CARDIOMETABOLIC RISK IN 10 TO 11 YEAR OLD CHILDREN: THE IMPACTS OF PHYSICAL ACTIVITY, CARDIORESPIRATORY FITNESS, BODY COMPOSITION AND LIFESTYLE EDUCATION.

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UNIVERSITY HAVE REQUESTED THE FOLLOWING ITEMS TO BE REDACTED

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FIG 2.1 P15

FIG 2.2 P17

Abstract

The aim of this thesis was to investigate the impacts of physical activity (PA), cardiorespiratory fitness (CRF), body composition and lifestyle education on cardiometabolic (CM) risk in 10-11 year old children. This broad aim was approached using three studies. Studies 1 and 2 were cross sectional observational studies, and study 3 was a clustered randomised control trial, with intervention effects assessed at post intervention and again at 8 to 10 weeks after the intervention.

Initially, in the first cross sectional study (Chapter 4) the relationships between non-invasive (LV Mass, E/A, E'/A', E/E', trunk fat mass, whole body fat mass) and invasive CM risk markers (CRP, HOMA-IR, adiponectin, TC: HDL-C), and between all risk markers and CRF ($VO_{2\ peak}$), time spent sedentary, moderate to vigorous intensity PA (MVPA) and vigorous PA (VPA) were investigated in 10-11 year old children (n=62). The key findings were significant but generally weak relationships present between some of the non-invasive and invasive markers of CM risk and risk markers also had significant correlations with measures of CRF and PA. CRP was significantly positively correlated with whole body fat in boys (rho=0.486, $p<0.05$) and girls (rho = 0.485 , $p<0.01$) and with trunk fat mass in boys (rho = 0.384, $p<0.05$) and girls (rho =0.489, $p<0.01$). Adiponectin was negatively correlated with whole body fat (rho = -0.446, $p<0.05$, and R= -0.697, $p<0.01$) and trunk fat mass (rho = -0.614, $p<0.01$; rho = -0.475, $p<0.01$) in boys and girls respectively, and in girls adiponectin also correlated positively with E'/A' (r=0.356, $p<0.05$). In boys only, TC:HDL-C was positively correlated with whole body fat (rho =0.407, $p<0.01$) and trunk fat mass (rho =0.391, $p<0.05$). ; VO_{2Peak} was negatively correlated with CRP in boys (Rho = -0.492, $p<0.05$) and HOMA-IR in girls (Rho =-0.522, $p<0.01$). VO2Peak was also negatively correlated with whole body fat (rho =-0.515, $p<0.01$; r=-0.697, $p<0.01$) and trunk fat mass (rho=-0.494, $p<0.05$; rho =-0.706, $p<0.01$) in boys and girls respectively. Both MVPA and VPA correlated negatively with TC: HDL-C in girls (rho= -0.396, $p<0.05$; rho =-0.428, $p<0.05$) and MVPA correlated with whole body fat (rho= -0.602, $p<0.01$) and trunk fat mass (rho=-0.65, $p<0.01$) in boys. VPA also correlated with whole body fat in girls (rho= -0.544, $p<0.01$) and with trunk fat mass in both boys (rho= -0.428, $p<0.05$) and girls (rho= -0.468, $p<0.01$). Time spent sedentary had a positive correlation with whole body fat in boys (rho = 0.429, $p<0.05$). This study demonstrated that risk factors clustered in individuals and that relationships were present between invasive and non-invasive markers of cardiometabolic risk, and provided preliminary evidence to investigate this phenomenon further. The correlations described in this study suggest a clustered risk score which includes both invasive and non-invasive measures may add value to predicting overall risk. The second cross sectional study (Chapter 5) investigated clustered CM risk, by combining invasive markers with non-invasive 'pre-clinical' markers of CM risk into a clustered risk score, in a different cohort of 10 – 11 year old children. Clustered risk scores were negatively correlated with CRF and PA. $VO_{2\ peak}$ showed a moderate negative correlation with CRS A (r=-0.57, $p<0.01$) and CRS B (r= -0.60, $p<0.01$) VPA showed a moderate negative correlation with CRS A (r= -0.51, p= 0.01) and CRS B (r= -0.50, p=0.01). MVPA showed a moderate negative correlation with CRS A (r= -0.44, p= 0.03) and CRS B (r= -0.41, p=0.04). Sedentary time showed a moderate positive correlation with CRS A (r= 0.414, p= 0.049).

The evidence provided by these two observational studies, Study 1 (Chapter 4) and Study 2 (Chapter 5), along with other literature, as discussed throughout this thesis, gave rationale for an intervention with the aim to reduce negative lifestyle behaviours, of low

levels of PA, high levels of sedentary behaviour and poor nutritional balance, increase CRF and maintain a healthy body weight.

The final study was a clustered randomised control trial which investigated the immediate and short term (8 to 10 weeks follow up) effects of the Children's Health Activity and Nutrition: Get Educated! (CHANGE!), curriculum based multi-disciplinary PA and nutrition intervention, on CM risk in 10 to 11 year old children. Whilst there were some statistically significant intervention effects on waist circumference (WC) (Adjusted mean (SE) change for Control = +1.4 cm (0.3) [95% CI 0.7, 2.1]; Intervention = -0.1 cm (0.4) [95% CI -0.9, 0.6], p=0.006) and diastolic blood pressure (dBP) (control group adjusted mean (SE) = +3 (3) [95% CI -4, 9] mmHg; intervention = -14 (3) 95% CI [-21, -7] mmHg) at post intervention these were not sustained at 8 to 10 week follow up. There were however improvements demonstrated in CRF in the intervention group at follow up (Adjusted mean change for control = -2.8 ml/kg/min (1.5) [95% CI -5.9, 0.3]; Intervention= +3.8 ml/kg/min (1.6) [95% CI 0.5, 7.1], p=0.009).

Overall the studies included in this thesis have highlighted a number of relationships between CM risk markers, measures of body composition, CRF and PA. Hence there is still a need to intervene in this population to reduce modifiable risk. The lifestyle education intervention (Study 3) demonstrated some success; however this was limited due to a number of factors, namely the lack of statistical power, intervention fidelity, and the lack of prescriptive PA element. Investment in promoting healthy lifestyles is essential in ensuring the future health of children as they develop into adulthood. There is a clear need for interventions which are sustainable, and lifestyle education embedded into the school curriculum is a logical and feasible option to reach the whole target population. Further research is required to evaluate the optimum sustainable intervention to improve children's CM health in the long term.

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Statement of candidate's individual contribution

REACH (study 1)

The REACH project was a multidisciplinary project, with the following researchers sharing overall responsibility for data collection: The candidate (RG), LB, LF, LG, and NH. Participants were recruited by LB, RG was responsible for data collection and analysis of LV Mass and diastolic function, and DEXA. LG was responsible for PA analysis. LF was responsible for VO_2Peak and Fundamental Movement Skills (not included) and NH was responsible for FMD (not included). All researchers shared responsibility of anthropometric measurements. A team at Alder Hey children's hospital were responsible for analysis of the venous blood samples.

CHANGE! (Studies 2 and 3)

The CHANGE! Project was part of a collaborative multidisciplinary project with 3 distinct areas of responsibility; the candidate (RG) along with KM and GW had shared responsibility for data collection for the CHANGE project:

The candidate (RG) was responsible for measurement and analysis of the following variables: LV Mass, Diastolic Function, CIMT, capillary blood sampling, DEXA and blood pressure. VO_2 Peak was carried out by RG and KM. Anthropometrics (height, weight, and sitting height) were carried out by RG and GW. Waist Circumference and Hip circumference were measured by KM. The 20mSRT was administered by RG, KM and GW.

KM was responsible for PA analysis and assessment of psychosocial variables. GW was responsible for assessing dietary behaviour. Recruitment of participants was shared between RG, KM and GW.

Formative work which was used to inform the intervention design was carried out by KM and GW. The whole CHANGE! team were responsible for the design of the CHANGE! intervention.

The candidate was responsible for data analysis included within this thesis as well as writing of the thesis.

Publications and Communications

This thesis has resulted in the following publications and conference communications:

Publications:

Gobbi, R.M, Davies, I.G,. Fairclough, S.F., Hackett, A.F., Mackintosh, K.A., Warburton, G.L., Stratton, G., George, K.P., Boddy, L.M. (2012) Clustered Cardiometabolic Risk, Cardiorespiratory fitness and Physical Activity in 10-11 year old children. The CHANGE! Project Baseline. *Archives of Exercise in Health and Disease*, **3** (3), 207-213

Conference Communications:

Gobbi. R., Boddy, L.M., Thomas, N.E., Foweather, L., Graves, L.E.F., Hopkins, N., Green, D., Davies. I.G. Stratton, G. (2011) Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children. Oral presentation. *European Group of Pediatric Work Physiology XXVII Biennial Conference*, Exeter, UK, University of Exeter.

Gobbi, R., Davies, I.G., Fairclough, S.J., Hackett, A.F., Mackintosh, K.A, Warburton, G.L., Stratton, G., George, K.P., Boddy, L.M. (2011) Clustered Cardiometabolic Risk, Cardiorespiratory fitness and Physical Activity in 10-11 year old children. The CHANGE! Project. Poster presentation, *16th Annual Congress of the European College Sports Science*, Liverpool, UK, Liverpool John Moores University.

Gobbi, R., Davies, I.G., Fairclough, S.J., Hackett, A.F., Mackintosh, K.A, Warburton, G.L., Stratton, G., George, K.P., Boddy, L.M. (2011) The CHANGE! Project: group and gender differences in body composition, cardiorespiratory fitness, and cardiometabolic variables at baseline. Poster presentation, *16th Annual congress of the European College Sports Science*, Liverpool, UK, Liverpool John Moores University.

Gobbi, R., Davies, I.G., Fairclough, S.J., Abayomi, J.C., Mackintosh, K.A, Warburton, G.L., Stratton, G., George, K.P., Boddy, L.M. (2012) The impacts of Children's Health Activity and Nutrition: Get Educated (CHANGE!) pilot study on cardiorespiratory fitness, cardiometabolic risk and body size in 10 to 11 year old children. Poster presentation, *17th Annual congress of the European College Sports Science*, Bruges, Belgium

Conference communications not directly related to thesis:

Gobbi, R., Boddy,L.M., Fairclough, S.J.,Abayomi,J., Mackintosh, K.A, Warburton, G.L., Stratton, G., George, K.P., Davies, I.G. (2012). Macronutrient intake and relations to physical activity and sedentary behaviour in 10-11 year old children: The CHANGE! Project. Nutrition Society, Belfast

Gobbi, R., Boddy,L.M., Fairclough, S.J.,Abayomi,J., Mackintosh, K.A, Warburton, G.L., Stratton, G., George, K.P., Davies, I.G. (2012). Macronutrient intake and relations to cardiometabolic risk in 10-11 year old children: The CHANGE! Project. Nutrition Society, Belfast

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p<0.05; **Intervention group significantly different to control group p<0.01)

Abbreviations

%BF	Relative body fat (percentage)
%PF	Relative periferal fatt mass (percentage)
%TF	Relative Trunk Fat Mass (percentage)
20 m SRT	20 m Shuttle Run Test
A	Peak Atrial Trans Mitral Filling velocity
A'	Atrial myocardial velocity
AGT	Angiotensin
ANCOVA	Analsyis of Covariance
ANOVA	Analysis of Variance
AV	Aortic Valve
BIA	Bioelectircal Impedance Analysis
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
CHANGE!	Children's Health Activity and Nutrition: Get Educated!
CHD	Coronary Heart Disease
CIMT	Carotid Intima Media Thickness
CM	Cardiometabolic
CMD	Cardiometabolic Disease
CPM	Counts Per Minute
CRF	Cardiorespiratory Fitness
CRP	C Reactive Protein
CRS	Clustered Risk Score
CVD	Cardiovascular
CVD	Cardiovasular Disease
DALYs	Diasbility Adjusted Life Years
dBP	Diastolic Blood Pressure
DEXA	Dual Energy Xray Absorptiometry
E	Peak Early Diastolic Trans Mitral Filling velocity
E'	Early diastolic myocardial velocity
E/A	Left ventricular diastolic filling (Ratio of Early diastolic trans mitral filling to Atrial trans mitral filling)
E'/A'	Septal myocaridal tissue velocity (Ratio of Early diastolic myocardial velocity to Atrial myocardial velocity)
E/E'	LV filling pressures (Ratio of Early diastolic trans mitral filling velocity to early diastolci myocardial velocity)
ECG	Electrocardiogram
EYHS	European Youth Heart Study
FFM	Fat Free Mass
FFST	Fat Free Soft Tissue
Fg	Fibrinogen
FM	Fat Mass

FMD	Flow Mediated Dilation
Fr	Froude
HC	Hip Circumference
HDL-C	High Density Lipoprotein Cholesterol
HOMA-IR	Homeostasis Model for Insulin Resistance
HPG	Hepatocyte growth hormone
HR	Heart Rate
IDL-C	Intermediate Density Lipoprotein Cholesterol
IL-6	Interleukin-6
IMD	Indices of Multiple Deprivation
	Intima Media Thickness
IOTF	International Obesity Task Force
IVSd	Interventricular Septum in Diastole
IVSs	Interventricular Septum in Ssytole
LA	Left Atria
LDL-C	Low Density Lipoprotein Cholesterol
LM	Lean Mass
LPA	Light Intensity Physical Activity
LV	Left Ventricle
LV Mass	Left Ventricular Mass
LV Mass Index	Left Ventricular Mass Index
LVDs	Left Ventricular Dimension systole
LVH	Left Ventricular Hypertrophy
LVIDd	Left ventricular internal dimension in diastole
MPA	Moderate Intensity Physical Activity
MV	Mitral Valve
MVPA	Moderate to Vigorous intensity Physical Activity
NAFLD	Non Alcoholic Fatty Liver Disease
NEFA	Nonesterified fatty acids
NHS	National Health Service
PA	Physical Activity
PAI-1	Plasminogen actiation inhibitor-1
PFM	Periferal Fat Mass
PWs	Post Wall systole
PWT	Posterior wall thickness
RA	Right Atria
REACH	Research into Exercise Activity & Children's Health Project
RER	Respiratory Exchange Ratio
RV	Right Ventricle
sBP	Systolic Blood Pressure
SED	Sedentary
SSA	Serum amyloid protein
ST	Septal thickness
TC	Total Cholesterol
TDI	Tissue Doppler Imaging
TFM	Trunk Fat Mass

TNF-α	Tumor Necrosis Factor alpha
TV	Tricuspid Valve
VLDL-C	Very Low Density Lipoprotein Cholesterol
$VO_{2\ Peak}$	Peak Oxygen Uptake
VPA	Vigorous Intensity Physical Activity
WBF	Whole Body Fat
WC	Waist Circumference

Chapter 1

Introduction

1.1. Organisation of the Thesis

The central theme of this thesis is to study the phenomenon of CM disease risk markers in children (10-11 years) in relation to physical activity (PA), cardiorespiratory fitness (CRF) and body composition. The thesis includes two cross sectional studies on the above which, along with secondary research, highlights a strong rationale for intervening in this population. The main focus of the thesis was an intervention study, Children's Health Activity and Nutrition: Get Educated! (CHANGE!). The CHANGE! Project is a multidisciplinary project, another researcher was responsible for the nutritional aspect of the project, and another researcher was responsible for PA and psychosocial impacts of the intervention.

The introduction provides an overview of the research problem. Chapter 2 provides an in depth review of the literature on the topics which have briefly been discussed in the introduction. The key topics addressed are CM health in children; and the effects of PA, CRF and body composition on CM risk. The review critically appraises and identifies gaps in the current literature which provide a rationale for the current research. Chapter 3 provides a description of the general methods which are common to all studies. Where additional methods, specific to studies, were used these are described within the subsequent relevant chapters. Chapter 4, (Study 1) presents the relationships between invasive and non-invasive markers of CM risk, and describes relationships between individual risk markers and PA, and CRF. In Chapter 5 (Study 2) the relationships between clustered CM risk, PA, CRF and body composition are investigated and reported. Chapter 6 (Study 3) is a pilot cluster randomised controlled study which investigates the 20 week post intervention and 8 to 10 week follow up effects of the school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) PA and healthy eating curriculum pilot intervention on CM risk in 10-11 year old children. Chapter 7 provides a synthesis of the

results from all three studies and draws together conclusions from the research, and Chapter 8 provides recommendations for future research.

Thesis Study Map

A thesis study map appears at the start of each chapter to demonstrate the key objectives and key findings of the studies, and to elucidate where each study fits in the overall thesis.

Study	Objectives
Study 1: Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.	**Objectives:** • **To investigate the relationships between traditional invasive and non-invasive 'preclinical' cardiometabolic risk markers.** • **To establish the relationships between individual cardiometabolic risk markers and cardiorespiratory fitness (CRF) and physical activity (PA).** • **To determine which measures would be most appropriate to use in future studies.**
Study 2: Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project	
Study 3: The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.	

Table 1-1: Time frame of studies

Project		**Thesis Study and Chapter/ Reference**	**Time Frame**
REACH	REACH data collection	Study 1, Chapter 4	June to July 2010
CHANGE!	CHANGE! formative work and intervention design	Mackintosh et al. (2012). Described in brief in Study 3, Chapter 6	March to September 2010
	CHANGE! baseline data collection	Study 2, Chapter 5; & Study 3, Chapter 6	October to November 2010
	CHANGE! Intervention starts		November 2011
	CHANGE! Intervention ends		March 2011
	Change! Post intervention data collection	Study 3, Chapter 6	March to April 2011
	CHANGE! Follow up data collection	Study 3, Chapter 6	June to July 2011

1.2. The Research Problem

For the purpose of this thesis the term CM risk is used to describe the constellation of interrelated risk markers which progress the development of CM diseases (CMD) such as cardiovascular diseases (CVD); for example, atherosclerosis, coronary heart disease (CHD), and metabolic disorders such as type 2 diabetes and insulin resistance.

CVD is one of the major public health concerns for the world (World Health Organisation, 2002). Worldwide, deaths attributed to CVD increased from 14.5 million in 1990 to 17.5 million by 2005, and this is projected to increase to 20 million deaths by 2015 (Institute of Medicine, 2010). More than 1 in 3 people die of CVD in the UK (Allender et al., 2008;) with similar findings reported in developed and developing countries (Institute of Institute of Medicine, 2010). Since the 1960s it has been well established that CVD, in particular CHD is associated with a combination of genetic (unmodifiable) and environmental (modifiable) risk factors and influences (Dawber et al., 1962; Kannel et al., 1961). Whilst genetic risk factors cannot be changed the modifiable, or lifestyle influences should be targeted in order to prevent or delay CMD (Hardman and Stensel, 2009). Research suggests that almost one third of deaths from CHD are attributable to unhealthy diets (World Health Organisation, 2002) whilst physical inactivity accounts for 23% of CVD deaths in men and 22% in women (World Health Organisation, 2002). Furthermore, around one third of CHD and ischemic stroke and 60% of hypertension are associated with excessive adiposity (World Health Organisation, 2002).

Negative lifestyle behaviours such as physical inactivity and poor dietary habits are often initiated during youth (Berenson, 2001) and there is an emerging body of evidence which suggests that CRF is inversely associated with CM risk markers in children and adolescents (Andersen et al., 2008; Anderssen et al., 2007; Bailey et al., 2012; Eisenmann, 2007; Ruiz

et al., 2009; Ruiz et al., 2007a) as well as incidence of CM events later in life (Ruiz et al., 2009). It is widely accepted that CVD and metabolic syndrome have their origins in childhood, although clinical symptoms may not become apparent until later in life (Gutin and Owens, 2011; Strong et al., 1999; Williams et al., 2002). There has been recent, consistent evidence that a high proportion of young people exhibit one or more risk markers (Thomas and Williams, 2008) and since they are likely to retain these risks into adulthood (Andersen et al., 2004; Camhi and Katzmarzyk, 2010) it is paramount to identify those at risk and implement intervention strategies at an early age to address these modifiable risk factors.

CM risk factors and biomarkers include: hypertension, type 2 diabetes mellitus, high levels of serum cholesterol, a low serum concentration of high density lipoprotein cholesterol (HDL-C) and/or high concentration of low density lipoprotein cholesterol (LDL-C), and small, dense, LDL-C, atherosclerosis, ventricular hypertrophy and dysfunction, vascular dysfunction, cigarette smoking, high circulating levels of pro-inflammatory markers such as C Reactive Protein (CRP), low levels of fitness, physical inactivity and central adiposity (Styne, 2001). Figure 1-1 shows a schematic representation of the relationships between CM biomarkers with lifestyle behaviours whilst taking into consideration the predisposing, non-modifiable risk markers. These risk factors often cluster and therefore an individual with a high level of central adiposity increases their risk of developing hypertension, type 2 diabetes mellitus, dyslipidaemia, and likely engages in reduced levels of PA (Bailey et al., 2012). Therefore their overall risk of developing CMD is greatly increased (Andersen et al., 2006). This clustering effect dramatically increases relative risk for CMD, and with each additional risk factor in the cluster, there is a greater increase in relative risk (Andersen et al., 2003). Whilst traditional risk factors (high cholesterol, high blood pressure) are sometimes observed in

children or adolescents they are still primarily markers of CMD in adulthood (Berenson et al., 1988). The utility of other markers that are early or "pre-clinical" markers of CMD in younger children is of interest. Furthermore, several of these pre-clinical markers can be measured using non-invasive techniques and thus are suited to paediatric research. Ultrasound can be used to measure cardiac structure and diastolic function, flow mediated dilation (FMD) (which is an indicator of vascular endothelial function) and carotid intima media thickness (CIMT), an indirect measure of atherosclerotic burden (Coumo et al., 2002). Some of these non-invasive techniques have been previously used to measure CM risk in paediatric research and have provided evidence that these CM risk factors are evident in youth and increase with increasing adiposity, low PA and low CRF (Henaghan et al., 2008; Hopkins et al., 2009a).

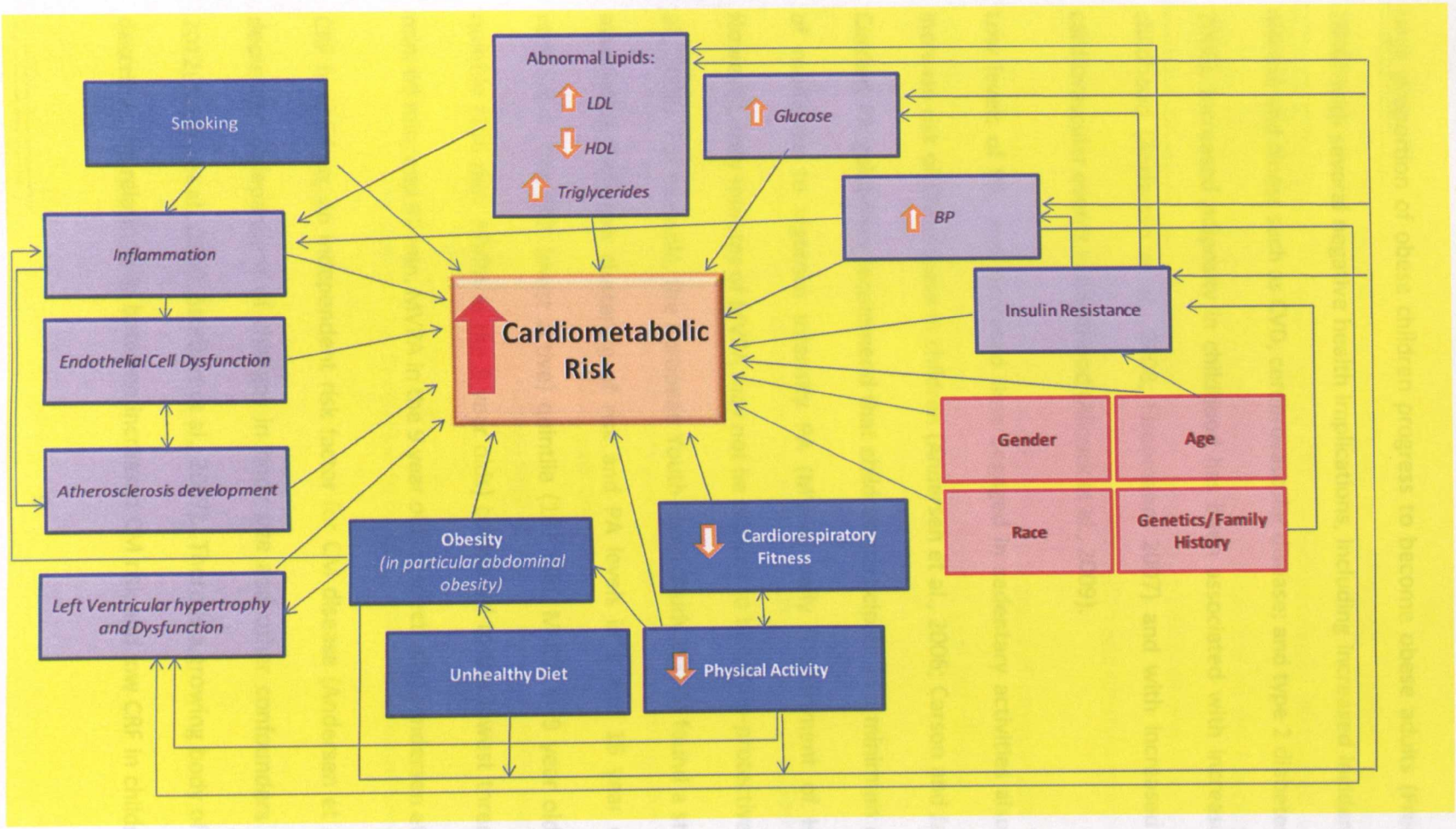

Figure 1-1: Schematic representation of potential relations among lifestyle behaviours (blue), CM biomarkers (purple) and predisposing factors (red). Drawn by author

Levels of childhood overweight and obesity have increased substantially over the last few decades (Boddy et al., 2009; Chinn and Rona, 2001). Recent studies have described a plateau in levels of obesity (Boddy et al., 2010; Lissner et al., 2010), but childhood obesity is still of serious public health concern (Gutin et al., 2005). Furthermore, it is known that a large proportion of obese children progress to become obese adults (Freedman et al., 2006) with several negative health implications, including increased incidence of chronic disease and illness such as CVD, cerebrovascular disease; and type 2 diabetes (Flynn et al., 2006). Increased adiposity in childhood has been associated with increased CM risk in childhood (Andersen et al., 2008; Eisenmann, 2007) and with increased incidence of cardiovascular events in adulthood (Allcock et al., 2009).

Low levels of PA, and increased time engaged in sedentary activities also substantially increase risk of CM disease in children (Andersen et al., 2006; Carson and Janssen, 2011). Current PA guidelines recommend that children participate in a minimum of 60 minutes of moderate to vigorous intensity PA (MVPA) daily (Department of Health, 2011). However, sixty minutes of MVPA may not be enough to be cardio-protective (Andersen et al., 2006). For example, the European Youth Heart Study (EYHS) found a strong negative association between clustering of risk and PA levels in 9 and 15 year olds, risk was reduced in the fifth (most active) quintile (167 min. MVPA in 9 year olds) and fourth quintile (116 min. MVPA in the 9 year olds) compared to the lowest three quintiles (38 min; 69 min; and 92 min. MVPA in the 9 year olds respectively) (Andersen et al., 2006).

CRF in children, an independent risk factor for CM disease (Andersen et al., 2004), has decreased independent of changes in body size and other confounders (Boddy et al., 2012; Boddy et al., 2010; Stratton et al., 2007). There is a growing body of evidence that describes the relationship between increased CM risk and low CRF in children (Adegboye

et al., 2011; Andersen et al., 2008; Bailey et al., 2012; Gutin et al., 2011; McGavock et al., 2009). The Literature Review [Chapter 2] will explore relationships between CM risk and CRF, body composition and PA in more detail.

In summary, CM disease has its origins in childhood. Obesity, physical inactivity, sedentary behaviour and low levels of CRF are independently associated with increased CM risk. However there are gaps in the paediatric literature on the interactions of some markers of risk, clustered CM risk which combines traditional and 'preclinical' markers, and measures of physical activity, CRF, body composition and lifestyle education.

The general aim of this thesis is to investigate the impacts of physical activity, CRF, body composition and lifestyle education on CM risk in 10-11 year old children.

The specific aims were:

- To investigate the relationships between invasive and non-invasive markers of CM risk
- To establish the relationships between the individual risk markers with objectively measured PA, and CRF in 10-11 year old children.
- To report clustered risk scores that combine both invasive and non-invasive markers of CM risk
- To assess clustered risk in relation to PA, CRF and body composition in 10-11 year old children.
- To investigate the immediate effects of a school based PA and healthy eating curriculum intervention [Children's Health Activity and Nutrition: Get Educated (CHANGE!)] on markers of CM risk in 10-11 year old children.

- To investigate the short term (8-10 weeks) follow up effects of the CHANGE! intervention on markers of CM risk in 10-11 year old children.

Chapter 2

Literature Review

Literature Review

2.1. Cardiometabolic Disease

The term cardiometabolic (CM) risk is used to describe the constellation of interrelated risk markers which progress the development of CM diseases (CMD) such as cardiovascular diseases (CVD); for example, atherosclerosis, coronary heart disease (CHD), and metabolic disorders such as type 2 diabetes and insulin resistance. It is widely accepted that CMD's have their origins in childhood, although clinical symptoms may not become apparent until later in life (Gutin and Owens, 2011; Strong et al., 1999; Williams et al., 2002). There has been recent, consistent evidence that a high proportion of young people exhibit one or more risk markers, such as hypertension, endothelial dysfunction, high cholesterol levels, and inflammatory mediators (Bailey et al., 2012; Thomas and Williams, 2008).

2.2. Risk factors for Cardiometabolic disease

A reduced risk of developing CMD is independently associated with the maintenance of a healthy body composition, and adequate PA and CRF levels (Ferrucci et al., 2006; King, 2005). Within this review of literature the clinical impact of body composition, PA and CRF, on health and more specifically on CM risk in children will be discussed. Individual risk markers as well as clustered CM risk will be explored.

2.2.1. Obesity and Overweight

For the purpose of this thesis, overweight and obesity are defined as the accumulation of excess body mass defined using age and sex specific cut off points as reported by Cole et

al., (2000) [Table 2-1]. Obesity is a chronic disease caused by a sustained energy mismatch where energy consumption exceeds energy expenditure (Power, 2012). Nutrition and PA play key roles in maintaining the homeostasis of the energy continuum and if energy consumed exceeds energy expended, excess energy is stored as triglycerides in adipose tissue; these fat cells can increase in number (hyperplasia) and/ or size (hypertrophy) and can contribute to surplus body weight (Sun et al., 2011). This surplus bodyweight is the fifth most significant risk factor contributing to the overall burden of disease worldwide (World Health Organisation, 2009). Hypertrophic fat cells release an increase in free fatty acids and peptides that can lead to clinical complications, such as type 2 diabetes mellitus, CVD, non-alcoholic fatty liver disease (NAFLD) and some forms of cancer (Guh et al., 2009). An increase in the number of fat cells can also lead to conditions such as osteoarthritis and sleep apnoea (Bonsignore et al., 2012; Issa and Griffin, 2012).

Table 2-1: International cut off points for body mass index for overweight and obesity by sex between 10 and 12 years, defined to pass through body mass index of 25 and 30 kg/m^2 at age 18 (Cole et al., 2000).

	Overweight		Obese	
Age	Boys	Girls	Boys	Girls
10	19.8	19.9	24.0	24.1
10.5	20.2	20.3	24.6	24.8
11	20.6	20.7	25.1	25.4
11.5	20.9	21.2	25.6	26.1
12	21.2	21.7	26.0	26.7

Obesity related diseases reduce life expectancy and quality of life; Haslam and James (2005) estimated the number of years of ill health and lives lost as a result of excess body weight worldwide, between the ages of 30 and 75 years [Figure 2-1]. According to these

estimates, the biggest burden of obesity is CM diseases in adults, with globally, over two and a half million deaths, associated with ischaemic heart disease and type 2 diabetes, attributable to excess BMI (Haslam and James, 2005).

Figure 2-1: Disability-adjusted life years (DALYs) as a result of obesity in men and women worldwide (Haslam and James, 2005, pg 1199).

2.2.1.1 Prevalence of Overweight and Obesity

Current data and trends in paediatric obesity are particularly alarming, as it is known that a very high proportion of obese children progress to become obese adults (Freedman et al., 2006). It is estimated that between the 1980s and 1990s prevalence of paediatric overweight and obesity increased by up to five fold in developed countries (Flynn et al., 2006). Data from the Liverpool SportsLinx project demonstrated an increase in

overweight and obesity between 1998 and 2006, from 17.4% in 9 year old boys and 22.5% in 9 year old girls to 26.5% and 33.9% respectively (Boddy et al., 2009), and similar trends have been found worldwide (Wang and Lobstein, 2006). In more recent years studies have described a plateau in prevalence of paediatric overweight and obesity (Boddy et al., 2010; Cali and Caprio, 2008; Lissner et al., 2010). However, obesity levels remain high and of great public health concern, with an estimated 110 million children classified as overweight or obese (Cali and Caprio, 2008). Recent data from the 2010/2011 UK National Child Measurement Programme found that 14.3% of Year 6 boys and 14.4% of Year 6 girls are overweight, and 20.6% and 17.4% of Year 6 boys and girls respectively are obese (The NHS Information Centre, 2011).

2.2.1.2. Measurement of Body Composition

Body composition can be measured using a number of different methods, for the purpose of this thesis body mass index (BMI), WC, and Dual Energy X-Ray Absorptiometry (DEXA) will be discussed.

2.2.1.2.1 Body Mass Index

Overweight and obesity are often measured using body mass index (BMI), which is calculated by using the following formula: body mass (kg) ÷ height^2 (m^2). In adults, overweight is defined as a BMI ≥25 kg/m^2 and obesity is defined as BMI ≥ 30 kg/m^2 (WHO, 2006). However, when defining overweight and obesity in children, it is not appropriate to apply these adult cut points due to the various stages of child development and growth. Therefore age and sex specific cut points have been developed. Such cut points have been developed using growth curves calculated from six nationally representative

cross sectional surveys, which were extrapolated from these adult cut points [Figure 2-2] (Cole et al., 2000).

Figure 2-2: International cut off points for BMI by sex for overweight and obesity passing through BMI 25 and 30 kg/m^2 at age 18 (data from Brazil, Britain, Hong Kong, Netherlands, Singapore and United States). (Cole et al., 2000)

An overweight child is expected to continue growing at a rate in line with growth curves so that they will have a BMI ≥25 kg/m^2 at the age of 18, and an obese child will have a BMI ≥ 30 kg/m^2 at age 18. Table 2-1 displays overweight and obese BMI cut points for children aged 10 to 12 years old.

2.2.1.2.2 Waist Circumference

It has been suggested that BMI may not be a sensitive measure of fatness in children as it gives no indication of fat distribution (Reilly et al., 2010). Therefore additional measures are needed to assess fat distribution. An increase in central adiposity, or greater fat

deposited around the waist, has a stronger association with increased CMD risk, than total adiposity or BMI (Burns and Arslanian, 2009). Waist circumference (WC) is a relatively convenient method of assessing fat distribution and has been useful in assessing risk for obesity related diseases such as CM diseases in adult populations (McCarthy et al., 2001). More recently WC has also been regarded a useful indicator of CM risk in children (Panagiotopoulos et al., 2012). Several studies have described the relationship between WC and CM risk, including clustered CM risk (Liu et al., 2010) and individual risk markers such as elevated blood pressure (Flores-Huerta et al., 2009; Genovesi et al., 2010), atherogenic lipoproteins and biomarkers of vascular smooth muscle cell dysfunction (Burns and Arslanian, 2009). Furthermore, WCs have been growing at a greater rate than BMI in children (McCarthy et al., 2003). WC centiles have been generated, to define overweight and obesity and identify those at greater risk of obesity related disease in UK children (McCarthy et al., 2001), and other paediatric populations (Aeberli et al., 2011; Brannsether et al., 2011; Fernandez et al., 2004). Table 2-2 shows WC by percentiles for 10 to 12 year olds in the UK.

Table 2-2: Waist circumference (cm) by percentiles of age and sex based on UK growth curves (McCarthy et al., 2001).

		Waist Circumference (cm) Percentiles						
Sex	**Age (y)**	**5th**	**10th**	**25th**	**50th**	**75th**	**90th**	**95th**
Boys	10-10.99	50.8	52.3	55.0	58.2	61.9	65.6	67.9
	11-11.99	51.9	53.6	56.6	60.2	64.1	67.9	70.4
Girls	10-10.99	50.7	51.8	53.9	56.7	60.0	63.6	66.2
	11-11.99	52.0	53.2	55.4	58.2	61.6	65.4	68.1

2.2.1.2.3. Dual Energy X-ray Absorptiometry (DEXA)

Dual Energy X-Ray Absorptiometry (DEXA) has also been used to accurately estimate body composition at a low radiation dose, by measurement of three components, fat mass (FM), fat free soft tissue (FFST) and bone mineral content (BMC). Fat free mass (FFM) is a combination of FFST and BMC (Gutin et al., 1996). DEXA can be used to detect small changes in body composition, and has a strong correlation with other measures of body composition such as skinfold thickness, and BIA (van der Sluis et al., 2002). The 'gold standard' body composition measure utilises a four compartment model with a combination of methods, FM and FFM measured using hydrodensitometry or air displacement plethysmography; total body water determined by isotope dilution, and bone mineral density (BMD) measured by DEXA. Total body water and BMD are subtracted from FFM to obtain the residual compartment (consisting of protein, glycogen and non-bone minerals) (Toombs et al., 2012). Whilst studies have demonstrated an under estimation of body fat using DEXA compared to this four compartment model, DEXA is considered a convenient and useful diagnostic body composition assessment tool due to technological advances, its relatively high precision, and low radiation dose (Toombs et al., 2012).

Normative data for body fat percentage, derived from DEXA analysis, in children has been published for various countries including the Netherlands (van der Sluis et al., 2002), New Zealand (Taylor et al., 2002), and Canada (Sala et al., 2007). To the author's knowledge there are no published normative values for British children which have been derived from DEXA data.

2.2.2. Physical (in) activity

Physical inactivity is estimated to cost the UK economy £0.9 billion per year (Scarborough et al., 2011) and is the fourth leading risk factor for global mortality, accounting for an estimated 3.2 million deaths worldwide (World Health Organisation, 2009).

Promoting PA in childhood is said to elicit three main benefits: A direct improvement in quality of life and health status in childhood; a direct improvement in adult life status by delaying the onset of chronic diseases; an indirect health gain through the increased likelihood of maintaining positive activity behaviours into adulthood (e.g. forming positive behaviours in childhood), again resulting in an improvement in adult heath status (Boreham and Riddoch, 2001). However the intensity and duration of PA plays an important role in the resulting health benefits (Hagstromer et al., 2007). PA can be defined as 'any bodily movement produced by the skeletal muscles which results in energy expenditure' (Freedson et al., 2000), pg. S77). Health enhancing PA is a type of PA which benefits health and fitness without undue harm or risk, and not all PA is beneficial to health (Hagstromer et al., 2007). PA of either moderate or vigorous intensity has health enhancing benefits. Moderate Intensity PA (MPA) refers to activities which results in increased heart rate, increased body temperature and being slightly out of breath. MPA is the equivalent of 51-69% VO_2 Max and increases the body's metabolism during the activity by 3 to 6 times resting level (3-6 METs) (Hagstromer et al., 2007); examples of activities of moderate intensity include brisk walking (3.8 METs), mowing the lawn (4.5 METs), and playing golf (4.5 METs) (Ainsworth et al., 2000). Vigorous PA (VPA) is the equivalent of ≥70% VO_2 Max , 6 METs, examples include high impact aerobics (7 METs) and running (at 5mph = 8 METs, or at 7mph = 11.5 METs) (Ainsworth et al., 2000).

2.2.2.1 Physical Activity Guidelines

Current UK guidelines recommend children participate in at least 60 minutes of daily moderate to vigorous intensity PA (MVPA) whilst engaging in vigorous intensity activities at least 3 times per week (Department of Health, 2011). However, few children reach 60 minutes of MVPA daily, with one study reporting as little as 2.5% of children meeting this guideline (Riddoch et al., 2007). Furthermore, PA levels decrease with age (Sallis, 2000) with older children reportedly accumulating less daily MVPA, and subsequently fewer meet the PA guidelines (The NHS Information Centre, 2009).

The estimates of the proportion of children meeting the PA guidelines vary by study and method of assessment (Corder et al., 2008). Numerous PA measures have been used in paediatric research, such as self-report PA, direct observation and objectively measured techniques such as accelerometry (Corder et al., 2008). The percentage of children meeting these guidelines tends to be overestimated when using self-report methods. The Health Survey for England (2008) reported that 32% of boys and 24% of girls met the recommended PA levels. Objectively measured PA assessment is a more accurate method of measuring PA and one study found that as little as 2.5% of children (mean age 11.8 years) achieved at least 60 minutes of daily MVPA (Riddoch et al., 2007).

2.2.2.2 Measurement of Physical Activity

Measurement of PA in children is notoriously difficult due to the sporadic intermittent nature of children's PA behaviour (Baquet et al., 2007). Self-report measures of PA using questionnaires, interview and diaries have been widely used in large scale paediatric research, due to its low cost, and ability to capture large samples relatively quickly and easily (Biddle et al., 2011). However, reliability and validity problems exist with self-report

measurements (Chinapaw et al., 2010). For example, individuals may sometimes exaggerate or underestimate the activity levels, perceptions on intensities of activities vary between individuals, and therefore one individual may perceive certain intensity as vigorous whereas another may only consider it moderate. People may also have problems remembering what activity they have participated in particularly if the activity was unplanned and unstructured such as walking; in addition intensity may vary substantially during a short space of time and therefore estimating the time spent at different intensities is difficult (Chinapaw et al., 2010). To overcome these problems of self-report measures, objective measurements have been employed in paediatric research (Riddoch et al., 2004). A feasible and accurate objective tool to measure PA in children is accelerometry (Ekelund et al., 2001; Metcalf et al., 2002; Pate et al., 2002). Accelerometers translate accelerations to a quantifiable measurement which allows different intensities of activity to be recorded by applying pre-determined cut points of accelerometer counts (Welk, 2005). Accelerometers are unobtrusive and can store large amounts of data, including intensity and duration of activity over several days. However, they cannot be used in contact sports or water based activities, and they do not measure load or gradient; in addition, they are relatively expensive in comparison to self-reported methods (Riddoch et al., 2004). Comparisons between studies can also be difficult, with number of days of monitoring, length of epochs and participant compliance differing between studies. There has also been much debate over the most appropriate thresholds used to define different intensities of PA (Trost et al., 2011).

2.2.3. Sedentary Behaviour

Prolonged sedentary behaviour is independently and positively associated with all-cause mortality and CM risk (Katzmarzyk et al., 2009; Tremblay et al., 2011b). PA and sedentary behaviours are separate entities, and can co-exist, with a child engaging in the recommended 60 minutes of MVPA, however also spending prolonged periods of the day engaged in sedentary activities (Tremblay et al., 2011a). The Bristol 3P's study recognised that 10-11 year old children could be clustered into three distinct typologies of PA and sedentary behaviours, these were: high sedentary and high active; medium sedentary and low active; and low sedentary and high active, suggesting that interventions should be tailored according to the typology of the intended target group (Jago et al., 2010b).

Whilst there is growing evidence of the importance of MVPA in reducing CM risk in children (Andersen et al., 2006; Ekelund et al., 2007), the relationship between sedentary behaviour and CM risk is less clear. Studies have demonstrated a positive association between clustered CM risk and volume of sedentary behaviour in children and adults (Ekelund et al., 2007; Martinez-Gomez et al., 2010) however neither of these studies adjusted for MVPA. Another study, found that volume of sedentary behaviour was not a predictor for high clustered CM risk when adjusting for MVPA in children and adolescents, which suggests that MVPA is more important than time engaged in sedentary activities (Carson and Janssen, 2011). Type of sedentary behaviour has also been linked to increased CM risk, and studies have demonstrated a positive association between TV viewing and CM risk (Carson and Janssen, 2011; Ekelund et al., 2006). Carson and Janssen (2011) found that children that watched in excess of 4 hours TV per day were 2.53 (95%CI 1.45-4.42) times more likely to have high CM risk than those that watched less than 1 hour of TV per day, however after adjustments for WC the relationship between CM risk

and TV time was attenuated. Ekelund et al (2006) also support this finding concluding that the association between TV viewing and clustered metabolic risk is mediated by adiposity.

2.2.3.1. Sedentary Guidelines

Recently the Canadian Society for Exercise Physiology (CSEP) published the first evidence based guidelines on sedentary behaviour for children and adolescents (Tremblay et al., 2011a). These guidelines have been produced in light of the growing evidence that suggests that sedentary behaviour has an independent and significant impact on health. The CSEP guidelines recommend that children limit sedentary transport (i.e. motorised transport) and reduce daily screen time (TV, computer etc.) to less than 2 hours (Tremblay et al., 2011a). UK guidelines recommend that sedentary time (sitting) should be minimised, but there are no specific time recommendations (Department of Health, 2011).

2.2.3.2. Measurement of Sedentary Behaviour

Volume and types of sedentary behaviour can be estimated using a combination of self-report and objective measurement tools (Carson and Janssen, 2011). Types and duration of sedentary activities, such as TV viewing are estimated using self-report questionnaires. It is estimated that approximately 29% of boys and 23% of girls aged between 9 and 16 years, in North America, watch in excess of 4 hours TV per day, with similar estimates reported in European countries (Biddle et al., 2004). As with the reliability and validity issues associated with self-reported PA, self-report sedentary time therefore also has such issues. Objective measures, such as accelerometry, can be used to measure volume but not type of sedentary behaviour. An accelerometer threshold of <100 CPM has been

used to define sedentary behaviour in several paediatric studies (Carson and Janssen, 2011; Evenson et al., 2008; Mattocks et al., 2008; Steele et al., 2010).

2.2.4. Cardiorespiratory Fitness

Studies have demonstrated an inverse relationship between CRF and all-cause mortality in healthy adults (Kodama et al., 2009; Lee et al., 2010). Furthermore, there is an emerging body of evidence which suggests that CRF is inversely associated with CM risk markers in children and adolescents (Andersen et al., 2008; Anderssen et al., 2007; Bailey et al., 2012; Eisenmann, 2007; Ruiz et al., 2009; Ruiz et al., 2007a) as well as incidence of CM events later in life (Ruiz et al., 2009).

CRF, or aerobic fitness as it is sometimes termed, is defined as 'the ability to deliver oxygen to the muscles and to utilise it to generate energy to support muscle activity during exercise' (Armstrong et al., 2011). CRF has a large genetic influence, although environmental factors, may also have an effect (Hopkins et al., 2010). In adults CRF has a strong positive association with habitual PA, however in children the relationship is less convincing (Armstrong et al., 2011). Whilst exercise training has been found to increase CRF levels in young people, a relationship between habitual PA and CRF is not evident (Armstrong et al., 2011).

2.2.4.1. Measurement of Cardiorespiratory Fitness

CRF can be measured accurately and objectively in the laboratory. Peak oxygen uptake ($VO_{2\ peak}$) is thought to be the best measure of CRF in young people (Armstrong et al., 1998). $VO_{2\ peak}$ relates to the highest rate of oxygen consumption during exercise

(Armstrong et al., 2011) and is generally measured in the laboratory using a treadmill or cycle ergometer protocol. Laboratory based testing is time consuming, and requires qualified technicians and sophisticated equipment to administer and therefore the use is limited in paediatric populations (Castro-Pinero et al., 2010).

A widely used field based measure of CRF in children is the 20 m shuttle run test (20m SRT) (Boddy et al., 2012). The 20m SRT is low in cost to administer, requires little equipment and allows measurement of large samples simultaneously, and is therefore suited to school based and community testing. A systematic review of field based fitness testing concluded that the 20m SRT was a valid, reliable tool for assessing CRF in children (Castro-Pinero et al., 2010).

At all ages boys tend to have higher $VO_{2\ peak}$ than girls, with girls mean $VO_{2\ peak}$ (ml/min) values approximately 10% lower than boys during childhood. In boys there tends to be a linear relationship between $VO_{2\ peak}$ (ml/min) and chronological age, whereas in girls $VO_{2\ peak}$ (ml/min) increases in a linear trend until a plateau at around 14 years of age (Armstrong et al., 2011). $VO_{2\ peak}$ has a positive relationship with body mass and therefore in order to control for this $VO_{2\ peak}$ is expressed in relation to body mass (ml/kg/min). When scaling $VO_{2\ peak}$ for body mass the trends for boys show that $VO_{2\ peak}$ (ml/kg/min) values remain relatively consistent between the ages of 6 and 18, whereas girls $VO_{2\ peak}$ (ml/kg/min) values decrease with age (Armstrong et al., 2011). Over the last couple of decades CRF levels in childhood have decreased independent of changes in body size and other confounders (Boddy et al., 2012; Boddy et al., 2010; Stratton et al., 2007).

2.2.4.2 Cardiorespiratory Fitness Recommendations

The EYHS recently published recommended levels of CRF for optimal CM health for children and adolescents (Adegboye et al., 2011). The recommended $VO_{2\ peak}$ for 9 year old children (age range 8.2-11.3 years) was 37.4 ml/kg/min for the girls and 43.6 ml/kg/min for the boys (Adegboye et al., 2011).

2.2.5. Summary of Risk Factors

Overweight and obesity, PA, sedentary behaviour and CRF levels are independently associated with CM risk and mortality. The following sections will describe the CM disease process, identify markers of risk and evaluate the impacts of body composition, PA and CRF in relation to individual risk markers, and clustered risk. Lifestyle interventions will then be explored.

2.3 Cardiometabolic Disease Process: Atherosclerosis

Atherosclerosis is an inflammatory process characterised by the progressive thickening of the artery walls and narrowing of the lumen (Libby, 2002). Atherosclerotic lesions primarily occur in large and medium-sized elastic and muscular arteries. Ischemia, or insufficient blood supply to an organ, caused by lesions in such arteries can result in tissue-death known as infarction, including myocardial infarction (heart attack), and cerebrovascular infarction (stroke) (Libby et al., 2011). The inflammatory process begins following injury to the endothelial cells of the artery wall, which in turn triggers an inflammatory response. It is thought that injury to the endothelial cells is caused by CM risk factors, such as elevated LDL-C, elevated free radicals caused by hypertension and

other factors, cigarette smoking, diabetes mellitus, and elevated plasma homocysteine (Libby et al., 2010b). The atherosclerotic process begins in the first decade, with endothelial cell dysfunction followed by the development of an inflammatory lesion, known as the fatty streak, which consists of monocyte-derived macrophages and T lymphocytes (Libby et al., 2010a; Libby et al., 2011). During this process the endothelium becomes more adhesive and permeable, adhesion molecules and platelets migrate to the artery wall and there is an increase in leukocyte permeation (Ross, 1999). As a result this stimulates smooth muscle proliferation and migration which develops into an intermediate lesion, causing thickening of the artery wall. As endothelial cell dysfunction progresses, there is an increase in oxidative stress, monocytes increase adherence and lipids accumulate. The continued inflammatory response leads to increased numbers of macrophages and lymphocytes, which emigrate from the blood and proliferate within the lesion, the activation of these cells encourages release of hydrolytic enzymes, cytokines, chemokines and growth factors which cause further damage and lead to necrosis (Libby, 2002). The continuous cyclic process of accumulation of adhesion molecules, smooth muscle cell proliferation and fibrous tissue formation enlarges the lesion, which becomes a core of lipid (foam cells) and necrotic tissue covered in a fibrous cap. This advanced, complicated, lesion may then obstruct blood flow as it intrudes into the lumen, clinical signs and symptoms may become evident when there is over 75% lumen occlusion. Over time the lesion may become disrupted, the plaque becomes unstable and could lead to rupture of the fibrous cap or ulceration of the plaque, which causes thrombosis (blood clot) (Libby et al., 2011). It is estimated that approximately 50% of incidence of acute coronary syndromes and myocardial infarction may be the result of plaque rupture and thrombosis (Ross, 1999). The thickening of the inner most layers of the arteries, the

intima media complex (IMT), is an early marker for atherosclerosis, and can be measured non-invasively (Cuomo et al., 2002).

2.3.1. Non-invasive Cardiometabolic Risk Markers

Whilst traditional risk factors (high cholesterol, high blood pressure) are sometimes observed in children or adolescents they are still primarily markers of CVD in adulthood (Berenson et al., 1988). The utility of other markers that are early or "pre-clinical" markers of CVD in younger children is of interest. Furthermore, several of these pre-clinical markers can be measured using non-invasive techniques and thus are suited to paediatric research (George et al., 2010; Hopkins et al., 2010; Hopkins et al., 2009a). Ultrasound can be used to measure cardiac structure and diastolic function, flow mediated dilation (FMD) (which is an indicator of vascular endothelial function) and carotid intima media thickness (CIMT), the latter being indirect measures of atherosclerotic burden (Coumo et al., 2002). Some of these non-invasive techniques have been previously used to measure cardiovascular (CV) risk in paediatric research and have provided evidence that these CV risk factors are evident in youth and increase with increasing adiposity (Henaghan et al., 2008; Hopkins et al., 2010; Hopkins et al., 2009a). The combination of these "preclinical" markers with invasive markers of CV risk in paediatric studies is novel, and this thesis will address this in order to fully understand the interactions.

2.3.1.1 Carotid Intima Media Thickness

CIMT is one way of assessing atherosclerotic burden indirectly (Cuomo et al., 2002). CIMT is positively associated with prevalence of CVD (O'Leary et al., 1999). As the number of other CV risk factors increases so does the severity of atherosclerosis of the carotid and aortic arteries and severity increases with age (Berenson et al., 1998). CIMT may also be an early predictor for other CV complications, and is positively correlated with other

markers of CM risk (Sorof et al., 2003). Sorof et al., (2003) measured CIMT and left ventricular mass (LVM) in hypertensive individuals. Left ventricular hypertrophy was prevalent in 89% of individuals with increased CIMT compared to 22% in individuals with normal CIMT. CIMT was also positively correlated with body mass index as well as interventricular septal thickness and posterior wall thickness of the heart (Sorof et al., 2003. An increased CIMT is also related to atherosclerosis in other areas of the body, for example atherosclerosis in the abdominal aorta as well as in the arteries of the lower extremities (Bots et al., 2003; Mattace Raso et al., 1999). CIMT in obese children is associated to systolic (sBP) and diastolic blood pressure (dBP) (Elkiran et al., 2011; Wunsch et al., 2005). In a study by Wunsch et al., (2005) children with CIMT in the highest quartile had a significantly higher blood pressure than those in the lower quartile ($p < 0.001$, median systolic pressure 137 mmHg versus 119 mmHg, median diastolic pressure 71 mmHg versus 60 mmHg) (Wunsch et al., 2005). Furthermore relationships have been found between CIMT and markers of inflammation, such as fibrinogen and C-Reactive Protein (CRP) (Meyer et al., 2006b) and CIMT is also inversely associated with HDL-C (Ayer et al., 2009). In obese children there were also significant correlations found between CIMT and serum glucose (Elkiran et al., 2011) and indices of insulin resistance (HOMA-IR, Glucose/ Insulin ratio, and whole body insulin sensitivity index) (Giannini et al., 2008).

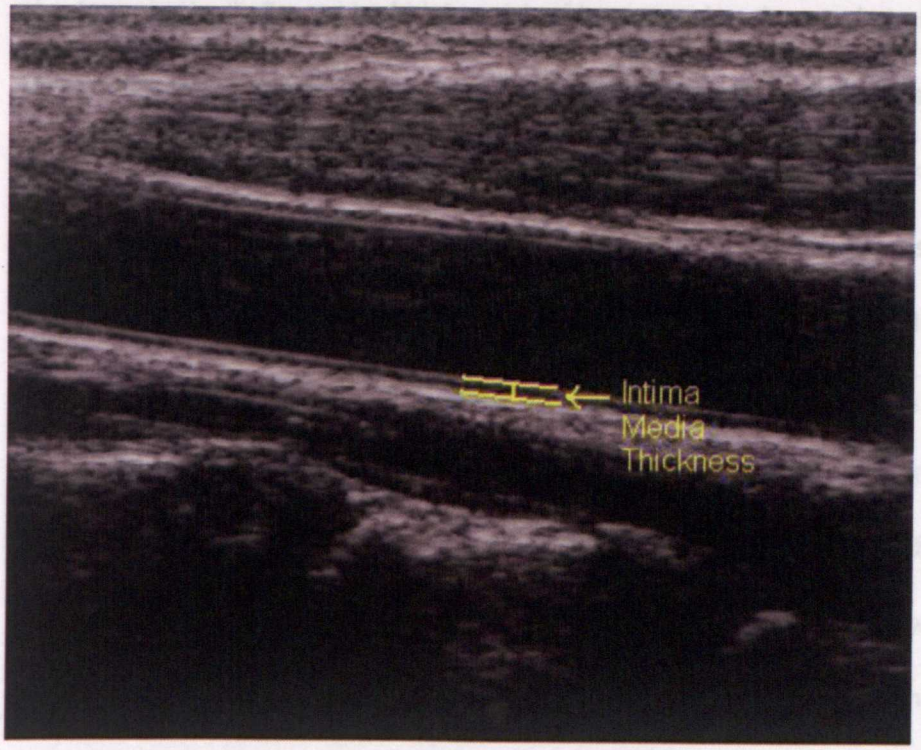

Figure 2-3: B Mode ultrasound scan indicating Intima Media Thickness. Author's own scan: Image taken from one of participants in study 2.

2.3.1.1.1 CIMT in relation to body composition, physical activity, and cardiorespiratory fitness.

Obesity in childhood significantly increases the risk of developing atherosclerotic disease and death later in life (Whincup and Deanfield, 2005). Childhood obesity has significant effects on the function of the arteries of the CV system including impaired endothelial function, weakened arterial distensibility and adverse changes in intima-media thickness (Meyer et al., 2006b; Whincup and Deanfield, 2005). Studies have found significantly higher CIMT in obese children and adolescents compared to lean controls (Iannuzzi et al., 2004; Meyer et al., 2006b). Meyer et al (2006b) investigated brachial FMD and CIMT in 32 obese adolescents (mean age 13.7 ± 2.7 years) in comparison to 20 age matched lean controls. The obese children presented impaired FMD and significantly increased CIMT compared to the lean controls, they also found that children with increased CIMT were

also less physically fit and had higher risk of hypertension. Iannuzzi et al (2004) supported this finding that obese children (n = 100, aged 6-14 years) had significantly greater CIMT and stiffness than controls of healthy weight. Furthermore a positive association was found between CIMT and BMI in adolescents (mean age 14.6 years) (Atabek, 2008). Conversely, other studies have not found significant differences in CIMT of children of healthy weight, overweight or obese (Ayer et al., 2009; Tounian et al., 2001). Juonala *et al.*, (2005) found that obesity in childhood was associated with CIMT in adulthood (aged between 24 and 39), however only if obesity persisted into adulthood. If an individual was obese as a child but non-obese as an adult they had a significantly lower CIMT (mean = 0.627 mm) than if they were also obese in adulthood (mean = 0.642mm). However, those who had always been non-obese had lower CIMT in adulthood (mean = 0.610 mm).

There is an apparent lack of literature on the relationship between PA and CIMT in children, and therefore this will be investigated further within this thesis. However, PA has been found to slow down the progression of atherosclerosis in both men and women (Nordstrom *et al.*, 2003). Nordstrom *et al.*, (2003) took baseline measures of CIMT in 500 subjects and then monitored the change over three years and found that CIMT progression was about threefold higher in the sedentary group compared to the regularly active group. Significant differences were evident between the sedentary group (change of 14.3 ± 1.7 microns per year) and the moderately active group (change of 10.2 ± 1.0 microns per year) but a greater slowed progression was evident in the vigorously active individuals (change of 5.5 ± 1.5 microns per year). Studies have also found that exercise training interventions can improve IMT in overweight and obese children (Meyer et al., 2006a; Woo et al., 2004). Overweight children (n= 82, aged 9 to 12 years) were assigned to either a diet or combined diet and exercise training group, and after 1 year there were significant improvements in CIMT in the combined diet and exercise group compared to

the diet only group (Woo et al., 2004). Meyer et al. (2006a) also found that CIMT was reduced in obese adolescents (mean age 14.7 ± 2.7 years) after 6 months of exercise training. Another study also found that structured exercise training over 9 weeks can also reduce IMT in healthy weight 11 year old children (Henaghan et al., 2008). Conversely, a study by Ayer et al (2009) found no significant relationships between PA levels and CIMT in 8 year old children. Further research is required to fully understand the interactions of CIMT with PA, and CRF in children.

2.3.1.2. Left Ventricular Structure and Function

The left ventricle (LV) works under greater pressure and resistance than the right ventricle, and therefore the walls of the LV are thicker (Tortora and Grabowski, 2003). LVM can be determined accurately using echocardiography [Figure 2-4], and gives an indication of overall cardiac structure. Cardiac structure can be affected by exercise and disease (Vella and Robergs, 2008) however, body growth directly influences organ growth and therefore LVM also increases with increases in body size (De Simone et al., 2005). Thus it is important, especially during childhood and adolescence, to index LVM by height to detect abnormal LVM dimensions (De Simone et al., 2005). Left ventricular hypertrophy (LVH), the term used to describe increased LVM, has been associated with increased CV morbidity and mortality (Chien et al., 2001).

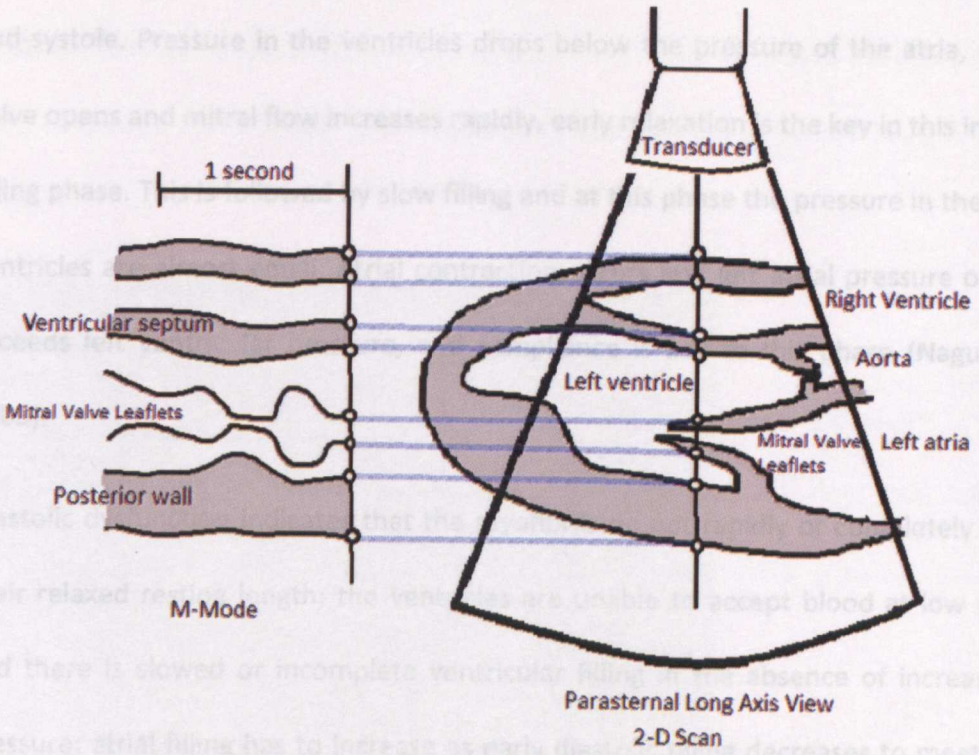

Figure 2-4: 2D Image of assessing LV Mass in parasternal long axis view.Drawn by author.

The cardiac cycle can be split into two distinct phases, systole and diastole. During systole the heart contracts and ejects blood into the arteries, the relaxation of the heart which follows contraction allows for refilling of blood is termed diastole. The efficiency of the functioning of the LV depends on its capability to alternate between its two key functions; systolic ejection and diastolic filling (Nagueh et al., 2009). In order for optimal function, the ventricles must be able to cycle from a compliant chamber which allows LV to fill from low left atrial pressure, to a stiff chamber, which under rapidly increasing pressure, in systole that ejects the stroke volume (SV) (Nagueh et al., 2009). Furthermore, SV must be able to increase when in demand, for example during exercise, in response to only minimal increase in left atrial pressure (Nagueh et al., 2009). The term diastolic dysfunction is used to describe abnormal, impaired functioning of the heart during filling

(Gaasch and Zile, 2004). In normal diastolic functioning, ventricular relaxation begins at end-systole. Pressure in the ventricles drops below the pressure of the atria, the mitral valve opens and mitral flow increases rapidly, early relaxation is the key in this initial rapid filling phase. This is followed by slow filling and at this phase the pressure in the atria and ventricles are almost equal. Atrial contraction occurs and left atrial pressure once again exceeds left ventricular pressure, and compliance is key to this phase (Nagueh et al., 2009).

Diastolic dysfunction indicates that the myofibrils do not rapidly or completely return to their relaxed resting length; the ventricles are unable to accept blood at low pressures and there is slowed or incomplete ventricular filling in the absence of increased atrial pressure; atrial filling has to increase as early diastolic filling decreases to meet demand for SV (Gaasch and Zile, 2004). Diastolic dysfunction precedes systolic dysfunction and is therefore an early marker for the development and progression of a number of CVDs, and is therefore of clinical importance and interest (George et al., 2010).

LV diastolic function can be measured non-invasively using ultrasound. Pulsed Doppler echocardiography measures blood flow velocity at the mitral valves in the apical four chamber view [Figure 2-5] (George et al., 2010). Trans mitral flow velocity is separated into two components; peak early (E) and peak late or atrial (A) filling velocities. In normal diastolic function, the majority of ventricular filling occurs in the early filling phase therefore E is greater than A, and E/A ratio >1.0 (Rakowski et al., 1996). An additional measure of diastolic function utilises tissue Doppler imaging (TDI). This technique evaluates wall movement, which is indicative of relaxation and contraction, by measuring the velocity of segments of the myocardium (George et al., 2010). Myocardial velocities which correspond to early diastole (E') and late diastole (A') are measured and E'/A' ratio

is reported. LV filling pressures can also be estimated by calculating the ratio of mitral inflow (E) velocity to tissue Doppler (E') (E/E'). An E/E' ratio <8 usually indicates normal LV filling pressures, and a ratio >15 is indicative of increased filling pressures (Ommen et al., 2000).

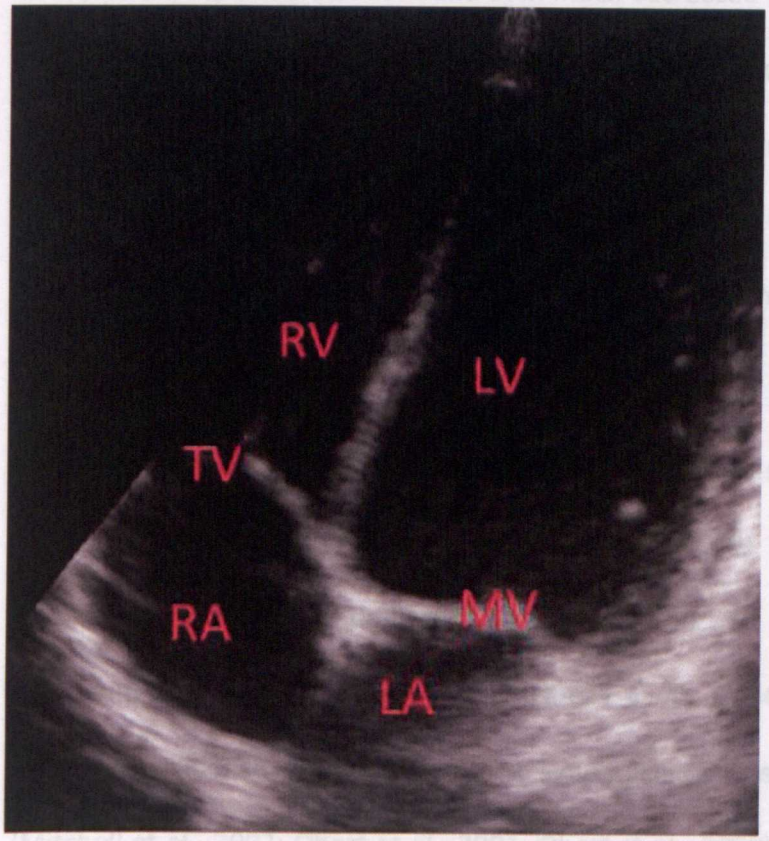

Figure 2-5: Apical four chamber view of heart. Author's own Scan: Image taken from one of participants in Study 2.

Key: LV = Left Ventricle, RV= Right Ventricle, LA= Left Atria, RA= Right Atria, MV = Mitral Valve, TV= Tricuspid Valve

2.3.1.2.1 LV Mass and LV diastolic function in relation to body composition, physical activity and cardiorespiratory fitness.

An increase in BMI is associated with increased LVM (Dekkers et al., 2002; Zeybek et al., 2010b) and weight reduction is a successful mechanism for treatment and prevention of LVH (Hinderliter et al., 2002). Zeybek et al. (2010) found that LVM and LVM Index were significantly higher in obese 9-13 year old children than in age matched lean children. This

is also supported by other studies who found that LVM index was greater in obese children compared to healthy weight controls (Di Salvo et al., 2006; Mitchell et al., 2002). Mitchell et al., (2002) also found that improvements in CRF through an 8-month physical training programme did not alter these adverse LV effects of obesity. Moreover, Zeybek et al., (2010) reported that LVM and LVM Index decreased slightly, in 9-13 year old obese children following a six month intervention of low carbohydrate diet combined with moderate exercise, though these reductions did not reach statistical significance. Furthermore, another study found that in non-obese children a 13-week exercise programme resulted in favourable improvements in LV structure and function (Obert et al., 2001).

LV dysfunction has been found to be associated with obesity in children (Zeybek et al., 2010) and low fitness in adults (Turzyniecka et al., 2010). Improvements in LV diastolic function have also been demonstrated in trained 11-13 year old male cyclists when compared with age matched controls (Nottin et al., 2004). However, there has been conflicting evidence on the effects of training programmes on LV function in children (Mitchell et al., 2002; Obert et al., 2001; Obert et al., 2009). Children, of healthy weight, enrolled on a two month high intensity aerobic training programme, which resulted in a significant increase in $VO_{2\ peak}$ by 6.5%, however this improvement in fitness did not result in changes in LVM, transmitral flow (E/A) or early (E') or late (A') wall movements measured by TDI (Obert et al., 2009). Obese adolescents, aged 13 to 16 years, enrolled on an 8 month physical training programme, which resulted in a significant improvement in CRF, and reductions in % body fat and visceral adipose tissue, however there were no significant differences between the training group and control group for changes in diastolic function (midwall fractional shortening) (Mitchell et al., 2002). In contrast to this favourable improvements in diastolic function have been demonstrated following a 13

week running programme in pre pubertal (9-11 years) children, however improvements induced by training were lost following two months of detraining. Training consisted of 3 x 1 hour sessions per week of VPA (>80% HR max). A significant increase in early diastolic passive filling (E) and a decrease in late diastolic filling (A) occurred in the training group (Obert et al., 2001).

Diastolic filling abnormalities are also associated with hypertension in children (Border et al., 2007) and elevated LVM has been found to be a significant independent predictor of diastolic filling abnormalities in hypertensive children (Border et al., 2007). The pattern of abnormalities found in these children suggests alterations in both LV relaxation and compliance with an increase in LVM predicting impaired LV relaxation (reduced E'), and reduced compliance (increased E/E') (Border et al., 2007). There appears to be no published research investigating the relationship between PA and diastolic function in children. Therefore this will be investigated in study 1 of this thesis.

2.3.2 Blood Pressure

The pressure of the blood within the arteries can also be measured non-invasively. Systolic blood pressure (sBP) is the pressure of the blood in the arteries after cardiac contraction, and diastolic blood pressure (dBP) is the pressure of the blood within the arteries after cardiac relaxation. Hypertension, or chronic high blood pressure, contributes to one-half of the CHD burden, and approximately two-thirds of the cerebrovascular disease burden, and is therefore considered the most important CVD risk factor worldwide (Farpour-Lambert et al., 2009).

Hypertension in adults is diagnosed if sBP is greater than 140 mmHg and dBP is greater than 90 mmHg. However, in children the classification of hypertension is the 95th

percentile of blood pressure or above dependent on age, sex and height [Table 2-3] (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004).

Table 2-3: Blood Pressure levels for the 90th (prehypertensive) and 95th percentile (hypertensive) of Blood Pressure for 10 and 11 year old boys and girls by percentiles of height.

		Systolic BP (mmHg)							Diastolic BP (mmHg)						
Height Percentile		5	10	25	50	75	90	95	5	10	25	50	75	90	95
Age 10 (pre)	Boys	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	Girls	112	112	114	115	116	118	118	73	73	73	74	75	76	76
Age 10 (hyp)	Boys	115	116	117	119	121	122	125	77	78	79	80	81	81	82
	Girls	116	116	117	119	120	121	122	77	77	77	78	79	80	80
Age 11 (Pre)	Boys	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	Girls	114	114	116	117	118	119	120	74	74	74	75	76	77	77
Age 11 (hyp)	Boys	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	Girls	118	118	119	121	122	123	124	78	78	78	79	80	81	81

2.3.2.2 Blood Pressure in relation to body composition, physical activity and cardiorespiratory fitness

Clinical studies have demonstrated a strong relationship between obesity and hypertension in adults (Rahmouni et al., 2005). This association is also present in children and adolescents with studies reporting a higher prevalence of hypertension in obese children compared to those that are lean (Sorof and Daniels, 2002). In a study of 12-16

year olds (n=2460) a significantly larger percentage of obese children (33%) were hypertensive compared to children of normal weight (11%, $p<0.001$) (Sorof et al., 2002).

Inconsistencies exist in the relationship between PA levels and BP in children between studies, with no clear association between PA and BP in normotensive children (Kelley et al., 2003). A significant curvilinear relationship is evident between CRF and sBP and dBP in both 9 and 15 year olds, with the greatest difference in blood pressure evident between children with low and moderate fitness levels (Klasson-Heggebo et al., 2006). However studies that have investigated training effects on BP in children have been inconclusive, a meta-analysis of 12 randomised control trials, with a total of 1266 participants, demonstrated a non-significant reduction in resting BP, of only a 1% and 3% reduction in sBP and dBP respectively, following exercise intervention (Kelley et al., 2003). Further investigation is needed to understand the impact of PA with BP in children. This thesis will also investigate the impacts of a lifestyle education intervention on BP (Study 3).

2.4 Invasive Cardiometabolic Risk Markers

Traditional metabolic risk markers such as cholesterol and glucose have been measured in several paediatric studies (Andersen et al., 2004; Andersen et al., 2008), and there has been growing focus on the role of markers of inflammation in the development of atherosclerosis (Thomas and Williams, 2008), therefore metabolic and inflammatory markers will be discussed in the following sections.

2.4.1 Metabolic Markers

Triglycerides, esters of glycerol and three fatty acids, provide highly concentrated sources of nonesterified fatty acids (NEFA), which are used in cell signalling and for producing metabolic energy (Mietus-Snyder and Krauss, 2008). Cholesterol is an essential component of cell membranes, forms bile secretions that aid digestion and is essential for synthesis of steroid hormones, and Vitamin D (Mietus-Snyder and Krauss, 2008). Fats are insoluble in water and therefore triglycerides and cholesterol are carried by transport vehicles in the plasma known as lipoproteins. Lipoproteins are made up of proteins and lipids, and can be classified according to their size and density, determined by their relative content of four major lipids; phospholipids, cholesterol, cholesterol esters and triglycerides (Blasiole et al., 2007). The common macromolecular structure of lipoproteins includes the hydrophobic cholesterol ester and triglyceride core, which is encompassed in a hydrophilic surface made of phospholipids and free cholesterol. The major classes of lipoproteins are chylomicrons, very low density lipoproteins (VLDL-C), low density lipoproteins (LDL-C) and high density lipoproteins (HDL-C) (Mietus-Snyder and Krauss, 2008).

LDL-C makes up around 60-70% of total serum cholesterol, is the major atherogenic lipoprotein since it delivers cholesterol to cells including arteries (National Cholesterol Education Program (NCEP) Expert Panel on Detection, 2002). HDL-C is inversely related to CM risk and makes up around 20-30% of total serum cholesterol and carries cholesterol from the cells to the liver for synthesis and excretion (National Cholesterol Education Program (NCEP) Expert Panel on Detection, 2002). VLDL-C is triglyceride rich, produced by the liver and contains around 10-15% of total serum cholesterol. VLDL-C is a precursor for LDL-C and is also associated with greater CM risk. Chylomicrons are formed in the intestines from dietary fats and are also triglyceride rich (National Cholesterol Education

Program (NCEP) Expert Panel on Detection, 2002). Studies have demonstrated that high levels of total cholesterol (TC), LDL-C and triglycerides are associated with increased CM risk, whereas high levels of HDL-C are associated with reduced CM risk (National Cholesterol Education Program (NCEP) Expert Panel on Detection, 2002).

Metabolic homeostasis relies on regulation of the equilibrium of energy intake, storage and energy expenditure (Mietus-Snyder and Krauss, 2008). When glucose levels in the blood drop below a certain threshold, glucagon is secreted by the pancreas. As a result adipose tissue hydrolyses its stored triglycerides and releases NEFA into the blood stream, which are subsequently required for energy by the muscles (Blasiole et al., 2007). However if normal homeostasis is not maintained, for example in conditions such as insulin resistance and diabetes, dyslipidaemia can occur (Mietus-Snyder and Krauss, 2008).

The homeostasis model assessment (HOMA-IR) is a method used to quantify insulin resistance. It is calculated using the formula [Glucose (mmol/min) x Insulin (μU/mL)]/22.5 (Matthews et al., 1985). Impaired insulin resistance increases relative risk for progression to type 2 diabetes mellitus by 2.1 fold over a four year period in non diabetic adults (Rosenbaum et al., 2007).

2.4.1.1 Metabolic markers in relation to body composition, physical activity and fitness

An adverse lipid profile (high TC, high LDL-C, high triglycerides, low HDL-C) is associated with higher adiposity in children (Lamb et al., 2011). Furthermore, 80-90% of adults and children with type 2 diabetes are obese (Caprio and Tamborlane, 1999), and it is estimated that adiposity accounts for 55% of the variance in insulin sensitivity in children (Arslanian and Suprasongsin, 1996). A study which compared 9 to 11.5 year old obese and

lean children, found that the obese children had significantly greater HOMA-IR compared to the lean children. Furthermore insulin, and insulin resistance (HOMA-IR) were positively correlated to WC and total adiposity, and also inversely associated with PA (Krekoukia et al., 2007). Other studies have also found that PA is negatively associated with insulin resistance in children and adolescents (Brage et al., 2004; Jago et al., 2005). Furthermore CRF has an inverse relationship with HOMA-IR (Kriemler et al., 2008). Associations between PA and lipid profiles are generally weak in children (Andersen et al., 2006), however some studies have demonstrated a weak beneficial effect of exercise training on HDL-C and triglycerides (Eliakim et al., 2000; Stoedefalke et al., 2000). Studies of overweight and obese children and adolescents have demonstrated more favourable improvements in lipid profiles following multidisciplinary exercise and lifestyle intervention (Evans et al., 2009; Nemet et al., 2005). A study of 168 overweight adolescents (mean age 13.4 ± 1.8 years) demonstrated a decrease in total cholesterol by 7.2% and LDL-C by 8.4% following 6 months of a multidisciplinary lifestyle intervention which involved nutrition, PA and other weight management behaviours (Evans et al., 2009). Study 3 of this thesis will investigate the impact of a multidisciplinary lifestyle intervention on metabolic risk markers in healthy weight children.

2.4.2 Inflammatory Markers

There has been increasing focus on the role of inflammation in the pathogenesis of atherosclerosis including the function of inflammatory markers of CVD such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), adiponectin, C-reactive protein (CRP), angiotensin (AGT), plasminogen activation inhibitor-1 (PAI-1), serum amyloid protein (SAA), and fibrinogen (Fg) (Balistreri et al., 2010; Thomas and Williams, 2008). Risk

factors, such as hypertension and hypercholesterolaemia, cause injury to the endothelial layer of the artery, this triggers an inflammatory response and inflammatory markers, including various proteins such as CRP and Fg and cytokines such as IL-6 are released into the circulatory system. These in turn progress the development of atherosclerosis and endothelial dysfunction (Libby and Ridker, 1999).

Adipose tissue releases both anti-inflammatory and pro-inflammatory factors, including adiponectin, leptin, resistin, vistafin as well as IL-6 and TNF-α (Balistreri et al., 2010). Therefore obesity can have an effect on metabolic and immune responses. Impaired metabolic homeostasis triggers an inflammatory process, activated by increased adipose tissue in metabolically active sites, including adipose tissue itself, the liver and immune cells. This response regulates an increase in circulating pro-inflammatory cytokines, hormones and other inflammatory markers collectively termed 'adipokines' (Balistreri et al., 2010). Adipokines have an effect on glucose and lipid metabolism, as described further below, as well as influencing appetite and satiety, blood pressure regulation, inflammation and immune function (Lago et al., 2007; Lago et al., 2009). The adipokine and cytokine network is altered by an increase in adipose tissue, and therefore obesity contributes to an inflammatory state and impaired adipocyte metabolism (Balistreri et al., 2010).

CRP, an acute phase protein is secreted from the liver in response to inflammatory cytokines. Cytokines are proteins secreted by cells which alter the behaviour or properties of the cell itself or other cells (Balistreri et al., 2010). One example of a cytokine is IL-6, a pro-inflammatory mediator, secreted by several cell types including monocytes, adipocytes, and endothelial cells (Balistreri et al., 2010). CRP binds to damaged tissue, to nuclear antigens and some pathogenic organisms (Du Clos, 2000). It

possesses pro atherogenic properties such as promoting activation of endothelial cells to express adhesion molecules (Pasceri et al., 2000), decreases bioavailability of endothelial nitric oxide synthase in endothelial cells (Verma et al., 2002) and augments the uptake of LDL (Zwaka et al., 2001). Higher levels of CRP therefore demonstrates greater CM risk and studies have demonstrated that CRP is a strong predictor of future CV events in the general population (Blake and Ridker, 2002; Ridker et al., 2002).

Adiponectin, a hormone produced by adipocytes, is an indirect regulator of glucose metabolism; it also increases insulin sensitivity, improves glucose tolerance, is antioxidant and inhibits inflammation (Jeffery et al., 2008). Therefore a higher level of adiponectin appears to be protective for CM events.

Markers of inflammation are also associated with other CM risk markers. CRP, HPG and PAI-1 was significantly correlated with a clustered metabolic risk score which was calculated by summing z-scores of HOMA-IR, triglycerides, sBP, and HDL-C (Steene-Johannessen et al., 2010).

2.4.2.1 Inflammatory markers in relation to body composition, physical activity and cardiorespiratory fitness

Pro inflammatory markers, such as CRP, IL-6, Fg, and TNF-α are positively correlated with increasing adiposity (Cook et al., 2000; Shin et al., 2008; Steene-Johannessen et al., 2010). Steene-Johnnessen and colleagues (2010) found that WC was related to low grade inflammation in 9 and 15 year old children, the 10 participants with the highest waist circumferences (HWC) for each age and sex category were assessed (n=40) in relation to a random sample of control participants (n=40) selected from a cross sectional analysis of

2,299 9 and 15 year olds. Those in the HWC group had significantly elevated CRP, PAI-1, and hepatocyte growth hormone (HPG) in comparison to the control group.

Unlike other adipokines, serum levels of adiponectin do not increase with increasing adipose tissue (Balistreri et al., 2010). Adiponectin has been found to be in lower concentrations with increasing adiposity in children (Nemet et al., 2003; Shin et al., 2008; Stefan et al., 2002). Furthermore higher levels of habitual PA have been found to be associated with higher adiponectin levels in children (Emken et al., 2010; Metcalf et al., 2009; Rubin et al., 2008b) and exercise training which improves CRF by 15% has been shown to increase adiponectin levels in adults (Ring-Dimitriou et al., 2006).

There have only been a few studies which have investigated the effects of exercise training intervention on CRP in children and adolescents, and these are limited to obese and overweight participants. CRP was significantly reduced ($p<0.05$) following a 6 month progressive aerobic exercise intervention in obese adolescents. The exercise programme consisted of 3 sessions per week, which included one session of 60 minutes swimming and aqua aerobic training, a 90 minute sports games session, and one 60 minute session of walking (Meyer et al., 2006a). This was supported by another study which offered 4 months of exercise training to adolescents (mean age 13.7±0.1 years), three times per week (Rosenbaum et al., 2007). Conversely a 12 week exercise intervention in overweight and obese girls (mean age 13 ±13.8 years) which resulted in an increase in CRF by 18.8%, did not significantly change CRP (Nassis et al., 2005). Some studies have suggested that changes in inflammatory cytokines following exercise training interventions may be explained by changes in adiposity (Hulver et al., 2002; Kelly et al., 2007).

Whilst there is growing evidence on the role of PA in lowering of inflammatory factors in adults the evidence in children is less convincing (Thomas and Williams, 2008). In order to

fully understand the metabolic and inflammatory risk markers, in relation to other CM risk markers, invasive measures would provide novel evidence as well as build a clustered picture of individual risk (Steene-Johannessen et al., 2010). This will be investigated throughout this thesis.

2.5 Clustered Cardiometabolic Risk

As discussed throughout the introduction and literature review CM risk markers tend to cluster in individuals. The EYHS investigated the incidence of CHD risk factors in a random cross sectional sample (n = 1020), of 9 and 15 year old children, risk factors measured were total cholesterol, HDL-C, triglycerides, serum insulin and blood pressure. It was reported that more children than had been expected had four or five CHD risk factors, and these participants were more likely to have lower than average CRF levels (1.2 SD below the mean) and higher than average BMI (1.6 SD above the mean) (Andersen et al., 2003). Therefore, studies have estimated CM risk by combining several risk markers in one overall clustered risk score (Andersen et al., 2006; Andersen et al., 2008; Bailey et al., 2012). This clustered risk score may be more clinically meaningful than investigation of individual risk markers due to the range of structural, functional and biochemical disturbances associated with CM disease, and the day to day variation in individual risk markers (Ruiz et al., 2007a). The EYHS also demonstrated that when tracking risk factors over an 8 year period, the relationships between CRF and CVD risk markers was stronger when risk markers were clustered rather than analysing markers individually (Andersen et al., 2004). There has not been a standard clustered risk score established and studies have included various combinations of cardiometabolic risk markers, even amongst

studies the markers included have been different depending on what the clustered risk score was compared against.

The EYHS investigated PA and clustered cardiovascular risk in a cross sectional study of 9 and 15 year olds from Denmark, Estonia and Portugal (n = 1732). Risk factors included in the composite risk score were sBP, triglycerides, TC: HDL-C, insulin resistance (HOMA-IR), sum of four skinfolds and aerobic fitness. Individuals with a risk score 1SD above the mean were defined as being at risk (Andersen et al., 2006). Those in the least active quintile had an odds ratio of 3.29 (95% CI 1.96-5.52) for having clustered risk when compared to the most active quintile. Odds ratios for the second, third and fourth quintile were 3.13 (1.87-5.25), 2.51 (1.47-4.26), and 2.03 (1.18 – 3.5) respectively (Andersen et al., 2006). Another EYHS study investigated clustered metabolic risk in relation to CRF in 873 randomly selected 9 to 10 year old children from Sweden and Estonia (Ruiz et al., 2007a). The risk score was calculated by summing z-scores of the following variables: insulin, glucose, HDL-C (inversed), triglycerides, sum of five skinfold thicknesses and blood pressure (both systolic and diastolic). Individuals with a risk score greater than 1 SD above the mean were defined as having high metabolic risk, and those that had a risk score greater than 1 SD below the mean were defined as having low metabolic risk. Cardiovascular fitness, estimated using a maximal cycle ergometer test, was negatively associated with clustered risk score. The CRF level for those in the low metabolic risk group was 37.0 and 42.1 ml/kg/min in boys and girls respectively (Ruiz et al., 2007a). Andersen and colleagues (2008) investigated fatness and fitness in relation to clustered CM risk in a cross sectional study of 1769 children from Denmark, Estonia and Portugal (aged 9 and 15 years). WC and sum of skinfolds were associated with clustered risk score, which included the following variables; sBP, triglycerides, HOMA-IR, TC: HDL-C and CRF. The odds ratio for clustered CV risk in the highest quartile compared to lowest quartile

was 9.13 (95% CI 5.78-14.43) for WC and 11.62, (95%CI 7.11-18.99) for skinfolds. However when fitness was removed from the clustered risk score the relationship with fatness was weakened, and only the highest quartile of the fatness parameters were significant after further adjustment for fitness. Fitness was also strongly associated to clustered risk score, which included sBP, triglycerides, HOMA-IR, and TC: HDL-C, with an odds ratio for the upper quartile of 4.97 (95% CI:3.20-7.73). After adjusting for fitness and fatness, PA was also associated with clustered risk score, with an odds ratio of 1.81 (95% CI: 1.18-2.76) (Andersen et al., 2008). The relationships between clustered risk score, fitness, and PA have since been investigated by other study groups. Bailey and colleagues (2011) investigated differences in clustered risk according to CRF levels and time spent at different intensities of PA in 10 to 14 year old children (n = 100). The clustered risk score included WC, blood pressure, TC: HDL-C, triglycerides and glucose. Children were separated into a high and low fitness group and those in the high fit group had significantly lower clustered risk than those in the low fit group. However conversely to the EYHS studies, no significant differences were found between PA tertiles, this may be due to the smaller sample size.

Previous clustered risk scores have only included traditional markers such as TC, HDL-C and blood pressure (BP) they have rarely included non-invasive risk markers such as left ventricular (LV) mass or estimates of adiposity using reference standard measures such as dual-energy x-ray absorptiometry (DEXA). The European Youth Heart Study (EYHS) employs skin fold thickness as an estimate of body fat (Andersen et al., 2006; Andersen et al., 2008; Ruiz et al., 2007c), and Bailey and colleagues used WC as a measure of body size and neither study group employed non-invasive measures of cardiac structure and function. Therefore this thesis aims to report a clustered risk score, which combines both

traditional and preclinical risk markers, and then will investigate the interactions between this clustered risk score and PA, and CRF (Study 2) and lifestyle education (Study 3).

2.6 Possible mechanisms for increased cardiometabolic risk in obesity

As discussed throughout the literature review, it is clear that obesity increases cardiometabolic risk.

There are a number of proposed mechanisms, involving both haemodynamic and metabolic factors, which are proposed to be responsible for the changes in cardiac structure and function associated with obesity. The pathophysiology of cardiac hypertrophy may involve plasma volume expansion, the presence of hypertension, and activation of the sympathetic nervous system.

An increase in BP and cardiac contractility, due to factors observed in obese individuals such as increased activation of the sympathetic nervous system, and increased secretion of angiotensin from adipocytes, (Grassi and Giannattasio, 2005; Grassi et al., 2003) causes pressure overload which leads to concentric remodelling. (Abel et al., 2008). In addition central blood volume is increased in obese individuals; furthermore, stroke volume and cardiac output are increased due to the increased metabolic demand from increased adipose tissue (Kaltman and Goldring, 1976). The combination of these factors causes volume overload which may also lead to an eccentric form of hypertrophy (Abel et al., 2008).

Animal studies investigating changes in cardiac structure and function suggest that obesity is associated with a shift in myocardial substrate utilisation which is characterised by an increase in fatty acid utilisation and a reduction in glucose utilisation. These

alterations are associated with increased myocardial oxygen consumption and reduced cardiac efficiency (Buchanan et al., 2005). An increase in mitochondrial number has also been observed in obese mice; however despite the increase in mitochondria, mitochondrial dysfunction is also present (Boudina et al., 2005). It was hypothesised that mitochondrial dysfunction and impaired myocardial energetics may contribute to contractile dysfunction in obese hearts (Abel et al., 2008) and this may also impact on relaxation as a result.

Pro-inflammatory cytokines, such as IL-6 and TNF-α, which increase with increasing adiposity, may also play a role in myocardial remodelling by directly influencing hypertrophy and contractility (Abel et al., 2008). Adiponectin is found in higher concentrations in lean individuals compared to obese individuals. Studies have demonstrated that adiponectin has both direct and indirect effects on the heart. In-vivo animal studies have demonstrated that adiponectin diminished endothelin induced hypertrophy in cardiomyocytes (Fujioka et al., 2006). Adiponectin may also induce changes in energy metabolism by stimulating an increase in glucose and fatty acid uptake in cardiomyocytes (Pineiro et al., 2005). Adiponectin also has indirect effects on cardiometabolic risk markers, including anti-inflammatory, antidiabetic, and antihypertensive effects which may impact on cardiac structure and function (Abel et al., 2008).

One potential mechanism for the relationship between obesity and increased CIMT also involves adipokines. Low adiponectin levels stimulate production of adhesion molecules in endothelial cells, encourage proliferation of smooth muscles cells and promote foam cell formation (Fasshauer et al., 2004). In the early stages of atherosclerosis development, up-regulation of endothelial adhesion molecules play a key role, by binding and

recruitment of monocytes into the intima layer of the artery wall, and thus leading to increased IMT. Higher levels of adhesion molecules such as endothelial-leukocyte adhesion molecule (E-selectin), vascular cell adhesion molecule-1 (VCAM-1) and intercellular cell adhesion molecule-1 (ICAM-1) have been found in obese children compared to lean children (Desideri et al., 2005). As atherosclerosis develops the arteries stiffen and therefore systemic vascular resistance increases leading to an increase in BP. The actions of adiponectin on endothelial cells may also explain the relationship between obesity and hypertension, as previously described adiponectin protects against endothelial damage and delays progression of vascular atherosclerosis, thereby reducing hypertension (Hong et al., 2004).

2.7 Possible mechanisms for reduced cardiometabolic risk with higher levels of PA and CRF.

Several mechanisms have been proposed in the literature to explain the possible mechanisms responsible for the associations between increased cardiometabolic risk and low levels of CRF. Possible mechanisms which explain the inverse relationship between IMT and CRF have been proposed, for example reduced body fat, improved endothelial function, improved antioxidant capacity, reduced inflammation and improved insulin sensitivity (Jae et al., 2009). Furthermore, autonomic nervous system function also appears to be related to inflammation. Evidence suggests that vagus nerve stimulation can moderate inflammatory cytokines through cholinergic anti-inflammatory pathways (Borovikova et al., 2000). Individuals with increased CRF have enhanced autonomic nervous system function and therefore it is feasible that increased PA and improved CRF may have favourable improvements in the cholinergic anti-inflammatory pathway, via improved autonomic function (Jae et al., 2009). It is also feasible therefore to speculate that exercise training, and improvements in CRF, may prevent increases in IMT via this

impact on inflammatory factors. Vascular tone also directly influences arterial wall thickness, and studies have demonstrated that exercise training alters vascular tone; and therefore may lead to reductions in CIMT (Thijssen et al., 2012). Exercise training is also associated with antioxidant effects; therefore improved CRF may lower oxidative stress in the arterial walls and therefore prevents increased IMT (Gomez-Cabrera et al., 2008). Increases in PA may lead to improvements in CRF and reductions in body fat, both of which could impact on LV structure and function. Possible mechanisms include decreased volume over load and cardiac output, attenuating inflammatory activation, reducing neurohormonal disturbances involving the sympathetic nervous system, adiponectin, and angiotensin. Exercise training may also induce cardiac structural changes such as myocyte hypertrophy, sodium retention and changes in myocardial metabolism (Kosmala et al., 2009).

2.8 Interventions

As previously discussed, over the last decade childhood obesity has increased in the United Kingdom (UK) (Boddy et al., 2010; Stratton et al., 2007) which, along with poor nutritional intake, low CRF and physical inactivity, increases the risk of developing CVD disease and metabolic syndrome (Andersen et al., 2006; Andersen et al., 2008; Freedman et al., 2007). Therefore an intervention which aims to reduce adiposity, and improve CRF, through promotion of increased PA, reduced sedentary time and improved nutritional intake could have a positive impact on reducing CM risk in children. Schools provide an ideal opportunity to implement an intervention since children spend approximately half of their waking hours in school (Fox et al., 2004), and school-based implementation also enables the whole target population to be reached. Several intervention studies have

aimed to increase PA, reduce sedentary time and improve nutritional intake in children in order to reduce obesity related risk through curriculum based interventions, often reporting mixed levels of success [Table 2-4]. The majority of the studies in Table 2-4 have reported changes in body composition, PA and fitness. However, with the exception of Gorely et al (2009) measures of self-report PA were used; and only crude measures of adiposity were used such as BMI, skin fold thickness and WC. Furthermore CRF was assessed in the field using 20m SRT in the majority of studies. Some studies have reported the impact of the intervention on markers of CM risk; however these are mostly limited to body composition and metabolic markers (TC, HDL-C, LDL-C, and triglycerides) (Harrell et al., 1998; Manios et al., 2002; Slawta and DeNeui, 2009), one investigated inflammatory markers (Rosenbaum et al., 2007) and one study investigated blood pressure (McMurray et al., 2002).

Comprehensive intervention studies investigating both invasive and non-invasive markers in combination with objectively measures PA, CRF (VO2 Peak) and body composition (DEXA) in children are rare. Study 3 of this thesis will investigate the impacts of lifestyle education on a number of CM risk markers, including TC, HDL-C, glucose, blood pressure, LVM, diastolic function, CIMT; and a clustered risk score which will be calculated with a combination of these markers.

2.9 Summary

As discussed throughout the introduction and literature review it is clear that CM risk is impacted by overweight and obesity and low CRF levels; as well as negative lifestyle behaviours such as low levels of PA, sedentary behaviours and poor dietary intake.

Comprehensive physiological intervention studies in children are rare, in particular those which investigate both invasive and non-invasive measures, in combination with objective measures of PA, fitness and estimates of food intake. Many of the risk markers for CM disease are modifiable and therefore there is scope to improve CM risk profile in children through an intervention which aims to improve negative lifestyle behaviours.

Aims and Objectives

- To investigate the impacts of PA, CRF, body composition and lifestyle education on CM risk in 10-11 year old children.

2.9.1 Individual Study Aims

Study 1: a) Investigate the relationships between invasive and non-invasive markers of CM risk; and b) To establish the relationships between the individual risk markers with objectively measured PA, and CRF in 10-11 year old children.

Study 2: To report clustered risk scores that combine both invasive and non-invasive markers of CM risk and assess clustered risk in relation to PA, CRF and body composition in 10-11 year old children.

Study 3: a) Investigate the immediate effects of a school based PA and healthy eating curriculum intervention [Children's Health Activity and Nutrition: Get Educated (CHANGE!)] on markers of CM risk in 10-11 year old children. And b) to investigate the short term (8-10 weeks) follow up effects of the CHANGE! intervention.

Table 2-4: Summary of multidisciplinary curriculum based interventions

Ref	Participants	Intervention Details	Outcome Measures	Key Findings
(Gorely et al., 2009)	7-11 years n= 589 children 4 intervention (INT) schools (n=310) 4 control (CON) schools	10 months curriculum based aiming to promote healthy lifestyles, teaching resources, interactive website, 2 x PA events. Nutrition and PA both promoted	PA (pedometers in all participants and accelerometers in 50%) Fruit and Veg consumption BMI Waist Circumference % body fat Knowledge Psychological Variables	MVPA increased in INT (9 mins/day) CON decreased MVPA by 10 mins/day Older participants in INT showed slowing of rate of % body fat, BMI and WC. No diff in fruit and veg consumption
(Jansen et al., 2011b)	2622 children aged 6 to 12 years 20 Schools (10 INT n=1240; CON n= 1382)	The 'Lekker Fit' Intervention which aimed to promote healthy eating and active living. Implementation of 3 PE sessions per week; education component consisting of lessons on active living, healthy nutrition, and healthy lifestyles; voluntary extra-curricular sports activities also made available.	BMI Waist Circumferences Fitness (20 m SRT)	Significant positive intervention effects were found for percentage overweight children (OR 0.53; 95% CI 0.36 – 0.78), waist circumference (- 1.29 cm; 95% CI - 2.16 to - 0.42 cm) and 20 m shuttle run (0.57 laps; 95% CI 0.13 – 1.01 laps) among pupils of grades 3 – 5 (6 – 9-year olds).

Ref	Participants	Intervention Details	Outcome Measures	Key Findings
(Manios et al., 2002)	5.5-6.5 year olds at baseline followed over 6 years INT (n= 250) CON (n=191)	6 year intervention multidisciplinary health and nutrition education: Nutrition education approx. 13-17 hours annually delivered by class teacher. PA and fitness had practical and theoretical component (4-6 hours annually) delivered by PE teachers.	Year 1 and Year 6 measurements taken: Anthrops Food frequency for week completed by parents Weighed 3 day food diary of Nutrient intake in subsample (30%) Serum lipids, TG, TC, HDL, LDL Eurofit tests incl. 20mSRT Self-report questionnaire for MVPA (for older children) parents completed for younger children.	Nutrient intake: Sig. diff between INT & CON for change in: Total Energy [INT<CON] Total Fat [INT<CON] MUFA [INT<CON] SFA [INT<CON] Protein [INT<CON] 20m SRT [INT>CON] MVPA [INT>CON] Weight [INT<CON] Height [INT>CON] BMI [INT<CON] Biceps skinfold [INT<CON] Triceps skinfold [INT<CON] LDL [INT Δ= -0.3, CON=Δ -0.08 TC:HDL [INT Δ= -0.07, CON=Δ +0.24] LDL:HDL [INT Δ= -0.13, CON=Δ +0.24]
(Gortmaker et al., 1999)	Mean age 11.7 years n=1295 5 INT schools (n=641) 5 CON schools	2 year curriculum intervention 'Planet Health' focussed on 4 key behaviour change components: Reduced TV viewing to less than 2 hours per day. Increased MVPA. Decreased consumption of high fat foods Increased consumption of fruits and vegetables to more than 5 per day	BMI; Triceps Skinfold TV (hours/day) (self-report) MVPA (self-report - Youth Activity Questionnaire) Dietary Intake including energy from fats (%), energy from saturated fats (%), fruit and vegetables (servings)(self-report – Youth Frequency Questionnaire)	Prevalence of obesity in girls in INT reduced compared with controls [odds ratio 0.47, 95% confidence interval 0.24-0.93, p=0.03]. No significant difference in boys. INT reduced TV in both boys and girls.INT increased fruit and vegetables intake in girls INT smaller increment in total energy intake in girls

Ref	Participants	Intervention Details	Outcome Measures	Key Findings
(Slawta and DeNeui, 2009)	INT n=45; CON n=20 Aged 6 to 12 years	'Be a Fit Kid' 10 week intervention. PA: 40 min. x 3 times per week emphasized CRF, muscular strength, and bone development. Nutrition: 45mins, once a week focussed on current dietary guidelines Parents involvement: Invited to 5 bimonthly meeting covered PA and nutrition principles	Fitness: 1 mile timed run; number of sit ups in 60 seconds Nutrition Knowledge: Questionnaire Diet: 24 hour food log Body Composition: BMI, skinfolds (triceps, subscapular and calf) Lipids and lipoprotein: TC, LDL, HDL, triglycerides	Fitness (both 1 mile run and sit ups) increased significantly in INT ($p<0.01$) and difference was significant from change in CON ($p<0.01$) Nutrition knowledge significantly improved in both INT & CON ($p<0.01$); however change in knowledge was significantly better in INT than in CON ($p=0.01$) % body fat decreased significantly in INT ($p<0.01$) and difference was significant from change in CON ($p<0.05$) Saturated fat, sodium, TC, TC:HDL-C all reduced in INT ($p<0.01$) but were not significantly different to change CON
(Prochaska and Sallis, 2004)	Mean age 12.1 years n=138	3 month intervention with 2 strands: INT Group 1 (PA): 30 min. health education, focused on PA behaviour change INT Group 2 (PAN): As above but with nutritional intervention	PA accelerometer 3-day diet log	Both Interventions (PAN and PA) interventions improved PA in boys ($p<.001$) but not girls ($p=.663$) relative to the control condition. Dietary change was non-significant
(Frenn et al., 2005)	12 – 13 year olds n=132	8 x 40mins blackboard based (internet) sessions in science classes, individual feedback on stages of change to increase PA and improve diet	PA (self-report 3 day log) (INT=43 CON=60) Food habits questionnaire (INT=40, CON=49)	INT: MVPA increased by 22 mins CON: MVPA decreased by 38 mins ($p=0.05$) INT: Dietary intake of fat (%) decreased from 30.7 to 29.9 ($p=0.008$)

Ref	Participants	Intervention Details	Outcome Measures	Key Findings
(Sahota et al., 2001)	Mean age 8.4 years n= 636 INT n=314 CON n= 322	'APPLES' intervention: Teacher training, modification of school meals, and the development of school action plans targeting the curriculum, physical education, tuck shops, and playground activities.	BMI Diet (24 hour recall and 3 day food diary) PA (questionnaire 7 days) psychological state	Vegetable consumption by 24 hour recall was higher in children in the intervention group than the control group (weighted mean difference 0.3 portions/day, 95% confidence interval 0.2 to 0.4), There was no difference in body mass index, other psychological measures, or dieting behaviour between the groups. Focus groups indicated higher levels of self-reported behaviour change, understanding, and knowledge among children who had received the intervention.
(Rosenbaum et al., 2007)	Mean age 13.7 (±0.1) years n=73 INT n=49	3 to 4 month classroom intervention: nutrition education and diet modification, education on importance of exercise. PE: exercise sessions offered 3 times per week consisting of dance and non-contact kickboxing.	Body fatness (bioelectrical impedence) Insulin sensitivity Lipid profiles Inflammatory markers: IL-6, CRP, adiponectin, TNF-α	Sig reductions in INT group for: % body fat Insulin resistance CRP IL-6
(Harrell et al., 1998)	Mean age 9 (±0.8) years n=412 with at least 2 CV risk factors (low aerobic power, obesity or high TC) 2 interventions & a control group	2 interventions over 8 weeks; 1) Classroom intervention: consisting of knowledge and attitude education to whole class; adapted P.E lessons delivered by normal teachers 2) Intervention delivered in smaller groups with known CV risk factors only.	Cholesterol Blood pressure, BMI Body fat, Eating and activity habits Health knowledge	Both intervention groups sig. reduced total cholesterol (-10.1 mg/dL and -11.7 mg/dL). There was a trend for systolic blood pressure to increase less in both intervention group

Ref	Participants	Intervention Details	Outcome Measures	Key Findings
(McMurray et al., 2002)	n= 1140 aged 11 to 14 years (mean age 12±1 year) 4 treatment groups: Exercise only (n=266) Education only (n=319) Exercise and Education (n=308) Control (n=247)	Cardiovascular Health in Children and Youth Study (CHIC II): 8 week intervention: Exercise only: 30mins aerobic exercise 3 times a week; Education only: knowledge programme of 2 sessions per week included information on nutrition, smoking, and exercise. Exercise and education combined: both exercise and knowledge programmes as other groups received.	Heights, weights, skinfold thicknesses and body mass index (BMI) Blood pressure Maximal oxygen uptake was predicted from a submaximal cycle ergometer test	Systolic and diastolic blood pressures increased more in the control group than in the intervention groups ($p = 0.001$). BMI did not change significantly ($p = 0.709$), but the sum of skinfolds increased less in subjects in the exercise intervention groups than the education only or control groups ($p = 0.0001$). The small increase in VO_2 Peak of the combined exercise and education group was significantly greater than the education only group ($p = 0.0001$).

Chapter 3

General Methods

3.1. Introduction

This chapter discusses the common methods used throughout this thesis and any additional procedures, specific to a study, will be described in the relevant chapter. All measures were carried out by fully trained individuals.

3.2. Preliminary information

All studies gained ethical approval from Liverpool John Moores University ethics committee. All studies obtained informed parental consent, informed participant assent and all parents/ guardians completed medical screening forms on behalf of their child prior to commencement of the studies [Appendix B and C].

3.3. Habitual Physical Activity

Habitual PA was objectively measured in the field using a uni-axial accelerometer (ActiGraph GT1M LLC, Pensacola, FL, USA) worn on the right hip over a 7 day period. The ActiGraph has previously been validated with children (Trost et al., 1998) and is a common tool used to assess the volume and intensity of PA. Children were asked to wear the monitor during waking hours and were only advised to remove for water based activities (e.g. showering or swimming) or where wearing it could cause injury (e.g. during contact sports). To distinguish total wear time children completed a log sheet, recording the wear and removal times as well as the reasons for removal. These log sheets were checked and initialled by parents at the end of each day. During the monitoring period PA was recorded using 5 second epochs of data collection. Sustained 20 minute periods of zero counts indicated that the ActiGraph had been removed, and total 'missing' counts for those periods represented the duration that monitors were not worn (Catellier et al.,

2005). Children were included in the data analysis if they wore the monitors for at least 540 minutes on week days (Graves et al., 2010) and 480 minutes on weekend days (Rowlands et al., 2008) for a minimum of 3 days (Mattocks et al., 2008). These inclusion criteria have previously shown acceptable reliability in similarly aged children (Mattocks et al., 2008).

3.4. Physical Activity Intensity Cut Points

The PA intensity accelerometer cut points for the REACH Study (Chapter 4) are described in the Materials and Methods section of Chapter 4.

The PA accelerometer cut points applied for the CHANGE! study (Chapters 5 and 6) were derived from a sub-study (Mackintosh et al., 2012). Population-specific accelerometer cut points generated were 2160 CPM for moderate intensity PA (MPA), 4806 CPM for vigorous intensity PA (VPA), sedentary was defined as less than 100 CPM (Mackintosh et al., 2012). These cut-points were appropriate to the age group of interest and were similar to those reported by Evenson et al. (2008) which were recently recommended as they demonstrate acceptable classification accuracy at moderate and vigorous activity intensities (Trost et al., 2011). Total daily time spent in moderate-to-vigorous PA (MVPA) was calculated and adjusted for valid daily ActiGraph wear time.

3.5. Cardiorespiratory Fitness (VO_{2peak})

Peak oxygen uptake (VO_{2peak}) was assessed using a continuous incremental treadmill (H P Cosmos, Traunstein, Germany) test to volitional exhaustion, under ambient conditions, using an online gas analysis system (Jaeger Oxycon Pro, Viasys Health Care, Warwick, UK).

All participants wore an accelerometer (Actigraph GT1M, ActiGraph LLC, Pensacola, FL, USA) on the right hip and a heart rate monitor (Polar, Kempele, Finland) throughout the test. As large variation in biological age of the participants was evident, the VO_{2peak} test speeds were calibrated individually by setting treadmill speeds to set Froude (Fr) numbers. Dynamic similarity theory suggests that geometrically, individuals will have similar gait dynamics if the Fr number is kept constant (Alexander, 1989). According to this theory optimum walking speed will be at Fr 0.25, with the transition between walking and running occurring close to Fr 0.5 regardless of variation in body size (Minetti, 2001). Therefore treadmill speeds were calculated individually using the equation:

$$Fr = v^2 / (g \times l)$$

[Where v is speed of movement (m/sec), g is gravity, l is leg length (m)]

The protocol involved 2 minute incremental stages; stage 1 was programmed to individual walking speed equivalent to Fr 0.25; stage 2 was programmed to a speed equivalent of Fr 0.5; subsequent stage increments were based on researcher judgement using respiratory exchange ratio (RER) and heart rate (HR) of participant as a guide and either involved an increase in speed, determined by the difference in speed for stages one and two (approximately 1 to 2 km/h), or by an increase in gradient. VO_{2peak} was determined as the highest 15-s averaged oxygen uptake achieved during the test when participants exhibited subjective indicators of peak effort that were confirmed by a RER $\geq$ 1.05 and/or HR $\geq$ 195 beats$\cdot$min^{-1}.

3.6. Anthropometrics

Stature and sitting stature were measured to the nearest 0.1 cm and body mass to the nearest 0.1 kg using a stadiometer (Seca, Bodycare, Birmingham, UK) and calibrated electronic scales (Seca, Bodycare, Birmingham, UK) using standard techniques (Lohman et al., 1991). Body Mass Index (BMI) was calculated using the equation body mass (kg) ÷ height $(m)^2$. WC and hip circumference (HC) were measured using a non-elastic anthropometric tape. Measurements were taken at the narrowest point between the bottom of the ribs and the iliac crest and from the widest point around the hips and gluteals by one researcher.

3.7. Body Composition

Body composition was assessed using fan beam dual energy x-ray absorptiometry (DEXA) (Hologic QDR series, Delphi A, Bedford, Massachusetts, USA) in the whole body scan mode. Participants were scanned in a supine position in lightweight clothing and without shoes. All scans were carried out by the same qualified researcher and were analysed using Hologic QDR software for Windows version 11.2. All scans were completed in accordance with standard operating procedures and after completing the necessary quality control checks including daily calibration. Key variables assessed from the whole body scan were absolute (kg) fat mass (FM) and lean tissue mass (LM), and relative (%) body fat (BF%). Segmental analysis was also carried out to assess the distribution of body fat and the key variables of interest were trunk fat mass (TFM), and relative (%) trunk fat (TF%), peripheral (arms and legs) fat mass (PFM), and relative (%) peripheral fat (PF%).

3.8. Somatic Maturation

Somatic maturation was estimated using the sex specific regression equations (Mirwald et al., 2002) by determining years from peak height velocity.

In girls:

Maturity Offset = -9.376 + [0.0001882 x (leg length x sitting stature)] + [0.0022 x (age x leg length)] + [0.005841 x (age x sitting stature)] + [0.002658 x (Age x body mass) + [0.07693 x (Body Mass: stature ratio)]

In boys:

Maturity Offset = -9.236 + [0.0002708 x (leg length x sitting stature)] + [0.007216 x (age x sitting height)] + [0.2292 x (body mass: stature ratio)]

This method has been used previously in similar paediatric populations (Graves et al., 2010; Hopkins et al., 2009b) and shows acceptable agreement with skeletal age (Mirwald et al., 2002).

3.9. Cardiac Structure

Participants rested in a supine position. Electrodes were attached for a three lead ECG system intrinsic to the Ultrasound Imaging System (Esoate Mylab 30CV, Italy). Echocardiographic images were then obtained with the participant lying in the left lateral decubitus position. A two dimensional image of the left ventricle in the long axis was obtained by placement of a 2.5 MHz transducer at the parasternal window. M-Mode recordings were taken at the tip of the mitral valve leaflets [Figure 3-1]. With a

concomitant ECG trace, septal thickness (ST), posterior wall thickness (PWT) and left ventricular internal dimension in diastole (LVID) were digitized at the peak of the R-Wave. LVM was estimated using a previously validated regression-corrected 'cube formula' ($LVM = 1.04\ (ST + LVID + PWT)^3 - (LVID^3) - 13.6$ g) (Devereux et al., 1986). All ultrasound scans were performed by one technician. LVM was adjusted for height of participants (LVM index) using the equation $LVM\ (g)/Height(m)^{2.7}$ (De Simone et al., 1995).

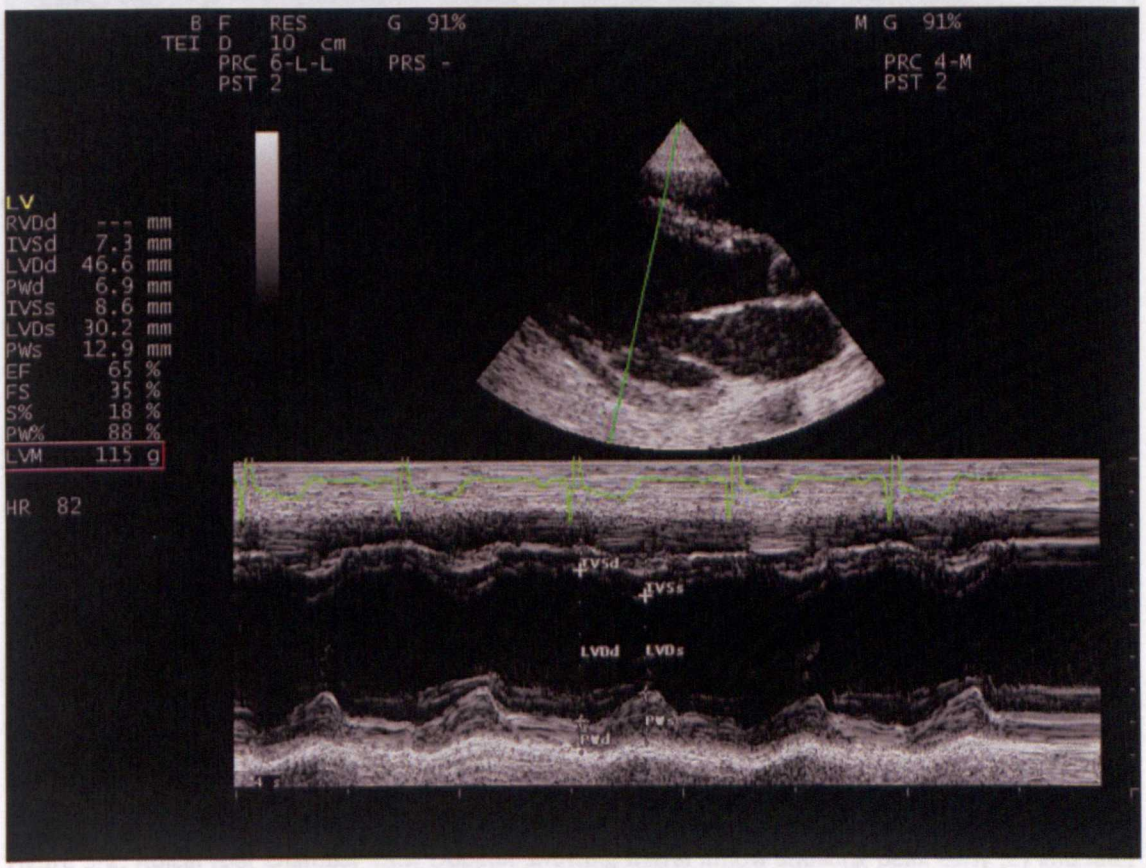

Figure 3-1: M –Mode echocardiography image of LVM in parasternal long axis view showing placement of measurements (Key: IVSd =Interventricular Septum in Diastole; LVDd = Left Ventricular Dimension diastole; PWd = Post wall diastole; IVSs = Interventricular Septum systole; LVDs = Left Ventricular dimension systole; PWs = Post wall systole). Image taken from one of participants in Study 2.

3.10. Diastolic Function

From the apical four-chamber view Doppler recordings were taken of mitral inflow by placing a 2 mm sample volume at the tips of the mitral leaflets and parallel with flow.

Peak early (E) and late/atrial (A) flow were obtained from the septal annular site using a 2 mm sample volume [Figure 3-2]. Peak early diastolic (E') and late diastolic (A') myocardial tissue velocities were recorded [Figure 3-3] and E'/A' ratio and E/E' ratio was calculated (George et al., 2010).

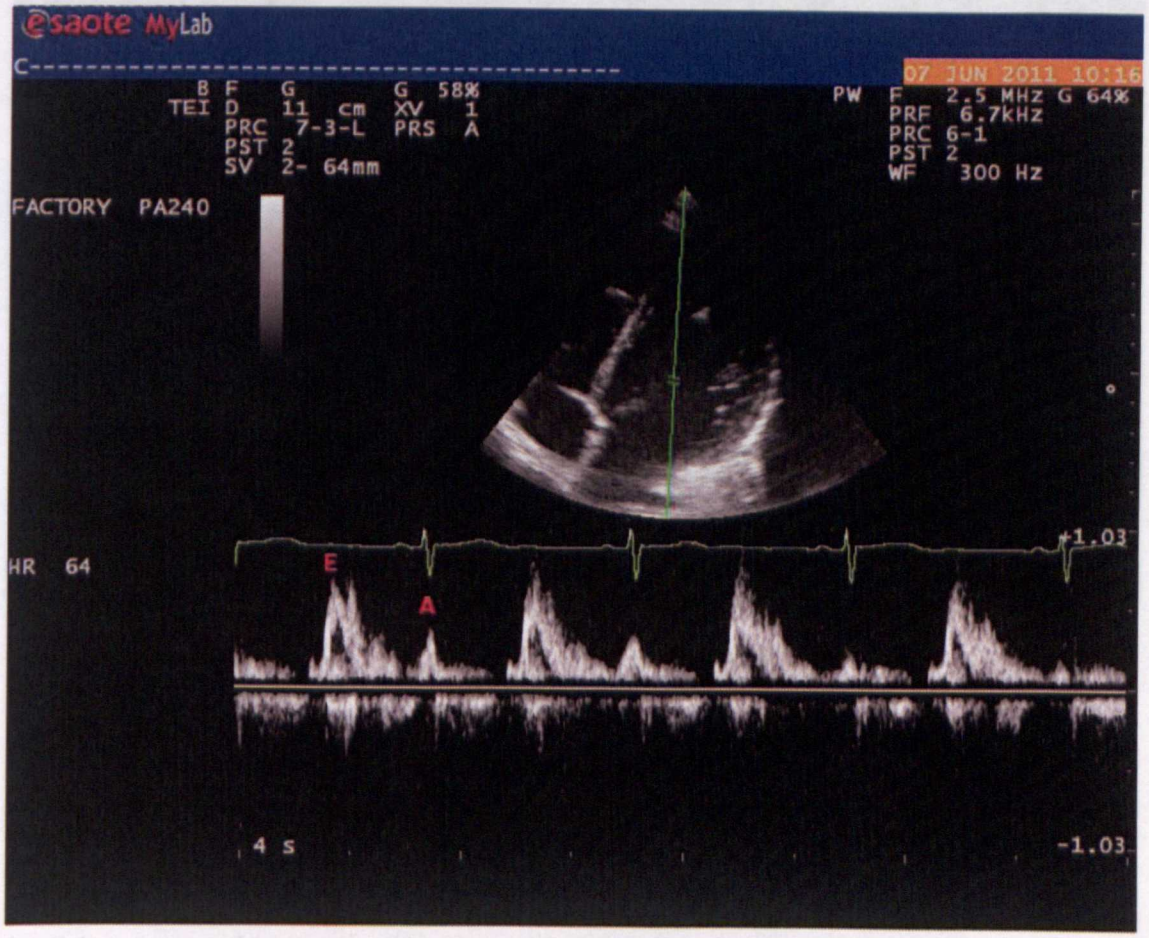

Figure 3-2: Apical four chamber view Doppler showing mitral inflow showing peak early (E) and late/ atrial (A) flow. Image taken from one of participants in Study 2.

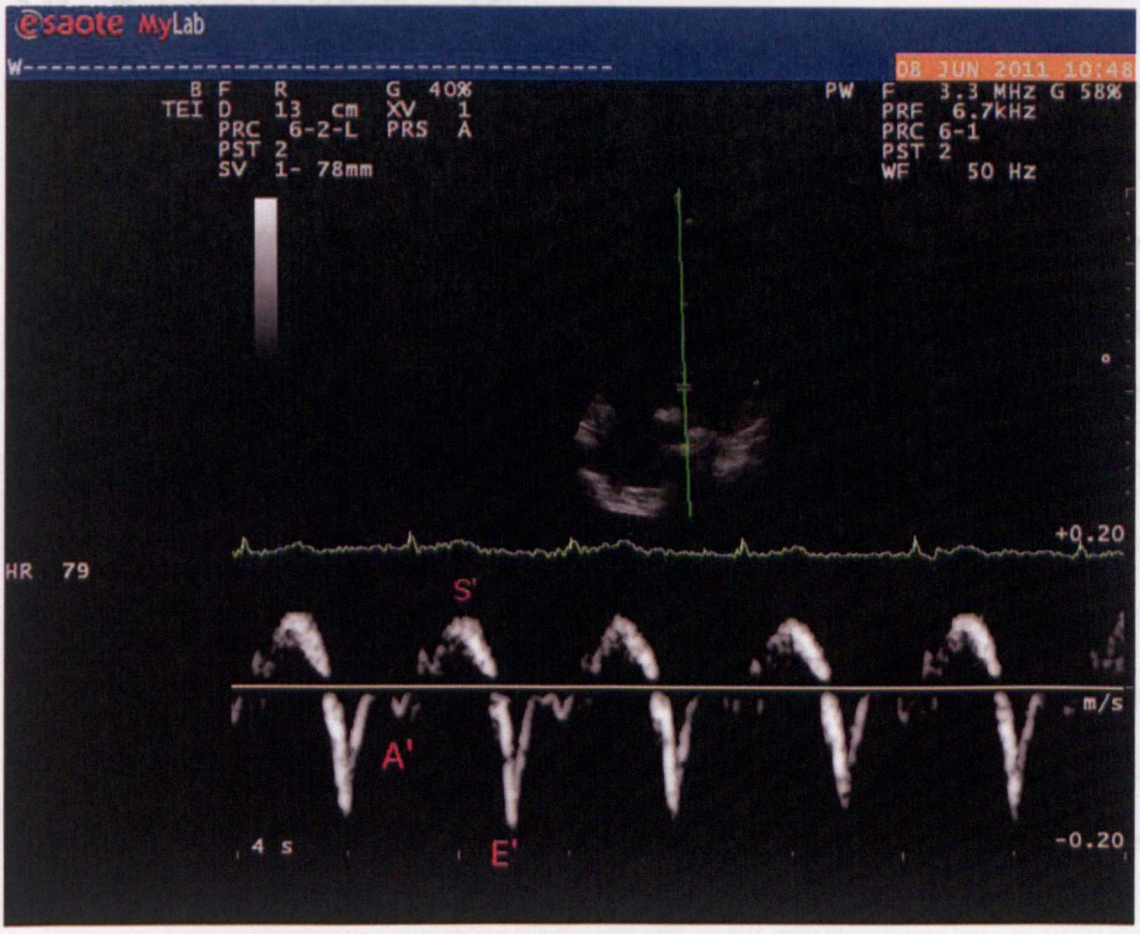

Figure 3-3: Tissue Doppler Image showing peak early diastolic (E') and late diastolic (A') and systolic (S') tissue velocity. Image taken from one of participant in Study 2.

3.11. Carotid Intima Media Thickness

Participants rested in a supine position with their neck slightly extended. A ten millimetre segment of the far wall of the common carotid artery 1-2 cm proximal to the carotid bulb was imaged using a 10-15 MHz linear transducer. Images were analysed offline (IMT. Lab V 2.0, Pie Medical Equipment, Netherlands). This software provided mean values for carotid IMT by tracking of the lumen-intima and media adventitia.

3.12. Cholesterol, Lipid Profile and Glucose

For the CHANGE! Study (Chapter 5 and 6) participants attended a blood sampling session at the school. After verbal confirmation of overnight fasting, seated finger prick capillary blood samples were taken between 8.30-10:00 am. Samples were collected in 35 μl capillary tubes and immediately analysed for total cholesterol, HDL-C, and glucose using the Cholestech LDX analyser (Alere, Stockport, UK). LDL-C was calculated using the Friedewald formula (Friedewald et al., 1972). Breakfast was provided for all participants following blood sampling. This method has been used previously in similar paediatric populations (Bailey et al., 2012) and studies have demonstrated that the precision and accuracy of the measurements obtained using the Cholestech LDX is consistently within the National Cholesterol Education Programme Guidelines (Issa et a., 1996; Panz et al., 2005; Parikh et al., 2009). The coefficient of variation for the Cholestech LDX can be found in Table 3-1.

Table 3-1: Precision and Accuracy of Cholestech LDX (www.cholestech.com, 2002)

Analyte	**R^2**	**Mean Bias (%)**	**Values Exceeding NCEP Total Error (%)**	**Clinical Misclassification (%)**	**CV (%)**
TC	0.98	-2.7	0	0	2.1
HDL-C	0.96	0.2	0	0	4.1
LDL-C	0.96	-3	0	0	4.7

3.13. Method Development

3.13.1. Inter observer reliability for Echo measurements

Echocardiography is generally regarded as the standard reference technique as it is more accurate at detecting LV hypertrophy than electrocardiography (Killian et al., 2010); however echocardiography is also affected by several sources of variability. Guidelines have been produced in order to improve accuracy of measurements (Wallerson and Devereux, 1987). These include strict adherence to quality control to generate echocardiograms of the highest technical quality including correct plane angulation, and adopting a uniform convention of measurement such as the American Society of Echocardiography recommendations for general measurement. It is also recommended that several cardiac cycles are measured with the mean being calculated and reported (Wallerson and Devereux, 1987).

A random selection of 20% of the CHANGE! Study (all 3 time points) echocardiograph images were measured by two separate sonographers in order to establish inter observer reliability and determine the suitable approach for measurement accuracy. Table 3-2 below reports means for each technician, absolute limits of agreement and inter correlation coefficients for each of the measures of LV structure and function.

Table 3-2: Means for each technician, absolute Limits of Agreement and ICC for each variable

Measure	Technician 1 Mean	Technician 2 Mean	Difference (SD)	Absolute Limits	ICC
LV Mass	101.0	101.0	0.045 (12.2)	23.4 (0.6)	0.877
E/A	2.55	2.44	0.11 (0.35)	0.69 (0.1)	0.753
E'/A'	3.06	2.85	0.21 (0.49)	0.98 (0.2)	0.824
E/E'	6.81	6.5	0.30 (0.66)	1.22 (0.35)	0.889

Wallerson and Devereux (1987) recommend that more than one technician analyse scans with the mean of several cardiac cycles from both technicians reported. However, due to the practical implications of having the same two technicians available to analyse all the scans (over a 2 y, multiple measurement period) a pragmatic solution was that the same technician analysed all scans to maintain consistency. Scan quality is also an important factor in the accuracy of the measurements (Wallerson and Devereux, 1987) therefore scans which did not meet the quality required for measurement accuracy were excluded from analysis. The absolute limits of agreement (Table 3-2) show acceptable agreement between the two technicians, furthermore the ICC for each measure are high, which demonstrates good intra observer reliability and therefore it was deemed acceptable and pragmatic for one technician to analyse all scans. One technician therefore performed all measurements for each project calculating a mean of 3 cardiac cycles to maintain consistency and eliminate inter- and minimise intra-observer errors.

Thesis Study Map

A thesis study map appears at the start of each chapter to demonstrate the key objectives and key findings of the studies, and to elucidate where each study fits in the overall thesis.

Study	Objectives
Study 1: Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.	**Objectives:** • **To investigate the relationships between traditional invasive and non-invasive 'preclinical' cardiometabolic risk markers.** • **To establish the relationships between individual cardiometabolic risk markers and cardiorespiratory fitness (CRF) and physical activity (PA).** • **To determine which measures would be most appropriate to use in future studies.**
Study 2: Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project	
Study 3: The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.	

Chapter 4

Study 1:

Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.

4.1. Introduction

Whilst traditional risk factors, such as adverse metabolic profiles, are sometimes observed in children or adolescents they are still primarily markers of CVD in adulthood (Berenson et al., 1988). The utility of other markers that are early or "pre-clinical" markers of CVD in younger children is of interest. Furthermore, several of these pre-clinical markers can be measured using non-invasive techniques and thus are suited to paediatric research (George et al., 2010; Hopkins et al., 2010).

In recent years there has also been increasing focus on the role of inflammation in the pathogenesis of atherosclerosis including the function of inflammatory markers of CVD such as C-reactive protein (CRP), adiponectin, interleukin-6 (IL-6) and fibrinogen (Fg) (Thomas and Williams, 2008). Low grade inflammation is present in overweight and obese children, and studies have investigated the relationships between adipokines, anthropometric measures, and markers of CM risk in overweight and obese children and adolescents (Herder et al., 2007; Shin et al., 2008; Steene-Johannessen et al., 2010; Valle et al., 2005; Warnberg et al., 2004). It is hypothesised that obese children will have an adverse CM risk profile, elevated levels of proinflammatory markers (e.g. CRP, IL-6) and decreased levels of adiponectin (Andersen et al., 2008; Steene-Johannessen et al., 2010). Metabolic risk has been shown to be negatively correlated with PA and CRF in adults, and whilst there is growing evidence on the role of PA and CRF in lowering of inflammatory factors in adults the evidence in children is less convincing (Thomas and Williams, 2008). This may be partly due to study methods and protocols, with subjective measures of PA, such as self-reported 7 day recall, being common in studies (Cook et al., 2000; Thomas et al., 2008). Further studies have suggested that changes in inflammatory markers following exercise training interventions may be explained by reductions in adiposity (Hulver et al., 2002; Kelly et al., 2007).

To the author's knowledge few studies have investigated relationships between invasive markers (inflammatory and metabolic markers) and non-invasive "pre-clinical" markers (LV Mass, diastolic function) of CM risk in healthy children across a range of weight status, in comparison to each other as well as objective measures of PA and CRF.

Therefore the objectives of this study were: 1. To investigate the relationships between traditional invasive and non-invasive CM risk markers. 2. To establish the relationships between CM risk markers and CRF and PA in 10 to 11 year old healthy children.

4.2. Materials and Methods

4.2.1. Participants and Study Design

Data were collected in schools and the University laboratories. Prior to recruitment institutional ethical approvals for all procedures were received; in addition, Local NHS Research Ethics Committee approvals were received for blood sampling protocols and analysis that involved the local Children's Foundation NHS Trust.

Participants were recruited from six primary schools throughout Liverpool. Within each school all Year 6 (10.0-11.9 year old) children were invited to take part in the REACH Y6 study (n=192). After gaining informed parental consent, participant assent and medical screening 62 participants agreed to take part in all components of the study (33% participation rate). The breakdown of participants by school was as follows: School 1 = 16; School 2 = 5; School 3 = 26; School 4 = 4; School 5 = 8; School 6 = 3. Table 4-1 demonstrates percentage of participants in the study by IOTF classification (Cole et al., 2005) in comparison to the percentage of Liverpool children by IOTF according to the National Child Measurement Programme (NCMP)(Department of Health, 2011).

4.2.2. Outcome Measures

Participants attended the laboratories on one occasion and undertook measurements, as described in the relevant section of the General Methods Chapter 3, of CRF [Section 3.5], anthropometrics [Section 3.6] body composition [Section 3.7], and cardiovascular structure [Section 3.9] and function [Section 3.10]. The participants also attended one school-based blood sampling morning. PA was assessed using accelerometry in the field over a 7-day period.

Blood sampling morning: Participants attended one blood sampling morning at their school site. After verbal confirmation of overnight fast, samples were drawn from the vena antecubitus by one experienced phlebotomist. Samples (~10ml) were taken between 8.30-10.30 am and were transported to the pathology laboratories at the local Children's Foundation NHS Trust for analysis. After giving a blood sample children were provided with breakfast and then returned to their usual school timetable. Full blood count, markers of inflammation and cytokines were assayed. Insulin, glucose, total cholesterol (TC), HDL-C, high sensitivity-C-reactive protein (hs-CRP) and adiponectin were included in the analysis for this study. Insulin was converted from pmol/l to μU/mL by dividing by 7.217 as per manufacturer's instruction. HOMA-IR was calculated using the equation: [Glucose (mmol/L) x Insulin (μU/mL)]/22.5 (Matthews et al., 1985).

Assessments of habitual physical activity: Habitual PA was measured objectively using accelerometry over a seven day consecutive period as described in General Methods-Chapter 3, Section 3.3. Because large individual differences exist in counts at different activity intensities (Rowlands, 2007) data were analysed using individually calibrated thresholds. These individually calibrated thresholds were generated from accelerometer

data collected during the CRF treadmill protocol, and this approach has been described previously (Hopkins et al., 2010). Briefly, using individual count thresholds, and a sedentary (SED) threshold of 100 counts per minute (CPM) (Treuth et al., 2004), the time spent per valid day sedentary, between sedentary and Fr 0.25 (Light PA), Fr 0.25 to Fr 0.5 (MPA), and ≥ Fr 0.5 (VPA) was established.

Outcome measures included in this study were invasive markers of adiponectin, hs-CRP, HOMA-IR, TC:HDL-C, LDL-C and triglycerides; non-invasive markers of LV diastolic filling (E/A), septal myocardial tissue velocities (E'/A'), the ratio of early diastolic filling to early diastolic tissue velocity (E/E'), LVM which was indexed for height$^{2.7}$ (LVM Index) (De Simone et al., 1995), TFM and relative whole body fat (%), CRF ($VO_{2\,Peak}$), SED, MPA, VPA and MVPA.

4.2.3. Statistical Analysis

All analyses were conducted using SPSS v 17 (SPSS Inc., Chicago, IL.). Data was initially explored for normality separately by sex using the Kolmogorov-Smirnov test of normality. The following were not normally distributed ($p<0.05$): CRP, HOMA, TFM, VPA, MVPA and SED in both boys and girls; and TC: HDL-C, whole body fat (%) were not normally distributed in boys. One way analysis of variance (ANOVA) was used to assess sex differences. For the parametric measures Pearson's correlation coefficients, controlling for somatic maturation, were completed separately by sex to assess the relationship between risk markers. For non-parametric variables Spearman's correlation was performed separately by sex.

A weak correlation is represented by an r value of less than 0.39; a moderate correlation is represented by an r value of 0.4 to 0.69 and a strong correlation is represented by an r greater than 0.7 (Cohen and Holliday, 1982).

4.3. Results

4.3.1. Descriptive characteristics

The percentage of participants included in the study by IOTF classification can be seen in Table 4-1. In comparison to the National Child Measurement Programme, more underweight children and more overweight children but less obese children were included in the study in comparison to the population norm.

Table 4-1: Percentage of participants by IOTF classification (Cole et al., 2000) in comparison to data from national Child Measurement Programme for Wigan PCT (NCMP)

	Participants in study	NCMP
Underweight	8%	1%
Healthy Weight	63%	61.8%
Overweight	21%	15.4%
Obese	8%	22.1%

The descriptive characteristics of the participants by sex can be seen in Table 4-2. Girls were significantly more mature ($p < 0.01$), had higher body fat (%) ($p < 0.01$), higher TC:HDL-C ratio, higher insulin levels, and were more sedentary ($p < 0.01$) than boys. Boys had greater fitness ($p < 0.01$), larger LVM Index ($p < 0.01$), higher HDL-C, and spent more time engaged in MVPA ($p < 0.05$) than girls. Of those that had valid PA data 10 out of 30

girls, and 12 out of 22 boys met the recommended PA guidelines of 60 minutes MVPA daily.

With regards to the invasive and non-invasive markers of cardiometabolic risk there are no normative values for children, however children did not differ greatly from participants of similar age in other studies. In comparison to slightly younger participants in the EYHS (Andersen et al., 2003) (n=312 girls and 279 boys, mean age 9.6) boys in the present study had lower insulin levels (boys in EYHS = 7.6 (5.2) μU/mL), girls insulin levels were similar (girls in EYHS = 8.6 (4.2) μU/mL). HDL-C in the girls in the present study was slightly lower, whereas boys were similar (both boys and girls in EYHS = 1.5 (0.3) mmol/L). Total Cholesterol was slightly lower in the present study in both sexes (boys in EYHS = 4.5 (0.7), girls = 4.6 (0.7). In comparison to slightly older children in a study by Thomas et al., 2008 (n= 75 boys and 89 girls, mean age 12.9 (0.3), children in the present study had lower CRP levels (Thomas et al., boys = 1.07 (1.33; girls = 1.24 (1.87) mg/L).

In comparison to similar aged children in a study by Eisenman et al., (2007) (n=74 boys [mean age 11.1 (0.8) years] and 53 girls [mean age 10.9 (1.0) years]) LVM index was lower in the present study (Eisenmann et al., boys = 42.9 (10) and girls = 37.7 (9.8 g/ht$^{2.7}$), and diastolic function variables were similar in the present study to baseline value in a study by Obert et al., 2009 (n=50, aged 9-11 years)[E/A = 2.21 (0.48) in experimental group and 2.1 (0.45) in control group; E'/A' = 2.4 (0.4) in the experimental group and 2.3 (0.4) in the control group; E/E' = 5.6 (0.9) in the experimental group and 6.0 (0.6) in the control group].

Table 4-2: Descriptive characteristics by sex

	Boys (n=28)		Girls (n=34)	
	Mean	**(SD)**	**Mean**	**(SD)**
Age (years)	11.4	(0.3)	11.3	(0.3)
Maturation Offset (years)	-2	(0.1)	-0.6**	(0.6)
BMI (kg/m2)	18.6	(3.2)	19.8	(4.1)
% body fat	23.6	(6.6)	29.4 **	(7.4)
Trunk fat mass (kg)	3.6	(3.1)	4.8	(3.2)
LV mass index ($g/m^{2.7}$)	30.8	(6.1)	26.2 **	(3.6)
E/A	2.06	(0.44)	2.09	(0.36)
E'/A'	3.04	(1.21)	3.01	(0.84)
E/E'	6.30	(1.17)	6.10	(1.27)
TC (mmol/l)	4.09	(0.7)	4.15	(0.61)
HDL-C (mmol/l)	1.46	(0.22)	1.29*	(0.3)
TC:HDL-C	2.83	(0.58)	3.3**	(0.6
Glucose (mmol/l)	4.58	(0.31)	4.61	(0.30)
Insulin (μU/mL)	4.86	(5.74)	8.65*	(8.44)
HOMA-IR	1.03	(1.40)	1.82	(1.93)
CRP (mg/L)	0.67	(1.1)	0.93	(1.5)
Adiponectin (μg/mL)	11.6	(5.0)	12.0	(5.8)
VO_{2peak} (ml/kg/min)	53.7	(6.0)	45.1**	(8.4)
MVPA [PA above Fr0.25] (mins)	74.1	(32.2)	54.4*	(22.5)
VPA [PA above Fr0.5] (mins)	8.7	(6.6)	5.6	(5.1)
SED (mins)	452.0	(65.3)	501.2**	(62.3)

Difference between boys and girls (**p < 0.01, *p < 0.05)

4.3.2. Invasive v non-invasive markers:

There were significant correlations present between invasive and non-invasive markers of CM risk; these can be seen in Table 4-3 CRP had a moderate positive correlation with whole body fat (%) in both boys and girls. CRP had a weak positive correlation with trunk fat mass in boys (kg) and a moderate positive correlation in girls. Adiponectin had a moderate negative correlation with whole body fat (%) in boys. In girls, when controlling for maturity, Pearson's correlation showed that adiponectin had a strong negative correlation with whole body fat (%). Adiponectin had a strong negative correlation with trunk fat mass (kg) in boys, and a moderate negative correlation in girls. TC: HDL-C had a moderate positive correlation with whole body fat (%) and a weak positive correlation with trunk fat mass in boys but there were no significant correlations in girls. HOMA-IR had a strong correlation with whole body fat (%) and trunk fat mass (kg) in girls but not boys.

Table 4-3: Correlations between invasive and non-invasive CM risk markers

		Whole Body Fat (%)	Trunk Fat Mass	E/A	E'/A'	E/E'	LV Mass Index
CRP	Girls	Rho=0.485 **	Rho=0.489 **	Rho=0.014	Rho=-0.196	Rho = 0.3	Rho= 0.067
	Boys	Rho= 0.486*	Rho= 0.384*	Rho=-0.085	Rho=0.025	Rho=0.146	Rho-0.103
Adiponectin	Girls	R=-0.697**$^{\$}$	Rho=-0.475**	R= 0.073$^{\$}$	R=0.356*$^{\$}$	R= -0.245$^{\$}$	R=0.175$^{\$}$
	Boys	Rho= -0.446*	Rho= -0.614**	R=-0.134$^{\$}$	R=0.176$^{\$}$	R=-0.361$^{\$}$	R=-0.095$^{\$}$
HOMA-IR	Girls	Rho=0.631**	Rho=0.694**	Rho= 0.171	Rho=-0.176	Rho =0.153	Rho =0.167
	Boys	Rho=0.213	Rho=0.166	Rho=-0.314	Rho=-0.267	Rho=0.187	Rho=-0.114
TC:HDL-C	Girls	Rho=0.315	Rho = 0.317	R= 0.012$^{\$}$	R= -0.212$^{\$}$	R= 0.012$^{\$}$	R= 0.208$^{\$}$
	Boys	Rho =0.407*	Rho=0.391*	Rho= -0.11	Rho=-0.136	Rho=0.139	Rho=0.154

Correlations between risk markers are statistically significant **p<0.01; *p<0.05; $^{\$}$controlling for maturity (parametric only)

4.3.3. CRF and CM risk markers:

CRF correlated significantly with several of the CM risk markers, these can be seen in Table 4-4. CRF had a moderate negative correlation with CRP in boys but the relationship was non-significant in girls. CRF also had a moderate negative correlation with HOMA-IR in girls but not boys. CRF had a strong negative correlation with whole body fat (%) and trunk fat mass in boys, and was correlated moderately with both adiposity measures in girls.

4.3.4. Physical activity and CM risk markers:

PA was significantly correlated with several of the CM risk markers [Table 4-4]. TC: HDL-C had a significant weak negative correlation with MVPA and VPA in girls but not boys. MVPA also had a significant strong negative correlation with whole body fat (%) and trunk fat mass in boys but not girls, and VPA had a strong negative correlation with whole body fat in girls and with trunk fat mass in both boys and girls. Time spent sedentary was also correlated positively with whole body fat (%) in boys.

Table 4-4: Correlations between risk markers and CRF, MVPA, VPA and SED

		VO_2 Peak	MVPA	VPA	SED
CRP	Girls	Rho=-0.244	Rho=-0.153	Rho=-0.189	Rho=0.132
	Boys	Rho=-0.492*	Rho=-0.248	Rho=0.039	Rho=0.160
Adiponectin	Girls	R=0.079$^{\$}$	Rho=0.231	Rho=0.313	Rho=0.1
	Boys	R=0.227$^{\$}$	Rho=0.379	Rho=0.317	Rho=-0.023
HOMA-IR	Girls	Rho=-0.522**	Rho=-0.005	Rho=-0.216	Rho=-0.063
	Boys	Rho=0.011	Rho=0.126	Rho=0.369	Rho=0.043
TC:HDL-C	Girls	R=0.011$^{\$}$	Rho=-0.396*	Rho=-0.428*	Rho=0.1
	Boys	Rho=-0.294	Rho=-0.287	Rho=0.090	Rho=0.23
E/A	Girls	R=0.052$^{\$}$	Rho= -0.062	Rho=0.181	Rho=0.024
	Boys	R=0.057$^{\$}$	Rho=-0.136	Rho=-0.141	Rho=0.165
E'/A'	Girls	R=0.273$^{\$}$	Rho=-0.081	Rho=-0.115	Rho=0.125
	Boys	R=-0.110$^{\$}$	Rho=-0.007	Rho=0.099	Rho=-0.055
E/E'	Girls	R=-0.337$^{\$}$	Rho=-0.212	Rho=-0.075	Rho=0.082
	Boys	R=0.04$^{\$}$	Rho=-0.239	Rho=-0.405	Rho=0.024
LV Mass Index	Girls	R=-0.170$^{\$}$	Rho=0.238	Rho=-0.083	Rho=-0.335
	Boys	R=-0.003$^{\$}$	Rho=-0.364	Rho=-0.141	Rho=0.165
Whole body fat (%)	Girls	R=-0.697**	Rho=-0.195	Rho=-0.544**	Rho=0.05
	Boys	Rho=-0.515**	Rho=-0.602**	Rho=-0.281	Rho=0.429*
Trunk fat mass	Girls	Rho=-0.706**	Rho = -0.169	Rho=-0.468**	Rho=0.036
	Boys	Rho=-0.494*	Rho=-0.65 **	Rho=-0.428 *	Rho=0.296

Correlations between risk marker and CRF/ PA statistically significant **p<0.01; *p<0.05; $^{\$}$controlling for maturity (parametric only)

4.3.5. Other significant relationships:

There were also significant correlations between the inflammatory markers and metabolic markers. CRP and TC: HDL-C had a moderate positive correlation in boys but not girls (Rho = 0.522, p=0.004); TC: HDL-C was also positively correlated with HOMA-IR in boys (Rho = 0.463, p=0.013) and girls (Rho=0.346, p=0.045), although these were relatively weak to moderate correlations. Adiponectin was negatively correlated with HOMA-IR in boys (Rho=-0.428, p=0.023) but not significantly in girls, again this was a relatively moderate correlation.

There were also significant correlations for measures of adiposity and diastolic function. Whole body fat (%) had a moderate positive correlation with E/E' in boys (Rho = 0.472, p = 0.011) and a moderate negative correlation with E'/A' in boys (Rho = -0.319, p=0.04); and trunk fat mass, when controlling for maturity a moderate negative correlation with E'/A' in girls was observed (r = -0.430, p = 0.041).

4.4. Discussion

The REACH study aimed to investigate the relationships between traditional invasive and non-invasive CM risk markers and to establish the relationships between CM risk markers and objectively measured CRF and PA.

The key findings were that there were significant relationships present between some of the non-invasive and invasive markers of CM risk; and some risk markers also had significant correlations with measures of CRF and PA.

The present study demonstrated that adiposity (trunk fat mass and whole body fat %) correlated significantly with markers of inflammation, CRP and adiponectin [Table 4-2]. This is consistent with other studies that have also demonstrated a positive correlation between measures of total adiposity and central adiposity (assessed by WC) and CRP (Brown et al., 2010; Galcheva et al., 2011; Mendoza et al., 2012) and a negative correlation with adiponectin (Rubin et al., 2008a), in both children and adolescents. An increase in adiposity can have an effect on metabolic and immune responses. Impaired metabolic homeostasis triggers an inflammatory process, activated by increased adipose tissue in metabolically active sites (Balistreri et al., 2010). The adipokine and cytokine network is altered by an increase in adipose tissue, and therefore increased trunk fat will contribute to an inflammatory state and impaired adipocyte metabolism (Balistreri et al., 2010). CRP possesses pro atherogenic properties such as promoting activation of endothelial cells to express adhesion molecules (Pasceri et al., 2000), decreases bioavailability of endothelial nitric oxide synthase in endothelial cells (Verma et al., 2002) and augments the uptake of LDL-C (Zwaka et al., 2001). Adipokines are believed to have an effect on glucose and lipid metabolism. For example adiponectin and leptin both trigger the decrease in lipogensis and the induction of fatty acid oxidation, whereas

proinflammatory cytokines such as TNF-α, inhibit triglyceride storage in adipose tissue (Lago et al., 2007; Lago et al., 2009).

The present study demonstrated a positive correlation between trunk fat mass and TC: HDL-C in boys, it also found significant relationships between markers of inflammation and metabolic markers in boys, but not girls. In boys there was a positive correlation between CRP and TC: HDL-C and a negative correlation between HOMA-IR and adiponectin. Other studies have also found a negative relationship between adiponectin and insulin resistance (Haluzik et al., 2004). Adiponectin gene regulation involves hormonal and environmental factors, for example adiponectin gene expression and thus adiponectin production is decreased by obesity, glucocorticoids and TNF-α, and is increased by leanness, cold exposure and IGF-1 (Fasshauer et al., 2002). Insulin also appears to be an important regulator of adiponectin gene expression; however it appears to have different effects dependent on the dose and duration of action. Some studies have demonstrated an increase in adiponectin gene expression in-vitro after short term insulin stimulation, whereas others have found a decrease following more prolonged exposure to insulin (Haluzik et al., 2004).

CRP is secreted from the liver in response to an increase in circulating inflammatory cytokines. Inflammatory cytokines such as TNF-α and IL-6 adversely affect lipid metabolism through a number of proposed mechanisms. TNF-α inhibits free fatty acid (FFA) uptake, regulates lipoprotein lipase expression, and reduces synthesis of proteins which are involved with fatty acid synthesis and esterification, leading to diminished triglyceride storage in adipose tissue (Lago et al., 2009). The positive correlation found between trunk fat mass and TC: HDL-C, is consistent with other studies. A similar relatively weak positive correlation ($r = 0.22$, $p < 0.01$) was reported in a cross sectional

study of slightly older Portuguese children (n = 159) , mean age 13.2 ± 1.6 years) (Teixeira et al., 2001). Abdominal adipocytes are thought to have higher lipolytic rates than peripheral adipocytes and therefore an increase in trunk fat mass has an impact on lipid metabolism (Ibrahim, 2010). As adipose tissue increases there is an increase in circulating free fatty acids, therefore VLDL production is stimulated by the liver, there is proliferation of triglycerides and an increase in lipid exchange between lipoproteins. This in turn increases total cholesterol, and plasma triglycerides and triglyceride rich lipoproteins (VLDL-C, VLDL-C remnants and small dense LDL) and reduces HDL-C, and therefore increasing CM risk (van de Woestijne et al., 2011).

There were also significant correlations for measures of adiposity and diastolic function, which differed by sex. Whole body fat (%) had a moderate positive correlation with E/E' and a moderate negative correlation with E'/A' in boys and trunk fat mass, when controlling for maturity had a moderate negative correlation with E'/A' in girls. These findings were consistent with other studies who found that obese children had significantly higher E/E', and significantly lower E'/A' than lean controls (Sharpe et al., 2006; Zeybek et al., 2010a). The increase in E/E' suggests that with increasing adiposity there is an increase in diastolic filling pressures, LA has to generate more pressure to fill LV, therefore causing a greater work load. This is likely due to poor early relaxation and compliance. The present study also found a significant positive correlation between adiponectin and E'/A' in girls when controlling for maturation. As already discussed E'/A' and adiponectin were both negatively correlated with measures of adiposity. Therefore it is speculated that adiposity may play a role in the relationship between adiponectin and E'/A'. A study of healthy adults found a negative relationship between adiponectin and A' (Kozakova et al., 2008), which is consistent with the findings of the present study, since a higher A' will equate to a lower E'/A'. Another study demonstrated that adiponectin had

an independent effect on diastolic function in hypertensive adults and suggested that this may be due to the influence of adiponectin on growth factors (Horio et al., 2005). To the author's knowledge no other studies have investigated the relationships of adiponectin and E'/A' in paediatric populations, and further research is required to understand this relationship. Studies have demonstrated that adiponectin has both direct and indirect effects on the heart. In-vivo animal studies have demonstrated that adiponectin diminished endothelin induced hypertrophy in cardiomyocytes (Fujioka et al., 2006). Adiponectin may also induce changes in energy metabolism by stimulating an increase in glucose and fatty acid uptake in cardiomyocytes, which therefore may lead to alterations in cardiac function (Pineiro et al., 2005).

CRF (VO_{2peak}) was only very weakly correlated with CRP (r= -0.273, p=0.046, Table 4-3). Another study found an association between absolute VO_{2peak} and CRP but relationships were lost when adiposity was included in the model (Ruiz et al., 2007b). A similar negative correlation (r= - 0.32, p<0.01) was demonstrated for CRF and CRP in 3-17 year old boys but not girls (Isasi et al., 2003). However CRF was assessed using the physical work capacity treadmill protocol at a heart rate of 170 bpm (PWC_{170}). This is a progressive exercise test where work load increases every 2 minutes, the fitness level is reported as the work load reached at test termination when heart rate reaches 170bpm. Other studies which have investigated CRF using the 20 m SRT have found no significant relationships between CRP and CRF (Thomas et al., 2008; Warnberg, 2006). There was also a weak negative correlation demonstrated between $VO_{2\ peak}$ and HOMA-IR in girls but not boys. A study by Kriemler et al., (2008) investigated CRF, assessed using the 20m SRT, in relation to cardiovascular risk markers, and reported a similar negative relationship in both boys and girls between 20m SRT stage completed and HOMA-IR, the present study was not able to control for maturity in the correlation between fitness and HOMA-IR, due

to the non-parametric test being used and therefore the different relationships observed between sexes may be due to differing maturation levels. The mechanisms responsible for the relationships between increased CRF and reduced insulin resistance are not clear, however it is likely to be due to enhanced insulin action and improved glucose homeostasis involving structural and biochemical adaptations in skeletal muscles, such as increased fibre size, improved capillary density and blood flow, improved insulin signalling kinetics, increased myoglobin, and an increase in enzymes responsible for glucose metabolism, increased CRF is also related with increased oxygen uptake and increased lipoprotein lipase which could also reduce insulin resistance (LaMonte et al., 2005). PA was significantly correlated with the metabolic risk markers [Table 4-4]. TC: HDL-C had a significant weak negative correlation with MVPA and with VPA in girls but not boys. This is similar to other observational studies which have demonstrated generally weak relationships between PA and TC:HDL-C (Andersen et al., 2006). In the present study there were no significant correlations present between insulin resistance (HOMA-IR) and PA. However, studies have hypothesised that PA is important in preventing insulin resistance due to its effects on the energy continuum leading to decreased body weight and increased metabolic rate, PA may also have a direct impact on insulin through short term activation of the GLUT-4 receptors which encourages glucose uptake and decrease in circulating insulin (Jago et al., 2008).

PA also correlated significantly with measures of adiposity (Table 4-3). MVPA had a significant strong negative correlation with whole body fat (%) and trunk fat mass in boys but not girls, and VPA had a strong negative correlation with whole body fat in girls and with trunk fat mass in both boys and girls. Time spent sedentary was also correlated positively with whole body fat (%) in boys. This is what would be expected since PA plays a key role in the energy continuum, and if energy consumed exceeds energy expended,

fat cells increase in number and size (Bray, 2004). These findings are also consistent with other studies, a recent systematic review concluded that higher levels of habitual PA may be protective against child and adolescent obesity (Jimenez-Pavon et al., 2010). However, since the present study is cross sectional, like the majority of other studies who have demonstrated this finding, causality of this relationship cannot be conferred.

Strengths and Limitations

The combination of these high-quality invasive and non-invasive measures, in conjunction with objective measures of PA and CRF is rarely observed in similar studies that are conducted on a larger scale. However, the present study had a relatively low sample size and therefore lacks statistical power at this stage. Small but clinically significant relationships may be missed due to the relatively small sample size. Similar to other studies involving invasive measures of risk markers sample size was limited due to financial constraints as well as in obtaining consent for taking blood samples from children. In order to increase statistical power, and to investigate if the relationships found in the present study exist in a wider sample, the study will be repeated and the samples will be pooled. Furthermore, this was a cross sectional study with measurement taken only on one occasion, and since markers of inflammation are sensitive for example to daily fluctuations, common colds, and acute exercise bouts, a one off measurement may not accurately assess chronic inflammation (Ruiz et al., 2007b). Another limitation was that it was not possible to control for maturity in the Spearman's correlations for the non-parametric measures.

Conclusions

The present study documented significant correlations between inflammatory markers, lipids and non-invasive markers which provide preliminary evidence to investigate this phenomenon further. Causality of relationships cannot be concluded, therefore in order to fully understand the impacts of changes in PA and CRF on CM risk markers there is clear need to conduct a prospective intervention trial (Chapter 6).

Thesis Study Map

Study	Objectives and Key Findings
Study 1: Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.	Objectives: • To investigate the relationships between traditional invasive and non-invasive cardiometabolic risk markers. • To establish the relationships between individual cardiometabolic risk markers and cardiorespiratory fitness (CRF) and physical activity (PA). • To determine which measures would be most appropriate to use in future studies. Key findings: • Relationships are present between invasive markers (CRP and TC: HDL-C +ve relationship; adiponectin –ve relationship) and adiposity measures (whole body fat % and trunk fat mass) • Relationships evident between some risk markers (CRP in boys, HOMA-IR in girls, whole body fat and trunk fat mass)and CRF • Some relationships found between TC: HDL-C and physical activity. • Lack of relationships found between measures of PA (MVPA & VPA) and inflammatory markers or measures of cardiac structure and function, this needs further investigation. • CRP seems to be a good representative marker to measure due to correlations with other markers.
Study 2: Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project	**Objectives:** • **To report clustered risk scores (CRS) that combine traditional invasive with non-invasive cardiometabolic risk markers; and to determine the relationships between individual risk markers, CRS and objectively measured PA, CRF and body composition.**
Study 3: The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.	

Chapter 5

Study 2:

Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project

Gobbi, R., Davies, I.G,. Fairclough, S.F., Hackett, A.F., Mackintosh, K.A., Warburton, G.L., Stratton, G., George, K.P., Boddy, L.M. (2012) Clustered Cardiometabolic Risk, Cardiorespiratory fitness and Physical Activity in 10-11 year old children. The CHANGE! Project Baseline. *Archives of Exercise in Health and Disease,* **3** (3), 207-213 [See Appendix D]

5.1. Introduction

Studies have estimated CM risk by combining several risk markers in one overall clustered risk score (Andersen et al., 2006; Andersen et al., 2008; Bailey et al., 2012). This clustered risk score may be more clinically meaningful than investigation of individual risk markers due to the range of structural, functional and biochemical disturbances associated with CM disease, and the day to day variation in individual risk markers (Andersen et al., 2006; Ruiz et al., 2007a).

While previous clustered risk scores have included traditional markers such as TC, HDL-C and blood pressure (BP) they have rarely included non-invasive risk markers such as left ventricular (LV) mass or estimates of adiposity using reference standard measures such as dual-energy x-ray absorptiometry (DEXA). Furthermore, few studies have combined measures of clustered CM risk with objective measures of PA and CRF. The current study used reference standard measurement techniques to assess body composition (DEXA), PA (accelerometry) and CRF (individually calibrated treadmill based VO_{2peak} protocol). Study 1 (Chapter 4), utilised this approach and similar studies are rare. In larger scale studies the combination of such high quality measures are rarely utilised. For example, The European Youth Heart Study (EYHS) employed skinfold thickness as an estimate of body fat (Andersen et al., 2006; Andersen et al., 2008), and the HEALTHY study (n = 6358, mean age 11.8 (± 0.6) years) measured BMI as an indicator of fatness, 20 m SRT as a measure of fitness (Jago et al., 2010a) and self-reported estimated PA respectively (The HEALTHY Study Group, 2009). Neither study employed non-invasive measures of cardiac structure or function. Following on from Study 1, a composite score of CM risk incorporating measures of structural, functional and biochemical variables was calculated rather than solely focussing on one or two of these measures.

The overall aim of this chapter was to investigate CM risk in 10 to 11 year old children at baseline for a randomised controlled trial. The objectives were to report clustered risk scores that combine traditional invasive with non-invasive CM risk markers; and to determine the relationships between clustered risk score and objectively measured PA, CRF and body composition.

5.2. Materials and Methods

5.2.1. Participants and Study Design

The CHANGE! pilot study was a clustered randomised controlled trial (RCT) and is registered with Current Controlled Trials (ISRCTN03863885). Twelve schools from the Wigan Borough in North-West England were recruited to the study, 6 randomly assigned to the intervention condition. Wigan is a large municipal borough with a population of over 300,000, which is recognised as an area of high deprivation and health inequalities (Wigan Borough Partnership, 2007). The borough is divided into six Neighbourhood Management Areas, and two schools were selected from each area, stratified by free school meal entitlement. This cross-sectional analysis used baseline data from CHANGE! with control and intervention groups pooled. Ethical approval was granted by the local institutional ethics committee. All children within Year 6 (10-11.9 years) were invited to take part in the CHANGE! Study from each school (N=420). Out of those invited to take part 318 children agreed (75.7% participation rate) and from those a random sub-sample of sixty participants (5 participants from each school), were invited to take part in additional study measures and are included in this study. If the selected children did not wish to participate another participant was randomly selected from the volunteers in the school. Approximately 95% of the children were of white British ethnicity, which is

representative of the school age population in Wigan (Wigan Council, 2011). Table 5-1 demonstrates the percentage of children by IOTF classification in the study in comparison to data from the National Child Measurement Programme.

5.2.2. Outcome Measures

School based:

Anthropometrics and Somatic Maturity: stature, sitting stature, body mass, WC and HC were assessed in the field as described in General Methods, Chapter 3, Section 3.6. Somatic maturation was calculated using the Mirward formula (Mirwald et al., 2002) as described in General Methods, Chapter 3, Section 3.8.

Physical Activity: Habitual PA was objectively measured over a 7 day period as described in General Methods, Chapter 3, Section 3.3. Briefly, PA intensity cut points were 2160 CPM for moderate intensity PA (MPA), 4806 CPM for vigorous intensity PA (VPA), sedentary (SED) was defined as less than 100 CPM (Mackintosh et al., 2012).

Blood Pressure: After 10 minutes rest, seated blood pressure was assessed on the left arm in the field (Omron Healthcare UK Limited, Milton Keynes, UK), and the mean of two assessments was retained for analysis. If the BP readings were different by more than 10mmHg a third reading was taken and the mean of the second and third was retained for analysis. It has been reported that the coefficient of variation for intra-individual

measurements of blood pressure are 9.9% and 9.2% for sBP and dBP respectively (Marshall, 2004).

Capillary blood sample: Participants also attended a blood sampling session at each school. After verbal confirmation of overnight fasting, seated finger prick capillary blood samples were taken and analysed for TC, HDL-C, and glucose, as described in General Methods, Chapter 3, Section 3.12.

Laboratory based:

Participants attended the laboratories on one occasion and undertook measurements, as described in the relevant section of the General Methods Chapter 3, of CRF [Section 3.5], body composition [Section 3.7], and cardiovascular structure [Section 3.9] and function [Section 3.10]. The following outcome measures are included in this study: VO_{2Peak}, whole body fat percentage (WBF %), trunk fat mass (TFM), peripheral fat percentage (PF %), WC, BMI, LV Mass Index, Total Cholesterol, HDL-C, sBP & dBP.

Clustered risk scores: Standardized z-scores were calculated separately by sex and summed to create continuous clustered risk scores. This approach has been used previously in similar aged participants (Andersen et al., 2008; Bailey et al., 2012). Two clustered risk scores (CRS A and CRS B) were calculated for each participant. Both CRS included TC: HDL-C; glucose; sBP; LV Mass Index ($g/m^{2.7}$). CRS A also included trunk fat mass and CRS B included WC. Two CRS were created to allow for comparison in Study 3 (Chapter 6). DEXA (trunk fat) was only assessed at baseline and follow up and therefore

an alternative risk score using WC instead of trunk fat can be used at all three time points. CRS A has been calculated since trunk fat is a more accurate measure of abdominal adiposity than WC.

5.2.3. Statistical Analysis

All analysis was conducted using SPSS v 17. Data was initially explored for normality, and all variables were normally distributed. Pearson's correlation coefficients, controlling for sex and maturation, were completed to assess the relationship between, clustered risk scores (CRS A and CRS B) and VO_{2peak}, MVPA, VPA, and sedentary time (SED). A weak correlation is represented by an r value of less than 0.39; a moderate correlation is represented by an r value of 0.4 to 0.69 and a strong correlation is represented by an r value greater than 0.7 (Cohen and Holliday, 1982), Statistical significance is described at $p<0.05$.

Group Comparisons

Participants with a clustered risk score greater than 1 SD above the grand mean, were categorised as 'higher' risk (n = 6); all others were categorised as 'normal' risk (n = 23). This method has been used previously in similar studies (Andersen et al., 2006). ANCOVA, with somatic maturity and sex as covariates were conducted to determine differences in $VO_{2\ peak}$; MVPA, VPA, and SED between groups.

Grouped by fitness level:

Participants were grouped as high fit (HF) (n = 20) or low fit (LF) (n = 9) based on whether they met the EYHS recommended fitness for metabolic health (Adegboye et al., 2011). The recommended VO_{2peak} is 37.4 ml/kg/min and 43.6 ml/kg/min in girls and boys respectively.

Grouped by PA level:

Participants were grouped based on whether they met (n = 12) or did not meet (n = 15) the recommended daily PA guidelines of at least 60 min of MVPA daily (Department of Health, 2011).

5.3. Results

Girls (n = 34) were more mature, had higher %BF and WFM, and lower HDL-C, VO_{2peak} and PA. The percentage of the sample classified as underweight (UW), normal weight (NW), overweight (OW) and obese (OB) (Cole et al (2000) can be found in Table 5-1. When comparing children in the study to data from the NCMP, more children in the study were underweight, more boys were normal weight with fewer boys overweight or obese. However more girls in the study were overweight and less were obese compared to NCMP data. Table 5-2 displays mean and standard deviation values for anthropometrics, body composition, CRF, PA levels and CM risk by sex for the subsample.

Table 5-1: Percentage of participants by IOTF classification (Cole et al., 2000) in comparison to data from national Child Measurement Programme for Ashton, Leigh and Wigan PCT (NCMP)

	Boys	Girls	NCMP
UW	3.8%	14.7%	1.1%
NW	88.5%	61.7%	65.1%
OW	7.7%	20%	14.6%
OB	0%	2.9%	19.3%

More girls (69.7%) than boys (23.8%) failed to meet the recommended daily PA guidelines of 60 min. MVPA. However, 76% of girls and 64% of boys achieved the EYHS recommended fitness level, which were 37.4 ml/kg/min for girls and 43.6 ml/kg/min for boys.

Table 5-2: Mean and SD for anthropometrics, CM risk markers, PA and CRF by sex for the subsample.

	Boys			Girls		
	N	Mean	SD	N	Mean	SD
Maturity Offset (Years to PHV)	26	-3.1	0.3	34	-1.2**	0.6
Height (m)	26	1.4	0.1	34	1.5	0.1
Sitting Height (m)	26	0.8	0	34	0.8	0
Body Mass (kg)	26	36.2	6.6	34	39.7	9.5
BMI (kg/m^2)	26	17.7	2.5	34	18.5	3.4
Total Cholesterol (mmol/l)	14	3.9	0.5	17	4.3	0.6
HDL-C (mmol/l)	13	1.5	0.3	17	1.3*	0.2
TC:HDL-C	13	2.8	0.4	17	3.4**	0.6
Glucose (mmol/l)	14	4.9	0.4	17	4.8	0.3
Systolic BP (mmHg)	26	117	17	34	111	16
Diastolic BP (mmHg)	26	74	22	34	69	19
Whole Body Fat %	26	22.3	5.8	34	26.6*	6.9
Whole Body Fat Mass (kg)	26	8.5	3.7	34	11.1*	5.7
Whole Body Lean Mass (kg)	26	28.2	3.4	34	28.8	4.8
Trunk Fat Mass (kg)	26	2.7	1.5	34	3.8	2.7
LV Mass Index (g/height $m^{2.7}$)	24	39.3	7.5	29	35.7	7.4
Sedentary Time (Mins Per Day)	21	500	69	33	511.7	48.1
Light PA (Mins Per Day)	21	171	30.5	33	173.2	25.9
Moderate PA (Mins Per Day)	21	54.8	16.5	33	41.6**	10.6
VPA (Mins Per Day)	21	21.7	9.9	33	13.5**	5.2
MVPA (Mins Per Day)	21	76.5	24	33	55.1**	14.1
Relative VO_{2Peak} (ml/min/kg)	25	46.5	9.6	33	40.8*	8.8
Clustered Risk Score A (trunk)	12	0.5	3.08	15	0.11	2.7
Clustered Risk Score B (WC)	12	0.56	3.13	15	0.04	2.75

Difference between boys and girls significant *p<0.05 **p<0.01

Of the 60 subsample children that took part in the study 29 had complete risk scores and $VO_{2\ peak}$ data, and 27 had complete risk scores and PA data. These reduced numbers were due to non-compliance for PA monitoring or blood sampling. The children with complete risk scores (n=29) did not differ in terms of anthropometrics to those who did not have complete clustered risk scores (n=31, p<0.05).

PA and Clustered Risk

VPA showed a moderate negative correlation with CRS A (r= -0.51, p= 0.01) and CRS B (r= -0.50, p=0.01) [Figure 5-1]. MVPA showed a moderate negative correlation with CRS A (r= -0.44, p= 0.03) and CRS B (r= -0.41, p=0.04) [Figure 5-2]. SED showed a moderate positive correlation with CRS A (r= 0.414, p= 0.049) [Figure 5-3].

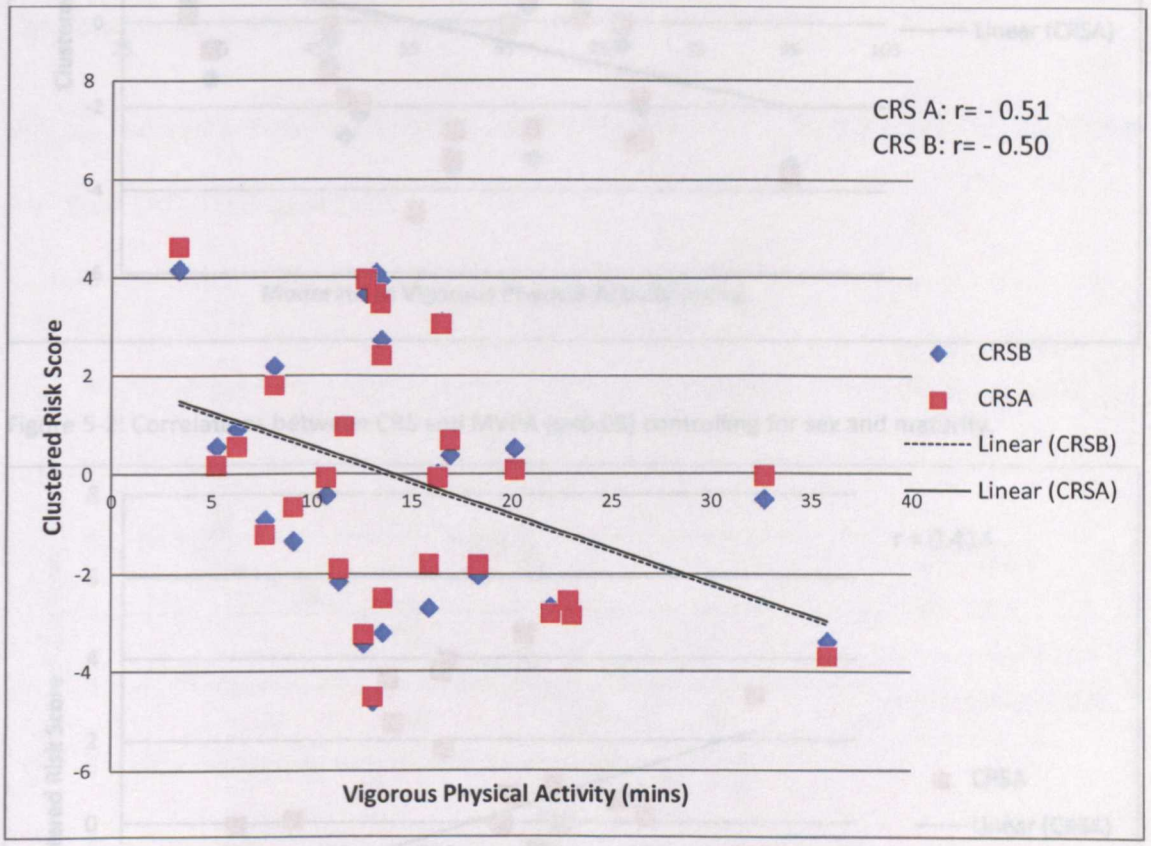

Figure 5-1: Correlations between CRS and VPA (p<0.05) controlling for sex and maturity.

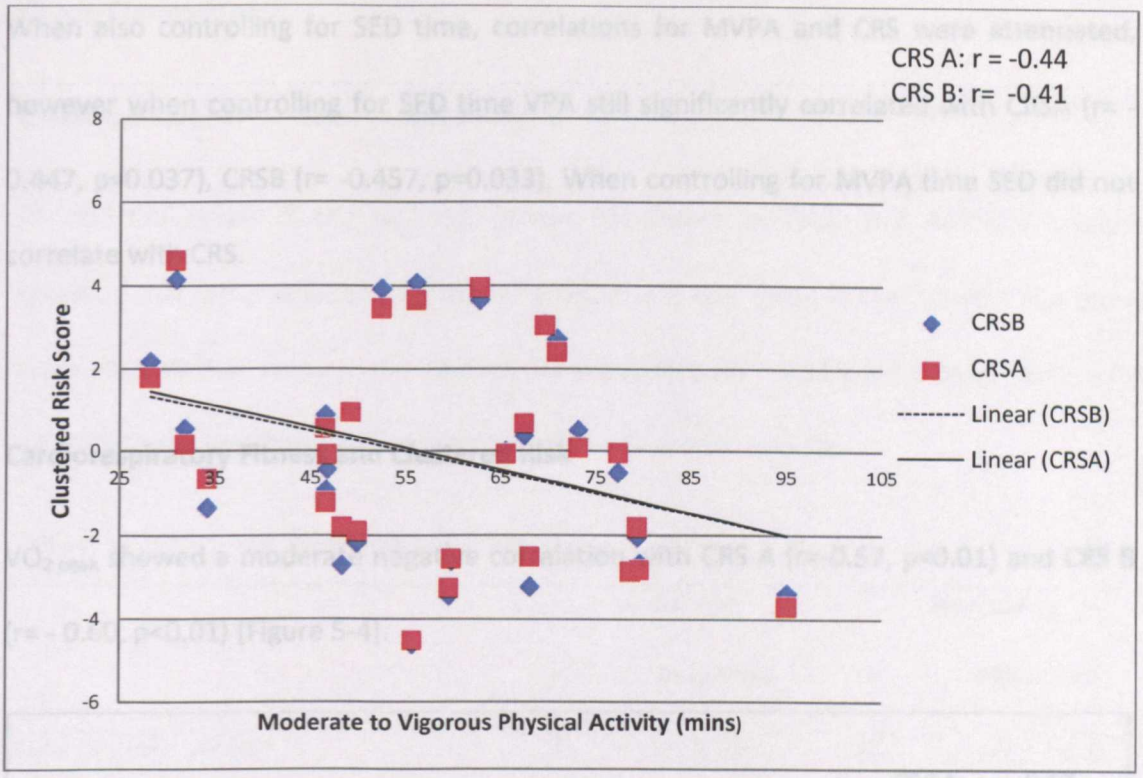

Figure 5-2: Correlations between CRS and MVPA ($p<0.05$) controlling for sex and maturity.

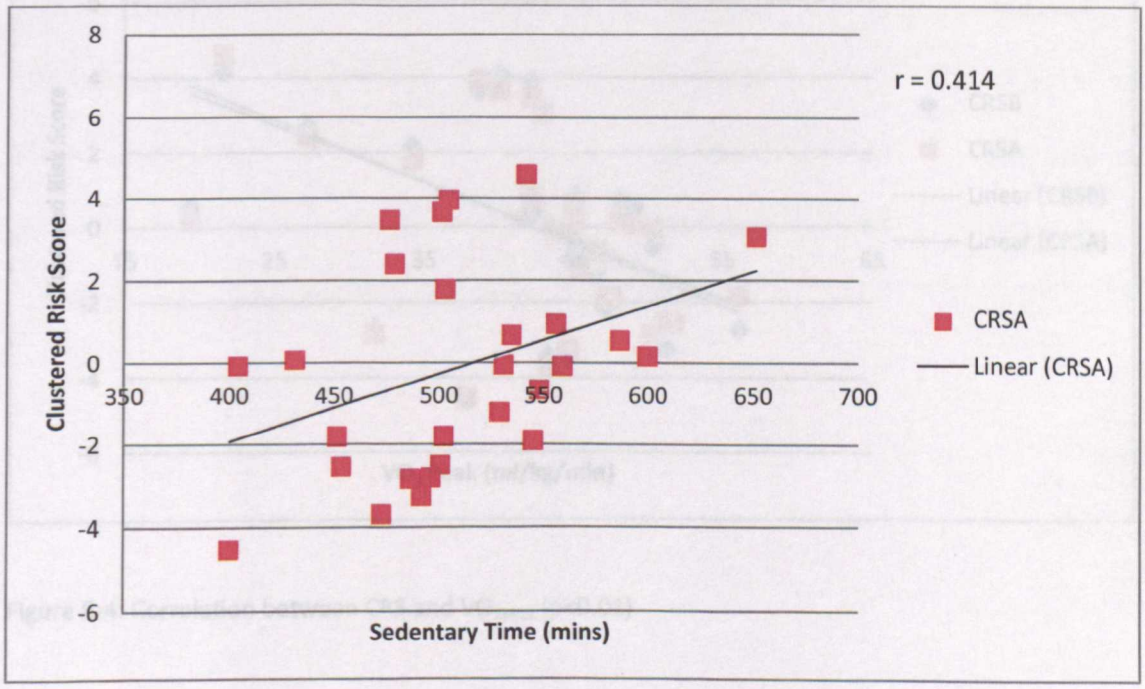

Figure 5-3: Correlation between SED and CRS A ($p<0.05$) controlling for sex and maturity.

When also controlling for SED time, correlations for MVPA and CRS were attenuated, however when controlling for SED time VPA still significantly correlated with CRSA (r= -0.447, p=0.037), CRSB (r= -0.457, p=0.033). When controlling for MVPA time SED did not correlate with CRS.

Cardiorespiratory Fitness and Clustered Risk

$VO_{2\ peak}$ showed a moderate negative correlation with CRS A (r=-0.57, p<0.01) and CRS B (r= - 0.60, p<0.01) [Figure 5-4].

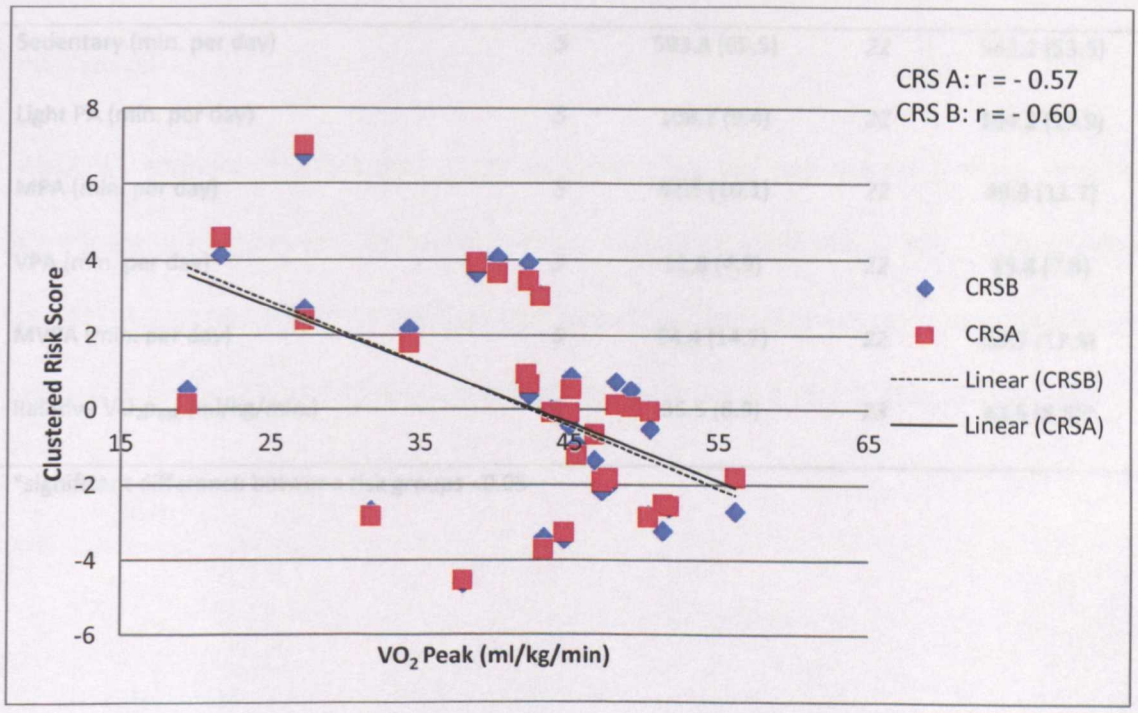

Figure 5-4: Correlation between CRS and VO_{2peak} (p<0.01)

Group Comparisons:

Clustered Risk Score Mean (+1SD) Groups.

PA and CRF levels of the two risk groups are shown in Table 5-3. ANCOVA analysis revealed that, after adjusting for maturity offset and sex, those in the 'normal' risk group were more fit than those in the 'higher' risk group [f(1,24) = 4.518, p = 0.044]. There were no statistically significant differences between risk groups and PA.

Table 5-3 PA Levels and CRF of both risk groups

	Higher Risk		Normal Risk	
	n	Mean (±SD)	n	Mean (±SD)
Sedentary (min. per day)	5	593.8 (69.5)	22	562.1 (53.5)
Light PA (min. per day)	5	108.7 (9.4)	22	104.2 (19.9)
MPA (min. per day)	5	42.5 (10.1)	22	43.9 (11.7)
VPA (min. per day)	5	11.8 (4.9)	22	15.8 (7.9)
MVPA (min. per day)	5	54.4 (14.7)	22	59.7 (17.5)
Relative VO_2p_{eak} (ml/kg/min.)	6	35.5 (8.9)	23	43.5 (8.5)*

*significant difference between risk groups <0.05

Fitness Groups

ANCOVA analysis revealed that, after controlling for sex and maturity, those that did not meet the EYHS recommended fitness level had significantly higher CRS B [Mean CRS B = 1.96 (± 3.28)]; than those that met the EYHS fitness guideline [Mean CRS B= -0.58 (±2.3) $p<0.05$]. CRS A was also higher in participants that did not meet the EYHS fitness guidelines [Mean CRS A= 1.84 (±3.44)] than those that met the EYHS guidelines [Mean CRS A= -0.63 (±2.1)] but the difference did not quite reach statistical significance ($p=0.056$).

PA Groups

ANCOVA analysis revealed that, after controlling for sex and maturity, there were no significant differences for CRS between those that met PA guidelines (Mean CRS A =-0.26 (±2.64); Mean CRS B = -0.33 (±2.53)) and those that did not meet the recommended 60 min. daily MVPA (Mean CRS A = 0.27 (±2.14); Mean CRS B = 0.28 (±2.85) $p>0.05$).

5.4. Discussion

This pilot study reports clustered risk scores that combine traditional invasive with non-invasive pre-clinical CM risk markers, and aimed to determine the relationship of this clustered risk score with objectively measured PA, and CRF. Participants categorised as 'higher' risk, as defined by 1 SD above the mean, were less fit than those in the 'normal' risk category ($p \leq 0.05$), furthermore VO_{2peak} was negatively correlated with clustered risk ($p \leq 0.01$). These findings are supported by other studies that have found a similar relationship between clustered risk and CRF in children (Andersen et al., 2008; Bailey et al., 2012). However, this study has included different risk markers in the overall clustered risk score to those of the EYHS, emphasizing the importance of fitness on other risk markers, such as LV Mass, as well as the traditional markers employed by EYHS and similar studies.

Participants who did not meet the EYHS recommended fitness levels (Adegboye et al., 2011) had significantly higher CRS B. This finding is unsurprising since Adegboye and colleagues defined the fitness cut points based on optimal CM health in a large cohort of children. Whilst the present study and the EYHS used different risk markers in the clustered risk score the risk levels appear to be comparable. However when including trunk fat measured by DEXA rather than WC in the CRS, which is arguably a more accurate method of assessing central adiposity, the difference between those that met the EYHS fitness level and those that did not, was no longer statistically significant, however the value was close to significance ($p=0.056$). The relatively small sample size may have reduced statistical power and hence the lack of statistical significance.

Children in the 'higher' risk group participated in 4 minutes less VPA per day than those in the 'normal' risk group; whilst this difference was not statistically significant it could have

clinical significance. In line with findings of other studies (Andersen et al., 2006; Carson and Janssen, 2011) MVPA and VPA were both moderately negatively correlated with CRS ($p<0.05$). SED correlated positively with CRS but this was slightly weaker than the relationships found between VPA and MVPA and CRS. When controlling for MVPA, the relationship between SED and CRS was diminished, as was the relationship between MVPA and CRS when controlling for SED. Similar findings are reported in a large scale cross sectional study of US children and adolescents, which found that SED as measured with accelerometry was not correlated with CRS when MVPA was controlled for (Carson and Janssen, 2011). Nevertheless they did find that self-reported high TV use was a predictor of CRS when controlling for MVPA (Carson and Janssen, 2011). Since type of sedentary activity was not measured in the present study conclusions on sedentary activity types cannot be made. CRS was more strongly correlated with VPA than MVPA or SED; furthermore significant correlations between VPA and CRS A and B remained after controlling for SED. This suggests that VPA may be more important in protecting against CM risk than MVPA, or SED.

UK PA guidelines recommend at least 60 minutes of MVPA daily (Department of Health, 2011). When participants were grouped by whether they met or did not meet these guidelines there were no significant group differences for CRS. There are possible reasons for the lack of differences, firstly due to the low sample size; there may not be appropriate statistical power to observe differences between the groups. Secondly, 60 minutes of MVPA may not be enough to be cardioprotective. The EYHS separated the population into quintiles of PA and found that risk was raised in the lowest three activity quintiles when compared to the most active quintile, and time spent at MVPA in the fourth quintile was 116mins, almost double the recommendations (Andersen et al., 2006). Furthermore, in the present study, VPA had a stronger correlation with clustered

risk than MVPA which suggests that VPA may be more important than MPA in CM risk reduction. There are currently no time recommendations for daily VPA in children; the only recommendation is that children should engage in VPA on 3 or more days per week (Department of Health, 2011).

The participants categorised as 'higher' risk in the present study are based on being the highest risk for the population sampled, however this does not necessarily mean that they are clinically at high risk. The EYHS recently recommended fitness levels for metabolic health based on the clustered risk scores from the EYHS population. Recommended VO_{2peak} levels were 37.4 ml/kg/min and 43.6 ml/kg/min in 9 year old girls and boys respectively (Adegboye et al., 2011). In this study, girls in the 'higher' risk group had a mean VO_{2peak} of 34.2 ml/kg/min, and boys had a mean of 36.7 ml/kg/min which is lower than the recommended levels for 9 year olds, which suggests the 'higher' risk participants may have also been classified 'at risk' according to EYHS criteria. Further research is required to accurately classify children as 'at risk' by using clustered risk score using longitudinal designs.

There are several proposed mechanisms which may be responsible for the relationships between increased CRF and increased PA with reduced cardiometabolic risk. Improvements in CRF and higher levels of PA are related to structural and biochemical adaptations in skeletal muscles, such as increased fibre size, improved capillary density and blood flow, improved insulin signalling kinetics, increased myoglobin, increased oxygen uptake and increased lipoprotein lipase which has impacts on several CM risk markers such as glucose homeostasis, insulin resistance, and endothelial function. Evidence suggests that vagus nerve stimulation can moderate inflammatory cytokines through cholinergic anti-inflammatory pathways (Borovikova et al., 2000). Individuals

with increased CRF also have enhanced autonomic nervous system function and therefore it is feasible that increased physical activity and improved CRF may have favourable improvements in the cholinergic anti-inflammatory pathway, via improved autonomic function (Jae et al., 2009). It is also feasible therefore to speculate that exercise training, and improvements in CRF, may reduce CM risk via this impact on inflammatory factors.

Strengths and Limitations

There are limitations within this study. Primarily the study lacked statistical power due to the small sample size. The sample size was small due to poor compliance for some of the measurements used to create a clustered risk score. Because of the small sample size and narrow age range of participants, the results may not be generalised to a wider population. Furthermore, as this study was cross-sectional causality cannot be conferred. In addition, the clustered risk score does not highlight which of the individual risk components contribute the greatest risk, as each variable has equal weighting within the calculation of the score. A further limitation is the exclusion of whole body fat mass as a covariate. As trunk fat was included in CRSA and WC in CRSB, and body mass was accounted for in the VO_{2peak} score, whole body fat mass was excluded to prevent co-linearity within analyses. Finally, although the study includes a range of markers within the risk score, an estimate of systemic inflammation is absent.

However, the evidence obtained does highlight some interesting findings that suggest an increase in VPA and CRF was related to CM risk but further investigation is warranted and future research should include larger sample sizes, and include an estimate of systemic inflammation, such as C-reactive protein, within the clustered risk score. Furthermore, this study was conducted at baseline for a healthy eating and PA intervention and the

impact of this intervention on clustered CM risk will be investigated as part of the CHANGE! study (Chapter 6).

Conclusions

The present study reports clustered risk scores which combined both traditional invasive markers with non-invasive preclinical markers of CM risk. This clustered risk score was significantly related to VPA and CRF. This study further emphasises the importance of promoting CRF and VPA in childhood, especially for those already with increased CM risk. Furthermore, this study provides rationale for an intervention which aims to improve CRF, and promote PA.

Thesis Study Map

Study	Objectives and Key Findings
Study 1: Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.	Objectives: • To investigate the relationships between traditional invasive and non-invasive cardiometabolic risk markers. • To establish the relationships between individual cardiometabolic risk markers and cardiorespiratory fitness (CRF) and physical activity (PA). • To determine which measures would be most appropriate to use in future studies. Key findings: • Relationships are present between invasive markers (CRP and TC: HDL-C +ve relationship; adiponectin –ve relationship) and adiposity measures (whole body fat % and trunk fat mass) • Relationships evident between some risk markers (CRP in boys, HOMA-IR in girls, whole body fat and trunk fat mass)and CRF • Some relationships found between TC: HDL-C and physical activity. • Lack of relationships found between measures of PA (MVPA & VPA) and inflammatory markers or measures of cardiac structure and function, this needs further investigation. • CRP seems to be a good representative marker to measure due to correlations with other markers.
Study 2: Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project	Objectives: • To report clustered risk scores (CRS) that combine traditional invasive with non invasive cardiometabolic risk markers; and to determine the relationships between CRS and objectively measured PA, CRF and body composition. Key Findings: • CRS significantly correlated with CRF. • CRS correlated significantly with VPA after relevant adjustments. • Children categorised as 'High Risk' had significantly lower CRF.

Study 3: The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.	**Objectives:** • **To report baseline characteristics of the whole sample and subsample CHANGE! Participants** • **To assess the effects of the school-based Children's Health Activity and Nutrition Get Educated! (CHANGE!) physical activity and healthy eating intervention on cardiometabolic health in a subsample of 10 to 11 year old children.** • **To investigate the short term (8 to 10 week follow up) effects of the CHANGE! Intervention on cardiometabolic health in 10 to 11 year old children.**

Chapter 6

Study 3:

The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.

Chapter 6: Study 3

6.1. Introduction

Over the last decade childhood obesity has increased and reached plateau in the United Kingdom (UK) (Boddy et al., 2010; Stratton et al., 2007) which, along with poor nutritional intake, low CRF and physical inactivity, increases the risk of developing cardiovascular disease and metabolic syndrome (Andersen et al., 2006; Andersen et al., 2008; Freedman et al., 2007). Furthermore, CRF, an independent risk factor for CM disease and a product of PA, has decreased independent of changes in body size and other confounders (Boddy et al., 2012; Boddy et al., 2010; Stratton et al., 2007).

Current UK guidelines recommend children participate in at least 60 minutes of daily moderate to vigorous intensity PA (MVPA) whilst engaging in VPA at least 3 times per week (Department of Health, 2011). However, few children reportedly meet 60 minutes of MVPA daily (Ness et al., 2007; Riddoch et al., 2007). An intervention which aims to reduce adiposity, and improve CRF, through promotion of increased PA, reduced sedentary time and improved nutritional intake could have a positive impact on reducing CM risk in children. Schools provide an ideal opportunity to implement an intervention since children spend approximately half of their waking hours in school (Fox et al., 2004), and school-based implementation also enables the whole target population to be reached. Health promoting curriculum based interventions have been found to be successful in similar aged children, especially when utilising a multi-disciplinary approach, which combines PA, and diet and uses established behaviour change and social support processes (Greaves et al., 2011). Several intervention studies have aimed to increase PA, reduce sedentary time and improve nutritional intake in children in order to reduce CM

disease risk, often reporting mixed levels of success as discussed in the Literature Review [Table 2-4].

The Children's Health, Activity and Nutrition: Get Educated! (CHANGE!) Project targeted PA and healthy eating through a school-based curriculum intervention delivered by in-service teachers. This approach has previously been utilised in the USA with some degree of success through programmes such as Planet Health (Gortmaker et al., 1999). Behaviour change can often be complex and difficult to sustain (NICE, 2007), there are several health promotion models which have been developed in order to influence positive changes effectively. The model utilised for the CHANGE! study was Green et al's (1980) PRECEDE-PROCEED Planning model. The PRECEDE-PROCEED model provides a comprehensive structure for assessment of health and health needs and for designing and implementing health promotion programmes to meet those emerging needs. PRECEDE (Predisposing, Reinforcing, and Enabling Constructs in Educational Diagnosis and Evaluation) outlines an indicative planning process to assist in the development of targeted and focused health programmes, whist PROCEED (Policy, Regulatory and Organisational Constructs in Educational and Environmental Development) aids in the implementation and evaluation of programmes. A review of reviews of behaviour change intervention studies revealed that the most effective school based PA interventions included printed educational materials and curricula that promoted PA during the whole day (Jepson et al., 2010). Furthermore, health promotion models recognise the importance of knowledge and education in behaviour change, therefore improving knowledge is fundamental to the intervention design.

The aim of this study was to assess the effects of the school-based CHANGE! PA and healthy eating intervention on CM risk in 10 to 11 year old children, at post intervention and again at 8 to 10 weeks follow up.

6.2. Materials and Methods

6.2.1. Participants and Study Design

After receiving institutional ethical approvals 12 primary schools from the Wigan Borough in North West England were recruited to participate within the clustered randomized controlled pilot trial, registered with Current Controlled Trials (ISRCTN03863885). All children within Year 6 (10 - 11.9yrs) were invited to take part in the CHANGE! study from each school (N = 420). At baseline informed consent was received from 318 participants (75.7% participation rate) A stratified random sub-sample of sixty participants (5 participants from each school), were invited to take part in additional study measures. If the selected children did not wish to participate another participant was randomly selected from the volunteers in the school using the random number generator function in SPSS V.17 (SPSS Inc., Chicago, IL.) Approximately 95% of the children were of white British ethnicity, which is representative of the school age population in Wigan (Wigan Council, 2011). Schools were randomised to an intervention (N = 6 schools) or control condition and baseline measures were completed in October 2010. Randomisation occurred prior to baseline measures to allow enough time for the teacher training sessions to take place, and was completed using the random number generator function in SPSS v17 (SPSS Inc., Chicago IL). Post intervention measures were completed after the 20 week intervention period in March and April 2011. Follow up measures were taken 8 to 10 weeks after post intervention, prior to the school summer holidays. One

intervention school dropped out shortly after baseline measurements, there were also some technical issues with some measures hence reduced sample sizes for these risk markers (see Table 6-2). The full flow of subsample participants and schools through the study can be found in Figure 6-1.

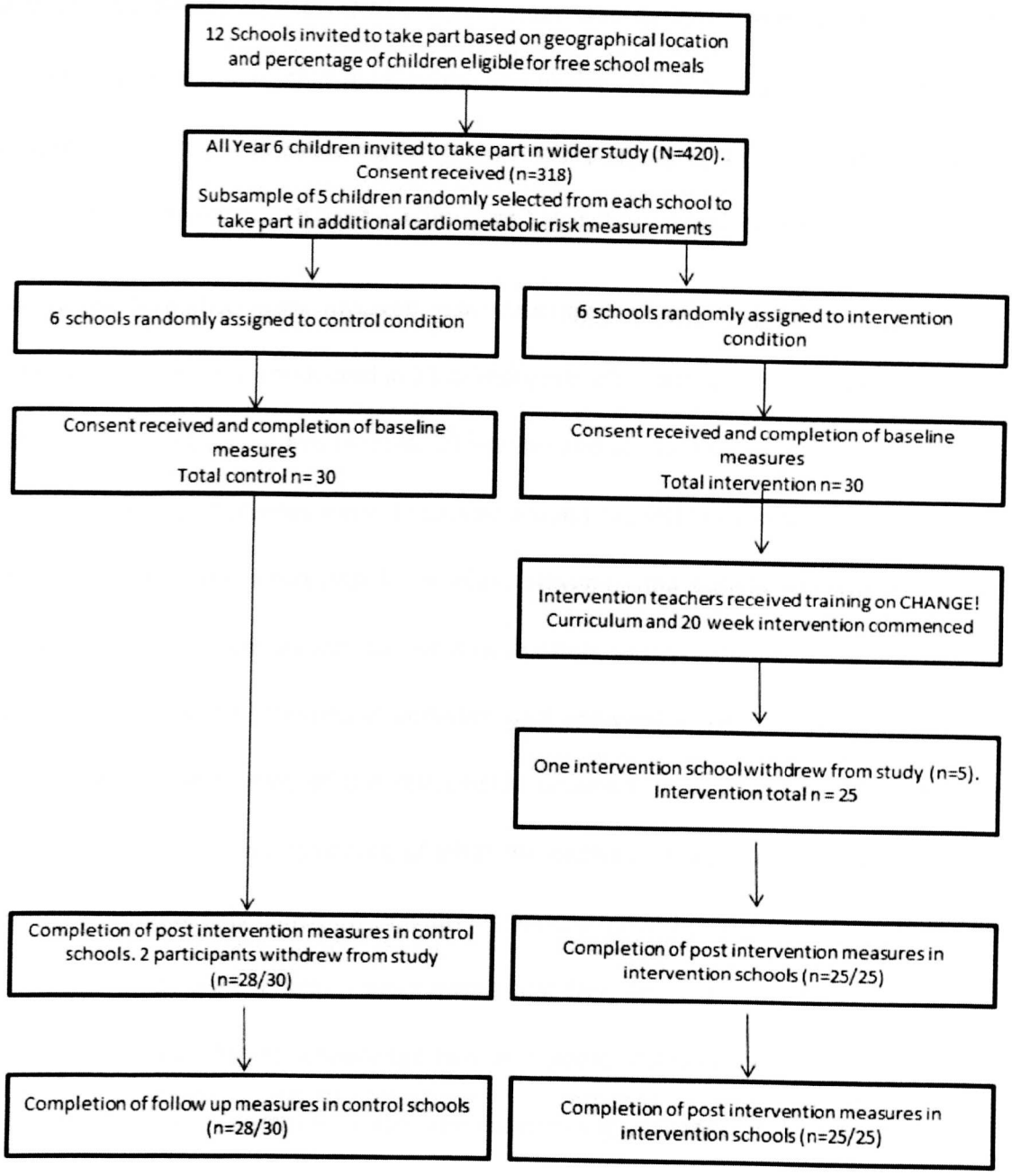

Figure 6-1: Flow of schools and subsample participants through the study

6.2.2. Intervention Design

Health promotion models recognise the importance of knowledge and education in behaviour change; therefore improving knowledge through education was key to the

intervention design. The CHANGE! intervention was designed and adapted from the Planet Health resources that have been used in the USA (Gortmaker et al., 1999). The adaptations were made following formative work (completed by the CHANGE! team in Year 1 of the project) which has been described elsewhere (Mackintosh et al., 2011).

Briefly the formative work involved semi-structured mixed-sex interviews (group and individual) which were conducted in 11 primary schools, with 60 children aged 9-10 years (24 boys, 36 girls), 33 parents (4 male, 29 female) and 10 teachers (4 male, 6 female). The questions for the interviews were structured around the PRECEDE stage of the PRECEDE-PROCEDE model and addressed knowledge, attitudes and beliefs towards PA, eating behaviour and attitudes as well as views on barriers to participation in PA and healthy eating. All data were transcribed verbatim and analysed using Pen Profiles. Analyses revealed an understanding of the relationship between PA and health, although some children had limited understanding of what PA involves. Views elicited by children and parents were generally consistent. Children's knowledge of healthy eating was generally good, specifically many children were aware that fruit and vegetable consumption was 'healthy' (N = 46). Adults' knowledge was also good, including restricting fatty foods, promoting fruit and vegetable intake, and maintaining a balanced diet. Fun, enjoyment and social support were essential predictors of PA participation, and barriers such as lack of parental support were identified across all group interviews. The important role parents play in children's eating behaviours and food intake was evident. It was suggested that barriers to healthy eating were external drivers such as advertising, the preferred sensory experience of "unhealthy" foods, and food being used as a reward.

The Planet Health resources were anglicised, and guidelines for diet and PA were adapted to those specific to the UK. The key findings from the formative work were used to select

the lessons from Planet Health resources, furthermore some of the lessons were adapted for the local context, after seeking copyright permission from the publishers. The CHANGE! topics were aligned with the UK Healthy Schools programme and were cross-referenced to English National Curriculum objectives in Personal Social Health and Economic Education (PSHE) PE, Maths, Science, ICT, English, Geography and History (Qualifications and Curriculum Authority, 1999). In total the CHANGE! Intervention consisted of 20 lesson plans which included worksheets, and other resources, and were also supported by homework tasks which involved the whole family, since the formative work emphasised the importance of family support. The lesson content and themes can be found in Table 6-1. Teachers from the intervention schools attended a 4 hour Wigan Council led training session on delivery of the curriculum resource and therefore were able to familiarise with the resource prior to the intervention commencing.

Table 6-1: CHANGE! Themes, Lessons and content summary

Theme	Resource Lesson	Content Summary
Introduction	Healthy Living	Lifestyle options, choices and consequences; Eatwell Plate
Introduction: What is PA and where do we do it?	'Map Maker' Lifetime activities sheet	PA definitions, intensities, guidelines for health, opportunities in local environment (mapping), types of activities [2 lessons]
Monitoring and Goal Setting	'What does your day look like' Survey the class' Where did the day go?' & 'Go for the goal'	Simple monitoring of PA (diary/pedometers), goal setting principles
Reducing Sedentary Time	'Power down' 'Impact of Technology'	Identifying sedentary behaviours, when they occur, how technology has changed our lifestyles, goal setting for reducing screen time [2 lessons]
Components of Fitness	'Muscle mysteries' 'The Human Heart'	Simplify the concept of fitness as representing 'heart health', 'muscle health', 'body composition', incorporate FITT principle as means of enhancing fitness, basic physiological principles to demonstrate effects of PA on body (e.g. pulse rate, etc) [2 Lessons]
Energy Balance	Keeping the Balance	Fuel; intake; expenditure; balance; negative/positive monitoring; nutrient function and sources
Carbohydrate	Carb Smart	Types; processing; starchy foods; why important; fibre; good sources
Sugar	Sugar Water Beverage Buzz	Terminology & Types; requirement; labels; sources- hidden; amounts; added sugar; consumption calculations
Fat	Hunting Hidden Fat	Terminology & Types; requirement; labels (graphing activity); sources; effect of cooking; fish oils
Fruit & Vegetables	Chain Five Menu Monitoring Alphabet Fruit (& vegetables) Veggie Mania	Benefits (source of variety of nutrients); portions; preparation; variety; storage; cooking; access; other foods containing fruit & vegetables; menu planning
Breakfast	Brilliant Breakfast Breakfast Bonanza	Benefits (energy); portions; choices; sugar; salt; nutritional comparison types of breakfast

Theme	Resource Lesson	Content Summary
Snacks (fat/sugar/salt)	Snack Attack Fast Food Frenzy Snack Decisions	Frequency of eating; swaps; snacks at bedtime requirements; hidden sources of fat/sugar/salt; amounts
Variety	Balancing Act Keeping the Balance	Why variety needed; balanced diet & Eatwell Plate; nutrient functions & sources; food swaps; access; monitoring task
Awareness	Foods Around the World	Food production- growing; local specialities; history; access; food miles; mapping locality
Conclusion		Summary of Principles of Healthy Living

6.2.3. Outcome Measures

Outcome measures were assessed at baseline, post intervention and at 8-10 week follow up. All children completed the following measures in the field:

Anthropometrics and Somatic Maturity: stature, sitting stature, body mass and waist (WC) and hip (HC) circumference were assessed in the field as described in General Methods, Chapter 3, Section 3.6. Somatic maturation was calculated using the Mirwald formula (Mirwald et al., 2002) as described in General Methods, Chapter 3, Section 3.8.

Estimation of Deprivation: To give an estimate of deprivation for each participant, postcodes for the primary address of each participant were collected and indices of multiple deprivation score (IMD) were calculated using Geoconvert (http://geoconvert.mimas.ac.uk/) which uses data from the National Statistics Postcode Database November 2010.

***Physical Activity*:** Habitual PA was objectively measured over a 7 day period as described in General Methods, Chapter 3, Section 3.3. Briefly, PA intensity cut points were 2160 CPM for MPA, 4806 CPM for VPA, sedentary (SED) was defined as less than 100 CPM (Mackintosh et al., 2012). In the whole sample 38 participants at baseline did not meet the inclusion criteria and their MVPA data was coded as missing. Within the subsample 9 participants did not meet the inclusion criteria, 6 at baseline (Control n = 4), 2 post-intervention (Control n = 1), and 1 at follow up (Control n = 1) and their MVPA data were coded as missing.

20 metre Multi-stage shuttle run test (20mSRT): This test provides an estimate of CRF and has been widely used in children of similar age in the past as part of the standardised EUROFIT test battery (Adam et al., 1998; Stratton et al., 2007). The total number of completed shuttles was used as a marker for CRF.

Blood Pressure: After 10 minutes rest, seated blood pressure was assessed on the left arm in the field (Omron Healthcare UK Limited, Milton Keynes, UK), and the mean of two assessments was retained for analysis. If the BP readings were different by more than 10mmHg a third reading was taken and the mean of the second and third was retained for analysis. It has been reported that the coefficient of variation for intra-individual measurements of blood pressure are 9.9% and 9.2% for sBP and dBP respectively (Marshall, 2004).

Additional Subsample measurements:

School based:

Participants also attended a blood sampling session at each school. After verbal confirmation of overnight fasting, seated finger prick capillary blood samples were taken and analysed for TC, HDL-C, and glucose, as described in General Methods, Chapter 3, Section 3.13.

Laboratory based:

Participants in the subsample attended the laboratories for one day on three occasions, at baseline, at post intervention and again at 8 to 10 weeks follow up, and undertook measurements as described in the relevant section of the General Methods Chapter 3, of CRF [Section 3.5], anthropometrics [Section 3.6] and cardiac structure [Section 3.9] and function [Section 3.10] and CIMT [Section 3.11]. At baseline and follow up body composition measurements were assessed using dual energy x-ray absorptiometry (DEXA) as described in General Methods, Chapter 3, Section 3.7. Due to local guidelines on radiation exposure, it was deemed unethical to retest at post intervention as well as at follow up 8 to 10 weeks after the intervention. Therefore body composition data, whole body fat mass (WBFM), relative whole body fat (WBF%), whole body lean mass (WBLM), trunk fat mass (TFM), relative trunk fat mass (TF%) and peripheral fat mass (PFM), relative peripheral fat (PF%), bone mineral content (BMC) and bone mineral density (BMD) are reported at baseline and at follow up only.

Clustered risk scores: Standardized z-scores were calculated separately by sex and summed to create continuous clustered risk scores. This approach has been used previously in similar aged participants (Andersen et al., 2008; Bailey et al., 2012). Two clustered risk scores (CRS A and CRS B) were calculated for each participant as previously explained in Chapter 5 [Section 5.2.2]. Both CRS included TC: HDL-C; glucose; sBP; LV Mass Index ($g/m^{2.7}$). CRS A also included trunk fat mass and CRS B included WC.

The following outcome measures were obtained at all three time points: VO_2Peak, LVM Index, LV diastolic filling (E/A) and septal myocardial tissue velocity (E'A'), and the ratio of early diastolic filling to early diastolic tissue velocity (E/E'), sBP & dBP, CIMT, and CRS B was calculated. DEXA measures were obtained at baseline and follow up and CRS A was calculated.

There were a number of technical issues with some of the measurements and therefore resulted in lower sample sizes for some of the measurements. The issues and final sample sizes for each measurement are described in Table 6-2.

Table 6-2: Measurement issues and final sample size for each variable

Issue	Variables	Sample Size (n) Baseline		Sample Size (after one school withdrew from INT; 2 participants withdrew from CON) Data for all 3 time points		Did the removed participants differ from population for anthropometrics (BMI & WC)?	Did the removed participants differ from population for fitness level?	Did the removed participants differ from the population for PA/ sedentary time?
		CON (N=30)	INT (N=30)	CON (N=28)	INT (N=25)			
Blood sampling specimen failed to react or failed to withdraw sufficient quantity of blood	Blood Markers:							
	TC	19	12	11	8	No	No	SED at post only[1]
	HDL-C	19	12	11	8	No	No	SED at post only[1]
	TC:HDL-C	19	12	11	8	No	No	SED at post only [1]
	Glucose	19	12	12	8	No	No	SED at post only [1]
Children failed to meet PA inclusion criteria	PA & Sedentary data	26	28	22	22	No	No	
Children failed to reach RER of >1.05 to indicate peak	VO_2 Peak	29	29	26	23	No		No
Ultrasound image quality did not meet required standard for accurate anatomical definition	LVM	28	26	25	20	No	Yes at baseline & post[2]	No
	E/A	27	28	25	22	Yes[3]	Yes at baseline & post[4]	No
	E'/A'	28	29	25	23	Yes[5]	Yes at baseline & post[6]	MVPA post, SED baseline & follow up[7]
	E/E'	27	28	25	22	Yes[3]	Yes at baseline & post[4]	No
	IMT	25	21	22	21	No	No	No

Notes from Table 6-2:

ANOVA revealed the following differences between excluded and included participants highlighted in Table 6-2 above.

1. Those excluded from the bloods markers were less sedentary at post intervention than those included (Excl. = 498.5 (61.9); Incl. = 510.1 (58.8) min. p=0.034). There were no significant differences for PA, or SED at other time points.

2. Those excluded were less fit at baseline than those included (Excl. = 34.6 (10.2); Incl. = 44.4 (9.2) ml/kg/min, p=0.019) and post intervention (Excl. 39.8 (6.8); Incl. 47 (6.8) ml/kg/min).

3. Those that were excluded had higher BMI (Baseline: Excl. 20.8 (3.8); Incl. 17.5 (2.5) p =0.003; Post: Excl. 21 (3.4); Incl. 17.7 (2.5)p=0.003; Follow up (Excl. 21.2 (4.2), Incl. 17.5 (2.5)p=0.002), and higher WC (Baseline: Excl. 71.0 (12.6), Incl. 60.8 (5.7)p=0.001; Post: Excl. 72.2 (12) Incl. 61.3, p<0.001); Follow up: Excl. 71.7 (11.6); Incl. 61.6 (6.1) p=0.004)

4. Those that were excluded were less fit at baseline and post intervention than those included (Baseline: Excl. 34 (14); Incl. 44.5 (8.5), p=0.012; Post: 39 (10.2); 47.1 (6.2), p=0.008)

5. Those that were excluded had higher BMI (Baseline: Excl. = 21.2 (4); Incl. = 17.5 (2.4) p=0.002; Post: Excl. = 21.3 (3.6); Incl. 17.7 (2.5) p=0.003; Follow up: Excl. =21.6 (4.5); Incl. = 17.6 (2.4)p=0.001) and higher WC at all three time points (Baseline: Excl. =73.0 (13)cm , Incl. 60.8 (5.6)cm p<0.001; Post Excl. = 74.1 (12.3)cm; Incl. = 61.4 (5.6)cm, p<0.001; Follow up: Excl = 72.3 (12.2)cm; Incl. = 61.6 (6)cm p=0.002)

6. Those that were excluded were less fit at baseline (Excl. 29.3 (9); Incl. 44.7 (8.6), <0.001) and post (Excl. 35.4 (5.8), Incl. 47.1 (9.2), p<0.001)

7. Those that were excluded participated in less MVPA at post intervention (Excl. 50.5 (16.8) min. Incl. 71.2 (20.9) min. p=0.038), they were also more sedentary at baseline and follow up (Baseline: Excl. 553.4 (48.8) min, Incl. 496.2 (59) p=0.045; Follow up: Excl. 575.6 (56.5), Incl. 502.3 (68.7) min. p=0.028).

6.2.4. Statistical Analysis

Descriptive Characteristics

All analyses were conducted using SPSS V.17 (SPSS Inc., Chicago, IL.). Baseline characteristics of the whole population are described to demonstrate the differences between the whole sample and subsample participants. Data were initially explored for normality using the Kolmogorov-Smirnov test. A number of measures in the whole sample were not normally distributed (sitting height, mass, WC, HC, Waist: Hip, BMI, sBP, dBP, Bleep Test score, LPA, MPA, VPA, MVPA), however since ANOVA is relatively robust to violations of the normality assumption, data were not transformed (Vincent, 2005).

Whole sample and subsample differences and differences between boys and girls at baseline were assessed using one way analysis of variance (ANOVA). Differences between participants in the intervention and control groups at each time point were assessed using ANCOVA with somatic maturation and sex as covariates.

Intervention effects

Change scores between baseline and post intervention, between baseline and follow up, and between post intervention and follow up were calculated for each measure.

Baseline to post intervention: Group differences between mean change scores were assessed using one way analysis of covariance (ANCOVA) with sex, somatic maturity at baseline, change in maturation between time points, IMD, school and baseline measure value as covariates. The unadjusted mean change scores and mean change scores adjusted for covariates are reported in Table 6-8, Table 10-1, Table 10-2, and Table 10-3.

Baseline to follow up changes: Group differences between mean change scores were assessed using one way analysis of covariance (ANCOVA) with sex, somatic maturity at baseline, change in maturation between time points, IMD, school and baseline measure value as covariates. The unadjusted mean change scores and mean change scores adjusted for covariates are reported in Table 6-8, Table 6-9, Table 10-1, Table 10-2, and Table 10-3.

Post intervention to follow up changes: Group differences between mean change scores were assessed using one way analysis of covariance (ANCOVA) with sex, somatic maturity at post intervention, change in maturation between time points, IMD, school and post intervention measure value as covariates. The unadjusted mean change scores and mean change scores adjusted for covariates are reported in Table 6-8, Table 10-1, Table 10-2, and Table 10-3.

This method has been recommended for use in RCTs, and generally has greater statistical power than other methods when analysing the effects of randomised control trials (Vickers and Altman, 2001).

At baseline 6 participants in the control group and 9 participants in the intervention group did not meet CRF guidelines for optimal CM health, as defined by Adegboye et al., (2011). Therefore in addition these participants have been analysed separately to determine if the intervention had a greater impact on those that were deemed to be at

higher risk at baseline. ANCOVAs of mean changes between time points was performed using the same method described above. The results can be found in Appendix A.

6.3. Results

At baseline, ANOVA showed that participants in the subsample did not differ from the wider sample group for anthropometric measures, seated BP, SED, PA or CRF as assessed by bleep test shuttles completed ($p > 0.05$). Within the whole sample there were significant differences between boys and girls. Girls were more mature ($p < 0.001$), had greater body mass ($p = 0.033$), hip circumference ($p < 0.001$), BMI ($p = 0.013$), and were more sedentary ($p = 0.003$), they had lower waist: hip ratio ($p < 0.001$), completed less shuttles in the 20m SRT ($p < 0.001$), and accumulated less MPA, VPA and MVPA ($p < 0.001$) compared to boys. Table 6-3 shows baseline characteristics of the whole sample, non-subsample and subsample participants and demonstrates significant differences between boys and girls.

Groups were well matched for most variables, however ANCOVA with covariates of sex and somatic maturation as covariates, revealed that subsample participants in the control group were of significantly shorter stature at baseline ($p = 0.005$), and had significantly greater BMI at baseline ($p = 0.035$) and post intervention ($p = 0.032$). sBP was significantly higher in the control group at baseline ($p = 0.034$) and post intervention ($p = 0.035$). dBP was also significantly higher in the control group at post intervention ($p = 0.001$). E'A' was significantly higher in the intervention group at post intervention ($p = 0.025$).

Table 6-3: Differences between subsample and non-subsample participants at baseline

		Non Subsample			Subsample			Whole Sample		
	Sex	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)
Age	Girl	133	10.64	-0.32	34	10.63	-0.3	167	10.64	-0.31
	Boy	120	10.64	-0.32	25	10.58	-0.24	145	10.63	-0.31
	Total	253	10.64	-0.32	59	10.61	-0.28	312	10.63	-0.31
Stature (m)	Girl	133	1.433	-0.08	34	1.461	-0.076	167	1.439	-0.08
	Boy	120	1.439	-0.069	25	1.435	-0.071	145	1.438	-0.069
	Total	253	1.436	-0.075	59	1.45	-0.074	312	1.439	-0.075
Sitting stature (m)	Girl	133	0.715	-0.048	34	0.723	-0.048	167	0.716	-0.048
	Boy	120	0.713	-0.037	25	0.716	-0.03	145	0.713	-0.036
	Total	253	0.714	-0.043	59	0.72	-0.041	312	0.715	-0.043
Mass (kg)	Girl	133	38.36	-9.95	34	39.11	-9.35	167	38.51	-9.81
	Boy	120	36.33	-7.88	25	35.75	-6.43	145	36.23*	-7.63
	Total	253	37.39	-9.07	59	37.69	-8.35	312	37.45	-8.92
WC (m)	Girl	133	0.621	-0.084	34	0.626	-0.08	167	0.622	-0.083
	Boy	120	0.619	-0.072	25	0.61	-0.062	145	0.617	-0.07
	Total	253	0.62	-0.079	59	0.619	-0.073	312	0.62	-0.077
HC (m)	Girl	133	0.705	-0.093	34	0.715	-0.097	167	0.707	-0.093
	Boy	120	0.67	-0.077	25	0.672	-0.061	145	0.670**	-0.074
	Total	253	0.688	-0.087	59	0.697	-0.086	312	0.69	-0.087
Waist: hip	Girl	133	0.88	-0.05	34	0.88	-0.04	167	0.88	(0.04
	Boy	120	0.92	-0.04	25	0.91	-0.04	145	0.92**	-0.04
	Total	253	0.9	-0.05	59	0.89	-0.04	312	0.9	-0.05
BMI	Girl	133	18.52	-3.71	34	18.16	-3.25	167	18.45	-3.62
	Boy	120	17.45	-2.93	25	17.3	-2.21	145	17.43*	-2.82
	Total	253	18.01	-3.4	59	17.79	-2.87	312	17.97	-3.3
BMI SDS	Girl	133	0.23	-1.34	34	0.15	-1.2	167	0.21	-1.31
	Boy	120	0.07	-1.32	25	0.14	-1	145	0.08	-1.27
	Total	253	0.15	-1.33	59	0.15	-1.11	312	0.15	-1.29
IMD Score	Girl	133	26.21	-17.13	34	26.66	-18.47	167	26.3	-17.36
	Boy	120	26	-16.9	25	25.72	-15.14	145	25.95	-16.56
	Total	253	26.11	-16.99	59	26.26	-17	312	26.14	-16.96
systolic BP (mmHg)	Girl	133	110	-17	34	112	-15	167	110	-16
	Boy	120	113	-15	25	117	-17	145	114	-15
	Total	253	111	-16	59	114	-16	312	112	-16
diastolic BP (mmHg)	Girl	133	69	-19	34	70	-19	167	69	-19
	Boy	120	72	-17	25	74	-21	145	72	-17
	Total	253	70	-18	59	72	-20	312	71	-18
20m SRT (shuttles)	Girl	129	24	-13	33	25	-12	162	24	-12
	Boy	114	35	-19	24	35	-18	138	35**	-19
	Total	243	29	-17	57	29	-16	300	29	-17

		Non Subsample			Subsample			Whole Sample		
	Sex	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)
Sedentary (min.)	Girl	128	520.4	-58.2	33	511.7	-48.1	161	518.6	-56.2
	Boy	109	497	-66.5	21	500	-69	130	497.5*	-66.6
	Total	237	509.6	-63.1	54	507.2	-56.8	291	509.2	-61.9
Light PA (min.)	Girl	128	173.9	-27.2	33	173.2	-25.9	161	173.8	-26.9
	Boy	109	178.8	-30.2	21	171.2	-30.5	130	177.6	-30.3
	Total	237	176.2	-28.7	54	172.4	-27.5	291	175.5	-28.4
MPA (min)	Girl	128	40.7	-11.8	33	41.6	-10.6	161	40.9	-11.6
	Boy	109	52.1	-13.6	21	54.8	-16.5	130	52.5**	-14.1
	Total	237	46	-13.9	54	46.8	-14.6	291	46.1	-14
VPA (min)	Girl	128	12.5	-6.6	33	13.5	-5.2	161	12.7	-6.4
	Boy	109	17.1	-8.1	21	21.7	-9.9	130	17.9**	-8.6
	Total	237	14.6	-7.7	54	16.7	-8.4	291	15	-7.9
MVPA (min)	Girl	128	53.3	-15.9	33	55.1	-14.1	161	53.7	-15.5
	Boy	109	69.2	-19.2	21	76.5	-24	130	70.4**	-20.1
	Total	237	60.6	-19.1	54	63.5	-21.2	291	61.1	-19.5
Somatic Maturity	Girl	134	-1.32	-0.58	34	-1.21	-0.57	168	-1.3	-0.58
	Boy	121	-3.07	-0.45	26	-3.07	-0.34	147	-3.07**	-0.43
	Total	255	-2.15	-1.02	60	-2.02	-1.05	315	-2.13	-1.02

Boys significantly different to girls* P<0.05 ** p<0.001

MPA= Moderate intensity physical activity; MVPA= Moderate to vigorous intensity physical activity. LPA = Light intensity physical activity; VPA= vigorous intensity physical activity

Table 6-4 shows unadjusted means (SD) for descriptive characteristics at baseline, post intervention and follow up. Table 6-5 shows unadjusted means (SD) for CM risk markers at baseline, post intervention and follow up. Table 6-6 shows unadjusted means (SD) for CRF and PA at baseline, post intervention and follow up. Table 6-7 shows unadjusted means (SD) for body composition measures at baseline, and follow up.

Table 6-4: Unadjusted means for anthropometrics at baseline, post intervention and follow up

		Control			Intervention		
		n	mean	(SD)	n	mean	(SD)
Age	Baseline	28	10.58	(0.26)	25	10.6	(0.3)
	Post Intervention		10.9	(0.26)		11.1	(0.3)
	Follow Up		11.1	(0.26)		11.3	(0.3)
Maturity Offset	Baseline	28	-1.98	(1.00)	25	-2.08	(1.14)
	Post Intervention		-1.50	(0.92)		-1.51	(1.16)
	Follow Up		-1.70	(1.50)		-1.34	(1.19)
Stature (m)	Baseline	28	1.430	(0.053)	25	1.452	(0.092)**
	Post Intervention		1.444	(0.052)		1.462	(0.091)
	Follow Up		1.464	(0.051)		1.478	(0.092)
Sitting Stature (m)	Baseline	28	0.756	(0.026)	25	0.752	(0.041)
	Post Intervention		0.762	(0.025)		0.761	(0.053)
	Follow Up		0.767	(0.026)		0.768	(0.053)
Mass (kg)	Baseline	28	39.0	(9.4)	25	36.8	(7.7)
	Post Intervention		40.5	(9.3)		38.7	(8.2)
	Follow Up		41.4	(9.5)		39.9	(8.2)
BMI	Baseline	28	18.93	(3.41)	25	17.31	(2.4)*
	Post Intervention		19.25	(3.32)		17.91	(2.51)*
	Follow Up		19.21	(3.34)		18.07	(2.42)
WC (cm)	Baseline	27	62.9	(8.8)	25	61	(5.6)
	Post Intervention		64.1	(8.7)		61	(5.3)
	Follow Up		63.8	(8.5)		61.4	(5.9)
HC (cm)	Baseline	27	70.1	(9.7)	25	68.7	(8.1)
	Post Intervention		72.3	(9.4)		70.0	(6.7)
	Follow Up		72.5	(8.5)		69.6	(6.7)
WC:HC	Baseline	27	0.89	(0.04)	25	0.89	(0.05)
	Post Intervention		0.89	(0.04)		0.87	(0.04)
	Follow Up		0.88	(0.04)		0.88	(0.05)

* Intervention Group significantly different to control group $p<0.05$; ** $p<0.01$

Table 6-5: Unadjusted means (SD) for CM risk markers by group at baseline, post and follow up (* Intervention group significantly different to control group p<0.05; **Intervention group significantly different to control group p<0.01)

Risk Marker	Time Point	Control			Intervention		
		n	Mean	(SD)	n	Mean	(SD)
sBP (mmHg)	Baseline	28	118	(17)	25	108	(15)*
	Post		113	(14)		105	(13)*
	Follow Up		110	(11)		107	(8)
dBP (mmHg)	Baseline	28	75	(20)	25	66	(20)
	Post		72	(19)		58	(9)**
	Follow Up		63	(12)		60	(7)
LV Mass Index ($g/m^{2.7}$)	Baseline	25	34.2	(8.4)	20	36.5	(8.1)
	Post		39.3	(10.4)		41.1	(8.2)
	Follow Up		34.1	(7.4)		39.1	(9.5)
E/A	Baseline	25	2.37	(0.38)	22	2.41	(0.52)
	Post		2.48	(0.51)		2.58	(0.79)
	Follow Up		2.51	(0.40)		2.49	(0.56)
E'/A'	Baseline	25	2.89	(0.63)	23	2.90	(0.72)
	Post		2.68	(0.66)		3.58	(1.68)*
	Follow Up		2.97	(0.90)		2.80	(0.61)
E/E'	Baseline	25	6.40	(1.07)	23	6.77	(1.47)
	Post		6.96	(1.23)		7.37	(2.81)
	Follow Up		6.66	(1.08)		6.96	(1.38)
CIMT (mm)	Baseline	22	0.428	(0.048)	21	0.411	(0.062)
	Post		0.424	(0.044)		0.418	(0.035)
	Follow Up		0.414	(0.067)		0.428	(0.062)
TC (mmol/L)	Baseline	11	4.29	(0.65)	8	4.01	(0.370
	Post		3.95	(0.48)		3.96	(0.270
	Follow Up		4.14	(0.67)		3.99	(0.38)
HDL-C (mmol/L)	Baseline	11	1.29	(0.14)	8	1.48	(0.30)
	Post		1.35	(0.19)		1.55	(0.31)
	Follow Up		1.31	(0.28)		1.36	(0.35)
TC:HDL-C	Baseline	11	3.36	(0.62)	8	2.75	(0.37)
	Post		2.98	(0.60)		2.64	(0.52)
	Follow Up		3.28	(0.64)		3.10	(0.25)
Glucose	Baseline	12	4.96	(0.40)	8	4.73	(0.37)
	Post		5.11	(0.52)		4.84	(0.52)
	Follow Up		4.85	(0.61)		4.78	(0.25)
CRS A (trunk fat)	Baseline	11	1.42	(2.58)	8	-1.15	(3.07)
	Post		NA	NA		NA	NA
	Follow Up		0.31	(2.03)		0.15	(2.08)
CRS B (WC)	Baseline	10	1.49	(2.63)	8	-1.16	(3.24)
	Post		1.79	(2.43)		-0.38	(3.11)
	Follow Up		0.30	(2.18)		0.00	(2.54)

Table 6-6: Unadjusted means (SD) for CRF and PA measures by group at baseline, post intervention and follow up

Measure	Time Point	Control			Intervention		
		n	mean	(SD)	n	mean	(SD)
VO_{2peak} (ml/kg/min)	Baseline	26	42.5	(9.7)	23	43.9	(10.0)
	Post		46.5	(6.8)		45.6	(7.7)
	Follow Up		44.0	(8.0)		49.0	(10.4)
Sedentary (mins)	Baseline	22	514.1	(58.6)	22	483.8	(59.3)
	Post		506.0	(59.4)		489.9	(71.7)
	Follow Up		509.4	(78.6)		509.4	(65.9)
LPA (mins)	Baseline	22	171.9	(19.5)	22	173.7	(26.3)
	Post		174.3	(20.8)		168.7	(26.2)
	Follow Up		179.9	(30.7)		180.4	(30.7)
MPA (mins)	Baseline	22	43.5	(11.9)	22	50.9	(17.3)
	Post		45.7	(12.9)		52.7	(13.4)
	Follow Up		49.4	(16.3)		53.2	(17.0)
VPA mins)	Baseline	22	16.4	(9.1)	22	17.3	(8.1)
	Post		18.4	(8.9)		21.7	(12.8)
	Follow Up		17.4	(8.8)		19.6	(13.5)
MVPA (mins)	Baseline	22	59.8	(20.0)	22	68.2	(23.7)
	Post		64.0	(20.5)		74.4	(22.1)
	Follow Up		66.8	(24.0)		72.9	(27.0)

Table 6-7: Unadjusted mean (SD) for body composition measures at baseline and follow up.

Measure	Time point	Control			Intervention		
		n	Mean	(SD)	n	Mean	(SD)
Whole Body Fat Mass (kg)	Baseline	28	10.72	5.96	25	9.15	4.16
	Follow Up		11.95	6.41		10.44	4.33
Whole Body Fat %	Baseline	28	25.79	7.53	25	23.70	5.99
	Follow Up		27.15	7.81		24.95	5.91
Trunk Fat Mass (kg)	Baseline	28	3.73	2.75	25	2.86	1.73
	Follow Up		4.36	3.10		3.38	1.72
Trunk Fat %	Baseline	28	20.35	7.87	25	17.53	5.94
	Follow Up		22.14	8.51		18.76	5.68
Peripheral Fat Mass (kg)	Baseline	28	6.20	3.18	25	5.51	2.48
	Follow Up		6.79	3.23		6.27	2.62
Peripheral Fat %	Baseline	28	31.57	9.44	25	29.39	8.07
	Follow Up		32.99	9.32		31.20	8.20
Whole Lean Body Mass	Baseline	28	28.67	4.00	25	28.02	4.52
	Follow Up		29.88	3.89		30.13	5.11
BMC	Baseline	28	1162.72	135.55	25	1175.96	142.98
	Follow Up		1244.78	154.37		1263.30	182.16
BMD	Baseline	28	0.85	0.06	25	0.86	0.05
	Follow Up		0.87	0.06		0.88	0.06

Intervention Effects

Table 6-8 shows actual and adjusted mean changes for the significant measures between baseline and post intervention, between baseline and 8 to 10 weeks follow up and between post intervention and 8 to 10 weeks follow up. Table 6-8 shows actual and adjusted mean changes for the significant variables. Table 6-9 shows actual and adjusted mean changes for body composition measures between baseline and 8 to 10 weeks follow up.

Table 10-1, Table 10-2, Table 10-3 (Appendix A) show actual and adjusted mean changes for all measures between baseline and post intervention, between baseline and 8 - 10 week follow up and between post intervention and 8 - 10 week follow up.

Changes between baseline and post intervention

The intervention had a positive impact on WC, with adjusted WC reducing by 0.1cm in the intervention group, and increasing by 1.4cm in the control group at post intervention. After relevant covariates were accounted for (maturity offset at baseline, change in maturity between time points, IMD, sex and baseline values), the change in WC was significantly different in the intervention group than in the control group ($F(1, 44) = 8.119$, $p = 0.007$) [Table 6-8]. There was a significant difference between groups for change in dBP between baseline and post intervention, with adjusted dBP decreasing by 14 mmHg in the intervention group and increasing by 3 mmHg in the control group ($F(1, 44) = 10.343$, $p=0.002$) [Table 10-2]. There were no statistically significant group differences for any of the other CM risk markers, or for measures of PA and CRF.

There were a number of significant covariates in the ANCOVA models for change between baseline and post intervention. Change in maturity had a positive interaction with several of the measures, including age, mass, sitting stature (Table 10-1) and IMT (Table 10-2). Values at baseline had a negative interaction with several of the measures, including sitting stature, HC, WC: HC (Table 10-1), sBP, dBP, E/A, E/E', IMT, TC (Table 10-2), $VO_{2\ Peak}$, SED, LPA, and MVPA (Table 10-3). Baseline maturity also had a positive interaction with sitting stature (Table 10-1), sBP, E'A' (Table 10-2), and VO_2 Peak (Table 10-3). Sex had a positive interaction with sitting stature (Table 10-1) and sBP (Table 6-9). School had a positive interaction with mass (Table 10-1). IMD had a negative interaction with E/A (Table 10-2).

Changes between post intervention and follow up

There was a positive impact on CRF at follow up, with an increase in adjusted VO_{2peak} in the intervention group of 3.8 ml/kg/min. VO_{2peak} decreased in the control group by 2.8 ml/kg/min between post intervention and follow up. This group difference was significant after relevant covariates were accounted for (maturity offset at post intervention, change in maturity between time points, IMD, sex and post intervention values), ($F(1, 41) = 28.051$, $p<0.001$) [Table 6-8]

There were a number of significant covariates in the ANCOVA models for change between post intervention and 8-10 week follow up. Values at post intervention had a negative interaction with HC, WC: HC, dBP, LV Mass Index, E/A, E/E', Glucose, CRS B (WC) (Table 10-2), SED, LPA, MPA, VPA, and MVPA (Table 10-3). Change in maturity had a positive interaction with glucose (Table 10-2). Maturity at post intervention had a negative interaction with glucose (Table 10-2). School had a positive interaction with sitting stature

(Table 10-1), and MVPA (Table 10-3). IMD had a positive interaction with HDL-C (Table 10-2). Sex had a positive interaction with MPA (Table 10-3).

Changes between baseline and follow up

There were no significant differences between groups for changes between baseline and follow up for any of the measures.

Between baseline and follow up the difference between groups for change in VO_{2peak} was close to significance (p=0.054). The intervention group increased adjusted VO_{2peak} by 6.1 ml/kg/min and the control group only increasing by 0.7 ml/kg/min. The positive intervention effects observed for WC at post intervention were not significant when assessing changes from baseline to follow up, with both groups change in WC adjusted to 0.7cm [Table 6-8]. The adjusted body composition (DEXA) measures showed favourable improvements in the intervention group in comparison to the control group; however none of these changes showed statistical significance (p > 0.05) [Table 6-9]. WBFM increased by 1.08 kg in the intervention group and by 1.92 kg in the control group, and %WBF actually reduced in the intervention group by 0.33 %, whereas the control group increased by 2.77 %. There was a slight increase in TFM of 0.19kg in the intervention group, and a bigger increase of 0.92 kg in the control group. TF% reduced in the intervention group by 0.62 % and increased by 3.43 % in the control group, and this group difference was close to statistical significance (p = 0.079). PFM also increased less in the intervention group than the control group, with the intervention increasing by 0.31 kg, and control group by 0.99 kg. PF% decreased by 0.07 % in the intervention group and increased by 3.1% in the control group. Furthermore, whole lean body mass increased

more in the intervention group than the control group (Intervention group 2.1 kg, control group 1.21 kg).

However there were a number of significant covariates in the ANCOVA models. Values at baseline had a negative interaction with several of the measures, including sitting stature, HC, WC: HC, (Table 10-1) sBP, dBP, LV Mass Index, E/A, E'/A', E/E', IMT, Glucose, CRS A (trunk) (Table 10-2), VO_2 Peak, LPA, MPA, MVPA, (Table 10-3) and all measures of body composition (WBFM, WBF%, TFM, TF%, PFM, PF%, WBLM) (Table 6-9). Change in maturity had a negative interaction with VO_2 Peak (Table 10-3). Sex had a positive interaction with sitting stature (Table 10-1) and MPA (Table 10-3). School had a positive interaction with mass (Table 10-1), E/A (Table 10-2), VO_{2peak}, and MPA (Table 10-3). IMD had a positive interaction with HDL-C (Table 10-2).

Table 6-8: Unadjusted change and adjusted change (Δ) between time points for significant variables. When covariates are included in the model these are reported as adjusted changes.

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
Age	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.34	(0.03)		0.46	(0.01)			Change in Maturity	0.04 (p=0.035)
		Adj. Δ Mean (SE)[95%CI]	0.34	(0.00)	[0.33, 0.34]	0.46	(0.00)	[0.45, 0.47]	<0.001		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.55	(0.02)		0.69	(0.010			NA	
		Adj. Δ Mean (SE)[95%CI]	0.55	(0.00)	[0.54, 0.55]	0.69	(0.00)	[0.68, 0.7]	<0.001		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.21	(0.02)		0.23	(0.01)			Change in Maturity	0.004 (p=0.041)
		Adj. Δ Mean (SE)[95%CI]	0.21	(0.00)	[0.21, 0.22]	0.23	(0.00)	[0.22, 0.23]	<0.001		
WC (cm)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	1.2	(1.2)		0	(2.1)			NA	
		Adj. Δ Mean (SE)[95%CI]	1.4	(0.30)	[0.7, 2.1]	-0.1	(0.4)	[-0.9, 0.6]	0.007		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.89	(2.38)		0.56	(2.20)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.7	(0.50)	[-0.2, 1.7]	0.7	(0.5)	[-0.3, 1.7]	0.981		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.30	(2.00)		0.44	(2.10)			IMD	0.000 (p=0.045)
		Adj. Δ Mean (SE)[95%CI]	-0.5	(0.40)	[-1.4, 0.3]	0.70	(0.40)	[-0.2, 1.6]	0.084		

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
dBP (mmHg)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-2	(27)		-8	(21)			Baseline	-0.981 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	3	(3)	[-4, 9]	-14	(3)	[-21, -7]	0.002		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-11	(23)		-6	(18)			Baseline	-0.919 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	-7	(2)	[-11, -2]	-10	(2)	[-15, -6]	0.278		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-9	(17)		3	(12)			Post	-0.776 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	-3	(2)	[-7, 2]	-4	(2)	[-9, 0]	0.644		
VO_{2peak} (ml/kg/min)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	4.0	(7.05)		1.7	(8.5)			Baseline	-0.696 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	3.3	(0.91)	[1.5, 5.2]	2.5	(0.98)	[0.5, 4.5]	0.566	Baseline Maturity	-4.548 (p=0.003)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	1.5	(9.4)		5.1	(12.6)			Baseline	-0.782 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	0.7	(1.7)	[-2.8, 4.2]	6.1	(1.9)	[2.3, 9.8]	0.054	Change in maturity	-19.9 (p=0.009)
										School	0.806 (p=0.036)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-2.5	(5.7)		3.4	(8.6)			NA	
		Adj. Δ Mean (SE)[95%CI]	-2.8	(1.5)	[-5.9, 0.3]	3.8	(1.6)	[0.5, 7.1]	0.009		

Table 6-9: Unadjusted and adjusted changes (Δ) for DEXA measures between baseline and follow up. When covariates are included in the model these are reported as adjusted changes.

Variable	Changes between baseline and follow up	Control			Intervention			Group Effect p	Sig. covariates in model	B (p)
Whole Body Fat Mass (kg)	Unadjusted Δ Mean (SD)	1.23	4.73		1.29	6.42			Baseline	-0.525 (p=0.006)
	Adj. Δ Mean (SE)[95%CI]	1.92	1.01	[-0.12, 3.96]	0.52	1.08	[-1.66, 2.7]	0.383		
Whole Body Fat %	Unadjusted l Δ Mean (SD)	1.36	7.78		1.25	8.85			Baseline	-0.749 (p<0.001)
	Adj. Δ Mean (SE)[95%CI]	2.77	1.35	[0.06, 5.49]	-0.33	1.44	[-3.28, 2.57]	0.15		
Trunk Fat Mass (kg)	Unadjusted Δ Mean (SD)	0.63	2.12		0.52	2.57			Baseline	-0.428 (p=0.014)
	Adj. Δ Mean (SE)[95%CI]	0.92	0.45	[0.02, 1.82]	0.19	0.48	[-0.77, 1.15]	0.304		
Trunk Fat %	Unadjusted Δ Mean (SD)	1.79	8.36		1.22	8.68			Baseline	-0.751 (p<0.001)
	Adj. Δ Mean (SE)[95%CI]	3.43	1.43	[0.55, 6.3]	-0.62	1.53	[-3.7, 2.5]	0.079		
Peripheral Fat Mass (kg)	Unadjusted Δ Mean (SD)	0.59	2.60		0.76	3.90			Baseline	-0.636 (p=0.002)
	Adj. Δ Mean (SE)[95%CI]	0.99	0.67	[-0.16, 2.13]	0.31	0.61	[-0.91, 1.5]	0.453		

Variable	Changes between baseline and follow up	Control			Intervention			Group Effect p	Sig. covariates in model	B (p)
Peripheral Fat %	Unadjusted Δ Mean (SD)	1.4	9.5		1.81	11.9			Baseline	-0.744 (p<0.001)
	Adj. Δ Mean (SE)[95%CI]	3.1	1.7	[-0.3, 6.5]	-0.07	11.8	[-3.7, 3.5]	0.235		
Whole Lean Body Mass	Unadjusted Δ Mean (SD)	1.21	2.51		2.11	7.3			Baseline	-0.672 (p=0.04)
	Adj. Δ Mean (SE)[95%CI]	1.21	0.93	[-0.66, 3.09]	2.10	0.99	[0.10, 4.13]	0.542		
BMC	Unadjusted Δ Mean (SD)	82.05	53.68		87.38	63.57				
	Adj. Δ Mean (SE)[95%CI]	83.79	11.13	[61.37, 106.21]	85.44	11.87	[61.52, 109.35]	0.925	NA	
BMD	Unadjusted Δ Mean (SD)	0.02	0.02		0.02	0.02				
	Adj. Δ Mean (SE)[95%CI]	0.02	0.00	[0.011, 0.029]	0.02	0.01	[0.014, 0.033]	0.611	NA	

6.4. Discussion

This pilot cluster randomised control study aimed to assess the effects of the school-based CHANGE! PA and healthy eating intervention on CM risk in 10 to 11 year old children.

Body size and body composition

There were positive intervention effects for WC at post intervention, which remained significant after covariates were added into the model. Furthermore, at follow up there were favourable improvements in the adjusted body composition (DEXA) measures in the intervention group in comparison to the control group; however none of these changes showed statistical significance ($p > 0.05$) [Table 6-9]. Whole body fat increased by 1.08 kg in the intervention group and by 1.92 kg in the control group, and relative whole body fat actually reduced in the intervention group by 0.33 %, whereas the control group increased by 2.77 %. There was a slight increase in TFM of 0.19kg in the intervention group but relative trunk fat reduced by 0.62%, whereas the control group increased TFM by 0.92 kg which was an increase in TF% of 3.43 %, and this group difference in relative trunk fat (%) was close to statistical significance ($p = 0.079$). PFM also increased less in the intervention group than the control group, with the intervention increasing by 0.31 kg, and control group by 0.99 kg. PF% decreased by 0.07 % in the intervention group and increased by 3.1% in the control group. Whole lean body mass increased in the intervention group by 2.1 kg, and only increased by 1.21 kg in the control group, therefore demonstrating that whilst group difference for change in WC did not remain significant at follow up, this could be explained by the increase in lean mass rather than fat mass. The improvements in body composition observed in the intervention group in the present study may be due to improved nutritional intake, however since dietary

intake is not reported here this is speculative. MVPA also increased more in the intervention group than the control group between baseline and post intervention (Control group adjusted mean (SE) change = 3.7 (3.6) [95% CI -3.6, 11.1] min.; Intervention adjusted mean (SE) change = 6.6 (3.6) [95% CI -0.7, 14] min.), whilst these group differences were not statistically significant, it may be clinically significant and therefore could explain the mechanism for reduced adiposity and increased lean mass.

The results of the present study adds support to the existing evidence of the effectiveness of combined curriculum based PA and nutrition interventions on healthy weight management. The reductions in WCs in the intervention schools at post intervention in the present study suggest that the multidisciplinary approach used in CHANGE! was successful in maintaining healthy weight and reducing the risk of overweight in participants in the short term. The 'Great Fun 2 Run' intervention, similar to CHANGE!, also focused on promoting healthy lifestyles through a 10 month curriculum based intervention in 7 to 11 year old children (Gorely et al., 2009). The 'Great Fun 2 Run' intervention resulted in a slowed rate of WC increase in the older children, who were similar age to the CHANGE! participants (Intervention increased WC by 1.8 cm vs. control increased by 2.8 cm per year) (Gorely et al., 2009) whereas WC in the subsample participants of CHANGE! was actually slightly reduced in the intervention group, whilst control group increased their WC (Adjusted mean (SE) change for Control = +1.4 cm (0.3) [95% CI 0.7, 2.1]; Intervention -0.1 cm (0.4) [95% CI -0.9, 0.6], p=0.006). The Lekker Fit! study in the Netherlands was also similar to CHANGE! in that it focused on promoting healthy nutrition and active lifestyles through a multi-component curriculum intervention (Jansen et al., 2011a). WC of 9-12 year olds reduced at follow-up by 0.71 cm in the intervention group compared to control (Jansen et al., 2011a). There were no statistically significant positive intervention effects on other measures of body size or body

composition within the subsample participants at post intervention or at follow up [Table 10-1; Table 6-9].

Cardiometabolic risk markers

The present study, demonstrated a statistically significant difference in change in dBP between groups from baseline to post intervention, after relevant adjustments (control group adjusted mean (SE) = +3 (3) [95% CI -4, 9] mmHg; intervention group adjusted mean (SE) = -14 (3) 95% CI [-21, -7] mmHg). However, there were no significant group differences for change in dBP between post intervention and follow up; or between baseline and follow up, suggesting this positive change was not maintained. An 8 week curriculum based randomised control study by McMurray et al., (2002) had three intervention groups (exercise only (ExO), education only (EdO), combined education and exercise (EE)) and a control group. The EdO intervention was similar in content to the CHANGE! intervention; however unlike the findings of the present study the EdO group demonstrated a slight increase in dBP at post intervention; yet the increase was significantly smaller than the increase observed in the control group. There was a decrease in dBP in both exercise groups, and the change in dBP in the ExO group was significantly different to the change in dBP in the EdO group, which suggests that inclusion of a prescriptive exercise component within the intervention may be more successful in reducing blood pressure and subsequent CM risk. However other studies who have investigated exercise training effects on blood pressure in children have been inconclusive, a meta-analysis of 12 randomised control trials, with a total of 1266 participants, demonstrated a non-significant reduction in resting blood pressure, of only a 1% and 3% reduction in systolic and dBPs respectively, following exercise intervention

(Kelley et al., 2003). The blood pressure changes observed in the present study may be due to measurement error; however speculative physiological mechanisms for the observed reduction in dBP may be associated to the improvements in waist circumference observed. As discussed in the literature review (Chapter 2, section 2.6) a reduction in adiposity is associated with improved endothelial function, and reduced levels of proinflammatory markers such as CRP, and increased levels of anti-inflammatory markers such as adiponectin. Furthermore adipocytes stimulate release of angiotensin and therefore activating the renin-angiotensin system which leads to hypertension via sympathoexcitation; therefore any reduction in adipose tissue will have positive effects on this system. Since endothelial function and markers of inflammation were not measured these are only speculative mechanisms, and further research is required to understand these mechanisms further.

There were no other significant intervention effects on any of the other CM health markers [Table 10-2]. This was in contrast to other longer term curriculum interventions that resulted in improvements in metabolic markers. A 6 year multidisciplinary curriculum intervention found that there were intervention effects on LDL-C; TC:HDL-C, and LDL:HDL-C (Manios et al., 2002). The CHANGE! intervention may not have been long enough to see such changes in lipid profiles and therefore a longer intervention and longer follow up would be required to assess longer term changes. However, another study which specifically targeted children with at least 2 CV risk factors (low aerobic power, obesity or high TC) found improvements in TC following an 8 week curriculum based intervention (Harrell et al., 1998). The intervention, which consisted of knowledge and attitude education as well as adapted P.E classes, was either delivered with the whole class or to smaller groups with children with known CV risk factors, both types of intervention delivery were successful in reducing TC (-10.1 mg/dL and -11.7 mg/dL) (Harrell et al.,

1998). The CHANGE! project was a whole school approach and children with risk factors were not separated in analysis. Furthermore the CHANGE! intervention did not include any prescriptive PA or exercise training, whereas both Harrel et al., (1998) and Manios et al., (2002) included some form of prescriptive PA element combined with the education aspect of the intervention and therefore this may explain the reasons for no immediate changes in many of the risk markers observed in CHANGE! Furthermore, changes may have been too small to detect because the population was healthy, and the CHANGE! study may have lacked statistical power to detect subtle changes, particularly for the metabolic markers. For the ultrasound measurements the scan quality for some participants was not good enough to provide accurate analysis and therefore participants were excluded from analysis. However, there were a number of significant differences for anthropometrics, fitness and PA measures between those included and those excluded. Participants that were excluded had higher BMI and WC, were less fit, accumulated less MVPA and were more sedentary than those that were included [Table 6-2]. Therefore these participants were arguably at greater CM risk and therefore should scan quality have been improved could have shown the biggest improvements.

Physical activity

Manios et al., (2002) also observed other intervention effects for MVPA at post intervention. However, MVPA was reported by parents at baseline, and self-reported by children at follow up, which raises concern over validity and reliability in comparison to the objective measures of MVPA used in CHANGE! There were no statistically significant intervention effects on PA levels. However both control and intervention groups increased MVPA at post intervention (Control group adjusted mean (SE) change = 3.7

(3.6) [95% CI -3.6, 11.1] min.; Intervention adjusted mean (SE) change = 6.6 (3.6) [95% CI -0.7, 14] min.) the difference between groups was not significant; however MVPA increased more in the intervention group. The improvements demonstrated by both groups could be explained by seasonal effects (Carson and Spence, 2010). The intervention group had a greater increase in VPA than the control group, however again this was not statistically significant (Control group adjusted mean (SE) change = 1.4 (2) [95% CI -2.6, 5.4] min; Intervention group adjusted mean (SE) change = 5, (2) [95% CI 1, 9] min.). This increase in VPA if sustained could lead to clinical benefits. However results at 8 to 10 weeks follow up established that VPA in both groups declined, yet still remained higher than baseline levels. The intervention group at baseline already participated in higher levels of MVPA than the recommended 60 minutes MVPA daily (mean 68.2 (± 23.7) minutes of MVPA daily) (Department of Health, 2011) and therefore this may have created a ceiling effect (Reilly, 2011), hence limiting the scope of the intervention effects on PA.

Cardiorespiratory fitness

Between baseline and post intervention both groups VO_{2peak} increased and there were no significant group differences, this increase observed could be due to familiarisation of the VO_{2peak} protocol, and motivation to 'beat' their previous performance. Throughout the intervention period other activities were not controlled for, therefore the increase in fitness could be as a result of other activities within the borough. However there was a significant group difference in change in VO_{2peak} between post intervention and follow up, with the intervention group increasing VO_{2peak} and control group decreasing VO_{2peak} (mean adjusted change CON = -2.8 ml/kg/min (1.5) [95% CI -5.9, 0.3]; INT= +3.8

ml/kg/min (1.6) [95% CI 0.5, 7.1], p=0.009). This suggests that the CHANGE! intervention may have had a short term impact on the intervention children. When assessing change in $VO_{2\ peak}$ from baseline to follow up the control group slightly increased VO_{2peak} (adjusted mean (SE) change = 0.7 (1.7) [95% CI -2.8, 4.2] ml/kg/min), whereas the intervention group increased $VO_{2\ peak}$ by over 6 ml/kg/min, (adjusted mean (SE) change = 6.1 (1.9) [95% CI 2.3, 9.8] ml/kg/min). Despite this relatively large difference in VO_{2peak} between groups the difference did not quite reach significance (p = 0.054). Other studies have demonstrated an increase in fitness immediately following multi-disciplinary curriculum based interventions (Jansen et al., 2011b; Manios et al., 2002; Slawta and DeNeui, 2009), however fitness was assessed using different methods to CHANGE!, Manios et al., (2002) and Jansen et al., (2011b) used the 20 m SRT and Slawta and DeNeui (2009) used a 1 mile run test to assess CRF rather than directly assessed $VO_{2\ peak}$ which is considered as the reference standard measure. The improvement in $VO_{2\ peak}$ in the intervention group between baseline and follow up equates to an increase of 13.9 %. In a review of 22 aerobic training studies, there was an average improvement in $VO_{2\ peak}$ of 5-6%, and greatest improvements were evident where training intensity exceeded 80% HR max (Baquet et al., 2003). In light of this, the improvement in the present study is particularly high, considering there was no prescriptive PA component to the intervention.

Strengths and Limitations

Over 75% of children invited to take part in the study consented to take part, therefore reducing risk of sampling bias. Randomisation into treatment groups was by school and therefore reducing risk of intervention contamination to control group children. The intervention content was informed by opinions and beliefs of the participants and

stakeholders (Mackintosh et al., 2011) and was relevant to the local context. Furthermore the intervention was a sustainable approach since existing class teachers delivered the lessons, which were able to be integrated into the existing curriculum.

Randomisation into treatment group was limited to clusters (by school) and therefore allows for the possibility of clustering of outcome observations within schools. However, at baseline control and intervention participants were well matched for the majority of outcome measures, furthermore statistical analysis has controlled for baseline results, as well as sex, school, deprivation (IMD), maturity at baseline and change in maturity therefore any baseline differences have been adjusted for, therefore adding strength to the analysis.

Due to time restrictions the order of testing meant that change in age between groups was significantly different. In order to fit the 20 week intervention into the term time intervention participants undertook testing first, followed by control participants, whereas at post intervention the order of testing was reversed.

Teachers received training on how to deliver the intervention lessons; however, there were no on-going procedures in place to monitor progress or to evaluate delivery of lessons. At the end of the intervention feedback was obtained from teachers which highlighted inconsistencies between schools on the delivery of lessons and the number of lessons completed, however these could not be addressed at the time, therefore increasing risk of intervention infidelity. Feedback suggested that lessons were too long for the allocated time and along with pressure of Standard Assessment Tests (SATS) and the fact that PSHE was no longer a compulsory subject, other SATS assessed subjects were prioritised. If the intervention were to be repeated it is recommended that it be adapted for Year 5 children (aged 9 to 10 years) who have less pressure for SATS

curriculum time. Another recommendation for future would be to maintain more regular contact with schools to monitor progress, however due to human resource constraints this was not feasible during the 20 week intervention in this study.

The CHANGE! study used reference standard measurement techniques to assess body composition (DEXA), PA (accelerometry) and CRF (individually calibrated treadmill based VO_{2peak} protocol). In larger scale studies the combination of such high quality measures are rarely utilised. However, the sample size for the subsample was relatively small, particularly for some measures such as the blood markers. This would have therefore reduced statistical power and may account for some between group and time-point differences failing to reach statistical significance, furthermore due to the small sample size and narrow age range of participants, the results may not be generalised to a wider population. A strength of the study was that it included a follow up investigation period. However, this was relatively short (8 to 10 weeks) and a longer term follow up is required to determine whether there were any longer term sustainable influences.

Conclusions

Despite the limitations, the present study demonstrated short-term positive intervention effects for WC and dBP at post intervention and for CRF at follow up. Since the CHANGE! intervention focused mainly on behaviour change, it is possible that any behavioural changes may not have clinical influence immediately after intervention. Furthermore, whilst education is key to behaviour change, other factors also affect behaviour for example the environment and therefore whilst knowledge may improve, if the environment does not support the behaviour change it may not be successful. Therefore longer term follow up research is required in order to establish if behaviour can transition into clinical health benefits over a longer term.

Thesis Study Map

Study	Objectives and Key Findings
Study 1: Relationships between non-invasive and invasive markers of cardiometabolic risk in 10 and 11 year old children, and the relationship of cardiometabolic risk markers with body composition, PA and CRF: The REACH project.	Objectives: • To investigate the relationships between traditional invasive and non-invasive cardiometabolic risk markers. • To establish the relationships between individual cardiometabolic risk markers and cardiorespiratory fitness (CRF) and physical activity (PA). • To determine which measures would be most appropriate to use in future studies. Key findings: • Relationships are present between invasive markers (CRP and TC: HDL-C +ve relationship; adiponectin –ve relationship) and adiposity measures (whole body fat % and trunk fat mass) • Relationships evident between some risk markers (CRP in boys, HOMA-IR in girls, whole body fat and trunk fat mass)and CRF • Some relationships found between TC: HDL-C and physical activity. • Lack of relationships found between measures of PA (MVPA & VPA) and inflammatory markers or measures of cardiac structure and function, this needs further investigation. • CRP seems to be a good representative marker to measure due to correlations with other markers.
Study 2: Clustered Cardiometabolic Risk, Cardiorespiratory Fitness and Physical Activity: The CHANGE! Project	Objectives: • To report clustered risk scores (CRS) that combine traditional invasive with non invasive cardiometabolic risk markers; and to determine the relationships between CRS and objectively measured PA, CRF and body composition. Key Findings: • CRS significantly correlated with CRF. • CRS correlated significantly with VPA after adjustments for time spent sedentary.

	• Children categorised as 'High Risk' had significantly lower CRF
Study 3: The effects of a school based Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum intervention on cardiometabolic risk in 10-11 year old children.	Objectives: • To report baseline characteristics of the whole sample and subsample CHANGE! Participants • To assess the immediate effects of the school-based Children's Health Activity and Nutrition Get Educated! (CHANGE!) physical activity and healthy eating intervention on cardiometabolic health in a subsample of 10 to 11 year old children. • To investigate the short term (8 to 10 week follow up) effects of the CHANGE! Intervention on cardiometabolic health in 10 to 11 year old children. Key Findings: • Waist circumference decreased in the intervention group and increased in the control group between baseline and post intervention, and group differences were significant. • dBP decreased in the intervention group and increased in the control group between baseline and post intervention. However this significant group difference was not sustained at 8 to 10 week follow up. • Cardiorespiratory fitness was significantly greater in the intervention group at 8 to 10 week follow up. • There were no other significant intervention effects on cardiometabolic risk markers.

Chapter 7

Synthesis of findings

7.1. Recap of thesis

The general aim of this thesis was to investigate the impacts of PA, CRF, body composition and lifestyle education on CM risk in 10-11 year old children. Three studies were included, the first cross sectional study (Chapter 4) provided evidence that relationships were present between some of the invasive and non-invasive markers of CM risk in 10 to 11 year old children, and that these markers were also related to CRF, PA, and sedentary behaviour. This study emphasised and provided support to the existing evidence of risk factors clustering in individuals (Andersen et al., 2003; Bailey et al., 2012). Other studies have demonstrated stronger associations between clustered risk and measures of CRF and PA than when assessing risk markers individually. Furthermore, clustered risk may be more clinically meaningful than investigation of individual risk markers due to the range of structural, functional and biochemical disturbances associated with CM disease, and the day to day variation in individual risk markers (Ruiz et al., 2007a). In light of this evidence, the second cross sectional study of this thesis (Chapter 5) investigated clustered CM risk, in children of the same age group as study 1, by combining invasive markers with non-invasive 'pre-clinical' markers of CM risk into a clustered risk score. Clustered risk scores were negatively correlated with CRF and levels of PA. The evidence provided by these two observational studies, Study 1 (Chapter 4) and Study 2 (Chapter 5), along with other literature, as discussed throughout this thesis, gave rationale for an intervention to reduce negative lifestyle behaviours, of low levels of PA, high levels of sedentary behaviour and poor nutritional balance, with the aims of increasing CRF and maintaining healthy body weight. The final study was a clustered randomised control trial, which investigated the immediate and short term (8 to 10 weeks follow up) effects of the CHANGE! curriculum based multi-disciplinary PA and nutrition intervention, on CM risk in 10 to 11 year old children. Whilst there were some statistically significant intervention

effects on WC and diastolic BP at post intervention these were not sustained at 8 to 10 week follow up. There was however improvements demonstrated in CRF in the intervention group at follow up. Overall this study lacked statistical power and therefore small changes may have been missed in the statistical analysis.

7.2. Overarching Issues

In all three studies the populations were studied without specific exclusion criteria (with the exception of lack of consent/assent or medical conditions that precluded participation) and did not specifically target children who were overweight or obese or of a particular fitness level, the aim was to investigate a 'normal' healthy cross section of the population, with a range of body size, CRF levels and PA levels. Furthermore, the intervention (Study 3) was a whole population approach and participants were not targeted based on body size, fitness, and PA or CM risk parameters. However, the majority of participants in all three studies were relatively fit. In the two cross sectional studies combined, 78% of participants (86% Study 1, and 70% Study 2) achieved the recommended fitness level for CM health (Adegboye et al., 2011). In the intervention study, 77% of the control group and 65% of the intervention group also achieved these fitness recommendations. If the intervention had specifically targeted those who had increased CM risk the intervention may have resulted in different outcomes.

There are no published normative data for children the cardiometabolic markers measured within this thesis, however when comparing participants with cardiometabolic measures obtained in similar aged children of other studies, those included in this thesis were very similar in most measures suggesting that the children may be representative of the population. More research is required to obtain normative data for this population.

In all three studies there was an evident lack of relationships for the preclinical non-invasive markers of risk (LV Mass Index, diastolic function, CIMT) with PA, CRF or lifestyle education intervention. Study 1 however demonstrated relationships between adiposity and diastolic function, which provided rationale to measure these markers. Nevertheless the limited relationships established with these preclinical risk markers suggest that these markers may not be very sensitive. Another explanation for the lack of relationships could be due to exclusion of the more overweight, less fit and less active participants from analysis due to scan quality as alluded to previously.

Other preclinical markers may have been better suited and been more sensitive to changes. Other cross sectional analysis of similar aged children have demonstrated significant relationships between endothelial cell dysfunction, assessed using flow mediated dilation (FMD), and both MVPA and adiposity (Hopkins et al., 2009a). Furthermore other studies have demonstrated improvements in vascular function after relatively short lifestyle interventions in overweight and obese children. A 6 week intervention of either dietary modification alone or dietary modification plus exercise, resulted in improvements in FMD in both intervention groups (Woo et al., 2004). Another study also established that exercise training could normalise endothelial dysfunction in obese children and adolescents independent of dietary modification and in the absence of changes in BMI (Watts et al., 2004). Furthermore, it has been suggested that improvements in endothelial cell dysfunction following exercise training occur before any other changes in CM risk markers in adults (Green et al., 2003). Therefore the results of these studies suggest that FMD may be a more sensitive non-invasive 'preclinical' marker to measure than those chosen in this thesis. It was not feasible to include any further measurements in the studies of this thesis due to human resource constraints.

7.3. Implications for childhood health and policy

Current UK guidelines recommend children participate in at least 60 minutes of daily MVPA (Department of Health, 2011). As study 2 highlighted, this may not be enough to be cardioprotective. Furthermore, VPA had a stronger correlation with clustered risk than MVPA which suggests that VPA may be more important than MPA in CM risk reduction. There are currently no time recommendations for daily VPA in children; the only recommendation is that children should engage in VPA on 3 or more days per week (Department of Health, 2011). Further research is required to determine how much VPA per day should be recommended.

The five leading global risks for all-cause mortality are high blood pressure (accountable for 7.5 m deaths per year), tobacco use (accountable for 5.1 m deaths per year), high blood glucose (accountable for 3.4 m deaths per year), physical inactivity (accountable for 3.2m deaths per year) and overweight and obesity (accountable for 2.8 m deaths per year) (World Health Organisation, 2009). All of these risk factors are modifiable through lifestyle changes, and with the exception of tobacco use have been targeted in the CHANGE! intervention (Study 3). Physical inactivity alone is estimated to cost the UK economy £0.9 billion per year (Scarborough et al., 2011). Therefore, investment in promoting healthy lifestyles is essential in ensuring the future health of children as they develop into adulthood, as well as reducing the economic burden of chronic diseases as a result of these risks. There is a clear need for interventions which are sustainable, and lifestyle education embedded into the school curriculum is a logical and feasible option to reach the whole target population. The previous UK government had planned on making Personal Social Health and Economic Education (PSHE) a compulsory subject; however this was removed from the coalition government's agenda in 2010 (PSHE Association,

2012). The CHANGE! intervention (Study 3) was designed to align with the national curriculum for PSHE, amongst other subjects, and should PSHE be made a compulsory subject in primary schools, this could have a lifelong impact on improving the health of children and future generations of adults.

7.4. Limitations, problems encountered and lessons learnt

The main limitation of all three of the studies was the relatively small sample sizes. However due to financial and logistical constraints the original sample recruited could not be larger. Furthermore there were a number of technical issues which resulted in reduced sample for some markers. In study 2 (Chapter 5) and study 3 (Chapter 6) the main markers affected were the capillary blood markers, TC, HDL-C and Glucose. Furthermore the original plan had been to take enough blood to analyse CRP in addition to lipids and glucose, however due to problems withdrawing sufficient blood from participants, CRP could not be measured. Study 1 (Chapter 4) highlighted several correlations between CRP and other risk markers and with CRF, and therefore the addition of CRP to the clustered risk score would have added strength to the study. Venous blood sampling may have eliminated this problem, as it is easier to withdraw larger quantities of blood and therefore would have allowed for analysis of more risk markers, however finances were restricted and therefore capillary blood sampling was chosen as a pragmatic alternative.

Maturity status of participants can have an influence on physiological parameters and therefore as with any study involving paediatric populations, differences between the maturational statuses of participants can affect results. In this thesis somatic maturity was determined using peak height velocity, and where possible this variable was entered into statistical analysis as a covariate in order to eliminate potential confounding results.

The CHANGE! curriculum was designed to be sustainable in the long term; the lessons were delivered by existing teachers in schools after an initial training session on how to deliver the resource. However, there were no on-going procedures in place to monitor progress or to evaluate delivery of lessons. At the end of the intervention feedback was obtained from teachers which highlighted inconsistencies between schools on the delivery of lessons and the number of lessons completed, however these could not be addressed at the time, therefore there was lack of control over delivery dosage. If the intervention were to be repeated it is recommended that it be adapted for Year 5 children who have less pressure for Standard Assessment Tests (SATS) curriculum time. Another recommendation for future would be to maintain more regular contact with schools to monitor progress.

7.5. Summary and Conclusions

The general aim of this thesis was to investigate the impacts of PA, CRF, body composition and lifestyle education on CM risk in 10-11 year old children. The thesis tackled these aims initially by two cross sectional observational studies, which investigated the relationships of individual risk markers (Study 1), and subsequently clustered CM risk (Study 2), with objective measures of CRF, body composition and PA, followed by a pilot randomised control trial, which aimed to assess the impact of lifestyle education (Study 3) - the Children's Health Activity and Nutrition: Get Educated! (CHANGE!) physical activity and healthy eating curriculum.

The studies mentioned above investigated CM risk from various study designs and overall several relationships were found that highlight need for further investigations. The lessons learnt from the CHANGE! pilot intervention can be used in future intervention

studies, and recommendations for future studies are outlined in Chapter 8. Investment in promoting healthy lifestyles is essential in ensuring the future health of children as they develop into adulthood, as well as reducing the economic burden of chronic diseases as a result of these risks. There is a clear need for interventions which are sustainable, and lifestyle education embedded into the school curriculum is a logical and feasible option to reach the whole target population. If such curriculums were enforced at government level, the success could be greater. Further research is required to evaluate the optimum sustainable intervention to improve children's CM health in the long term.

Chapter 8

Recommendations for Future Work

The findings and problems encountered during the studies included in this thesis have highlighted a number of areas for further research:

1. It is hypothesised that the CHANGE! intervention may have been more successful if it included a prescriptive PA element therefore an investigation to assess the impacts of lifestyle education only, in comparison to a combined lifestyle education with prescriptive PA is proposed with the following recommendations:
    a. Should include measures of CM risk, including those included in Study 3 of this thesis, in addition to FMD, and markers of inflammation through venous blood sampling, to fully understand health and links to PA, CRF and body composition.
    b. Intervention delivered to a younger age group (aged 9 to 10) so that SATS do not have an impact on intervention fidelity
    c. Procedures should be put in place to continually check progress of intervention schools
    d. Include a longer follow up period to assess long term impact.
    e. Future intervention studies should include larger sample sizes to address some of the power issues.
    f. More in depth analysis of nutritional intake is required to fully understand the impact of diet on CM risk; however this will require some pilot work to develop a relevant method.
2. Investigation into methods to accurately and reliably estimate dietary intake in children.

Chapter 9

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Chapter 10

Appendices

APPENDIX A

Results tables from Chapter 6

Table 10-1: Unadjusted change and adjusted change between time points for anthropometrics. When covariates are included in the model these are reported as adjusted changes.

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
Age	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.34	(0.03)		0.46	(0.01)			Change in Maturity	0.04 (p=0.035)
		Adj. Δ Mean (SE)[95%CI]	0.34	(0.00)	[0.33, 0.34]	0.46	(0.00)	[0.45, 0.47]	<0.001		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.55	(0.02)		0.69	(0.010			NA	
		Adj. Δ Mean (SE)[95%CI]	0.55	(0.00)	[0.54, 0.55]	0.69	(0.00)	[0.68, 0.7]	<0.001		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.21	(0.02)		0.23	(0.01)			Change in Maturity	0.004 (p=0.041)
		Adj. Δ Mean (SE)[95%CI]	0.21	(0.00)	[0.21, 0.22]	0.23	(0.00)	[0.22, 0.23]	<0.001		
Maturity Offset	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.47	(0.18)		0.56	(0.13)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.47	(0.03)	[0.40, 0.53]	0.57	(0.03)	[0.5, 0.63]	0.054		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.28	(1.33)		0.73	(0.15)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.42	(0.19)	[0.03, 0.8]	0.58	(0.20)	[0.17, 0.99]	0.588		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.2	(1.3)		0.17	(0.06)			NA	
		Adj. Δ Mean (SE)[95%CI]	-0.04	(0.18)	[-0.41, 0.33]	0	(0.2)	[-0.39, 0.4]	0.873		

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
Stature (m)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.015	(0.012)		0.011	(0.013)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.015	(0.003)	[0.009, 0.02]	0.011	(0.003)	[0.006, 0.017]	0.46		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.032	(0.01)		0.027	(0.01)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.032	(0.002)	[0.026, 0.037]	0.028	(0.003)	[0.023, 0.033]	0.37		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.017	(0.01)		0.016	(0.007)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.016	(0.002)	[0.012, 0.019]	0.017	(0.002)	[0.013, 0.021]	0.634		
Sitting Stature (m)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.008	(0.01)		0.009	(0.024)			Baseline	-0.391 (p=0.013)
		Adj. Δ Mean (SE)[95%CI]	0.008	(0.003)	[0.001, 0.015]	0.009	(0.004)	[0.002, 0.016]	0.871	Change in maturity Baseline maturity Sex	0.035 (p=0.041) 0.037 (p<0.001) 0.062 (p<0.001)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.011	(0.011)		0.016	(0.024)			Baseline	-0.302 (p=0.038)
		Adj. Δ Mean (SE)[95%CI]	0.009	(0.003)	[0.002, 0.016]	0.017	(0.004)	[0.010, 0.025]	0.142	Baseline maturity Sex	0.03 (p=0.002) 0.051 (p=0.003)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.005	(0.007)		0.007	(0.007)			School	0.001 (p=0.004)
		Adj. Δ Mean (SE)[95%CI]	0.004	(0.001)	[0.002, 0.006]	0.008	(0.001)	[0.005, 0.01]	0.068		

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
Mass kg)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	1.5	(1.2)		1.8	(1.3)			Change in maturity	3.487 (p=0.001)
		Adj. Δ Mean (SE)[95%CI]	1.5	(0.2)	[1, 1.9]	1.8	(0.2)	[1.4, 2.3]	0.29	School	0.102 (p=0.042)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	2.4	(1.7)		3	(1.5)			School	0.158 (p=0.027)
		Adj. Δ Mean (SE)[95%CI]	2.2	(0.3)	[1.6, 2.8]	3.2	(0.3)	[2.6, 3.9]	0.035		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.9	(1.0)		1.2	(0.7)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.9	(0.2)	[0.6, 1.3]	1.2	(0.2)	[0.8, 1.6]	0.292		
BMI	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.32	(0.77)		0.6	(0.66)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.33	(0.15)	[0.03, 0.62]	0.59	(0.16)	[0.28, 0.9]	0.269		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.28	(0.90)		0.76	(0.65)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.27	(0.16)	[-0.06, 0.59]	0.78	(0.17)	[0.43, 1.13]	0.053		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.04	(0.52)		0.16	(0.34)			NA	
		Adj. Δ Mean (SE)[95%CI]	-0.01	(0.09)	[-0.2, 0.18]	0.13	(0.10)	[-0.07, 0.33]	0.369		

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
WC (cm)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	1.2	(1.2)		0	(2.1)			NA	
		Adj. Δ Mean (SE)[95%CI]	1.4	(0.30)	[0.7, 2.1]	-0.1	(0.4)	[-0.9, 0.6]	0.007		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.89	(2.38)		0.56	(2.20)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.7	(0.50)	[-0.2, 1.7]	0.7	(0.5)	[-0.3, 1.7]	0.981		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.30	(2.00)		0.44	(2.10)			IMD	0.000 (p=0.045)
		Adj. Δ Mean (SE)[95%CI]	-0.5	(0.40)	[-1.4, 0.3]	0.70	(0.40)	[-0.2, 1.6]	0.084		
HC (cm)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	1.6	(2.1)		1.4	(2.7)			Baseline	-0.156 (p=0.003)
		Adj. Δ Mean (SE)[95%CI]	1.8	(0.5)	[0.9, 2.8]	1.1	(0.5)	[0.2, 2.1]	0.36		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	1.6	(2.5)		1	(3.2)			Baseline	-0.245 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	1.7	(0.5)	[0.7, 2.6]	1	(0.5)	[0, 2.0]	0.332		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.19	(2.80)		-0.24	(2.70)			Post	-0.185 (p=0.006)
		Adj. Δ Mean (SE)[95%CI]	0.10	(0.50)	[-0.9, 1.2]	-0.20	(0.60)	[-1.3, 0.9]	0.691		

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
WC:HC	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.00	(0.03)		-0.02	(0.04)			Baseline	-0.483 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	0.00	(0.01)	[-0.014, 0.01]	-0.02	(0.01)	[-0.032, -0.008]	0.057		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.01	(0.03)		-0.01	(0.04)			Baseline	-0.408 (p=0.005)
		Adj. Δ Mean (SE)[95%CI]	-0.01	(0.01)	[-0.02, 0.01]	-0.01	(0.01)	[-0.02, 0.01]	0.973		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.01	(0.03)		0.01	(0.04)			Post	-0.335 (p=0.035)
		Adj. Δ Mean (SE)[95%CI]	0.00	(0.01)	[-0.02, 0.01]	0.01	(0.01)	[-0.01, 0.02]	0.315		

Table 10-2: Actual change and adjusted changes between time points for cardiometabolic risk markers

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
sBP (mmHg)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-4	(19)		-3	(19)			Baseline	-0.872 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	1	(3)	[-5, 6]	-8	(3)	[-14, -2]	0.07	Baseline maturity	8.985 (p=0.022)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-8	(21)		-1	(16)			Sex	19.863 (p=0.02)
		Adj. Δ Mean (SE)[95%CI]	-3	(2)	[-7, 1]	-6	(2)	[-11, -2]	0.336	Baseline	-0.1.037 (p<0.001)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-4	(13)		1	(13)			NA	
		Adj. Δ Mean (SE)[95%CI]	-1	(2)	[-5, 3]	--1	(2)	[-5, 3]	0.965		
dBP (mmHg)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-2	(27)		-8	(21)			Baseline	-0.981 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	3	(3)	[-4, 9]	-14	(3)	[-21, -7]	0.002		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-11	(23)		-6	(18)			Baseline	-0.919 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	-7	(2)	[-11, -2]	-10	(2)	[-15, -6]	0.278		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-9	(17)		3	(12)			Post	-0.776 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	-3	(2)	[-7, 2]	-4	(2)	[-9, 0]	0.644		

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
LV Mass Index ($g/m^{2.7}$)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	5.1	(8.1)		4.6	(3.5)			NA	
		Adj. Δ Mean (SE)[95%CI]	5.1	(1.5)	[2.2, 8.1]	4.5	(1.7)	[1.2, 7.9]	0.8		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.1	(8.4)		2.6	(7.6)			Baseline	-0.417 (p=0.009)
		Adj. Δ Mean (SE)[95%CI]	-0.6	(1.6)	[-3.8, 2.6]	3.2	(1.8)	[-0.4, 6.8]	0.136		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-5.2	(8.4)		-2	(7.6)			Post	-0.451 (p=0.001)
		Adj. Δ Mean (SE)[95%CI]	-5.6	(1.5)	[-8.6, -2.5]	-1.5	(1.7)	[-5, 1.9]	0.1		
E/A	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.11	(0.54)		0.16	(0.83)			Baseline	-0.727 (p=0.002)
		Adj. Δ Mean (SE)[95%CI]	0	(0.14)	[-0.28, 0.28]	0.29	(0.15)	[-0.12, 0.59]	0.21	IMD	-0.013 (p=0.036)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.14	(0.56)		0.07	(0.62)			School	0.052 (p=0.036)
		Adj. Δ Mean (SE)[95%CI]	0.08	(0.10)	[-0.13, 0.29]	0.13	(0.11)	[-0.09, 0.36]	0.761	Baseline	-0.881 (p<0.001)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.03	(0.56)		-0.09	(0.56)			Post	-0.583 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	-0.01	(0.09)	[-0.18, 0.17]	-0.05	(0.09)	[-0.24, 0.14]	0.745	School	0.043 (p=0.041)

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
E'/A'	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-0.22	(0.74)		0.27	(0.87)				
		Adj. Δ Mean (SE)[95%CI]	-0.12	(0.16)	[-0.44, 0.21]	0.16	(0.17)	[-0.18, 0.50]	0.278	Baseline Maturity	-0.515 (p=0.049)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.21	(0.99)		-0.11	(0.58)			Baseline	-0.468 (p=0.013)
		Adj. Δ Mean (SE)[95%CI]	-0.12	(0.16)	[-0.45, 0.22]	-0.21	(0.17)	[-0.56, 0.14]	0.712		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.01	(0.88)		-0.39	(1.11)				
		Adj. Δ Mean (SE)[95%CI]	0.00	(0.219)	[-0.44, 0.45]	-0.38	(0.23)	[-0.84, 0.09]	0.289	NA	
E/E'	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.57	(1.5)		0.59	(3.26)				
		Adj. Δ Mean (SE)[95%CI]	0.28	(0.54)	[-0.82, 1.38]	0.91	(0.59)	[-0.27, 2.1]	0.477	Baseline	-0.907 (p=0.002)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.26	(1.63)		0.2	(1.47)				
		Adj. Δ Mean (SE)[95%CI]	0.08	(0.27)	[-0.46, 0.63]	0.41	(0.29)	[-0.18, 0.99]	0.447	Baseline	-0.736 (p<0.001)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.3	(1.49)		-0.39	(2.8)				
		Adj. Δ Mean (SE)[95%CI]	-0.53	(0.27)	[-1.06, 0.01]	-0.14	(0.29)	[-0.72, 0.44]	0.36	Post	-0.849 (p<0.001)

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
CIMT (mm)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-0.004	(0.055)		0.007	(0.067)			Baseline	-0.893 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	0	(0.009)	[-0.017, 0.017]	0.003	(0.009)	[-0.016, 0.022]	0.833	Change in maturity	-0.104 (p=0.01)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.014	(0.063)		0.017	(0.068)				
		Adj. Δ Mean (SE)[95%CI]	-0.013	(0.013)	[-0.039, 0.014]	0.015	(0.014)	[-0.014, 0.044]	0.188	Baseline	-0.434 (p=0.023)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.01	(0.057)		0.009	(0.063)				
		Adj. Δ Mean (SE)[95%CI]	-0.012	(0.013)	[-0.039, 0.015]	0.011	(0.014)	[-0.018, 0.040]	0.273	NA	
TC (mmol/L)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-0.35	(0.44)		-0.06	(0.29)				
		Adj. Δ Mean (SE)[95%CI]	-0.32	(0.10)	[-0.55, -0.09]	-0.1	(0.13)	[-0.38, 0.18]	0.242	Baseline	-0.457 (p=0.01)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.15	(0.47)		-0.02	(0.37)				
		Adj. Δ Mean (SE)[95%CI]	-0.06	(0.14)	[-0.37, 0.24]	-0.14	(0.17)	[-0.50, 0.22]	0.75	NA	
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.20	(0.40)		0.04	(0.39)				
		Adj. Δ Mean (SE)[95%CI]	0.25	(0.11)	[-0.004, 0.5]	-0.03	(0.14)	[-0.33, 0.27]	0.158	NA	

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
HDL-C (mmol/L)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.05	(0.21)		0.06	(0.19)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.02	(0.08)	[-0.14, 0.19]	0.11	(0.09)	[-0.09, 0.31]	0.535		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	0.02	(0.28)		-0.13	(0.18)			IMD	0.011 (p=0.034)
		Adj. Δ Mean (SE)[95%CI]	0.02	(0.08)	[-0.14, 0.19]	-0.13	(0.09)	[-0.33, 0.07]	0.262		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.04	(0.21)		-0.19	(0.22)			IMD	0.011 (p=0.009)
		Adj. Δ Mean (SE)[95%CI]	-0.02	(0.06)	[-0.15, 0.11]	-0.21	(0.07)	[-0.36, -0.06]	0.076		
TC:HDL-C	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-0.38	(0.57)		-0.11	(0.31)			NA	
		Adj. Δ Mean (SE)[95%CI]	-0.28	(0.18)	[-0.66, 0.11]	-0.26	(0.21)	[-0.73, 0.21]	0.95		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.08	(0.72)		0.35	(0.52)			NA	
		Adj. Δ Mean (SE)[95%CI]	-0.04	(0.24)	[-0.57, 0.49]	0.29	(0.29)	[-0.36, 0.93]	0.458		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	0.3	(0.36)		0.46	(0.47)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.27	(0.11)	[0.02, 0.52]	0.5	(0.14)	[0.20, 0.81]	0.247		

Risk Marker	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B= (p)
Glucose	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.15	(0.24)		0.11	(0.52)			NA	
		Adj. Δ Mean (SE)[95%CI]	0.14	(0.13)	[-0.14, 0.42]	0.12	(0.16)	[-0.23, 0.46]	0.923		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.115	(0.88)		0.053	(0.25)			Baseline	-1.187 (p=0.011)
		Adj. Δ Mean (SE)[95%CI]	-0.07	(0.16)	[-0.41, 0.28]	-0.02	(0.2)	[-0.45, 0.41]	0.864		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-0.26	(1.04)		-0.06	(0.4)			Change in maturity	6.357 (p=0.01)
										Maturity at post	-0.607 (p=0.048)
		Adj. Δ Mean (SE)[95%CI]	-0.2	(0.11)	[-0.43, 0.03]	-0.15	(0.13)	[-0.44, 0.14]	0.796	Post	-1.213 (p<0.001)
CRS A (trunk fat)	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-1.11	(3.25)		1.31	(2.39)			Baseline	-0.723 (p=0.006)
		Adj. Δ Mean (SE)[95%CI]	-0.31	(0.65)	[-1.75, 1.13]	0.21	(0.80)	[-1.54, 1.96]	0.660		
	Baseline to Post Changes	Unadjusted Δ Mean (SD)	0.29	(1.77)		0.78	(1.52)				
		Adj. Δ Mean (SE)[95%CI]	0.29	(0.55)	[-0.94, 1.5]	0.79	(0.63)	[-0.61, 2.2]	0.598	NA	
CRS B (WC)	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-1.19	(2.99)		1.16	(1.39)				
		Adj. Δ Mean (SE)[95%CI]	-0.76	(0.7)	[-2.32, 0.78]	0.63	(0.80)	[-1.16, 2.42]	0.264	NA	
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-1.5	(2.6)		0.4	(1.3)			Post	-0.454 (p=0.025)
		Adj. Δ Mean (SE)[95%CI]	-1.2	(0.63)	[-2.6, 0.16]	0.08	(0.71)	[-1.5, 1.7]	0.224		

Table 10-3: Actual change and adjusted changes between time points for cardiorespiratory fitness and physical activity

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B (p)
VO_{2peak}(ml/kg/min)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	4.0	(7.05)		1.7	(8.5)			Baseline	-0.696 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	3.3	(0.91)	[1.5, 5.2]	2.5	(0.98)	[0.5, 4.5]	0.566	Baseline Maturity	-4.548 (p=0.003)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	1.5	(9.4)		5.1	(12.6)			Baseline	-0.782 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	0.7	(1.7)	[-2.8, 4.2]	6.1	(1.9)	[2.3, 9.8]	0.054	Change in maturity	-19.9 (p=0.009)
										School	0.806 (p=0.036)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-2.5	(5.7)		3.4	(8.6)			NA	
		Adj. Δ Mean (SE)[95%CI]	-2.8	(1.5)	[-5.9, 0.3]	3.8	(1.6)	[0.5, 7.1]	0.009		
Sedentary (mins)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	-8.1	(56.7)		6.1	(65.9)			Baseline	-0.426 (p=0.014)
		Adj. Δ Mean (SE)[95%CI]	-8.6	(14.2)	[-37.7, 20.4]	6.7	(15.7)	[-25.2, 38.6]	0.525		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	-4.7	(57.1)		25.6	(75.1)			NA	
		Adj. Δ Mean (SE)[95%CI]	-9.8	(15.1)	[-40.4, 20.8]	31.5	(16.5)	[-2.0, 65.1]	0.106		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	3.4	(72.0)		19.5	(72.6)			Post	-0.580 (p=0.002)

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B (p)
LPA (mins)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	2.4	(20.8)		-5.1	(33.9)			Baseline	-0.727 (p=0.001)
		Adj. Δ Mean (SE)[95%CI]	2.8	(5.5)	[-8.5, 14]	-5.5	(6.0)	[-17.7, 6.8]	0.369		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	8.0	(28.1)		6.7	(26.1)			Baseline	-0.447 (p=0.018)
		Adj. Δ Mean (SE)[95%CI]	11.5	(5.8)	[-0.4, 23.4]	2.6	(6.4)	[-10.4, 15.6]	0.352		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	5.6	(25.1)		11.8	(29.7)			Post	-0.432 (p=0.017)
		Adj. Δ Mean (SE)[95%CI]	9.0	(5.8)	[-2.9, 20.8]	7.8	(6.3)	[-5.1, 20.8]	0.903		
MPA (mins)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	2.2	(10.3)		1.7	(13.9)			IMD	0.276 (p=0.009)
		Adj. Δ Mean (SE)[95%CI]	2.5	(2.3)	[-2.2, 7.2]	1.5	(2.3)	[-3.2, 6.2]	0.785	Baseline	-0.557 (<0.001)
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	5.9	(13.0)		2.3	(16.3)			School Sex	-1.436 (p=0.02) 15.616 (p=0.045)
		Adj. Δ Mean (SE)[95%CI]	7.4	(2.6)	[2.2, 12.7]	0.8	(2.6)	[-4.4, 6.0]	0.107	Baseline	-0.762 (p<0.001)
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	3.7	(12.1)		0.5	(14.9)			School	-1.63 (p=0.004)
		Adj. Δ Mean (SE)[95%CI]	5.0	(2.4)	[0.1, 9.8]	-0.7	(2.4)	[-5.6, 4.1]	0.133	Sex Post	14.71 (p=0.025) -0.549 (p=0.001)

	Changes between time points		Control			Intervention			Group Effect p	Significant covariates in model	B (p)
VPA mins)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	2	(6.7)		4	(9)			NA	
		Adj. Δ Mean (SE)[95%CI]	1.4	(2)	[-2.6, 5.4]	5	(2)	[1, 9]	0.256		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	1.0	(6.6)		2.3	(11.3)			NA	
		Adj. Δ Mean (SE)[95%CI]	2.2	(2.2)	[-2.4, 6.7]	1.2	(2.2)	[-3.4, 5.7]	0.78		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	-1.0	(6.4)		-2.1	(8.5)			Post	-0.262 (p=0.045)
		Adj. Δ Mean (SE)[95%CI]	-0.1	(1.8)	[-3.7, 3.6]	-3.0	(1.8)	[-6.7, 0.7]	0.307		
MVPA (mins)	Baseline to Post Changes	Unadjusted Δ Mean (SD)	4.2	(14.7)		6.2	(19.8)			Baseline	-0.5 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	3.7	(3.6)	[-3.6, 11.1]	6.6	(3.6)	[-0.7, 14.0]	0.618		
	Baseline to Follow Up Changes	Unadjusted Δ Mean (SD)	7.0	(18.0)		4.6	(25.0)			Baseline	-0.697 (p<0.001)
		Adj. Δ Mean (SE)[95%CI]	9.6	(4.3)	[0.9, 18.3]	2.0	(4.3)	[-6.7, 10.7]	0.263		
	Post to Follow Up Changes	Unadjusted Δ Mean (SD)	2.8	(17.1)		-1.6	(19.2)			School	-1.914 (p=0.024)
		Adj. Δ Mean (SE)[95%CI]	4.6	(3.7)	[-2.9, 12.1]	-3.4	(3.7)	[-10.9, 4.1]	0.174	Post	-0.424 (p=0.006)

Intervention effects on participants who did not meet Fitness guidelines at baseline:

At baseline 6 participants in the control group and 9 participants in the intervention group did not meet CRF guidelines for optimal CM health, as defined by Adegboye et al., (2011). Therefore these particpants have been analysed separately to determine if the intervention had a greater impact on those that were deemed to be at higher risk at baseline.

Due to measurement issues as described in Chapter 6, some measurements were not obtained for all participants and therefore there were insufficient sample size to perform statistical analysis for all measures. For the measures where statistical analysis was possible results are displayed in Table 10-4 as adjusted mean changes (SE) between time points. These have been adjusted for covariates as described in Chapter 6, Methods. For measurements where sample size was too small, results are displayed as unadjusted mean changes (SD) between time points, and no statistical analysis has been undertaken.

Table 10-4: Adjusted mean changes (SE) between time points for the subsample of participants that did not meet CRF recommendations at baseline.

	Baseline to Post Intervention							Baseline to Follow Up						
	Control			Intervention				Control			Intervention			
Marker	N	Adjusted Mean Change	SE	N	Adjusted Mean Change	SE	Significant group difference?	N	Adjusted Mean Change	SE	N	Adjusted Mean Change	SE	Significant group difference?
Waist Circumference (cm)	6	3.6	0.7	9	-0.6	0.6	p=0.006	6	0.7	1	9	0.1	0.7	p>0.05
Trunk Fat Mass (kg)								6	1.661	1.37	9	-0.387	1.03	p>0.05
Trunk Fat Mass (%)								6	4.2	4.5	9	-2.1	3.5	p>0.05
Whole Body Fat Mass (kg)								6	2.814	3.155	9	-0.653	2.38	p>0.05
Whole Body Fat (%)								6	1.9	4.5	9	-1.9	3.4	p>0.05
Peripheral Fat Mass (kg)								6	1.148	1.807	9	-0.304	1.37	p>0.05
Peripheral Fat (%)								6	0.7	5.7	9	-2.2	4.35	p>0.05
sBP (mmHg)	6	2	7	9	-7	5	p>0.05	6	6	16	9	-1	24	
dBP (mmHg)	6	9	7	9	-15	5	p=0.049	6	5	9	9	-12	7	p>0.05
LV Mass Index	5	7.6	1.8	5	4.9	1.8	p>0.05	5	-1	3.33	5	4.36	3.33	p>0.05
E/A	3	-1.15	0.23	8	0.87	0.1	p>0.05	3	-1.43	0.56	8	0.687	0.24	p>0.05
E'/A'	3	-0.63	1.1	8	0.7	0.5	p>0.05	3	-2.25	0.64	8	-0.01	0.3	p>0.05
E/E'	3	0.288	1.55	8	0.733	0.691	p>0.05	3	0.86	2	8	0.52	0.9	p>0.05
CIMT	3	-0.008	0.099	6	-0.048	0.051	p>0.05	3	-0.106	0.075	6	0.024	0.04	p>0.05
$VO_{2\ Peak}$ (ml/kg/min)	6	13.2	3.05	8	10.6	2.4	p>0.05	6	16.5	5.9	8	14.1	4.7	p>0.05
MVPA (mins)	4	-0.24	8.8	7	26	5.6	p>0.05	4	33	41.6	7	9.5	25.6	p>0.05
VPA (mins)	4	-3.1	4.9	7	15.5	3.2	p>0.05	4	19.3	18.9	7	0.45	11.7	p>0.05
SED (mins)	4	33.7	17.5	7	-53.7	12.5	p>0.05	4	28.6	36	7	-50.4	24.9	p>0.05

Table 10-5: Unadjusted mean changes (SD) between time points for the subsample of participants that did not meet CRF recommendations at baseline (sample too small for statistical analysis).

	Baseline to Post						Baseline to Follow Up					
	Control			Intervention			Control			Intervention		
	N	Mean Change	SD	N	Mean Change	SD	N	Mean Change	SD	N	Mean Change	SD
TC:HDL-C	4	-0.63	0.43	4	-0.03	0.39	4	-0.3	0.35	4	0.38	0.57
Glucose	4	0.12	0.27	4	0.41	0.42	4	-0.69	1.32	4	0.1	0.31
CRS A							4	-2.3	4.7	4	0.79	3.4
CRS B	4	-0.2	0.68	4	0.1	1.99	4	-1.9	4.3	4	0.6	1.8

Discussion

As displayed in Table 10-4, significant group differences are evident in WC and dBP, which follows the same pattern as the whole sample comparison displayed in Chapter 6.

DEXA measures also follow the same pattern, with non-significant group differences, however changes in the intervention group are in a favourable direction.

The main other points to note are that fitness improved in both control and intervention group and whilst group differences were non-significant, the control group actually improved $VO_{2\,Peak}$ more than the intervention group at both post intervention and follow up.

At post intervention the intervention group increased both MVPA and VPA, whereas the control group had a very slight reduction, however between baseline and follow up the control group had quite a large increase in MVPA and VPA, whereas the intervention group had smaller overall increases. Again, these group differences were non-significant.

Time spent sedentary decreased between baseline and post and between baseline and follow up in the intervention group, whereas in the control group time spent sedentary increased. Whilst there were no significant group differences, this suggests that the intervention was successful in reducing sedentary time in intervention participants that were deemed at higher risk.

APPENDIX B

Study 1: REACH study

- Ethical approvals
- Participant information sheet
- Participant blood sampling information sheet
- Parent's information sheet
- Parent's blood sampling information sheet
- Medical screening form
- Participant assent form
- Parent's consent form
- Parent's blood sampling consent form

North West 3 Research Ethics Committee - Liverpool East
North West REC Centre
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7827
01 June 2010

Dr Lynne Boddy
Research Officer
Faculty of Education, Community and Leisure
IM Marsh Campus
Barkhill Road
Liverpool
L17 6BD

Dear Dr Boddy

Study Title:	**The REACH Y6 Follow up Study: Blood Sampling Project**
REC reference number:	**10/H1002/15**
Protocol number:	**N/A**

Thank you for your letter of 26 April 2010, responding to the Committee's request for further information on the above research, and for submitting the revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

In terms of registering the study on a public database, either of the below databases would be appropriate:

http://www.actnow-database.co.uk/

http://www.invo.org.uk/index.asp

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk. *Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*	
Covering Letter		22 February 2010	
REC application	2.5	25 February 2010	
Participant Information Sheet: Parental/Guardian/Carer PIS	4.0	27 January 2010	
Participant Consent Form: Parental/Guardian/Carer Consent Form	2.0	27 January 2010	
Participant Consent Form: Assent Form for Children	1.0	27 January 2010	
Protocol	2.0	26 April 2010	
Participant Information Sheet: Blood samples	1.0	26 April 2010	
Participant Consent Form: Blood samples	1.0	26 April 2010	
Response to Request for Further Information		26 April 2010	

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

10/H1002/15	**Please quote this number on all correspondence**

Yours sincerely

Mrs Jean Harkin
Chair

Email: ellie.wilcox@northwest.nhs.uk

Enclosures: "After ethical review – guidance for researchers" -SL-AR1 for CTIMPs

Copy to: Professor Gareth Stratton
Professor of Paediatric Exercise Science
Liverpool John Moores University
Tom Reilly Building
Byrom Street
Liverpool
L3 3AF

From: McKeon, Jo
Sent: 27 January 2010 12:24
To: Stratton, Gareth
Subject: 09/SPS/033 – The REACH Year 6 Follow Up Study. Major Amendments

Dear Gareth,

Major Amendments - Provisional Approval

With reference to your application for Ethical approval:

The REACH Year 6 Follow Up Study

Liverpool John Moores University Research Ethics Committee (REC) has reviewed the above application at the meeting held on Thursday 21st January 2010. The Committee would be content to give a favourable ethical opinion of the research subject to receiving a complete response to the following request for further information:

Approved: Subject to the following provisos:

- The project requires a risk assessment because blood is being taken out of a controlled environment.
- Please assure that the Human Tissue Act is abided by.
- Please clarify how the blood will be processed.

When submitting any revised documentation with your response please underline or otherwise highlight the changes you have made.

No participants should be approached or recruited prior to receiving confirmation of ethical approval from LJMU REC. Please note that failure to obtain full ethical approval from LJMU REC may invalidate any insurance cover provided through LJMU.

Yours sincerely

PP

Brian Kerrigan
Chair of the LJMU REC
Tel: 0151 231 3119
E-mail: j.m.mcwatt @ljmu.ac.uk

Jo McKeon
Research Support Officer
Research Support Office
Liverpool John Moores University
Rodney House
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Email: j.m.mcwatt@ljmu.ac.uk
Website: http://ljmu.ac.uk/research_and_graduate/

LIVERPOOL JOHN MOORES UNIVERSITY

Title of Project The REACH Y6 Follow up study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy. Research into Exercise, Activity and Children's Health Group (REACH).

We would like you to take part in a research study. Before you decide whether you would like to take part it is important that you understand what we are doing and why. Please take time to read the following information. Ask us if there is anything that is you don't understand of if you want to know any more.

Why are we doing this project?

You took part in the SportsLinx project a while ago, where you did a number of fitness and health tests. We would like to go into a bit more detail with these tests, and we've invited all the Y6 children that took part in SportsLinx to come and take part in this project.

Do I have to take part?

No. It is up to you to decide whether or not you would like to take part. If you decide to take part you'll need to sign your 'Participant Assent Form'. Even if you have signed the form you can pull out of the project at any time without giving a reason.

What will happen if you take part?

You will take part in these activities and tests:-

Physical Activity Monitoring

You will be given an activity monitor to wear around your waist for seven days it looks at how active you are. It is important that you wear your monitor every day. The researchers will teach you how to put on your monitor, and let you know when you should wear it. At

the same time as the physical activity monitoring, we will ask to fill out a small diary to tell us what activities you have been doing each day, and tick boxes about foods.

Text Messaging

When you've been given your activity monitor we will send you a text message each day to remind you to wear it. We won't phone you or give your number to anyone else, and once you've finished the project we will delete your phone number.

Markers of heart and blood vessel health

It is important to have a healthy heart and healthy blood vessels. Blood vessels are things like arteries and veins that carry the blood pumped by your heart around your body.

This test and the heart and blood vessel scans will help us see how healthy your heart and arteries are. Make sure you haven't eaten anything on the morning of the blood test, you can drink water though. We will do this test at your school in an area we set up to take blood samples. We will give you some breakfast afterwards. During this test a researcher will take some blood from a vein in your arm. The researcher will explain to you what will happen and how you will feel. Researchers will make sure you are feeling OK and you can ask them questions whenever you like. After you have relaxed and had your breakfast you will go back to lessons as normal. Remember, you don't have to do this test, and if you choose not to that is fine.

<u>Lab measures:</u>

Ultrasound: Pictures of your heart and arteries

In these tests we will look at pictures of your heart and some of your blood vessels- we will show you these pictures during the testing. For one of the tests we will put a cuff around your arm that will fill full of air and become tight around your arm. This will then be deflated and become loose again and we will look at pictures to see how a blood vessel in your arm changes. We will also check your blood pressure. The researchers will talk you through the tests when you are in the lab and answer any questions you have.

DEXA whole body scan

This machine will scan your body, giving us a picture of your skeleton. The scan takes four minutes and you will be asked to lie as still as possible. You won't feel the scan at all, and researchers will explain the test when you are in the lab and answer any questions you have

Running on a Treadmill to look at fitness

We will ask you to walk and then run on a treadmill (running machine) until you are running as fast as you can. You will wear a harness around your waist so you can't fall off the treadmill, and you will wear a face mask and a monitor that will tell us how fast your heart is beating. We will give you lots of encouragement to keep on running.

Body Size Measurements

We will measure your height, weight, measure around your waist and hips, and we will also take some skinfold measurements. These are the same tests you did on the SportsLinx fitness fun day.

Questionnaires

We will also ask you to fill out some questionnaires whilst at the labs, these questionnaires look at things like if you take part in sport, and if you feel confident.

<u>After-School Assessments</u>

Fundamental movement skills

We will ask you to do some sports activities after-school to look at how well you perform at six sports skills - the hop, vertical jump, sprint run, kick, catch and throw. We will film you doing these assessments as we need to watch the video in slow-motion to see how well you perform.

Other Details:

Sports Kit

You should wear clean lightweight kit for the testing. Trainers should be non-muddy.

Time

Physical activity monitoring will be done at your school, and giving out the monitors should take no longer than a few minutes. Blood tests will also be done at your school and taking the blood will only take a few seconds, then you will eat your breakfast and return to lessons. The lab based testing will take up one school day, and you will be picked up from school at the start of the day, testing will take a while and then you'll be taken back to school at home time, so you will miss a full day of lessons. Your parents/guardians are welcome to come with you to the lab based testing. Once you're back at school after the lab visit we would like you to stay after-school to complete the sport skill assessments in the school playground or hall. This will take about an hour, and after this you can go home.

Eating

Make sure you don't eat on the morning of the blood test, but you can drink water. We will give you some breakfast after your blood test but you should bring a packed lunch and drinks to lab testing sessions.

If you would like any more information about the project please email or phone Lynne Boddy, Research Officer on 0151 231 5243 or l.m.boddy@ljmu.ac.uk .

Finally, we hope you will enjoy the lab visit if you decide to take part, and you will be given a pack containing your results when the project is finished.

Kind Regards,

Professor Gareth Stratton

Dr. Lynne Boddy

LIVERPOOL JOHN MOORES UNIVERSITY

PARTICIPANT BLOOD SAMPLING

Title of Project: The REACH Y6 Follow up study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy. Research into Exercise, Activity and Children's Health Group (REACH).

This sheet is to give you a bit more information about how the blood sample will be taken, how you might feel and how the testing morning will run.

When and where?

We will be at school to do the blood sampling on:_____

Make sure you don't eat on the morning of the blood sample, but you can drink water.

When you get to school we'll take you to a room to relax- we may have a DVD or TV for set up for you to watch.

We will walk with you through to the blood sampling area where one of our team from Alder Hey will take a blood sample from your arm.

You can then have some breakfast that we will have ready for you.

Once you've had your breakfast you can go back to class as normal.

How will you feel?

You might feel a bit nervous before the blood test- don't worry, you can talk to us and ask us any questions you like about it.

If you would like someone to go with you for the blood sample that's fine, just let us know.

You can ask the Alder Hey person any questions you like and they will tell you what will happen.

We will put some cream on your arm so it goes a bit numb and it should stop the needle hurting.

Once your arm is a bit numb the Alder Hey specialist will take some blood out of a vein in your arm using a needle. You might still feel a bit of a 'scratch' or 'pinch'.

One you have given your sample you may have a little mark or bruise on your arm- this will go away quickly. We will stay with you to make sure you are feeling OK, and we will take you round to have your breakfast.

If you really don't want to give a blood sample on the day don't worry, no one will force you to do anything.

LIVERPOOL JOHN MOORES UNIVERSITY

Title of Project: The REACH Y6 Follow up study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy. Research into Exercise, Activity and Children's Health Group (REACH).

We would like to invite your child to take part in a research study. Before you decide whether you would like to child to participate it is important that you understand why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the project?

Your child recently took part in the SportsLinx project that looked at your child's health and fitness. We are inviting all Year 6 children that took part in SportsLinx this year to participate in this project. This project follows on from the SportsLinx fitness fun day by looking in more detail at your child's health and fitness. There are a number of sophisticated lab and school based tests that we would like your child to take part in. The tests are designed to measure the amount of physical activity your child participates in, fitness, skill, heart and blood vessel function, markers of cardiovascular health, blood pressure, bone health and body composition.

Does my child have to take part?

No. It is up to you to decide whether or not your child may take part. If you decide to allow your child to take part you will be asked to sign a consent form. Your child will also receive information about the project and an assent form to sign if they would like to take part. Even after giving consent your child is still free to withdraw from the study or certain tests at any time without giving a reason.

What will happen if my child takes part?

Test details:-

Physical Activity Monitoring

Your child will be issued with a physical activity monitor at the start of the school day, which is worn around the waist for seven days, and measures the amount and intensity of physical activity your child participates in over a whole day. The monitor is handed back at the end of the monitoring period to the researchers. Monitoring takes place over a number of days in order to gain a realistic overview of the amount of activity your child participates in. At the same time as the physical activity monitoring, your child will be asked to complete a diary recording physical activity and some tick lists of foods. Researchers will explain how children should wear the monitors and when the wear them at the time of monitoring and you will receive further information about physical activity monitoring when children receive the monitors.

Text messaging:

It is important that children wear the physical activity monitors for 7 days. To help children to remember to wear and return the monitors, we have decided to text your child reminders. Texts will be sent from a university number and will only be sent for the above reason. No calls will be made or received by LJMU. We will only do this if you and your child have given permission on the consent form. All mobile numbers are kept in a secure file, which will be destroyed by 1st August 2010.

Markers of cardiovascular risk

For this your child should not have eaten breakfast, and only consumed water on the morning of blood sampling. This test will be completed at your child's school where we will set up a blood sampling area and a quiet area for them to relax in before and after sampling. During this test a fully trained and experienced researcher will take a blood sample from your child. They will fully explain the procedure to your child and will answer any questions your child may have. The sample will be taken from a vein in your child's arm in a safe and hygienic environment. This blood sample will be analysed to look for levels of cholesterol and fats in the blood, and see if any markers of inflammation are present. This information provides very useful information on the health of children, and results will be fed back to yourself and your child after analysis. Your child will be provided with breakfast after the blood test, and will be looked after by researchers to make sure they are OK. They will then return to lessons and carry on with the school day as normal after they have had their breakfast. Remember, your child can withdraw from tests at any point, and if they choose not to give a blood sample that is fine.

Lab Visit Measures

Ultrasound

During this test a researcher will scan the heart to measure its dimensions, and will also measure the thickness of some major arteries. This technique follows the same principle of scans used to produce images of a baby in the womb. We will also use another ultrasound technique to see how your child's arteries in the arms are functioning. To complete this test a blood pressure cuff will be inflated around your child's arm and then deflated, we then look at how your child's blood vessels react. Blood pressure will also be measured at this time. Researchers will fully explain the tests to children and answer any questions they may have.

DEXA whole body scan

This machine scans the whole body, providing a picture of the skeleton and measuring bone, fat and muscle tissue. The scan takes four minutes, and uses radiation that is the equivalent of a two-hour flight on an airplane. Children will receive a picture of their skeleton in their results pack.

Anthropometry

Simple height, weight, waist circumference, hip circumference and skinfolds measures will be taken. These are the same techniques used in the SportsLinx fitness fun days.

Aerobic fitness

This will involve a treadmill based running test to maximum, and should last between 9 and 15 minutes. The participant will wear a face mask and a heart rate monitor. We will ensure that your child is fully warmed up before the test and familiarised with the treadmill. Children will also wear a harness to prevent any fall risk whilst on the treadmill. We will also ensure your child completes a cool down, and monitor your child's heart rate throughout.

Questionnaires

Children will be asked to fill out a series of questionnaires whilst at the laboratories, these questionnaires examine things like participation in sport, and self-perceptions.

After-School Assessments

Fundamental movement skills

Following the visit to the labs, children will be assessed after-school performing skills such as the hop, vertical jump, sprint, kick, catch and throw. This will take about an hour. They will be filmed performing these skills to allow for slow motion analysis. These video's will be kept in a secure setting and will only be handled by approved persons.

Other Details:

Risks/Discomfort Involved:

Your child may become out of breath and flushed during the treadmill exercise, this is similar to what your child experiences when playing in the playground or taking part in sport. Your child's heart rate and condition will be monitored throughout, and they can stop at any point.

Your child may feel a slight 'scratch' sensation when the blood sample is taken. Researchers will explain the blood sampling technique and ensure your child is fully aware of what is happening. Children will be monitored by researchers during and after the blood sampling to ensure they are feeling OK.

The cuff used to take blood pressure and measure the function of blood vessels may cause a slight pins and needles sensation, this will go once the cuff is released.

The DEXA body scan emits a very small amount of radiation similar to that experienced in a transatlantic flight.

Benefits:

Your child will receive their results in a sealed pack at the end of the project, researchers will explain what these results mean, and you may contact researchers to discuss your child's results if you wish.

These results will help you understand how healthy and fit your child is at the time of testing.

Children usually find the laboratory visit interesting, enjoyable, and educational.

Confidentiality

All information about your child and their results will be treated with the strictest confidence. No identifiable information will be released by the project, and all data is securely stored by project staff, and may be accessed by approved persons only.

Sports Kit

Children should wear clean lightweight kit for the testing. Trainers should be non-muddy.

Time

Physical activity monitoring will be conducted at your child's school, and the distribution and collecting of the monitors should take no longer than a few minutes. Blood sampling should take no longer than a few minutes including explanations of the procedures to your child, and then your child will take several minutes to relax after sampling and eat breakfast. The lab based testing will require your child to be picked up from school at the start of the day and testing will take a full school day. You are welcome to accompany your child to the lab based testing. After the lab visit, your child will be returned to school for the end of the school day. We will then require them to stay for one hour after-school to complete assessments of fundamental movement skills (catch, hop, jump etc.) in the school playground or indoor hall.

Eating

Children should not consume food on the morning of the blood sampling and should only drink water. We will provide breakfast on the blood sampling morning, but your child will need to bring a packed lunch and drinks to lab testing session.

Illness

Participants should postpone their testing if they are feeling unwell.

For any further information regarding the project please don't hesitate to contact Professor Gareth Stratton on 0151 231 4334 or Dr. Lynne Boddy on 0151 231 5243 or l.m.boddy@ljmu.ac.uk .

Kind Regards,

Professor Gareth Stratton

Dr. Lynne Boddy

LIVERPOOL JOHN MOORES UNIVERSITY

PARENTAL/GUARDIAN/ CARER BLOOD

Title of Project: The REACH Y6 Follow up study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy. Research into Exercise, Activity and Children's Health Group (REACH).

This sheet is to give you a bit more information about how the blood sample will be taken, how your child will feel and how the testing morning will run.

Highly trained staff from Alder Hey will take all blood samples and will treat your child with the utmost care

When and where?

Blood sampling will take place between 8.30 and 10.30am at your child's school on:

_____

Please make sure your child doesn't eat breakfast and only consumes water on the morning of testing.

We will be on site with blood sampling specialists (Phlebotomists) from Alder Hey Children's Hospital.

Your child will be led to a room to relax- we may have a DVD or TV for them to watch.

We will then take children one at a time through to a room where a member of the Alder Hey team will take a blood sample from your child.

Your child will then be taken to eat breakfast. Breakfast will be supplied by the project at your child's school.

After breakfast your child will return to class and carry on with the school day.

How will my child feel?

Before a blood sample is taken your child may feel a bit apprehensive. The project team will reassure your child and explain fully what will be happening.

If your child would like someone to accompany them whilst the blood sample is being taken they can let us know and that would be fine.

When your child is sitting with the Alder Hey Phlebotomist they will be able to ask questions and will have the procedure explained to them.

The Phlebotomist will put some cream on your child's arm. This is a pain-killer cream that helps to numb the area where the sample will be taken.

The sample will be taken once the cream has numbed the area. Your child may still feel a 'scratch' or 'pinch' where the needle goes into the skin.

Once the sample has been taken your child may be left with a small mark where the needle went into the skin and some children may have a small bruise. Some children may feel faint after or before the blood sample. We will keep a close eye on your child before, during and after the sample to make sure they are feeling ok.

Remember, if your child decides not to give a blood sample then that is fine.

We will store the blood sample so that we can analyse it. Once we have finished the analysis we will destroy the sample.

For information:

This blood sample will be analysed to look for levels of cholesterol and fats, and to see if any markers of inflammation are present. We are interested in the links between these markers and levels of physical activity, fitness and body composition. We are working with healthy children in this study and we are not screening the blood for anything related to illness or immediate health problem

LIVERPOOL JOHN MOORES UNIVERSITY

MEDICAL SCREENING FORM

Project Name: The SportsLinx Y6 Follow Up Study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy

Research into Exercise, Activity and Children's Health Group (REACH)

Research Institute for Sport and Exercise Sciences, LJMU

This form should be completed as accurately as possible by the parent/guardian. All information will remain confidential. The form is designed to ensure that your child has no medical condition/illness that might compromise their safety to take part in the project. It will also be available in case of emergency.

Name of child _____

Address _____

_____

Doctors Address _____

_____

Home Tel No. _____

	YES	NO
Has your child ever had any surgery?		
Has your child ever suffered from any injuries?		
Has your child recently suffered from any illness?		
Has your child been involved in any major accidents?		
Is your child currently being treated by your doctor?		
Does your child have problems with:		
hearing		
vision		
bones/joints		
co-ordination		
diabetes		
epilepsy		
respiratory problems		

heart problems		
Is your child allergic to any medication?		
Does your child carry any medication in case of emergency?		
If you have answered yes to ANY questions please provide relevant details		

LIVERPOOL JOHN MOORES UNIVERSITY

ASSENT FORM FOR CHILDREN

Project Name: The REACH Y6 Follow Up Study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy

Research into Exercise, Activity and Children's Health Group (REACH)

Research Institute for Sport and Exercise Sciences, LJMU

To be completed by the child participant: Please circle your answer to the questions below.

Have you read (or had read to you) information about this project?	Yes/No
Do you understand what this project is about?	Yes/No
Have you asked all the questions you want?	Yes/No
Have you had your questions answered in a way you understand?	Yes/No
Do you understand it's OK to stop taking part at any time?	Yes/No
Are you happy to take part?	Yes/No
Are you happy to give your mobile number to the research team?	Yes / No

If any answers are 'no' or you **don't** want to take part, don't sign your name!

If you do want to take part, please write your name below

Your name _____

Date _____

LIVERPOOL JOHN MOORES UNIVERSITY

PARENTAL/GUARDIAN/ CARER CONSENT FORM

Project Name: The REACH Y6 Follow Up Study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy

Research into Exercise, Activity and Children's Health Group (REACH)

Research Institute for Sport and Exercise Sciences, LJMU

I confirm that I have read and understand the information provided for the above study. I have had the opportunity to consider the information, ask questions and if I have asked questions these have been answered satisfactorily. 1

I understand that my child's participation is voluntary and that my child is free to withdraw at any time, without giving a reason and that this will not affect mine or my child's legal rights. 2

I understand that any personal information collected during the study will be anonymised and remain confidential. 3

I give permission for photographs/video to be taken of my child during the project, which may be used for subsequent academic/promotional purposes associated with LJMU and SportsLinx. 4

I give permission for the research team to ask my child for his/her mobile number for the sole purpose of sending text message reminders to wear the physical activity monitors. 5

I give permission for the research team to transport my child with other children to LJMU. 6

7

I give permission for my child to stay for one hour after school on the day of the laboratory visit to complete fundamental movement skills assessments.

If yes, how will your child be transported home after the skills assessments?

(E.g. they will be collected, walk etc)_____

I give permission for researchers/phlebotomists to take a blood sample from my child if my child is happy for them to do so. 8

I agree my child can take part in the above study 9

Name of Participant _____

Parent/Guardian/Carer Signature_____Date_____

Note: When completed 1 copy for parent/guardian/carer and 1 copy for researcher

LIVERPOOL JOHN MOORES UNIVERSITY

Project Name: The REACH Y6 Follow Up Study

Researchers: Professor Gareth Stratton, Dr. Lynne Boddy

Research into Exercise, Activity and Children's Health Group (REACH)

Research Institute for Sport and Exercise Sciences, LJMU

(Please tick the appropriate boxes and fill in the gaps)

I give permission for phlebotomists to take a blood sample from my child if my child is happy for them to do so. ☐

Sometimes NHS regulatory authorities randomly pick studies to check up on. The authorities check that studies are being run properly and safely. As we are working with Alder Hey for the blood samples there is a chance that they may want to check out this study, so the sentence below covers them checking the study should they need too:

'I understand that relevant sections of my child's health records and data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to them taking part in this research. I give permission for these individuals to have access to my child's records'

Name of Participant

Parent/Guardian/Carer Signature Date

Note: When completed 1 copy for parent/guardian/carer and 1 copy for researcher

APPENDIX C

CHANGE! (Study 2 and 3):

- Ethical approvals
- Participant information sheet for whole sample
- Participant information sheet for subsample
- Parent's information sheet for whole sample
- Parent's information sheet for subsample
- Participant assent form
- Parental consent form for whole sample
- Parental consent form for subsample
- Medical screening form

From:	Williams, Mandy
To:	Fairclough, Stuart
Cc:	Boddy, Lynne
Subject:	Provisional Approval
Date:	24 June 2010 14:26:59

Dear Stuart

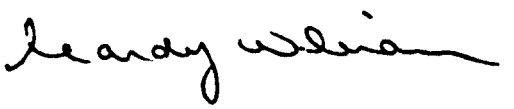
Provisional Approval

10/ECL/039 – Stuart Fairclough, Staff, CHANGE! (Children's Health Activity & Nutrition- Get Educated!) WIGAN (Lynne Boddy)

Liverpool John Moores University Research Ethics Committee (REC) has reviewed the above application at its June meeting. The Committee would be content to approve the research project subject to the following provisos:

- Parents should be reassured regarding the stages within the intervention,
- REC suggested that the Applicant check the issues regarding the mode of transport and insurance.
- Please clarify when the inventions will take place and if the Children will miss any school work or if it's an after School session.
- The Participant Information Sheet should state that the testing will cease immediately if the Child wishes to do so should they feel uncomfortable

Yours sincerely
PP



Brian Kerrigan
Chair of the LJMU REC
Tel: 0151 231 3110
E-mail:a.f.williams@ljmu.ac.uk
CC: Supervisor

From: Williams, Mandy
To: Boddy, Lynne; Fairclough, Stuart
Subject: Amendment to Ethical approval
Date: 26 May 2011 14:41:43

-

CHANGE! (Children's Health, Activity and Nutrition: Get Educated!) 10/ECL/039

Liverpool John Moores University Research Ethics Committee (REC) has reviewed the above notification of major amendments by Chair's action. I am happy to inform you that the Committee are content to give a favourable ethical opinion and recruitment to the study can now commence.

Approval is given on the understanding that:

- any adverse reactions/events which take place during the course of the project will be reported to the Committee immediately;
- any unforeseen ethical issues arising during the course of the project will be reported to the Committee immediately;
- any substantive amendments to the protocol will be reported to the Committee immediately.
- the LJMU logo is used for all documentation relating to participant recruitment and participation eg poster, information sheets, consent forms, questionnaires. The JMU logo can be accessed at www.ljmu.ac.uk/images/jmulogo

For details on how to report adverse events or amendments please refer to the information provided at http://www.ljmu.ac.uk/RGSO/RGSO_Docs/EC8Adverse.pdf

Please note that ethical approval is given for a period of five years from the date that the original approval was granted and therefore the expiry date for this project will be June 2010 An application for extension of approval must be submitted if the project continues after this date.

Yours sincerely
PP:

Brian Kerrigan
Chair of the LJMU REC
Tel: 0151 904 6467
E-mail:a.f.williams@ljmu.ac.uk
CC: Supervisor

Wigan Council

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

CHILD PARTICIPANT INFORMATION

Title of Project: CHANGE! (Children's Health, Activity and Nutrition: Get Educated!)

Name of Researchers and School/Faculty: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh (The Faculty of Education, Community and Leisure, Liverpool John Moores University).*

You are being invited to take part in a research project. Before you decide it is important that you understand why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you want to take part.

1. What is the purpose of the study?

In Wigan there are lots of opportunities for children to take part in physical activity and sport, and activities that encourage healthy eating. Being active and eating well is important because it is good for our health.

The purpose of this project is to improve eating habits and physical activity of Year 6 pupils and their families in Wigan. The project will also try and find out what children think about their own physical activity and eating habits. The information collected will help us to learn how well the sport, physical activity and healthy eating programmes in Wigan are working.

2. **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do you will be asked to sign the assent form. You are still free to drop out at any time and without giving a reason, and we will stop taking any measures or asking you to fill out any questionnaires as soon as you tell us you want to stop. Dropping out will not affect your school or sporting opportunities in any way.

3. What will happen to me if I take part?

If you decide to take part you will be asked to fill in questionnaires, asking about the types of physical activities you do, what you think about your own physical activity, how often you take part in physical activity, and aspects of your eating habits. A researcher will explain how to fill in each questionnaire and will be there whilst you complete them, in case you need to ask about anything you are not sure of.

a. We will measure everyone's weight, height, sitting height, blood pressure, the distance around your waist and hips and look at how much muscle and fat you have in your body. All of these measures will take place away from the rest of the group, and no one but the researchers will see the results.

b. Weight will be measured by asking you to stand on some weighing scales with your shoes taken off.

c. Height and sitting height will be measured using a height meter; you will be asked to stand and then sit with your back to the height meter and the researcher will record your standing and sitting height.

d. Blood pressure will be measured by placing a cuff around your arm which will squeeze your arm for a few seconds before releasing again.

e. The distance around your waist and hips will be measured using a measuring tape.

f. We will look at how much muscle, fat and water is in your body using a special type of scales. You will stand on the scales with your bare feet and it will give us a reading. We won't show any of your results to anyone else.

g. We will also do a fitness session, where we will ask you to complete a shuttle run test.

h. Completing the questionnaires and having the measurements taken should take no longer than two hours. All of these measures will take place at school in school time. Your class teacher will be there along with the researchers who will do the measurements with you.

i. To measure your physical activity we will ask you to wear an activity monitor attached to an elastic belt around your waist. These monitors measure and record how much activity you do and are a bit like pedometers.

j. We would like you to wear them for 7 days. You put them on when you get up on a morning and take them off when you go to bed. You also need to take the monitor off when doing any activities where they might get wet, like swimming, showering, taking a bath, etc. After 7 days the researchers will be at school to collect the monitors back from you. If you are happy for us to do so, we will send either your parent/guardian or yourself a message each day of the physical activity monitoring to remind you to wear it and to bring it back to school after seven days.

k. We will also be looking at the types of foods you and your family like to eat and see how much you know about foods. To do this we will ask you to fill in a couple of short questionnaires in school and there will also be a few things that we would like you to do at home such as making a simple report of a mealtime on a form we will give you, making a list of the foods in your cupboards at home and collecting a till receipt from the supermarket (with the financial information taken off).

You may also be invited to take part in some more research; you will be given information about this separately.

4. Will my taking part in the study be kept private?

All of the results of the research will only be viewed by the researchers. We will write reports about the project, but this will only give general information about your year group as a whole. At no time will your name be used when we write any of the results.

For more information or if you've got any questions please contact one of the researchers:
Rebecca Gobbi (R.Gobbi@2009.ljmu.ac.uk)
Kelly Mackintosh (K.A.Mackintosh@2009.ljmu.ac.uk)
Genevieve Warburton (G.L.Warbuton@2009.ljmu.ac.uk)
Address: Liverpool John Moores University, IM Marsh, Barkhill Rd, Liverpool, L17 6BD
Telephone: **0151 231 5271**

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

CHILD PARTICIPANT INFORMATION

Title of Project: CHANGE! (Children's Health, Activity and Nutrition: Get Educated!)

Name of Researchers and School/Faculty:
Dr Stuart Fairclough, Dr. Lynne Boddy, Dr. Allan Hackett, Dr. Ian Davies (Faculty of Education, Community and Leisure).

You are being invited to take part in a research project. Before you decide it is important that you understand why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you want to take part.

Why are we doing this study?
You have already taken part in the first stage of the study, where we assessed some measures such as height and weight. We would like to go into a bit more detail with these tests, and we've invited some children to take part in this second stage of the project.

1. **Do I have to take part?**
No. It is up to you to decide whether or not to take part. If you do you will be given this information sheet and asked to sign a consent form. You are still free to drop out at any time and without giving a reason. We will stop taking any measurements or doing any tests straight away when you tell us you want to stop. Dropping out will not affect your schooling or sporting opportunities in any way.

2. What will happen if you take part?
You will be invited to take part on 2 different testing days. Throughout these days you will take part in these activities and tests:-

Testing Day A: In School
Markers of heart and blood vessel health
It is important to have a healthy heart and healthy blood vessels. Blood vessels are things like arteries and veins that carry the blood pumped by your heart around your body.

These tests and the heart scans that we do in the lab will help us see how healthy your heart and arteries are. Make sure you haven't eaten anything on the morning of the finger tip test, you can drink water though. We will do this test at your school in an area we set up to take blood samples. We will give you some breakfast afterwards. During this test a researcher will take tiny bit of blood from your finger tip. The researcher will explain to you what will happen and how you will feel. Researchers will make sure you are feeling OK and you can ask them questions whenever you like. After you have had your finger prick test, we will look at some pictures of one of your blood vessels in your arm. For this we

will put a cuff around your arm that will fill full of air and become tight around your arm. This will then be deflated and become loose again and we will look at pictures to see how a blood vessel in your arm changes. We will also check your blood pressure. After you have relaxed and had your breakfast you will go back to class as normal. Remember, you don't have to do these tests, and if you choose not to that is fine.

Testing Day B: Lab Measures

DEXA whole body scan

You will be invited into the university to take part in a body scan. This machine will scan your body, giving us a picture of your skeleton. The scan takes four minutes and you will be asked to lie as still as possible. You won't feel the scan at all, and researchers will explain the test when you are in the lab and answer any questions you have.

Ultrasound: Pictures of your heart and arteries

In these tests we will look at pictures of your heart and some of your blood vessels- we will show you these pictures during the testing. The researchers will talk you through the tests when you are in the lab and answer any questions you have.

Running on a Treadmill to look at fitness

We will ask you to walk and then run on a treadmill (running machine) until you are running as fast as you can. You will wear a harness around your waist so you can't fall off the treadmill, and you will wear a face mask and a monitor that will tell us how fast your heart is beating. We will give you lots of encouragement to keep on running.

After School Skills Session

When you return to school after the lab visit you will stay at school for an hour and in this session we will ask you to do a number of skills, including hopping and throwing.

3. Other Details:

Sports Kit

You should wear clean lightweight kit for the testing. Trainers should be non-muddy.

Time

Blood tests will be done at your school and taking the blood will only take a few seconds, then you will eat your breakfast and return to lessons. The lab based testing will take up one day, and you will be picked up from school and taken back to school. Your parents/guardians are welcome to come with you to the lab based testing.

Eating

Make sure you don't eat on the morning of the blood test, but you can drink water. We will give you some breakfast after your blood test but you should bring a packed lunch and drinks to lab testing sessions.

For more information or if you have any questions please contact one of the researchers:
Rebecca Gobbi (R.Gobbi@2009.ljmu.ac.uk)
Kelly Mackintosh (K.A.Mackintosh@2009.ljmu.ac.uk)
Genevieve Warburton (G.L.Warburton@2009.ljmu.ac.uk)
Address: Liverpool John Moores University, IM Marsh, Barkhill Rd, Liverpool, L17 6BD
Phone: **0151 231 5271**

Wigan Council

NHS Ashton, Leigh and Wigan

Liverpool JMU

LIVERPOOL JOHN MOORES UNIVERSITY

PARENT/GUARDIAN/CARER INFORMATION

Title of Project: CHANGE! (Children's Health, Activity and Nutrition: Get Educated!)
Name of Researchers and School/Faculty: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh (The Faculty of Education, Community and Leisure, Liverpool John Moores University).*

Your child is being invited to take part in a research project. Before you decide it is important that you understand why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you want your child to take part

1. What is the purpose of the study?
In Wigan there are lots of programmes and opportunities for children to take part in physical activity and sport, and to encourage healthy eating. Being active and eating well is important because it is good for our health. The purpose of this project is to improve the eating habits and physical activity levels of Year 6 pupils in Wigan. The project will also try and find out what children think about their own physical activity and eating habits. The information collected will help us to learn how well the sport and physical activity programmes and the healthy eating messages in Wigan are followed.

2. **Does my child have to take part?**
No. It is up to you and your child to decide whether or not you want to them to take part. If you do you will be given this information sheet and asked to sign a consent form. **Your child is still free to withdraw from the project at any time and without giving a reason. Withdrawing will not affect your child's educational or sporting opportunities in any way.**

3. What will happen to my child if they take part?
If you decide to allow your child to take part they will be asked to complete questionnaires, asking about the types of physical activities they do, what they think about their own physical activity, how often they take part in physical activity, and about aspects of their eating habits. A researcher will explain how to fill in each questionnaire and will be there while the children complete them, in case they need to ask about anything they are not sure of.

We will measure each child's weight, height, waist circumference, hip circumference, body composition, sitting height and blood pressure. All of these measures will take place away from the rest of the group, and no one but the researchers will see the results. Weight will be measured by asking the child to stand on some weighing scales with their shoes removed. Height and sitting height will be measured using a height meter; each child will be asked to stand and then sit with their back to the height meter and the researcher will

record the standing and sitting height values. A non-elastic measuring tape will be used to measure the distance around your child's waist and hips. We will use a different type of scales to measure body composition, your child stands on the scales bare-footed and the scales give us a measure of muscle tissue, total body water and %body fat. After these measurements children will complete a fitness assessment using a shuttle runs test, also known as the bleep test.

Completing the questionnaires, and having the measurements taken should take no longer than two hours. All of these measures will take place during school time on school grounds.

To measure your child's physical activity we will ask them to wear an activity monitor attached to an elastic belt around their waist. These monitors measure and record how much activity a person does and are similar to pedometers. We would like the children to wear them for 7 days. We ask children to put on the monitor when they get up in the morning, and take it off when they go to bed. The only other times we would ask the children to remove the activity monitors would be during any activities where they might get wet, like swimming, showering, taking a bath, etc. After 7 days the researchers will be at school to collect the monitors back from the children. If you and your child agree to give us a contact mobile phone number we will send a maximum of one text message per day during the physical activity monitoring to remind children to wear the monitor and bring it back to school after seven days.

We will also be looking at the types of foods your family like to eat and see how much your child knows about foods. To do this we will ask your child to fill in a couple of short questionnaires in school and there will also be a few things that we would like your child to do at home such as making a simple report of a mealtime on a form we will give them, making a list of the foods stored in your home and collecting a till receipt from the supermarket (with the financial information taken off).

Your child may also be invited to take part in further research, however you will be given information about this and an additional consent form if your child is invited to take part.

4. Are there any risks / benefits involved?
Your child may feel apprehensive when researchers are taking measures such as height and weight. We will only share the results with your child and they can ask questions at any time. Your child may become out of breath and flushed during the fitness test, this is similar to what your child experiences when playing in the playground or taking part in sport. Your child will be monitored throughout, and they can stop at any point.

You and your child may find the information gained relating to health, physical activity levels and participation, and information relating to eating habits, interesting and informative.

5. Will my child's participation in the study be kept private?
All of the results of the research will only be viewed by the researchers. We will produce reports of the findings, but this will only give general information about the Year group as a whole. At no stage will your child's name be used when we report any of the results and we will treat all data in the strictest confidence.

For more information or if you have any questions about CHANGE! please don't hesitate to contact one of the researchers:
Rebecca Gobbi (R.Gobbi@2009.ljmu.ac.uk)
Kelly Mackintosh (K.A.Mackintosh@2009.ljmu.ac.uk)
Genevieve Warburton (G.L.Warburton@2009.ljmu.ac.uk)
Address: Liverpool John Moores University, IM Marsh, Barkhill Rd, Liverpool, L17 6BD
Telephone: **0151 231 5271**

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

PARENT/GUARDIAN/CARER

Title of Project: CHANGE! (Children's Health, Activity and Nutrition: Get Educated!)

Name of Researcher and School/Faculty: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh (The Faculty of Education, Community and Leisure, Liverpool John Moores University).*

We would like to invite your child to take part in a research study. Before you decide whether you would like to child to participate it is important that you understand why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you would like more information.

1. What is the purpose of the project?

Your child recently took part in the first stage of this study where we looked at a number of measures such as height and weight, physical activity levels and eating habits. We are now inviting a number of children to participate in the second stage of the project. This follows on by looking in more detail at your child's health and fitness. There are a number of sophisticated leisure centre, lab and school based tests that we would like your child to take part in. The tests are designed to measure, fitness, heart and blood vessel function, markers of cardiovascular health, blood pressure, bone health and body composition.

2. Does my child have to take part?

No. It is up to you to decide whether or not your child may take part. If you decide to allow your child to take part you will be asked to sign a consent form. Your child will also receive information about the project and an assent form to sign if they would like to take part. **Even after giving consent your child is still free to withdraw from the study or certain tests at any time without giving a reason. Testing will stop straight-away if your child wants to withdraw from the study.**

3. What will happen if my child takes part?

Your child will be asked to take part in a number of measurements which will be carried out on two different days. One will be done at school and should take less than an hour, and the other will be at Liverpool John Moores University and again should take a school day.

Testing Session A:
Markers of cardiovascular risk

For this your child should not have eaten breakfast, and only consumed water on the morning of blood sampling. This test will be completed at your child's school where we will set up a blood sampling area and a quiet area for them to relax in before and after sampling.

During this test a fully trained and experienced researcher will take a blood sample from your child. Your child will have a very small blood sample taken from their finger tip. This blood sample will be analysed to look for levels of cholesterol and fats in the blood, and see if any markers of inflammation are present. We will then use an ultrasound technique to see how your child's arteries in the arms are functioning. To complete this test a blood pressure cuff will be inflated around your child's arm and then deflated, we then look at how your child's blood vessels react. Blood pressure will also be measured at this time. Researchers will fully explain the tests to children and answer any questions they may have.

This information provides very useful information on the health of children, but we are not screening for any current health problems. Your child will be provided with breakfast after the tests are completed, and will be looked after by researchers to make sure they are OK. They will then carry on with the school day as normal after they have had their breakfast. Remember, your child can withdraw from tests at any point, and if they choose not to give a blood sample that is fine.

Testing Session B (At Liverpool John Moores University)
Children will be picked up from school at the start of the school day and will be returned by the end of the school day. Children will have completed all assessments no later than one hour after school finish time.

DEXA whole body scan
This machine scans the whole body, providing a picture of the skeleton and measuring bone, fat and muscle tissue. The scan takes four minutes, and uses radiation that is the equivalent of a two-hour flight on an aeroplane. Children will receive a picture of their skeleton in their results pack.

Ultrasound
During this test a researcher will scan the heart to measure its dimensions, and will also measure the thickness of some major arteries. This technique follows the same principle of scans used to produce images of a baby in the womb. Again, Researchers will fully explain the tests to children and answer any questions they may have.

Anthropometry
Simple height, weight, waist circumference, hip circumference and skinfolds measures will be taken.

Aerobic fitness
This will involve a treadmill based running test to maximum, and should last between 9 and 15 minutes. The participant will wear a face mask and a heart rate monitor. We will ensure that your child is fully warmed up before the test and familiarised with the treadmill. Children will also wear a harness to prevent any fall risk whilst on the treadmill. We will also ensure your child completes a cool down, and monitor your child's heart rate throughout.

After School Skills Assessment
We will also run an after school skills session which will be the same day as the lab visit. In this session, children will be assessed performing skills such as the hop, vertical jump, sprint, kick, catch and throw. They will be filmed performing these skills to allow for slow motion analysis. These video's will be kept in a secure setting and will only be handled by approved persons. Children should be finished no later than one hour after normal school finish time.

4. Other Details:

Risks/Discomfort Involved:

- Your child may become out of breath and flushed during the treadmill exercise, this is similar to what your child experiences when playing in the playground or taking part in sport. Your child's heart rate and condition will be monitored throughout, and they can stop at any point.

- Your child may feel a slight 'scratch' sensation when the blood sample is taken. Researchers will explain the blood sampling technique and ensure your child is fully aware of what is happening. Children will be monitored by researchers during and after the blood sampling to ensure they are feeling OK.

- The cuff used to take blood pressure and measure the function of blood vessels may cause slight pins and needles sensation, this will go once the cuff is released.

- The DEXA body scan emits a very small amount of radiation similar to that experienced in a two-hour flight.

Benefits:

- Your child will receive their results in a sealed pack at the end of the project, researchers will explain what these results mean, and you may contact researchers to discuss your child's results if you wish.

- These results will help you understand how healthy and fit your child is at the time of testing.

- Children usually find the laboratory visit interesting, enjoyable, and educational.

Confidentiality
All information about your child and their results will be treated with the strictest confidence. No identifiable information will be released by the project, and all data is securely stored by project staff, and may be accessed by approved persons only.

Sports Kit
Children should wear clean lightweight kit for the testing. Trainers should be non-muddy.

Time
Blood sampling should take no longer than a few minutes including explanations of the procedures to your child, and then your child will take several minutes to relax after sampling and eat breakfast. The lab based testing will require your child to be picked up from school at the start of the day and testing will take a full school day. You are welcome to accompany your child to the lab based testing. After the lab visit, your child will be returned to school for the end of the school day.

Eating

Children should not consume food on the morning of the blood sampling and should only drink water. We will provide breakfast on the blood sampling morning, but your child will need to bring a packed lunch and drinks to lab testing session.

Illness

Participants should postpone their testing if they are feeling unwell.

For more information or if you have any questions please don't hesitate to contact one of the researchers:

Rebecca Gobbi (R.Gobbi@2009.ljmu.ac.uk)

Kelly Mackintosh (K.A.Mackintosh@2009.ljmu.ac.uk)

Genevieve Warburton (G.L.Warburton@2009.ljmu.ac.uk)

Address: Liverpool John Moores University, IM Marsh, Barkhill Rd, Liverpool, L17 6BD
Phone: **0151 231 5271**

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

ASSENT FORM FOR CHILDREN

Project Name: *CHANGE! (additional physiological testing)*

Researchers: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh.*
The Faculty of Education, Community and Leisure, Liverpool John Moores University

To be completed by the child participant: Please circle your answer to the questions below.

Have you read (or had read to you) information about this project? Yes/No

Do you understand what this project is about?
Yes/No

Have you asked all the questions you want?
Yes/No

Have you had your questions answered in a way you understand?
Yes/No

Do you understand it's OK to stop taking part at any time?
Yes/No

Are you happy to take part?
Yes/No

If any answers are 'no' or you **don't** want to take part, don't sign your name!

If you do want to take part, please write your name below

Your name _____

Date _____

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

Project Name: *CHANGE!*

Researchers: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh.*
The Faculty of Education, Community and Leisure, Liverpool John Moores University

1. I confirm that I have read and understand the information provided for the above study. I have had the opportunity to consider the information, ask questions and if I have asked questions these have been answered satisfactorily. 1

2. I understand that my child's participation is voluntary and that my child is free to withdraw at any time, without giving a reason and that this will not affect mine or my child's legal rights. 2

3. I understand that any personal information collected during the study will be anonymised and remain confidential. 3

4. I give permission for photographs/video to be taken of my child during the project, which may be used for subsequent academic/promotional purposes associated with LJMU, Wigan Council and Ashton, Leigh and Wigan NHS. 4

5. I give permission for the research team to ask my child for his/her mobile number for the sole purpose of sending text message reminders to wear the physical activity monitors. 5

6. I agree my child can take part in the above study. 6

Name of Participant _____

Parent/Guardian/Carer Signature_____Date_____

_____

Note: When completed 1 copy for parent/guardian/carer and 1 copy for researcher

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

Project Name: *CHANGE! (Additional Physiological Testing)*

Researchers: *Dr. Stuart Fairclough, Dr. Lynne Boddy, Dr. Ian Davies, Dr. Allan Hackett, Rebecca Gobbi, Genevieve Warburton, Kelly Mackintosh.*
The Faculty of Education, Community and Leisure, Liverpool John Moores University

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3. I understand that any personal information collected during the study will be anonymised and remain confidential. 3

4. I give permission for photographs/video to be taken of my child during the project, which may be used for subsequent academic/promotional purposes associated with LJMU, Wigan Council and Ashton, Leigh and Wigan NHS. 4

5. I give permission for the research team to transport my child with other children to LJMU. 5

6. I give permission for my child to attend the after school skills assessment session, 6

   If yes, how will your child be transported home after the skills assessments?

   (E.g. they will be collected, walk etc) _____

7. I give permission for researchers/phlebotomists to take a blood sample from my child if my child is happy for them to do so. 7

8. I agree my child can take part in the above study 8

Name of Participant _____

Parent/Guardian/Carer Signature_____Date_____

Note: When completed 1 copy for parent/guardian/carer and 1 copy for researcher

NHS
Ashton, Leigh and Wigan

LIVERPOOL JOHN MOORES UNIVERSITY

MEDICAL SCREENING FORM

Title of Project: CHANGE (Children's Health, Activity and Nutrition: Get Educated!)

Name of Researcher and School/Faculty:
Dr Stuart Fairclough (Faculty of Education, Community and Leisure)

This form should be completed as accurately as possible by the parent/guardian. All information will remain confidential. The form is designed to ensure that your child has no medical condition/illness that might compromise their safety to take part in the project. It will also be available in case of emergency.

Name of child _____

Address _____

_____

Doctors Address _____

_____

Home Tel No. _____

	YES	NO
Has your child ever had any surgery?		
Has your child ever suffered from any injuries?		
Has your child recently suffered from any illness?		
Has your child been involved in any major accidents?		
Is your child currently being treated by your doctor?		
Does your child have problems with:		
• hearing		
• vision		
• bones/joints		
• co-ordination		
• diabetes		
• epilepsy		
• respiratory problems		
• heart problems		
Is your child allergic to any medication?		
Does your child carry any medication in case of emergency?		

If you have answered yes to ANY questions please provide relevant details