and BMI were able to walk further there is the confounding that current smoking was associated with a smaller waist and lower BMI (data not shown). These participants may also have had associated significant co-morbidities (not measured) such as chronic obstructive pulmonary disease.

It is well known that obesity and physical inactivity contribute to the development of dysglycemia (Rana et al. 2007) and MS. Clustering of risk factors is useful for prediction of risk in an individual but often relies on factors that do not measure the ability to perform activities of daily life. Few studies report the association of risk factors with an objective measure of physical performance. Okoro et al (Okoro et al. 2006) using the ATPIII criteria for MS (National Cholesterol Education Program Expert Panel 2001) in adults ≥50y found no association between gait speed (over 6.1m) impairment and MS. They were able to show in women only gait speed impairment was associated with waist (>88cm) and low HDL cholesterol. Our study has undertaken similar analyses and has reported similar results but without specific cut-points. No accepted metabolic syndrome diagnostic cut-off for waist Maori and other Polynesians has yet been defined (WHO Expert Consultation 2004; Alberti et al. 2006), so we are not able to repeat these analyses. Indeed, it is known that for the same height and weight Maori have more muscle and less fat than Europeans (Swinburn *et al.* 1999), but the longitudinal studies to equate waist to morbidity and mortality are lacking in

this population. It is interesting that in the multivariate analyses, the distance walked was associated with the number of components of MS, but not any specific components per se. We find this hard to explain, but speculate that this is due to the lower precision of the measurements from a biological view point. It is also possible that the relationship with the walk test is more with the underlying metabolic syndrome process, which leads to the clustering of its components

The 4MWT was administered safely by trained assistants as part of a comprehensive screening protocol. Participants who did not have other limiting factors took part willingly, did not require a lot of explanation and completed the whole process within 10 minutes, including the subsequent rest period. Very few participants (6%), who started the test were unable to complete, and no adverse events were reported. We suspect that having a shorter test than the current 6 minute test (Leung *et al.* 2006), may increase its utility in the general population and those with significant co-morbidities. With the growing obesity pandemic, it may become increasingly useful. The precision of this continuous measurement means that it would be sensitive enough to measure change, and therefore demonstrate effectiveness (or not) of intervention to improve function of an individual over time.

We conclude that the more MS components present, the slower the speed that individuals are able to walk or vice versa. The 4MWT is an easy, safe and relatively quick objective assessment of the ability to walk quickly across a diverse (by age, body size, and varying risk) population. While useful in screening populations, it could also have utility in the clinical setting for inclusion in the approach to assessing functional limitations, and may help with identifying those whose metabolic phenotype is more associated with sedentary behaviour, and therefore be more amenable to lifestyle intervention.

Declaration of Competing Interests: Nothing to declare

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Table I – *Descriptive characteristics of participants by sex*

	Women (n = 2115)	Men (n = 1088)	*P* value
Age (years)	45 (12)	46 (12)	0.01
Weight (kg)	84.0 (19.1)	98.1 (20.3)	<0.0001
Height (cm)	162.5 (5.9)	174.3 (6.7)	<0.0001
BMI (kg/m^2)	31.8 (7.0)	32.2 (6.2)	0.09
Waist (cm)	96.0 (15.6)	104.6 (15.8)	<0.0001
Body Fat (%)	41.6 (6.2)	30.7 (6.9)	<0.0001
Systolic blood pressure (mmHg)	130.8 (20.1)	138.4 (17.1)	<0.0001
Diastolic blood pressure (mmHg)	87.6 (12.0)	89.9 (11.6)	<0.0001
Resting pulse (bpm)	67.6 (9.4)	66.7 (10.9)	0.03
Blood pressure treatment (%)	11.3	11.2	1.0
Distance walked in 4 minutes (m)	359.1 (58.3)	371.3 (60.9)	<0.0001
Current smoker (%)	40.3	31.1	<0.0001
Never smoked regularly or at all in past (%)	38.7	47.7	<0.0001
Smoked heavily in past (%)	21.0	21.2	0.3
OGTT and lipids (n)	1902	976	
Fasting glucose (mmol/l)	5.2 (0.8)	5.5 (1.0)	<0.0001
Triglycerides (mmol/l)	1.4 (1.0)	1.8 (1.7)	<0.0001
HDL cholesterol (mmol/l)	1.40 (0.36)	1.25 (0.37)	<0.0001
Diabetes status Diabetes/IGT/IFG (%)	3.4/7.6/2.7	5.7/6.7/4.9	<0.0001

Metabolic Syndrome component (%)			
Fasting glucose ≥ 5.6 mmol/l	18.2	32.1	<0.0001
Triglycerides ≥ 1.7 mmol/l	21.1	35.3	<0.0001
HDL cholesterol ≤ 1.29 female, ≤ 1.03 male	19.3	10.7	<0.0001
Raised blood pressure, systolic ≥ 130 or diastolic ≥90 mmHg	62.9	79.2	<0.0001

Data are means (SD), unless otherwise indicated, P unpaired t test or chi squared for sex

Table II

Multiple regression analyses for prediction of walk test distance using waist and body fat percentage –sex, course length, height, age entered in all models

Model	Waist			Fat%		
Variable	*B*	*95% CI*	*Partial r*	*B*	*95% CI*	*Partial r*
Constant	223.3	167.6 to 278.9		253.4	196.2 to 310.7	
Sex	6.5	1.0 to 12.0	0.04	-13.0	-19.3 to -6.7	-0.07
Course Length, m	2.3	2.0 to 2.7	0.25	2.4	2.0 to 2.7	0.24
Height, cm	1.1	0.8 to 1.4	0.12	0.8	0.5 to 1.2	0.09
Age, year	-1.2	-1.4 to -1.0	-0.24	-1.2	-1.4 to -1.0	-0.24
Waist, cm	-0.75	-0.87 to -0.63	-0.21			
Fat%				-1.5	-2.0 to-0.2	
$R^2_{adjusted}$		0.18			0.17	
F for change in R^2		142.1			129.8	

Sex 0 Female, 1 Male, CI confidence interval, r correlation

Table III – *Multiple regression analysis of prediction of distance walked in 4 minutes, course length and participant characteristics.*

Distance walked Constant 241.16m	ß	95% CI	*P*	Partial correlation
Age y	-1.37	-1.54 to-1.20	<0.0001	-0.28
Course length, m	2.32	2.00 to 2.66	<0.0001	0.24
Fat mass, kg	-0.91	-1.05 to -0.76	<0.0001	-0.22
Community services card, 1 Yes 0 No	-15.66	-19.54 to -11.77	<0.0001	-0.14
Smoking status 1 now, 0 used to, -1 never smoked	-7.99	-10.17 to -5.81	<0.0001	-0.13
Height, cm	0.82	0.59 to 1.06	<0.0001	0.13

Adjusted R^2 =0.210 SEE =52.73m

Sex, waist, glycemic status, lipids or blood pressure were not significant entrants into the model

Legends for Figures

Figure 1 – *Flow diagram for eligibility for inclusion in walk test analysis.*

Figure 2 – *Distance walked in relation to metabolic risk, dysglycemia and smoking*

*Mean ((95%CI) distance walked in 4 minutes (adjusted by age, course length and height within each sex) by number of metabolic syndrome risk factors and dysglycemia (female 1902, male 976 determined using OGTT) and smoking status (female 2088, male 1084 including no OGTT). Number of participants in each category is shown within the bar * significantly different to preceding adjacent group mean. In each analysis presented the linear trend for performance to decrease with increasing risk is significant (P <0.001) and* R^2 *for each model is >0.10.*

Figure 1

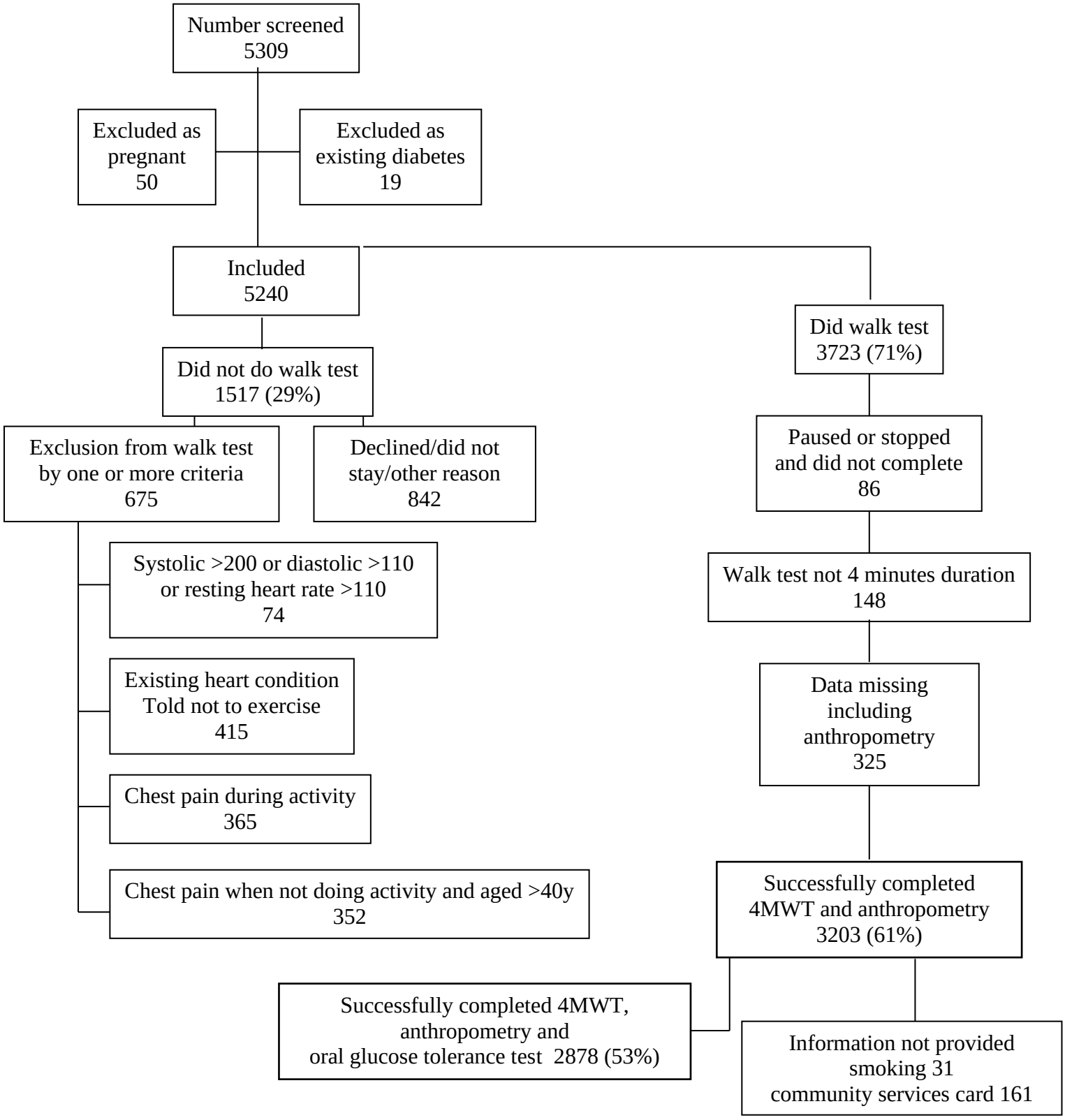
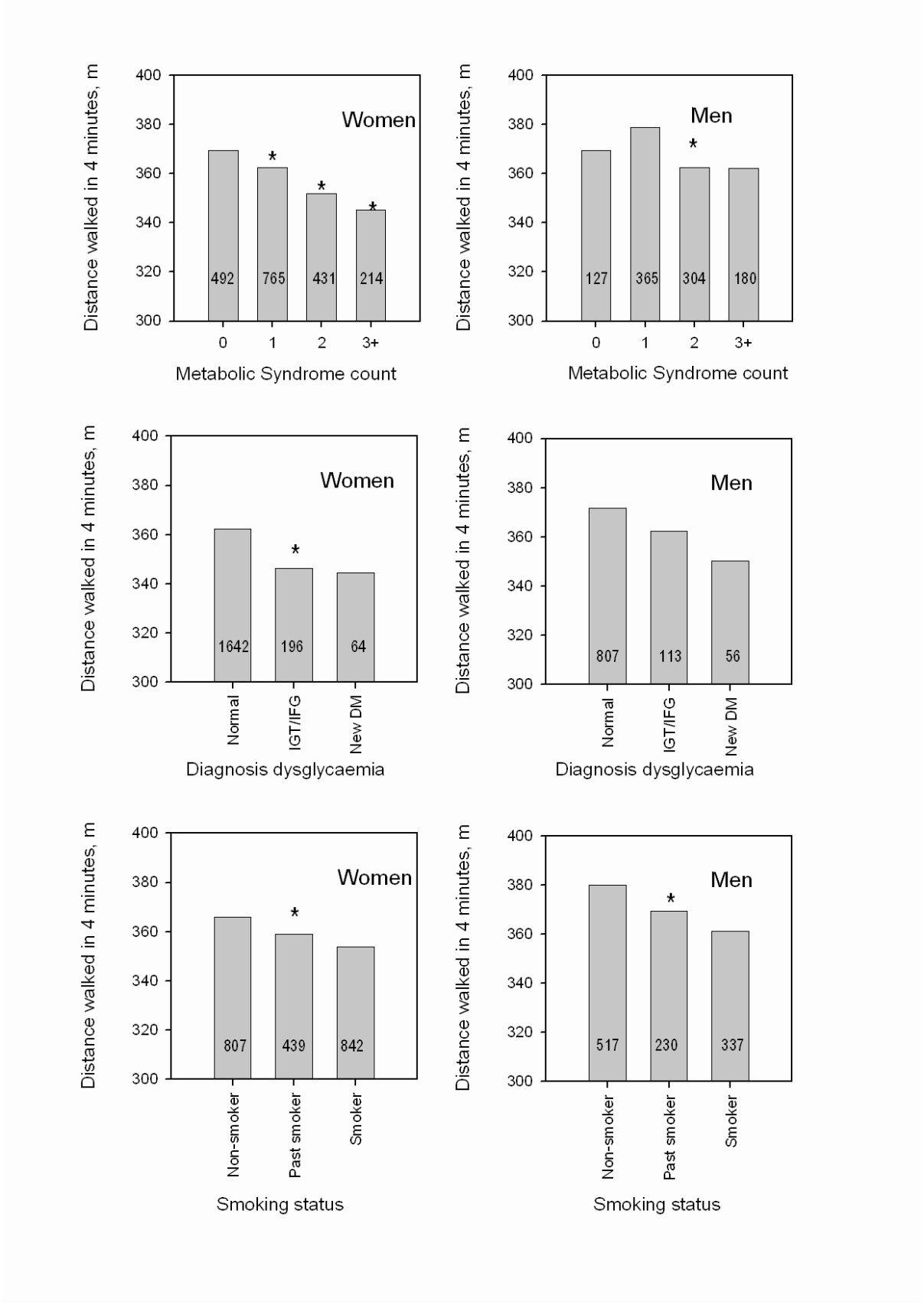

Number screened
5309
Excluded as pregnant
50
Excluded as existing diabetes
19
Included
5240
Did not do walk test
1517 (29%)
Did walk test
3723 (71%)
Exclusion from walk test by one or more criteria
675
Declined/did not stay/other reason
842
Paused or stopped and did not complete
86
Systolic >200 or diastolic >110 or resting heart rate >110
74
Walk test not 4 minutes duration
148
Existing heart condition Told not to exercise
415
Data missing including anthropometry
325
Chest pain during activity
365
Chest pain when not doing activity and aged >40y
352
Successfully completed 4MWT and anthropometry
3203 (61%)
Successfully completed 4MWT, anthropometry and oral glucose tolerance test 2878 (53%)
Information not provided
smoking 31
community services card 161

Figure 2


Distance walked in 4 minutes, m
Women
Men
Metabolic Syndrome count
0
1
2
3+
492
765
431
214
127
365
304
180
Diagnosis dysglycaemia
Normal
IGT/IFG
New DM
1642
196
64
807
113
56
Smoking status
Non-smoker
Past smoker
Smoker
807
439
842
517
230
337
400
380
360
340
320
300
*