

## The Combating Obesity in Māori and Pasifika Adolescent School-children Study: COMPASS Methodology and Study Protocol

Lee Stoner, Sarah P. Shultz, Danielle M. Lambrick<sup>1</sup>, Jeremy Krebs<sup>2</sup>, Mark Weatherall<sup>2</sup>, Barry R. Palmer<sup>1</sup>, Andrew M. Lane<sup>3</sup>, Geoff Kira<sup>4</sup>, Trevor Witter, Michelle A. Williams<sup>5</sup>

School of Sport and Exercise, Massey University, Wellington, New Zealand, <sup>1</sup>Institute of Food Nutrition and Human Health, Massey University, New Zealand, <sup>2</sup>Department of Medicine, University of Otago, Wellington, New Zealand, <sup>3</sup>School of Sport, Performing Arts and Leisure, Wolverhampton University, United Kingdom, <sup>4</sup>School of Sport and Exercise, Massey University, Palmerston North, New Zealand, <sup>5</sup>Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

### Correspondence to:

Dr. Lee Stoner,  
School of Sport and Exercise,  
Private Bag 756, Massey University,  
Wellington 6140, New Zealand.  
E-mail: dr.l.stoner@gmail.com

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### ABSTRACT

**Background:** Lifestyle modifications including, physical activity can reduce obesity-related morbidity and subsequent cardiovascular disease in youth. This study will investigate the efficacy of a culturally-sensitive, non-contact, boxing-orientated training program on obesity and related cardio-metabolic conditions in Māori and Pasifika adolescents. Details of the methodological aspects of recruitment, inclusion criteria, randomization, cultural sensitivity, intervention program, assessments, process evaluation, and statistical analyses are described.

**Methods:** This study will be a community based, New Zealand, randomized control trial (RCT). Male and female obese (body mass index >95<sup>th</sup> percentile) Māori and Pasifika adolescents aged 14-16 years will be recruited and the sample size will be confirmed through a feasibility study. Combating Obesity in Māori and Pasifika Adolescent School-children Study (COMPASS) is a 6-month, theory-based program, conducted 3-times/week in a culturally appropriate setting. Each session includes 40 min boxing-orientated training and 30 min resistance training. Assessments will be made at baseline, 3-months, 6-months, 12-months, and 24-months. Main outcomes include abdominal obesity, endothelial function, and insulin resistance. Other outcomes include arterial stiffness, lipid profile, inflammatory biomarkers, well-being, and aerobic fitness. Control measures include physical activity, sleep behavior, and dietary intake.

**Results:** As a protocol paper there are no specific results to present, our purpose is to share our RCT design with the scientific community.

**Conclusions:** COMPASS will be used to provide direction for exercise prescription policy in at-risk Māori and Pasifika adolescents.

**Keywords:** Cardiovascular, exercise, indigenous, lifestyle, metabolic syndrome, pediatrics

### INTRODUCTION

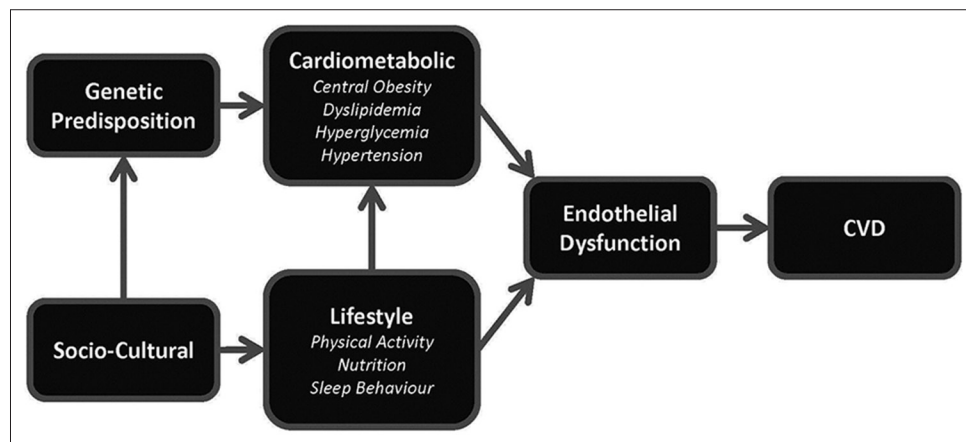
Within New Zealand, much higher rates of obesity have been reported for Pasifika (22.3%) and Māori (11.8%)

children (2-14 years) than their counterparts of European ancestry (5.5%).<sup>[1]</sup> The increased prevalence places these cohorts at greater risk for obesity-related cardio-metabolic conditions, including dyslipidemia, hypertension, and type 2 diabetes mellitus<sup>[2]</sup> [Figure 1].<sup>[3]</sup> These conditions independently and additively increase cardiovascular disease (CVD) risk,<sup>[3-7]</sup> even in children and adolescents.<sup>[5,8-17]</sup> Indeed, many of the pro-inflammatory and pro-atherogenic disorders associated with vascular disease in adults have also been demonstrated in obese children.<sup>[5,8-17]</sup> For example, overweight children were found to have elevated levels of interleukin-6 (IL-6) and tumor necrosis factors-alpha (TNF- $\alpha$ ) receptors, and plasma levels of C-reactive protein (CRP) that are approximately 3 times greater than normal-weight children.<sup>[5]</sup>

Although genetic factors might influence the susceptibility of individuals to weight gain,<sup>[18]</sup> there is a consensus that changes in lifestyle activities have driven the current obesity epidemic.<sup>[19]</sup> Dietary modification has been shown to be relatively ineffective in the long-term treatment of obesity in adults,<sup>[20,21]</sup> and it has been suggested that obesity prevention in childhood and adolescence should focus on physical activity rather than diet because of fears relating to eating disorders.<sup>[22]</sup> Dieting can also lead to loss of fat-free mass, which is of particular concern when considering an increase in muscle strength (and by proxy, muscle mass) decreases insulin resistance in children aged 10-15 years.<sup>[23]</sup> Conversely, exercise maximizes the proportion of weight lost from fat mass and minimizes the loss of fat free

mass.<sup>[22]</sup> The World Health Organization (WHO), in recognition of declining physical activity levels and the subsequent rise in cardio-metabolic conditions, including obesity, published the Global Recommendations on Physical Activity and Health.<sup>[24]</sup> The WHO recommends that children aged 6-17 years participate in at least 60 min of moderate-to-vigorous physical activity every day, and to perform vigorous exercise (high intensity), muscle-strengthening, and bone strengthening exercise, on at least 3 days/week.<sup>[24]</sup> However, obese children and adolescents are disadvantaged by physical and cardiovascular constraints, simply due to the excess body weight and the effort involved in moving a large mass, thus, limiting the capacity of these individuals to comply with WHO recommendations.

A meta-analysis of exercise treatment programs in obese children and adolescents has shown that the most effective exercise paradigm for this population incorporates high repetition resistance training combined with low-intensity, long duration aerobic exercise.<sup>[25]</sup> Resistance training has been shown to be well-tolerated by this population and results in positive changes to body composition,<sup>[26-28]</sup> as well as an improvement in elements of metabolic syndrome (i.e., levels of glycated hemoglobin,<sup>[29]</sup> insulin resistance,<sup>[28,29]</sup> low-density lipoprotein (LDL) cholesterol,<sup>[30]</sup> triglycerides,<sup>[30]</sup> total cholesterol,<sup>[30]</sup> intrahepatic lipid,<sup>[28]</sup> both systolic and diastolic blood pressure<sup>[29-31]</sup>) in obese adults. Low-intensity, long-duration aerobic exercise has been shown to have positive results on body weight and composition in obese children,<sup>[22]</sup> but ultimately is limited in capacity



**Figure 1:** Causal pathway for cardiovascular disease. Adapted from<sup>[145]</sup>

when compared to high-intensity exercise for decreasing obesity, cardio-metabolic conditions, and the progression of CVD.<sup>[32-34]</sup> There remains a pressing need to develop and assess vigorous exercise programs, which are safe, tolerable, enjoyable, and sustainable for at-risk obese children and adolescents. A mixed-modality program that incorporates both resistance and high-intensity aerobic training is optimal for producing the greatest impact to the health of obese adolescents.

Exercise programs designed for children and adolescents from indigenous backgrounds, including Māori and Pasifika, should not only be physiologically appropriate, but also culturally sensitive. An argument can be made that sport can be used as a vehicle to experience, discover, and reconnect to indigenous cultural heritage.<sup>[35]</sup> For example, Māori are attracted to sport not only because of their love of whakataetae (competition) and achievement (whakatutukitanga), but also, because it provides a forum to experience feelings of whanau (extended family).<sup>[36]</sup> In particular, many Māori show a decided preference for sports, which involve a team environment (whanaungatanga/kotahitanga) and that include bodily contact.<sup>[36]</sup> Boxing training is characterized by high-intensity, intermittent activities,<sup>[37,38]</sup> and, in previously untrained individuals, has been shown to result in favorable changes in gait and balance,<sup>[39]</sup> cardiovascular fitness,<sup>[40]</sup> and lipid profiles.<sup>[41]</sup> Besides health/fitness (hauora/oranga), boxing training can also lead to increased self-confidence (mana), self-discipline, character development, and comradery.<sup>[42]</sup> A non-contact, boxing-orientated program presents an accessible, relatively inexpensive, fun and engaging option for promoting healthy lifestyles that aligns with tikanga (Māori culture).

### Research objectives

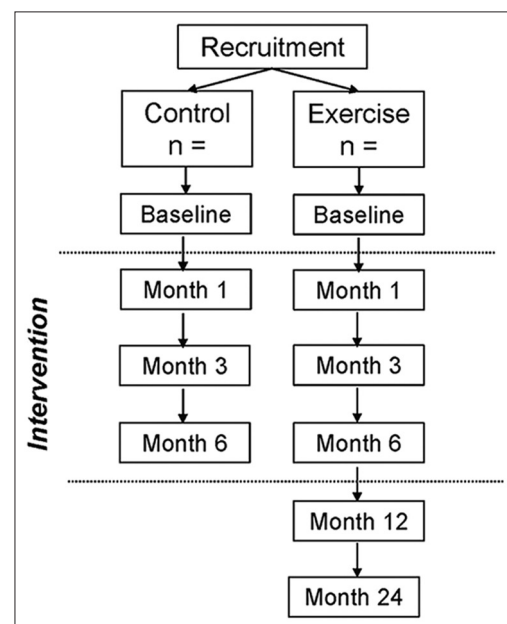
This study will investigate the efficacy of a culturally-sensitive, non-contact, boxing-orientated training program Combating Obesity in Māori and Pasifika Adolescent School-children Study (COMPASS) on obesity and related cardio-metabolic conditions in Māori and Pasifika adolescents aged 14-16 years. Three null hypotheses will be tested: H1: There will be no relationship between COMPASS participation and endothelial function (CVD risk), H2: There will be

no relationship between COMPASS participation and abdominal adiposity; H3: There will be no relationship between COMPASS participation and insulin resistance. An important objective is to also determine the strength of association between endothelial function, abdominal adiposity, and insulin resistance associated with the COMPASS intervention. Findings from COMPASS will provide direction for future exercise prescription policy in this at-risk cohort.

## METHODS

### Study design

The COMPASS intervention will be evaluated using a randomized control trial (RCT) study design [Figure 2]. A randomization envelope will be prepared by a member of the research team and an independent third party will allocate participants to the treatment or control (wait list) groups. Full assessments [Table 1] will be made on both groups at baseline, and at 3-months and 6-months. Follow-up assessments will be conducted on the intervention group at 12-months and 24-months. Analysis will be by intention to treat.<sup>[43]</sup> Ethical approval will be obtained from the regional Health and Disabilities Ethics Committee.



**Figure 2:** Design of the combating obesity in Māori and Pasifika Adolescent school-children study

**Table 1:** Study outcomes

Dependent variable	Method	Main/other/control
Abdominal obesity	Ultrasound	Main
Endothelial function	Flow mediated dilation	Main
Insulin resistance	2-h OGTT	Main
Arterial stiffness	Pulse wave analysis	Other
Lipid profile	Blood lipids	Other
Inflammation	Adipokine	Other
Well-being	Brunel mood scale	Other
Aerobic fitness	VO <sub>2</sub> max	Other
Genomics	1.25×10 <sup>6</sup> marker SNP/CNV chip	Other
Physical activity	Accelerometry IPAQ	Control
Diet	FFQ	Control
Sleep behavior/ quality	Accelerometry	Control

FFQ=Food frequency questionnaire, IPAQ=International physical activity questionnaire, OGTT=Oral glucose tolerance test, SNP=Single nucleotide polymorphism, CNV=Copy number variant

### Study participants and recruitment

Male and female adolescents aged 14-16 years will be recruited. Participants will be categorized as obese (Body mass index [BMI] >95<sup>th</sup> percentile), based on the age- and gender-specific recommendations of the International Obesity Task Force.<sup>[44]</sup> A self-reported Tanner scale will be used to determine pubertal status. Participants who have not reached Tanner IV staging will not be eligible. Participants receiving insulin or other pharmacological treatment for diabetes will be excluded, but will be eligible if diabetes is diet-controlled. Participants will also be excluded from the study, if they have had an orthopaedic injury or surgery that has prohibited full function within 4 weeks of commencing the intervention, or have been diagnosed with a neuromuscular disease or cardiovascular conditions that would exclude them from participating in high-intensity exercise. All female participants will be asked to submit a urine sample for a basic pregnancy test as pregnant participants are not eligible for participation.

Participants will be recruited from the greater Wellington area through press releases on local

radio and in newspapers, by physician referral, publicly posted advertisements, and via direct contact with the Māori and Pasifika boxing community. Recruitment will continue over a period of several months, with rolling study commencement occurring at 1-month intervals.

### Cultural sensitivity

A number of steps will be followed to ensure cultural sensitivity and long-term viability of COMPASS:

1. Māori academic consultants. To advise on cultural issues pertaining to the program and translate common boxing terminology to Te Reo (Māori) and Pasifika.
2. A steering committee. Comprised of Māori and Pasifika adolescents and parents who are currently involved with the boxing club or from the greater community.
3. Adherence to kawa and tikanga. Kawa are the protocols that apply in different situations. For boxing training (fight training) there are certain rules and conditions that Māori apply regarding expectations of behavior, outcomes, and standards, similar to martial arts training. Tikanga or customs apply in the treatment of individuals and groups and this would include awahi (inclusion), whakawhanaungatanga (relationship building) mana (self-esteem and empowerment), and noa (states of wellbeing). The merging of Māori culture and physical exercise serves to validate the interface between mātauranga Māori and science.<sup>[45]</sup>

### Adherence

To ensure adherence we will: (1) Have the participants sign an accountability contract, (2) ensure the program is fun and culturally sensitive, and (3) utilize social media group to aid social facilitation. The accountability contract will be independent of the ethics consent form. By signing this contract between the participant and program coordinator, the participant is agreeing to attend scheduled training sessions on time, or contact the program coordinator, if they will be late or absent. The participant also agrees to attend sessions in appropriate dress (i.e., gym attire) and maintain a positive attitude throughout the training sessions. The social media will be participant-led,

with minimal input from the research team except to vet the suitability of entries. Participants will be provided with pocket cameras and encouraged to share their personal journeys.

### Pilot studies

Two pilot studies will be conducted prior to the primary intervention trial.

#### Feasibility study

A 3-month trial of the COMPASS intervention will recruit 14 male/female adolescents who meet the study criteria outlined above. Assessments will be made at baseline, 1-month and 3-months. The outcomes will be: Abdominal obesity (ultrasound, central arterial stiffness (pulse wave analysis [PWA]), central blood pressures (PWA), carotid arterial stiffness (ultrasound), and insulin resistance (oral glucose tolerance test [OGTT]). Daily physical activity (accelerometry), nutrition (food frequency questionnaire) and sleep behavior and quality (accelerometry) will also be collected to ensure the COMPASS program does not interact with important lifestyle factors. A focus group will be held at the conclusion of the study, utilizing standardized semi-structured questions. This study will provide the data needed to adequately power the primary intervention trial, and to address unforeseen cultural issues.

#### Brunel mood scale validation

Mood will be assessed using the Brunel Mood Scale,<sup>[46,47]</sup> which is a 24-item scale that assesses anger, confusion, depression, fatigue, tension, and vigor. The BRUMS was designed with the intention of producing a scale that was easy to complete. Studies support the validity of use with children in different languages including, Italian, Hungarian,<sup>[48]</sup> Malaysian,<sup>[49]</sup> and Australian.<sup>[46]</sup> Consistent with the notion that the validation is an on-going process and that researchers should not assume that validity transfers from culture to another, we will investigate the factorial validity of BRUMS for use in New Zealand with the Māori and Pasifika population. Data will be gathered from a sample of 200 Pākehā (non-indigenous) and 30 Māori/Pasifika. BRUMS will be translated to Te Reo (Māori). A member of the research team is a Chartered Psychologist with the British Psychological Society.

### Treatment group

COMPASS is a 6-month mixed-modality exercise training program for Māori and

Pasifika adolescents. The participants will attend three 70 min training sessions per week, on non-consecutive days. Each session will consist of 40 min standard boxing training, consisting of skipping (3 min × 2 min), shadow boxing (3 min × 2 min), bag work (3 min × 2 min), and one-on-one focus-pad work (3 min × 2 min). The boxing training will be standardized in terms of content, and intensity will be gradually increased each month. Training intensity will be monitored using ratings of perceived exertion (RPE) and heart rate monitors. Session-RPE has been validated for use in range of intermittent sports,<sup>[50-52]</sup> including combat sports.<sup>[53,54]</sup> Then the participants will complete a 30 min progressive, closed kinetic, resistance training routine, consisting of 5 lower extremity, 5 upper extremity, and 3 abdominal exercises. Intensity will be increased non-linearly. One of the research team is a certified Athletic Trainer, and two members are accredited exercise physiologists with the British Association of Sport and Exercise Sciences. The training sessions will be held at Petone Sports and Boxing Club (Lower Hutt, Wellington, New Zealand). Compared to New Zealand as a whole, Lower Hutt has a higher proportion of Māori (14.7% vs. 17.1%, respectively) and Pasifika (6.9% vs. 10.5%, respectively).<sup>[55]</sup> Training sessions will be coordinated by the head coach of Petone Sports and Boxing Club, one of the co-investigators (a Level 1 boxing coach), and a trained research assistant.

### Control (wait list) group

The control group will continue at their typical levels of physical activity. The control group will have an opportunity to participate in COMPASS after the initial 6-month period and post-testing has been completed.

### Main outcome measures

#### Endothelial function

The flow-mediated dilation (FMD) test is the standard tool used to assess endothelial function.<sup>[56,57]</sup> Reduced FMD is an early marker of atherosclerosis<sup>[56]</sup> and has been noted for its capacity to predict future CVD events.<sup>[58-61]</sup> Furthermore, an impaired vascular response has been demonstrated in children as young as 7 years old with familial hypercholesterolemia.<sup>[62]</sup> Physical activity has been shown to improve FMD in obese children<sup>[32,33,63-66]</sup> with exercise-induced

improvement in FMD reversing after only 6 weeks of inactivity.<sup>[64,65]</sup> FMD will be conducted using high-resolution B-mode ultrasound (t3200; Terason, Burlington, Massachusetts) equipped with a 15-4 MHz linear array transducer (15L4), by a highly trained technician who has developed FMD guidelines.<sup>[67]</sup> In past research FMD has been expressed as percentile, and this is the basis of the sample size calculation. A change of 1% is a clinically relevant difference<sup>[61]</sup> and past research has found a wide range for the standard deviation (SD) for FMD in similar populations, of between 0.8% and 2.5%.<sup>[63,65]</sup> We have used the largest SD in the sample size calculation for the feasibility study. We will also express FMD as the absolute change in diameter and in analysis use the baseline diameter as a covariate.<sup>[68]</sup>

#### **Abdominal obesity**

The classification of an individual as obese is usually determined by BMI, not by a direct measure of adiposity. Whilst BMI is a surrogate of total body fatness it does not account for the differential health risks of excess fat within the abdominal and gluteal regions and is less predictive of health risk than measures of abdominal fat.<sup>[69]</sup> Visceral adiposity decreases the sensitivity of target tissues to insulin while subcutaneous abdominal fat has a more direct influence on insulin sensitivity.<sup>[69]</sup> While total body fat is important, studies have shown that visceral adiposity poses a higher risk for developing obesity related disorders than overall adiposity,<sup>[70-72]</sup> including in adolescents and children.<sup>[73-76]</sup> Therefore, intra-abdominal and subcutaneous abdominal adipose tissue will be measured by a highly trained sonographer using a portable, high-resolution, B-mode ultrasound device (t3200; Terason, Burlington, MA) equipped with a 6-1 MHz curved array transducer (6C1). Intra-abdominal thickness will be defined as the distance between the anterior wall of the aorta and the posterior surface of the rectus abdominis muscle, measured 1-5 cm above the umbilicus at the xipho-umbilical line. These measurements strongly agree with computed tomography (CT),<sup>[77-79]</sup> and magnetic resonance imaging (MRI),<sup>[80,81]</sup> based estimations and are reliable,<sup>[79,82,83]</sup> with high interobserver ( $P = 0.97$ , 95% CI: 0.90-0.99) and intraobserver (Intraclass Correlation Coefficient: 0.97, 95% CI: 0.88-0.99) reliabilities.<sup>[83]</sup> CT and MRI are reference methods, both MRI and CT are

high-cost technologies, and CT requires radiation exposure.<sup>[84]</sup> The clinically relevant difference in adiposity measured by ultrasound is unknown. The association between adiposity and FMD will be used to estimate the likely size of the clinically important difference for this variable.

#### **Insulin resistance**

There are many methods for estimating insulin sensitivity with reference methods including the hyperinsulinaemic euglycemic clamp<sup>[85]</sup> or intravenous glucose tolerance test with minimal modelling.<sup>[86]</sup> Both of these methods are invasive, time consuming and expensive. A variety of surrogate methods are based on either fasting state insulin and glucose concentrations, or insulin and glucose concentrations during an OGTT.<sup>[87-89]</sup> The homeostasis model assessment (HOMA) is perhaps the most commonly used simple method, and correlates well with the euglycemic clamp in those without diabetes.<sup>[89]</sup> The Matsuda index provides a more integrated measure combining both fasting and dynamic changes in glucose and insulin.<sup>[87]</sup> We will use both of these measures in the pilot study. This will enable accurate sample size calculations for the main study, and also an assessment of tolerability and acceptability of the 5 point OGTT in this adolescent population. To enable 5 blood samples to be collected at 30 min intervals an indwelling intravenous cannula will be inserted. Fasting plasma glucose and insulin will be analysed using standard commercial assays, and HOMA will use a computer generated program to calculate insulin resistance based on insulin and glucose values. Insulin resistance has been related to FMD in children,<sup>[66,90,91]</sup> adolescents<sup>[90]</sup> and adults.<sup>[92-95]</sup> For example, a strong, negative relationship between HOMA and FMD has been reported in adults with chronic kidney disease ( $R^2: -0.91$ ,  $\beta: -0.24$ ,  $P = 0.008$ ).<sup>[92]</sup> The association between HOMA, Matsuda index and FMD will be used to estimate the likely size of the clinically important difference for this variable in obese adolescents.

#### **Other outcome measures**

##### **Well-being**

Available evidence indicate that pleasant emotions are associated with good physical and psychological health.<sup>[96]</sup> The present study will use a measure of Total Mood Disturbance by subtracting the sum of unpleasant states (anger,

confusion, depression, fatigue, and tension) from vigor scores as assessed by the BRUMS.

#### **Aerobic fitness**

Cardiovascular health risk has been associated with low levels of cardiorespiratory fitness in youth. Therefore, participants will complete 2 phases of a maximal discontinuous cycle protocol. During the first phase, the initial workload will be set at 50 Watts and each stage will include an increased workload of 25 Watts. Stages will consist of 3.5 min of continuous cycling followed by 1.5 min of rest. During the cycling component, the participant will maintain a cadence of at least 60 rpm. When the cadence minimum is not maintained, the stage is considered incomplete and phase one is terminated. The participant will be given several minutes rest before a second attempt at the previous workload (Phase 2). If a participant completes this stage, then the workload is increased appropriately and protocol continued as described above. When the participant is unable to complete a stage (i.e., maintain a cadence of 60 rpm for 3.5 min), the testing session will be finished. A valid maximal test will have been achieved if at least 3 of the following criteria were met during the final 30 s of the last completed stage: Respiratory equivalent ratio less than 1.15, RPE less than 18, heart rate within 11 bpm of the age-predicted maximum ( $208 - [0.7 \times \text{age}]$ ), an increase in  $\text{VO}_2$  that is less than 50% of what would be expected for the change in mechanical work.<sup>[97]</sup>

#### **Central blood pressure and arterial stiffness**

The FMD test can be used to evaluate the functional health of the vascular system, whereas indicators of arterial stiffness and central blood pressures are used to assess structural characteristics.<sup>[98]</sup> PWA is a simple,<sup>[98]</sup> non-invasive, valid,<sup>[99-101]</sup> and reliable<sup>[102-104]</sup> technique that has been widely used in epidemiological<sup>[105]</sup> and interventional studies<sup>[106]</sup> to investigate central blood pressures and arterial stiffness. The PulseCor R7 CardioScope (PulseCor, Auckland, New Zealand) measures brachial artery pressure waves using the oscillometric method from an upper arm cuff and incorporates a POEM2 module (Welch Allyn, Skaneateles Falls, New York). Central blood pressures, derived from a generalized transfer function, have been validated against invasive catheter measurements and exceed the requirements of the Association for the Advancement of

Medical Instrumentation (sphygmomanometer committee 0) for measurement accuracy.<sup>[107,108]</sup> Using this device, Lydakis *et al.*<sup>[109]</sup> reported that obesity and adherence to the Mediterranean diet independently predicts arterial stiffness in 12-year-old children.

#### **Lipid profile**

A fasting blood sample will be collected at the time the cannula is inserted for analysis of lipid profile. Total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) concentrations will be determined using commercial assays. Low-density lipoprotein (LDL) cholesterol will be calculated combining values from the above measurements of TC, HDL cholesterol, and TG, using Friedwald's formula.<sup>[110]</sup>

#### **Inflammation**

Pro-inflammatory cytokines (i.e., IL-1 $\beta$ , IL-6 and TNF- $\alpha$ ) are secreted from adipose tissue macrophages and impair insulin signaling as well promote endothelial dysfunction. CRP and other markers of oxidative stress have been associated with increases in adiposity and atherosclerosis progression.<sup>[111]</sup> Contracting skeletal muscle releases myokines that lower blood pressure, enhance insulin sensitivity and lipid oxidation and protect against cardiovascular morbidity. These markers have been previously linked to published exercise interventions in obesity management.<sup>[112-116]</sup> Therefore, a clinical phlebotomist with experience in children and adolescents will collect serum from the arms of participants. Serum samples will be analysed, in duplicate, for TNF- $\alpha$ , IL-6, CRP, using high sensitivity enzyme linked immunosorbent assays (ELISA). Fasting plasma insulin and IL-1 will be analysed using standard ELISA kits. The adipokines (adiponectin, leptin, resistin, plasminogen activator-1) will be analysed using a human adipocyte multiplex kit.

#### **Genomics**

Genetic studies have revealed links between genetics and response to physical training<sup>[117]</sup> and obesity.<sup>[118]</sup> The COMPASS study provides an opportunity to add to this data in a Maori/Pasifika population. A whole blood sample will be collected by a clinical phlebotomist and genomic DNA isolated and stored as previously described<sup>[119]</sup> for future analysis with single nucleotide polymorphism/copy number variant (SNP/CNV)

chip and/or next generation sequencing technology. The study will focus on genetic analysis of genes that have been shown to be associated with response to physical training, including Alpha-actinin-3, IL-6, insulin-like growth factor-2, vitamin D receptor, peroxisome proliferator-activated receptor alpha, and angiotensin-converting enzyme.<sup>[117]</sup> Genes implicated in associations with obesity will also be analyzed, including fat mass and obesity-associated protein, uncoupling protein 2 and 3, transmembrane protein 18, pro-opiomelanocortin, and melanocortin receptor 4 genes.<sup>[120]</sup>

### Control measures

Other important lifestyle factors, including physical activity, nutrition, and sleep behavior, may be strongly associated with our main outcome variables. For example, a recent systematic review and meta-analysis<sup>[121]</sup> reported that physical activity interventions have had only a small effect on children's overall activity levels. Statistical adjustment for these factors will be necessary to account for possible uneven distribution between the randomized groups and to increase the precision of the estimates of the effect of the randomized treatment. As these factors will only be measured as part of the study design it will not be possible to stratify randomization by these factors.

### Physical activity

Accelerometry, in combination with a physical activity questionnaire will be used to interpret changes in physical activity. For both measurements, data collection will take place over 7-days at baseline, then over 7-days at the end of each stage [Figure 2]. The participants will be instructed to wear a 3-axis accelerometer (wActiSleep +; ActiGraph LLC, Fort Walton Beach, FL) at the right hip during their waking hours, but to remove when bathing, showering, or participating in water sports. A 60 s sampling period will be used throughout, and the count data expressed in counts per minute. This is a validated objective measure of physical activity for use with young people.<sup>[122]</sup>

Physical activity type and context (e.g., modality)<sup>[123]</sup> will be determined using the International Physical Activity Questionnaire (IPAQ) Long Form (<http://www.ipaq.ki.se/ipaq.htm>), a cross-national monitoring tool, which has been validated for use in children and

adolescents.<sup>[124-127]</sup> The IPAQ will be applied during an interview because there is evidence that interview measures have stronger characteristics than self-administered measures.<sup>[128]</sup>

### Nutritional intake

Direct observation is considered the “gold standard” for monitoring dietary intake.<sup>[129-132]</sup> However, this approach can be time consuming and impractical for use in large-scale studies. Alternatively, food frequency questionnaires are considerably less burdensome in both time and cost in than other measurement tools.<sup>[133,134]</sup> Therefore, food choice will be assessed using 12 questions from the Health Behavior in School Children (HBSC) questionnaire<sup>[135]</sup> that has been validated for use in New Zealand adolescents aged 14-18 years.<sup>[136]</sup> The frequency of consumption of food items will be recorded by asking the respondent how many times weekly each item is ate or drank. The food frequency questionnaire will be applied during an interview, along with the IPAQ.

### Sleep behaviour

Increasing evidence has indicated that short sleep duration may be related to childhood obesity,<sup>[137,138]</sup> high blood pressure,<sup>[139]</sup> and decreased insulin sensitivity<sup>[140]</sup> among children and adolescents. Sleep behavior will be assessed using the ActiSleep monitor described above. When worn during sleep episodes, the ActiSleep will monitor sleep onset, sleep latency, total sleep time, number and duration of awakenings, and sleep efficiency. An integrated ambient light sensor provides information on subject environment. Study participants will wear the ActiSleep monitor on their non-dominant wrists for intervals of seven consecutive days to provide objective estimates of sleep. Participants will be instructed to keep a record of logging time in bed and time out of bed for each measured sleep episode and to return a completed sleep log with the ActiSleep monitor to the research staff.

### Process evaluation

The feasibility of COMPASS will be examined using measures of recruitment, retention, adherence, and satisfaction. Evaluation questionnaires will also be administered to determine perceptions of the programme. A 6-point Likert scale format will be used with responses ranging from “Strongly Disagree” through to “Strongly Agree.” Focus group interviews involving 5-6 students and lasting



5-10 min will also be conducted by trained research assistants. The groups will be based on friendship groups (both single-sex and mixed-sex groups) and will utilize standardized semi-structured questions. The anonymous verbal responses will be recorded by the research assistant. At the end of the session the participants will also be asked if they have anything else to add or would like to discuss anything further.

### Sample size

The sample size for the feasibility study is based on FMD. Based on the research from a similar population,<sup>[63,65]</sup> for 90% power, alpha 5% a total of 14 participants, seven in each group are needed to detect a difference of 5% with an SD of 2.5%. The sample size calculation for the main study will be based on FMD and we plan to confirm the SD for this variable in the feasibility study as the range of SD in past research was so wide. If possible we also plan to estimate the SD for abdominal obesity and insulin resistance (OGTT). A sample size of 14 has reasonable precision to estimate variance. The variances and appropriate 95% confidence intervals will be estimated by Chi-square statistics.

### Statistical analysis

The analysis will by intention to treat, namely that participants will be analyzed as by their randomized intervention allocation. A secondary analysis will be a per protocol analysis, namely participants will be analyzed as by the intervention they actually completed. For missing data, we will take a multiple imputation approach based on the missing at random assumption for the main outcome variables at the main measurement time. The main outcome variables are: Abdominal obesity, endothelial function and insulin resistance. Other outcomes will include arterial stiffness, lipid profile, inflammatory biomarkers, well-being, and aerobic fitness. General linear models will examine the effect of randomized treatment on the outcome variables at the final measurement time. A sensitivity analysis will be by mixed linear models using all measurement time points as well as possible confounding variables: Daily physical activity, nutritional intake, and sleep behavior. Mixed linear models explicitly model the correlation of repeated measurements on the same individuals to examine rates of change with time and whether these differ by randomized treatment.

Associations between adiposity, insulin resistance and endothelial function will be examined by general linear models and logistic regression. These associations will be used to predict the expected proportional reduction in obesity or insulin resistance, for example, attributable to the COMPASS intervention – assuming all else remains constant in the study population.

## DISCUSSION

Multiple pediatric studies have demonstrated a clustering of cardio-metabolic complications with obesity.<sup>[2,141]</sup> The metabolic syndrome, manifested by the coexistence of central obesity, dyslipidemia, hypertension, and pre-diabetes, may affect as many as 30% of obese adolescents.<sup>[142,143]</sup> The symptoms of these conditions do not differ between adolescents and adults, however, the burden of disease is maintained for a longer period of time with less pharmaceutical options available for the younger population.<sup>[2]</sup> This increasing burden of obesity has created an urgent need to develop strategic prevention and management approaches for New Zealand youth of various ethnic backgrounds.

Although lifestyle modification is considered the cornerstone of the management of obesity, there are significant gaps in our understanding of the optimal modalities of exercise to use with an adolescent population, particularly with at-risk, obese adolescents. COMPASS will be one of the first RCTs to address obesity and related cardio-metabolic and CVD concerns in Māori and Pasifika adolescents. The combined study objectives will provide a unique opportunity to gain robust evidence for developing safe and effective exercise options in this cohort.

## IMPLICATIONS

This research study will provide much needed objective data in an area of research and population that to date has been largely ignored. Given the practical implications of the present study, we will examine the clinical significance for changes in each variable.<sup>[144]</sup>

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