THE EFFECTS OF RESISTANCE EXERCISE ON INSULIN SENSITIVITY IN ADOLESCENTS

by © Sarah A. Critch

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ABSTRACT

Background: An escalating incidence of type 2 diabetes among adolescents is causing concern. This is thought to be sparked by rising population-wide prevalence of insulin resistance. Resistance exercise has been shown to reduce insulin resistance, however only immediate, post-intervention effects have been demonstrated. The use of resistance exercise by adolescents in managing insulin resistance in the long-term has not been evaluated.

Purpose: To assess the effects, up to six months, of a physiotherapist-supervised, resistance exercise program on insulin sensitivity, cardiorespiratory fitness, muscle strength, physical activity levels, and anthropometric measures among adolescents with insulin resistance.

Methods: Participants with insulin resistance were recruited from a database of patients from a pediatric chronic disease prevention program. They completed a supervised 10-week resistance exercise program, 60-minutes, three times per week. A body positive approach was used focusing on health behaviours. Using a repeated-measures design, participants were assessed during an observational run-in control period then at pre, post, and 6-month follow-up assessments. The primary outcome was insulin sensitivity, measured by the oral glucose tolerance test. Secondary outcomes included cardiorespiratory fitness, muscle strength, physical activity level, and anthropometric measures.

Results: Thirteen participants (14.16±1.19 years old; 8 males, 5 females) completed the intervention. Improvements in insulin sensitivity were found, observed as reduced fasting insulin [$F_{(2,22)}$=7.54,p=0.003,ηp^2=0.41], fasting glucose [$F_{(2,22)}$=3.58,p=0.045,ηp^2=0.25], and HOMA-IR [$F_{(2,22)}$=7.60,p=0.003,ηp^2=0.41], which were maintained at follow-up. Cardiorespiratory fitness, waist circumference, and waist-to-hip ratio also significantly improved at post and follow-up. Daily physical activity levels improved but not significantly. Upper and lower body muscle strength significantly increased post-intervention but returned to pre-assessment values at follow-up.

Conclusion: The findings suggest that a supervised 10-week resistance exercise program (60-minute, three times per week) improves insulin sensitivity, cardiorespiratory fitness, waist circumference, and waist-to-hip ratio in adolescents who are at high risk of developing type 2 diabetes. Importantly, these benefits are maintained up to six months. Supervised, resistance exercise adds significant long-term benefit in the management of insulin resistance in adolescents.

For my husband, Darrell, and son, Chase.

Thank-you for your unconditional love, prayers, and constant support.

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LIST OF ABBREVIATIONS AND SYMBOLS

Symbol / Abbreviation	Meaning
ACSM	American College of Sports Medicine
ANOVA	Analysis of variance
AUC	Area under the curve
BMI	Body mass index
CDPP	Chronic Disease Prevention Program
cm	Centimetre
CON	Control period
DXA	Dual-energy x-ray absorptiometry
F	F-value or F-ratio
FOLLOW-UP	6-month follow-up assessment
FSIVGTT	Intravenous glucose tolerance test
G	Grams
GLUT-4	Glucose transporter type 4
HOMA-IR	Homeostasis model assessment of insulin resistance
hrs	Hours
Kg	Kilogram
L	Litre
M	Metre
m^2	Squared metre
mL	Millilitre
mL/min/kg	Millilitres per minute per kilogram
min	Minute
mmHg	Millimetres of mercury
mmol/L	Millimoles per litre
n	Number (of)
NL	Newfoundland and Labrador
ηp^2	Partial Eta Squared
OGTT	Oral glucose tolerance test
p	Probability

pmol/L/min	Picomoles per litre per minute
POST	Post-intervention assessment
PRE	Pre-intervention assessment
RCT(s)	Randomized Control Trial(s)
SD	Standard deviation
VCO_2max	Maximal carbon dioxide production
VO_2max	Maximal oxygen consumption
WHO	World Health Organization
±	Plus or minus
%	Percentage
=	Equal
<	Less than
>	Greater than
e.g.	For example

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CHAPTER ONE

As Canadians strive to improve their health, there is ongoing concern with the increasing incidence of type 2 diabetes among children.[1] A 2006 surveillance study showed an annual incidence of 1.54 per 100 000 cases of type 2 diabetes in Canadian children (<18 years). This incidence translates into at least 113 new cases of type 2 diabetes diagnosed in Canadian children annually.[1] In Canadian youth (>10 and <18 years), the incidence doubles to 3.10 per 100 000 cases of type 2 diabetes; the study found that the average age at diagnosis of type 2 diabetes was 13.7 years. Reasons for the incidence of type 2 diabetes among adolescents (13-18 years) have been discussed in the literature. It is mainly thought to be related to prevalence of insulin resistance amongst this population as 73% of those adolescents diagnosed with type 2 diabetes show symptoms of insulin resistance, such as acanthosis nigricans (dark, thickened skin along back of the neck, under the breasts, or axillae).[1]

An increasing rate of insulin resistance among adolescents is observed in Newfoundland and Labrador (NL).[2] Experts agree that prevention and management of risk factors must be the focus of care in the pediatric population to effectively reduce rates of insulin resistance; thus, preventing the cascade of diagnosis from insulin resistance to type 2 diabetes.[3-7] Canada's Centre for Chronic Disease Prevention implemented a strategic plan for 2016–2019 entitled "Improving Health Outcomes - A Paradigm Shift" in an effort to tackle the growing incidence of insulin resistance and type 2 diabetes in Canada.[3,7,8] NL has implemented a provincial pediatric chronic disease prevention program (CDPP), to help families address factors contributing to the development of insulin resistance.

The etiology of insulin resistance has been comprehensively described in the literature with non-modifiable (e.g., ethnicity and genetics)[1,7,9] and modifiable (e.g., dietary intake of glucose and saturated fat, excess fat, physical activity, and sleep)[1,3,4,6,7,10-12] factors identified as contributing to the increasing incidence. Physical activity has been shown to be a modifiable factor that can help reduce insulin resistance.[12-21] However, most adolescents are physically inactive and lead a sedentary lifestyle[22] and, therefore, they do not obtain health benefits observed with regular physical activity. An increase in physical activity is a tangible lifestyle modification some families can make that could reduce the risk of developing insulin resistance in adolescents. Therefore, the focus of this review will be discussing the role of physical activity in the development and management of insulin resistance.

The health benefits associated with regular physical activity are robust regardless of age, gender, or culture.[23-25] Specifically, in a pediatric population, research has shown that regular aerobic and resistance exercise can help improve insulin resistance.[12-21] Although this is useful information, it is unknown exactly how to prescribe exercise (e.g., frequency, intensity, repetitions, and duration) to adolescents with insulin resistance, as precise exercise guidelines have not been published. There are only a few studies looking at the effects of resistance exercise.[17] What is known from randomized controlled trials (RCT) completed using resistance-based interventions is that they were offered in 60-minute sessions, two to three times per week for 12-16 weeks.[26-31] Resistance was applied using a variety of equipment and exercises were set-up in a circuit.[14] How intensity was determined and progressed varied among studies.[14,26-31] Some research promotes the use of a 'body positive approach' when implementing a physical activity intervention to help manage chronic disease, as it focuses on long-term change of lifestyle behaviours.[32-37] However, the role of physical activity in the long-term management of insulin resistance has yet to be examined. In accordance with this observation, the systematic review and meta-analysis by Fedewa et al.[17] stated that more research was required to determine which type of physical activity would produce sustainable change and promote lifestyle modification. Therefore, the primary objective of this thesis was to help address this gap identified in the literature by evaluating effects, up to six months, of resistance exercise on insulin sensitivity in adolescents diagnosed with insulin resistance.

Chapter One will review the definition and etiology of insulin resistance, effects of physical activity on insulin resistance, barriers to adherence to physical activity in adolescents, gaps and limitations within the research, current clinical efforts to help adolescents manage insulin resistance, and objectives for this thesis. Written as a manuscript, Chapter Two will provide a brief review of the literature, details of the methods used to conduct this study, presentation of findings, and a brief discussion addressing how results may affect clinical care provided to adolescents with insulin resistance. Chapter Three will discuss, in more detail, the significance and implications of the results of this study, discussing how results may affect the clinical care provided to adolescents with insulin resistance, and address study limitations.

1.1 INSULIN RESISTANCE

1.1.1 What is insulin resistance?

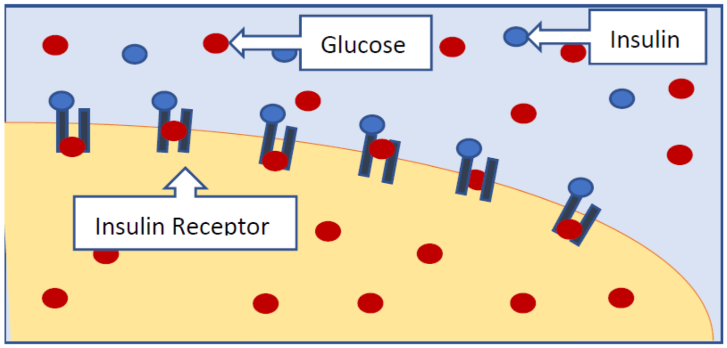
To understand insulin resistance, this section will review the role of insulin in blood hemostasis, discuss the effects of maturation on insulin production, differentiate insulin resistance from pre-diabetes, outline the characteristics of persons who have insulin resistance, and discuss diagnostic testing to determine the presence of insulin resistance.

1.1.1.1 The role of insulin in blood hemostasis

Insulin, an anabolic hormone made by the pancreas, is primarily responsible for assisting cells to metabolize glucose. The pancreas is made up of clusters of cells called islets. Pancreatic beta cells within these islets make insulin, which is released into the blood.[38] Insulin in the blood must bind to plasma membrane receptors or insulin receptors on cells, which then signal the transport of glucose into that cell, as shown in panel A of Figure 1.1. Once in the cell, glucose is used as energy. The pancreas must make enough insulin to complement the dietary intake of glucose.[38,39] In a person with normal insulin action, the pancreas can match the dietary intake of glucose by producing enough insulin to maintain blood hemostasis. Insulin does this by (1) helping muscle, fat, and liver cells absorb glucose from the blood, (2) stimulating muscle and liver cells to store extra glucose, and/or (3) reducing glucose production by the liver.[38] Insulin sensitivity refers to how responsive the body is to the effects of insulin. A person who has a normal physiological reaction to insulin is said to be insulin sensitive, meaning they require a small amount of insulin to lower their blood glucose levels.[38-40] Insulin sensitivity refers to the responsiveness of the cells to insulin.[38-40] As larger amounts of insulin are required to elicit a physiological response in cells, insulin sensitivity decreases. When cells become insensitive to insulin, the person is at risk of becoming insulin resistant.[41]

Insulin resistance is defined as the inability of insulin within the blood to perform normally in the process of glucose metabolism.[41] When the body is insulin resistant, insulin sensitive cells, mainly skeletal muscle cells, have a muted response to the role of insulin in transporting glucose from the blood into cells. In this state, insulin receptors on cells do not recognize insulin in the blood, thus insulin does not bind to the receptors. A main reason for insulin receptors not binding with the circulating insulin, is an increase in intramyocellular lipid within the skeletal muscle cell.[42,43] In the absence of receptor-bound insulin, glucose is prevented from travelling from the blood into cells, as shown in panel B of Figure 1.1. Thus, glucose accumulates within circulation resulting in hyperglycemia or elevated blood glucose levels. To compensate for hyperglycemia, pancreatic beta cells secrete more insulin, consequently causing an increase in blood insulin levels (sometimes called compensatory hyperinsulinemia).[38-40] Over time, the pancreas will become incapable of maintaining this compensation and will cease producing sufficient amounts of insulin, increasing the individuals' risk for developing type 2 diabetes and cardiovascular disease.[4,5,39,40]

Panel A: Normal Cell



Panel B: Insulin Resistant Cell

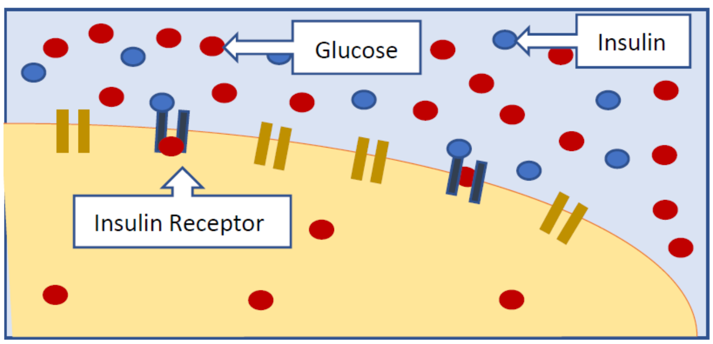


Figure 1.1: The basic physiology of a cell when insulin resistant

Red dots represent glucose; Blue dots represent insulin; Navy/orange rectangles represent insulin receptors; Orange area is the cell; Blue area is the blood.
Panel A: Normal cell – insulin binds to the insulin receptors allowing the transport of glucose into the cell. Panel B: Insulin resistance cell – insulin receptors are no longer sensitive to circulating insulin in the blood stream, thus do not bind to receptors therefore preventing the transport of glucose into the cell.

Furthermore, free fatty acid and intramyocellular lipid levels have been found to contribute to the pathology of insulin resistance.[42,43] An increase in free fatty acids (from dietary intake of saturated fat) in the blood has been shown to be accompanied by an increase in intramyocellular lipids or fat within skeletal muscle cells.[42,43] Intramyocellular lipids can inhibit glucose transporters preventing glucose from travelling from the blood into the cell to be used as energy. This results in a reduction in insulin sensitivity within the skeletal muscle cell.[43] Thus, glucose accumulates within circulation resulting in hyperglycemia. Similarly to the compensation required to control for excess dietary glucose, the pancreas must also compensate for elevated blood glucose due to the effects of intramyocellular lipids by producing more insulin.[42,43]

1.1.1.2 Effects of maturation on insulin sensitivity

The response of insulin is also influenced by puberty. Hormonal changes that take place during puberty cause insulin sensitivity to naturally decrease at the onset of puberty, which does not recover until the end of maturation.[4,44-46] Puberty proceeds in a predictable pattern of maturity that is often defined in stages using the Tanner scale, beginning at stage one at the onset of puberty and ending at stage five. The Tanner scale represents stages of puberty based on growth in stature and development of sexual characteristics.[47] The developmental pattern of insulin sensitivity is often described as 'transient physiological insulin resistance'; this is a natural occurrence of insulin resistance commencing during Tanner stage two, peaking during Tanner stage three, and returning to a baseline during Tanner stage five.[4,44,45] The emergence and disappearance of transient pubertal insulin resistance is an important factor to consider when determining the rates of insulin resistance among adolescents. Adolescents may be at greater risk of abnormal degrees of insulin resistance during puberty due to a combination of transient insulin sensitivity[4,44-46] and the adoption of unhealthy lifestyle habits, including decreased physical activity and increased sedentary behaviour.[22,46]

1.1.1.3 Insulin resistance compared to prediabetes

The terms 'insulin resistance' and 'prediabetes' are often incorrectly interchanged. As stated, insulin resistance is diagnosed once cells become resistant to insulin binding to insulin receptors. At this stage, pancreatic beta cells are still able to produce enough insulin to meet the dietary intake of glucose and saturated fat, thus blood glucose levels stay within the normal range. If insulin resistance is not managed properly, a person becomes at increased risk of developing prediabetes. When a person is prediabetic, pancreatic beta cells can no longer produce enough insulin to overcome insulin resistance; therefore, blood glucose levels rise above the normal range.[38,48] More specifically, prediabetes is defined by Goldenberg et al.[48] as "impaired fasting glucose, impaired glucose tolerance, or a glycated hemoglobin (A1C) of 6.0% to 6.4%, each of which places individuals at high risk of developing diabetes and its complications". If loss in function of pancreatic beta cells continue, this may lead to type 2 diabetes.[38,48]

1.1.1.4 Characteristics of a person with insulin resistance including diagnostic testing

The clinical diagnosis of insulin resistance co-occurs based on typical clinical features and results of laboratory testing. There is not one specific clinical feature that consistently presents in all people with insulin resistance. An adolescent with insulin resistance may be normal weight (a body mass index (BMI) between the 5th and 84th percentile as per the World Health Organization (WHO) growth charts[49]), overweight (a BMI between the 85th and 94th percentile as per the WHO growth charts[49]), or obese (a BMI >95th percentile as per the WHO growth charts[49]).[4,6,50,51] BMI is a measure of body weight relative to height.[49] In a pediatric population, body mass changes with age thus categories of underweight, healthy weight, overweight, and obese are defined as percentiles based on age and gender.[49] An adolescent with insulin resistance may have increased or normal waist circumference[4,6,50]; acanthosis nigricans (dark, thicken skin along back of the neck, under the breasts, or axillae)[1]; dyslipidemia (low high-density lipoproteins levels and high triglycerides)[52]; impaired glucose tolerance (glucose intolerance after a standardized glucose intake)[4]; impaired fasting glucose (poor glucose metabolism when fasting)[4]; hypertension[4]; non-alcoholic fatty liver disease[4,52]; polycystic ovary syndrome[4,53]; low cardiorespiratory fitness[10,12,15,21,54]; and/or a strong family history (genetics) of type 2 diabetes or cardiovascular disease[4,44]. Insulin resistance may also occur as part of a cluster of cardiovascular and metabolic symptoms commonly called metabolic syndrome (a waist circumference >90th percentile plus at least two of the following: impaired fasting glucose, hypertension, or dyslipidemia).[4,5,46]

In clinical practice, there is no single laboratory test to diagnose insulin resistance. Insulin sensitivity can be measured using two laboratory methods: (1) Whole-body assessments of insulin action (e.g.: euglycemic-hyperinsulinemic clamp (the gold-standard), intravenous glucose tolerance test (FSIVGTT), and oral glucose tolerance test (OGTT)) or (2) Indirect measures (e.g.: homeostasis model assessment of insulin resistance (HOMA-IR), whole-body insulin sensitivity index, fasting insulin concentration; fasting glucose/fasting index ratio, quantitative insulin-sensitivity check index, and insulin sensitivity index).[41,55,56] A commonly used laboratory test is the OGTT, from which the HOMA-IR is derived. Normative values for the OGTT and the HOMA-IR in a pediatric population are presented in Table 1.1. Presence of clinical features, as stated above, together with laboratory findings is indicative of a diagnosis of insulin resistance.

Table 1.1: Normative values for OGTT outcomes for children (<18 years)

Outcomes	**Normal values for children**
Fasting insulin (pmol/L)	0 – 170
Fasting glucose (mmol/L)	3.5 - 6.0
Insulin at 2 hrs (pmol/L)	<800
Glucose at 2 hrs (mmol/L)	<7.8
HOMA-IR	<2.5

Abbreviations: pmol/L = picomoles per litre; mmol/L = millimoles per litre; HOMA-IR = Homeostasis model assessment of insulin resistance

Once diagnosed with insulin resistance, adolescents are provided with information about managing this condition. In general, insulin resistance can be managed using medication (such as metformin), altering eating habits (such as increasing fruit and vegetable intake, increasing fibre consumption, and reducing intake of sugar), increasing daily physical activity time, and reducing daily sedentary time.[4,7,57] Changes in lifestyle are likely to result in metabolic improvements and consequently alleviate insulin resistance. However, changing lifestyle habits is not easy. Therefore, the role of the healthcare team is not only to prescribe appropriate medication, but also to help those diagnosed with insulin resistance to identify and change modifiable behaviours that may improve their insulin sensitivity. It follows that healthcare professionals must understand which lifestyle factors are typically associated with this condition. Thus, the next section will describe the etiology of insulin resistance.

1.1.2 Etiology of insulin resistance

The etiology of insulin resistance is widely addressed in the literature. Mainly modifiable factors contributing to insulin resistance are discussed; non-modifiable factors associated with the development of insulin resistance are lesser known. Both non-modifiable (e.g., ethnicity and genetics)[1,7,9] and modifiable (e.g., dietary intake of glucose and saturated fat, excess fat, physical inactivity, and sleep)[1,3,4,6,7,10-12] will be discussed in more detail.

1.1.2.1 Non-modifiable factors

A non-modifiable factor identified as having a role in the development of insulin resistance is genetic anomalies among certain ethnic groups. Within Canada, there are some ethnic groups, such as indigenous groups, who have a higher prevalence of insulin resistance, type 2 diabetes, and cardiovascular disease.[1,7] The annual incidence is 23.2 per 100 000 cases of type 2 diabetes in Canadian indigenous children (<18 years)[1], which is 15 times higher than the general Canadian population. Highly prevalent among indigenous groups are genetic abnormalities of proteins involved in the action of insulin, which can reduce effectiveness of insulin in maintaining blood hemostasis, thereby increasing susceptibility for insulin resistance.[7,9] Compounding the issue, Harris et al.[9] suggests that the increased prevalence among indigenous groups may also be attributed to modifiable factors such as the quality of their healthcare, particularly limited access to healthcare, fragmented health service, and limited health surveillance. Diminished healthcare quality impacts insulin resistance as people may not receive the support and information regarding the preventative measures, such as to decrease glucose intake and increase physical activity, they can take to reduce their risk.[9]

1.1.2.2 Modifiable factors

In addition to ethnicity and genetic susceptibility, specific modifiable factors have been shown to play a role in the development of insulin resistance. These include excess dietary intake of glucose and saturated fat, excess weight, excess visceral fat, physical inactivity, sedentary lifestyle, and lack of and/or interrupted sleep.[1,3,4,6,7,10-12] These factors are concerning given the current rate of type 2 diabetes in the Canadian pediatric population.

1.1.2.2.1 Consuming excess dietary intake of glucose and saturated fat

Excess dietary intake of glucose and saturated fat are common behaviours among Canadians. In a surveillance study conducted in 2004, Canadians were recorded as consuming 110 grams of sugar per day (equivalent to 26 teaspoons), accounting for 21.4% of their total daily calorie intake. The daily intake was recorded as even higher in adolescents at 24.1% and 24.6% for boys and girls respectively.[58] Canada's Food Guide encourages a limited intake of foods and beverages high in sugar and fat.[59] As high amounts of glucose and saturated fat are consumed, the pancreas must continue to produce appropriate amounts of insulin. As described in the previous section, the body can only endure this effort for so long before cells become resistant to insulin. Efforts to reduce the dietary intake of glucose and saturated fat may be key to reducing rates of insulin resistance[4,5,7] and, therefore, must be considered by healthcare professionals when discussing modifiable factors with adolescents diagnosed with insulin resistance.

1.1.2.2.2 Obesity

Pediatric obesity rates are increasing, with one in four Canadian adolescents now classified as overweight or obese.[60] It is uncertain whether obesity is an independent, modifiable factor which directly contributes to cells becoming resistant to insulin, or is an indirect result of the body attempting to manage excess dietary glucose.[4] Cruz et al.[4] suggest two theories which may explain the interaction between weight and insulin action. In terms of the 'direct' theory, it has been suggested that excess weight, particularly visceral fat, may directly cause insulin resistance for two reasons: dysfunction related to fat stored in organs and metabolic dysregulation. With increasing adiposity, there is an increase in fat deposition outside of adipose tissue, such as in muscles (called intramyocellular lipid), which has been shown to be a determinant of insulin resistance in adolescents.[42,43] As well, adipose tissue is critical in metabolic regulation as it produces and secretes adipocytokines (e.g.: leptin, adiponectin, and interleukin-6), which help control appetite and stimulate energy expenditure.[4,61,62] Dysregulation within this metabolic process may contribute to the development of insulin resistance.[4,61,62] The second or 'indirect' theory suggested by Cruz et al.[4] that connects obesity and insulin resistance suggests that obesity is indirectly a result of the body attempting to manage the excess intake of glucose and saturated fat, thus, the increased effort needed by the pancreas to produce insulin. Insulin, being an anabolic hormone, is efficient at encouraging the growth of tissues, in this case, fat. Since insulin is responsible for metabolizing glucose, it facilitates the conversion of excess glucose into fat, a process to help manage the excess intake of dietary glucose and saturated fat.[4,5,32,39,42,43] Although body weight does not equate directly with health[63,64], the ongoing strain on the body during either of these processes may contribute to the development of other chronic diseases, such as metabolic syndrome, cardiovascular disease, or type 2 diabetes.[4,5]

1.1.2.2.3 Physical inactivity

Physical inactivity and sedentary lifestyle, considered modifiable factors, have been shown to contribute to the current health status of the Canadian pediatric population, including the incidence of insulin resistance.[4,10,12,15,16,54] Unfortunately, only 5% of adolescents meet the Canadian Physical Activity Guidelines of 60 minutes of moderate-to-vigorous activity per day [22]; therefore, they do not obtain the health benefits attributed to regular physical activity.[24] Most adolescents live a sedentary lifestyle with only 10% meeting the Canadian Sedentary Behaviour Guidelines of no more than two hours of screen time per day.[22] The combination of reduced physical activity and increased sedentary time places many adolescents at higher risk of developing chronic diseases, such as insulin resistance.[24] Regular physical activity, both aerobic and resistance-based, has been shown to have many health benefits for adolescents.[24] As will be discussed later in this chapter, one of the effects of physical activity on blood hemostasis is the increased need for glucose to be converted to energy to be used by active muscles. The increased demand for glucose lowers blood glucose level, thus, lessening the requirements for the pancreas to synthesize insulin. An inactive lifestyle, therefore, may contribute to the increasing risk of developing insulin resistance.[4,5,12,39]

1.1.2.2.4 Sleep

Inadequate and interrupted sleep has also been identified as a modifiable factor to be considered when addressing insulin resistance.[11,65,66] Most Canadian adolescents are not obtaining the sleep they require each night (between eight and ten hours)[22], which potentially impacts their overall health status and lifestyle choices. With regards to insulin resistance, a lack of and/or interrupted sleep may affect a person's energy level, their ability to be physical active, to maintain or lose excess weight, and their food and beverage choices, all of which have been attributed to the development of insulin resistance.[11,65] Therefore, sleep may be an indirect factor contributing to insulin resistance as it influences other modifiable factors. Research has shown associations between sleep duration and risk of insulin resistance. For example, in a study by Matthews et al.[66] which recorded sleep duration and insulin resistance levels in 245 healthy adolescents, shorter sleep duration was associated with higher insulin resistance independent of age, gender, BMI, waist circumference, or ethnicity. Further, they reported that for every extra hour of sleep per night, a 9% improvement in insulin resistance was observed.[66] Whether there is a direct or indirect relationship between sleep and insulin resistance is unknown; however, for healthcare professionals working with adolescents at risk of insulin resistance, sleep is a compelling target for a behavioural intervention.

The modifiable factors contributing to insulin resistance discussed above (e.g., excess dietary intake of glucose, excess weight and visceral fat, physical inactivity, sedentary lifestyle, and lack of and/or interrupted sleep[22]) are also typical of adolescents' lifestyle in Canada[22,58,60], thereby exposing them to the risk of developing insulin resistance. Left unaddressed, these modifiable factors can precipitate the continuation of insulin resistance, and possible subsequent development of type 2 diabetes. The etiology of insulin resistance is multi-factorial. A number of modifiable factors have been shown to be associated with it, suggesting that preventative interventions to improve lifestyle behaviours are critical in preventing this disease. The next section will examine one of these modifiable factors, physical activity, as a method to help manage blood hemostasis and thus insulin resistance.

1.2 EFFECTS OF PHYSICAL ACTIVITY ON BLOOD HEMOSTASIS

Before discussing how physical activity can affect blood hemostasis and thus insulin resistance, terminology will be clearly defined. Physical activity is any bodily movement produced by our skeletal muscles which may not have a clear objective, whereas exercise is a subset of physical activity that is specific, structured activity with the intent to improve fitness.[67,68] There are two main forms of exercise: aerobic and resistance. These two terms will be used, not interchangeable, but as they are intended. Physical activity will be used when discussing activity in general, such as daily physical activity amounts. Exercise will be used when discuss structured activities, such as resistance exercises used in interventions.

Aerobic exercise involves continuous movement of large muscle groups, such as quadriceps, gluteus, and muscles within the back.[63] Examples include walking, bicycling, running, swimming, or playing leisure games, such as tag. Resistance exercise involves progressive, repetitive movements of the body against a resistance.[69,70] Resistance could be in the form of body weight, hand-held weights, resisted bands, or weight machines. Examples include wall climbing, sit-ups, push-ups, using weight machines, or playing leisure games, such as tug-of-war.

Regardless of type, physical activity has a profound impact on physical, mental, and social health, as listed in Table 1.2. Even modest amounts of physical activity can have tremendous health benefits in adolescents that are high-risk for disease (e.g., obese or insulin resistant).[5,24] Physical activity also helps prevent the development of many diseases, such as type 2 diabetes[21,68,71], cardiovascular disease[68], certain types of cancer[68], osteoporosis[72], stroke[68], and depression[24].

Table 1.2: The physical, mental, and social benefits attributed to regular physical activity (aerobic and resistance-based)

Physical Health	• Increases cardiorespiratory fitness[10,12,15,16,54,73-75] • Improves lipid profile (decreases level of triglycerides and increases level of HDL or healthy cholesterol)[14,16,23,24,76] • Helps maintain normal blood glucose levels thus reduces insulin requirements[14,17,18,20,23,24,69,76] • Lowers heart rate and blood pressure[16,23,24,76] • Increases bone mineral density[14,24,69,72,76] • Increases muscle strength and endurance[14,24,69,76] • Improves balance and coordination[24,69,76] • Improves sleep[24] • Helps maintain a healthy body weight[16,23,24,76] • Develops fundamental movement skills[24,69,76]
Mental Health	• Reduces stress[23,24,76,77] • Enhances mood[24,76] • Improves cognitive functioning[24,76] • Improves learning and attention[24,76] • Reduces risk of anxiety and depression[23,24,76,77]
Social Health	• Increases confidence[24,69,76,77] • Enhances self-esteem[23,24,69,76,77] • Improves body image[37,77] • Provides an opportunity to expand social connections[24]

When specifically discussing blood hemostasis, regular physical activity can create adaptations within the body to help control blood glucose. A systematic review and meta-analysis completed by Fedewa et al.[17] included 24 RCTs and analyzed data on 1599 children (age 6-19 years). The authors reported that exercise (combined results of aerobic and resistance-based interventions) decreased fasting insulin (effect size = 0.48) and reduced insulin resistance (effect size = 0.31), immediately post-intervention, in children and adolescents. These benefits will be discussed in more detail in the following sections.

1.2.1 Effects of aerobic exercise on blood hemostasis

Aerobic exercise may improve glycemic control[18,50,63,78,79], help with weight management[16,24,76], and increase cardiorespiratory fitness[10,12,15,16,54,73-75], which contributes to the overall improvement in insulin sensitivity in a pediatric population.[18]

As a person participates in aerobic exercise, the body requires more glucose to meet the increased energy demand.[50,63,78] Cells, such as skeletal muscle cells, increase their uptake of glucose and, in response, the pancreas lessens insulin production.[21,50,63] Alberga et al.[79] completed a review on 17 RCTs studying the effects of aerobic exercise on markers of insulin resistance among obese adolescents (13-18 years). These authors found that the effects of aerobic exercise on insulin resistance were inconsistent due to variability within the methods of the RCTs, such as studying aerobic exercise in combination with dietary restrictions. They did state that five RCTs studying only the effects of aerobic exercise, without dietary restrictions, noted an increase in insulin sensitivity.[79] Gracia-Hermoso et al.[18] completed a systematic review and meta-analysis including nine RCTs analyzing data on 367 (n=191 and n=176 in intervention and control groups respectively) children (age 6-18 years) from five countries. Aerobic exercise was applied using a variety of methods, including treadmills, cycle ergometers, rowers, sports, running, walking, cycling, snowshoeing, and skipping rope. The authors reported that aerobic exercise reduced fasting glucose (effect size = -0.39) and fasting insulin (effect size = -0.40) levels with moderate effect sizes.[18] As stated previously, Fedewa et al.[17] completed a systematic review and meta-analysis studying the effects of exercise in general on insulin resistance. They analyzed 24 RCTs with all but two studies using aerobic-based interventions, thus the results seen (including reduced fasting insulin and insulin resistance) are more likely attributed to aerobic exercise than resistance exercise. The results of these meta-analyses suggest that aerobic exercise may be an effective tool in the management of insulin resistance in adolescents.

An increase in cardiorespiratory fitness, or ability of the circulatory and respiratory systems to supply oxygen to the body, is an additional benefit associated with an increase in aerobic exercise.[63] In the review by Alberga et al.[79] of RCTs studying the effects of aerobic exercise on cardiometabolic risk factors among obese adolescents, five RCTs were identified as measuring cardiorespiratory fitness, noting a significant increase following an aerobic-based intervention.[79] The authors suggested that when considering the effects of aerobic exercise on cardiorespiratory fitness, intensity of the exercise and compliance with the program are the most important factors to consider.[79] Janssen et al.[24] reported in their review of the benefits of physical activity, including aerobic exercise, among school-aged children that even modest amounts of physical activity may increase cardiorespiratory fitness, in high-risk adolescents (e.g.; obese, insulin resistant). When reviewing the literature studying the association between cardiorespiratory fitness and insulin resistance, evidence (from well-conducted clinical trials and cross-sectional studies) suggests that an increase in cardiorespiratory fitness is independently associated with improvements in insulin sensitivity.[10,12,15,16,54,73,75] Specifically, in a well-conducted clinical trial studying 53 adolescents females, they reported that cardiorespiratory fitness, measured using a sub-maximal exercise test, was a predictor of HOMA, a measure of insulin sensitivity, even when accounting for change in percent body fat.[54] In addition to improving insulin sensitivity and, consequently, reducing the risk of developing insulin resistance, an increase in cardiorespiratory fitness can also reduce the risk of all-cause mortality and the development of type 2 diabetes, cardiovascular disease, certain types of cancer, hypertension, and stroke.[23,68,71,79]

In addition to improved cardiorespiratory fitness and glycemic control, aerobic exercise may also reduce body weight for some people, which may help to increase insulin sensitivity.[4,16,18,23,24] In the review by Alberga et al.[79] of RCTs studying the effects of aerobic exercise on cardiometabolic risk factor, they reported inconsistent findings on changes in body weight, BMI, waist circumference, or percent body fat (15 RCTs reported a significant decrease in one of these anthropometric measures, whereas seven RCTs report no change).[79] Along with this evidence, cross-sectional studies[12,13,15,21,75,80] have reported that regular aerobic exercises has been shown to improve insulin sensitivity, with and without changes in weight, BMI, waist circumference, and/or adiposity. However, a preliminary study on mice noted that when adiposity decreased, the density of insulin receptors and glucose transporter type 4 (GLUT-4 transporter) proteins increased, thereby augmenting the cells' glucose uptake, helping to increase insulin sensitivity.[81] Richter et al.[78] stated in their detailed review of the physiology of GLUT-4 proteins and their role in glucose delivery, transport, and metabolism that there is an increase in GLUT-4 proteins with exercise, enhancing the overall function of the cell. They report that exercise intensity and duration are the primary determinants of glucose uptake by skeletal muscles. Based on the findings from clinical research along with the knowledge of physiology, the improvements in insulin sensitivity due to aerobic exercise may be caused by physiological changes within the cells, such as an increase in GLUT-4 transporters, and not only alterations in anthropometric measures or body composition, such as reduced adiposity.

1.2.2 Limitations within research using aerobic-based interventions

Although the research, supporting aerobic exercise to help manage insulin resistance is compelling, there are limitations, including relative paucity of RCTs designs, clarity of diagnosis in selection criteria, compliance to the exercise trials, lack of control of diet and physical activity, and lack of follow-up. Two systematic reviews and meta-analysis on a total of 31 RCTs, in addition to well-conducted cross-sectional and cohort studies, have concluded that more robust RCTs are needed to make definitive statements about the effectiveness of aerobic exercise in the prevention and treatment of insulin resistance, providing details of the exercise prescription requried.[17,18] The second limitation is concerning recruitment of participants; in all published studies, participant selection was based on BMI and not on a diagnosis of insulin resistance.[18] It is known that not all adolescents with an elevated BMI are insulin resistant[33,54]; therefore, not all participants recruited necessarily had insulin resistance. Thirdly, compliance to the intervention was not reported for most studies (in only four of nine RCTs); however, of the studies that reported compliance, the rate was high (80-100%).[18] Lack of information about compliance is a concern for studies reporting non-significant effects, as readers are unable to discern whether there indeed could be a benefit if participants were compliant with the intervention. As well, compliance rates and the reasons for drop out provide valuable guidance for healthcare professionals prescribing aerobic exercise to improve insulin resistance. The fourth limitation, and perhaps the most important confounding variable which may or may not have influenced the results in this body of literature, is the impact of diet and physical activity performed outside of study protocols. Most studies did not account for dietary habits or physical activity levels of their participants during the study period.[17,18] Davis et al.[82] did measure habitual physical activity pre- and post- intervention using accelerometry, with no significant difference found. Potentially, participants that were feeling better and experiencing anthropometric changes during the physical activity intervention may also have been motivated to improve their eating and daily activity habits as well. These factors may contribute to over or underestimation of changes in primary or secondary outcomes resulting from the intervention. And finally, without exception, all studies have only reported effects immediately post-intervention with no follow up assessment.[17,18] Therefore, commentary cannot be made on the use of aerobic exercise for the long-term management of insulin resistance. In considering the limitations of this research and its application to clinical practice, the most significant clinical concern is the lack of long-term follow-up by any study.

1.2.3 Effects of resistance exercise on blood hemostasis

Effects of resistance exercise on insulin resistance is similar to aerobic exercise with improved glycemic control.[29-31,69] Also seen with resistance exercise is increased lean tissue mass[27,30,31,69,70] and increased muscle strength and endurance[30,31,69,70,73], both know to effect insulin resistance.

Similar to the improved glycemic control seen with aerobic exercise, as a person participates in resistance exercise the body requires more glucose to meet the increased energy demand.[50,63,78] Skeletal muscle fibres, specifically type II, are the primary site of insulin-stimulated glucose uptake.[15,78] With activity, the uptake of glucose by skeletal muscles increases, causing the pancreas to lessen insulin production.[21,50,63] It has been accepted in this field of research that improvement in glycemic control and thus insulin sensitivity with resistance exercise is attributable to changes in body composition, such as increase lean mass.[4] Therefore, it was not unexpected that RCTs and clinical controlled trials examining the effects of resistance exercise have consistently shown an increase in lean muscle mass or muscle strength along with a reduction in insulin resistance.[26-31] For example, in an RCT by Shaibi et al.[29] they examined the effects of a 16-week resistance exercise program (two days per week, 60 minutes per session) on insulin sensitivity among 22 overweight adolescent males. They reported a significant improvement in insulin sensitivity along with a significant increase in upper and lower body muscle strength. In a cross-sectional study by Benson et al.[73] studying 126 youth (10-15 years old), it was shown that muscle strength is an independent predictor of insulin sensitivity. This has lead researchers to study what alterations happen within the skeletal muscle cell during resistance exercise that helps improve blood hemostasis. Emerging research suggests that the etiology underpinning the beneficial effects of resistance exercise could extend beyond simply increasing muscle strength to physiological alterations at the cellular level.

It is now evident that physiological changes within skeletal muscle cells, as a result of resistance exercise, not *only* increase lean tissue mass, muscle strength, and muscle endurance, but also enhance the action of insulin and glucose metabolism.[27,29,30,78,83] The physiological, both morphological and neurological, adaptations within skeletal muscle cells are listed in Table 1.3. These physiological changes enhance glycemic control through muscle fibre modification, improved glucose metabolism, and enhanced insulin action. It is important to recognize that among children and adolescents, the primary reason for training-induced changes in muscle strength is due to neurological adaptations, not an increase in lean muscle mass. Among adults, in comparison, exercise-induced increases in muscle strength can be attributed solely to muscle hypertrophy.[69] This knowledge may help explain why RCTs, such as the one completed by Shaibi et al.[29], found an improvement in insulin sensitivity along with an increase in muscle strength, but independent of changes in total fat and lean body mass.

Table 1.3: Physiological adaptations within skeletal muscle cells in response to resistance exercise

Function	Physiological Adaptations
Muscle fibre modification	• Augments skeletal muscle capillary density, recruitment and proliferation[30,69,70,78] • Enriches endothelial function[30] • Alters muscle fibre type (changing from type IIb to IIa)[69,70]
Improved glucose metabolism	• Increases number and location of GLUT-4 transporter proteins in skeletal muscle[78,84] • Amplifies glycogen synthase activity[78] • Increases number and activity of mitochondrial enzymes that aid in glucose uptake[78] • Enhances ability for lipid uptake, transport, utilization and oxidation[84]
Enhanced insulin action	• Enhances insulin signaling in response to muscle contractions[83]

The combination of these adaptations helps to explain why resistance exercise improves glycemic control, thus improving insulin sensitivity and reducing insulin resistance. As well, because of neurological adaptations and motor learning in the still-developing younger person, it supports the need to provide a program that teaches proper technique and adjusts the volume of work at a pace in which adolescents' muscles can adapt.

In addition to improved glycemic control and increased muscle strength and endurance, resistance exercise may also alter body composition, such as decreased adiposity.[4] However, only one RCT has demonstrated that insulin sensitivity increased with a decrease in adiposity, seen as a reduction in weight, waist circumference, or BMI.[27] This RCT by Lee et al.[27] examined the effects of a three month resistance exercise program (3 days per week, 60 minutes per session) on 45 obese adolescent males. They did not report the same findings when they repeated the study on 44 obese adolescent females.[28]

With only four RCTs[26-29] and two controlled clinical trials[30,31] examining the effects of resistance exercise on insulin resistance compared to the broad body of knowledge on aerobic exercise (two systematic reviews and meta-analysis analyzing 31 RCTs[17,18], along with clinical trials and well-conducted cross-sectional studies), it leads the researcher and clinician to question, why so few studies? Up until the late 1990s, a myth existed amongst the general population that it was unsafe for children and adolescents to complete resistance exercise as it may damage their epiphyseal growth plates, thus stunting their growth.[69] This myth has been refuted in many position statements and review articles.[69] Resistance exercise is safe for children and adolescents when under the supervision of qualified personnel, using proper technique, and ensuring gradual progression of intensity.[69] However, a clinical concern is that since many adolescents may be unfamiliar with resistance exercise techniques prior to developing insulin resistance; knowledge of quality, safety, and appropriate intensity may have yet to be acquired. When working with adolescent participants, some points to consider to ensure safe and effective exercise include: instructing in proper technique, providing sufficient supervision, using appropriate volume of work (number of repetitions and sets), and including a warm-up and cool down.[69] The degree and quality of supervision is an often overlooked aspect in exercise research among adolescents. For example, of the four RCTs examining resistance exercise programs, three studies provided supervised programs in a community setting[27-29] and one study offered a home-based intervention.[26] The three community-based interventions showed improvement in insulin sensitivity[27-29], however, the home-based program reported no change[26]. This finding may not be unexpected considering the established benefits of supervised, compared to unsupervised, exercise programs, especially among younger populations where adult guidance is recommended.[69,70] Since we know that the current population of adolescents in Canada have lived a sedentary lifestyle and have had limited engagement in regular physical activity, likely from a young age[22], it is probably unrealistic to believe that they would be able to initiate resistance exercise independently. These findings support the notion that guidance provided by knowledgeable healthcare professionals, such as physiotherapists, is important to consider when implementing exercise in research and in clinical practice among adolescents.

Beyond ensuring participants' safety, healthcare professionals also need to prescribe exercise with appropriate parameters to meet target outcomes. All of the studies in this field have employed a combination of single or multi-joint exercises.[26-31] Resistance was applied using free weights or machine weights in programs completed in community centres,[27-31] whereas the home-based program targeted exercises using body weight as resistance.[26] It has been shown that when adolescents participate in supervised resistance exercise program of at least 30-minute duration, two or three times per week for 12 weeks, they may expect improvements in insulin sensitivity.[27-31] Reduced weight, BMI, and waist circumference may[27,30] or may not[26,28,29,31] accompany these outcomes; however, an increase in muscle strength was invariably noted in all RCTs and controlled trials.[26-31] Details of RCTs and controlled trials are provided in Table 1.4.

Table 1.4: Studies examining effects of resistance exercise on insulin resistance in adolescents

Study	Population			Intervention				Outcomes	Compliance	Quality§
	N	Age (yrs)	Cohort	Groups	Duration (min/day)	Frequency (day/wk)	Study Length (wks or mths)			
Randomized Controlled Trials										
Shaibi et al. (2008)[29]	22	15 ± 0.5	Male Obese Latino	RT: 10 single/multi-joint exercises using free weights and machines; progressive in intensity CON: no exercise	60	2	16 wks	Insulin sensitivity^{*+}; Weight (kg); BMI (kg/m^2); VO_2peak; Strength (kg)$^{*+}$	96%	Fair
Lee et al. (2012)[27]	45	12–18	Male Obese	AT: Treadmill, elliptical, bike RT: 10 whole body exercises using weight machines; 8-12 reps; > 60% 1RM CON: no exercise	60	3	3 mths	Insulin sensitivity^{*+}; Weight (kg)$^{*-}$; WC (cm)$^{*-}$; BMI (kg/m^2)$^{*-}$; VO_2peak^{*+} Strength (kg)$^{*+}$	99%	Fair
Lee et al. (2013)[28]	44	12–18	Female Obese	AT: treadmill, elliptical, bike RT: 10 whole body exercises using weight machines; 8-12 reps; >60% 1RM CON: no exercise	60	3	3 mths	Insulin sensitivity; Weight (kg); WC (cm); BMI (kg/m^2); VO_2peak; Muscle strength index^{*+}	97%	Fair
Kelly et al. (2015)[26]	26	14–18	Male Obese Latino	RT: Home-based; combination of upper, lower, and whole body resistance exercises; progressive in intensity CON: no exercise	60	2	16 wks	Insulin sensitivity; Weight (kg); WC (cm); BMI (kg/m^2); Strength (kg)$^{*+}$	89%	Fair
Controlled Clinical Trials										
Dias et al. (2015)[30]	24	14.1±1	Obese Males/ Females	RT: 12 exercises of large muscle groups; 1-3 sets; 8-15 reps; progressive in intensity CON: non-obese, completed same RT	30-40	3	12 wks	Insulin sensitivity^{*+}; Weight (kg); WC (cm)$^{*-}$ BMI (kg/m^2); Strength (kg)$^{*+}$	N/A	
Van der Heijden et al. (2010)[31]	12	15.5± 0.5	Obese Males/ Females	RT: 10 exercises of large muscle groups using free weights; 2-3 sets; 8-20 reps; progressive in intensity based No CON	60	2	12 wks	Insulin sensitivity^{*+}; Weight (kg)$^{*+}$; BMI (kg/m^2)$^{*+}$; Strength(kg)$^{*+}$	96%	

Abbreviations: n = sample size; yrs = years; RT = resistance training; AT = aerobic training; CON = control; 1RM = One-repetition maximum; min = minutes; wk(s) = week(s); mths = months; kg = kilograms; kg/m^2 = kilograms per metre; % = percentage; cm = centimetres; * = significant change in outcome; + = significant increase in outcome; - = significant decrease in outcome. §Note: Quality of RCTs was assessed using the US Preventive Services Task Force quality rating criteria[85]

1.2.4 Limitations within research using resistance-based interventions

Despite consistent findings, there are limitations noted within studies examining the effects of resistance exercise on insulin. These include few RCTs designs, clarity of diagnosis in selection criteria, low generalizability, and lack of follow-up. Fedewa et al.[17] included only three RCTs using resistance-based interventions in their systematic review and meta-analysis examining the effects of exercise on insulin resistance among adolescents. The authors concluded that more robust studies are needed to make definitive statements about the effects of exercise on the prevention and treatment of insulin resistance.[17] This research area would benefit from more RCTs and well-controlled clinical trials using resistance-base interventions. Like the research with aerobic-based interventions, the second limitation is concerning the selection of participants. Again, recruitment was not based on having a diagnosis of insulin resistance; all studies recruited participants based on BMI[26-31], despite it being recognized in the literature that BMI is a poor predictor of insulin resistance in a pediatric population.[33,54] Thirdly, two of the four RCTs recruited only adolescents of Latino descent[26,29] and three of the four RCTs recruited only male participants[26,27,29]. Clinical generalizability of these results may be limited due to over-representation of Latino ethnicity and males. The research group lead by S. Lee completed two very similar studies comparing the effects of aerobic and resistance-based interventions on insulin sensitivity conducting one study on adolescents' girls[28] and the other on boys[27]. Lee et al.[28] noted there was no change in insulin sensitivity with resistance exercise among girls. They observed that the girls did not appear to enjoy the resistance-based intervention as much as the aerobic-based intervention; thus, despite high attendance rates, the girls' effort may have been lacking. Thirdly, no studies controlled for physical activity level[26-31] and only one study controlled for dietary intake[31] of their participants during the study period. By not controlling for a change outside of the study intervention in diet or physical activity levels, the results of the primary and secondary outcomes due to the intervention may be over or underestimated. And finally, all studies, as with aerobic-based interventions, only examined effects immediately post-intervention with no follow-up assessment[26-31]; therefore, commentary cannot be made on the use of resistance exercise in the long-term management of insulin resistance.

1.2.5 Effects of combined aerobic and resistance exercise on blood hemostasis

Most physical activity when completed with children or adolescents is a combination of games and unstructured activities and is thus a combination of aerobic and resistance exercise. Therefore, it would be reasonable to think that taking a combined approach when designing a treatment program would target multiple outcomes while providing variety for adolescent participants in order to foster compliance. Although there are clinical guidelines for prescribing both aerobic and resistance exercise for adults with type 2 diabetes[71,77], similar guidelines have not been established for a pediatric population who have insulin resistance or have continued to develop type 2 diabetes. As a compromise, Sigal et al.[71] suggests that adolescents with insulin resistance or type 2 diabetes follow the Canadian Physical Activity Guidelines which recommend that adolescents participate in at least 60 minutes per day of moderate-to-vigorous physical activity (aerobic exercise) and participate in activities that strengthen muscle and bone at least three days per week (resistance exercise).[86]

In the most recent systematic review with meta-analysis conducted on studies of adolescents with insulin resistance, Fedewa et al.[17] completed their statistical analysis combining all modes of physical activity, showing a positive effect of physical activity on insulin resistance regardless of type. Four cross-sectional studies have been completed examining the combined aerobic and resistance-based interventions, investigating anthropometric, metabolic, and cardiorespiratory fitness changes in adolescents with insulin resistance.[13,82,87,88] Two of the studies were very similar in design, recruiting obese adolescents to participate in either an aerobic or an aerobic combined with resistance-based intervention continuing for one year.[87,88] Both studies reported that the aerobic plus resistance-based intervention was more effective than the aerobic-based intervention alone in increasing insulin sensitivity, decreasing visceral adiposity, improving blood lipid profile, and increasing lean mass.[(merged)] However, these results should be considered cautiously as both studies also provided participants with dietary education and counselling which may have contributed to the change in insulin sensitivity. However, this consideration may be somewhat controlled for since both intervention groups received the same dietary support.[87,88] The studies by Davis et al.[82] and Bell et al.[13] recruited obese adolescents to participate in a combined aerobic and resistance-based intervention lasting 8-16 weeks. Both studies reported that the combined intervention was effective in increasing insulin sensitivity, decreasing visceral adiposity, improving blood lipid profile, and increasing lean mass.[13,82,87,88] These findings may be attributed to the physiological adaptations within skeletal muscle fibres with resistance exercise that is not reported with aerobic exercise.[27,29,30,78,83] More research would be required to decipher the optimal dosage (frequency, intensity, duration, and type) and combination of activity to improve metabolic outcomes.

1.3 BARRIERS TO LONG-TERM ADHERENCE TO PHYSICAL ACTIVITY

We have discussed how physical activity can help maintain blood hemostasis and identified current knowledge regarding exercise prescription specifically for adolescents with insulin resistance. This review would be remiss if it did not identify the concerns, from both parents and healthcare professionals, of long-term adherence to physical activity for adolescents.

As stated, the participation rate among adolescents in regular physical activity is very low[22] and adherence is vital when trying to reduce risk factors for insulin resistance. Thus, barriers and facilitators affecting adherence to physical activity need to be considered. Typical barriers include socioeconomic status (adolescents of lower status are less active)[89], gender (males are more active than females)[22], age (physical activity decreases with age)[22], family and peer support (people with less support are less active)[22], time constraints[89], and availability and access to physical activity programs[89]. A systematic review by Martins et al.[90] evaluated qualitative studies which reported, from the adolescents' perspective, barriers and facilitators to physical activity. While the same sociodemographic barriers were identified, they went on to identify psychosocial barriers and facilitators which program leaders and healthcare professionals may not have previously considered. The authors stated that the main items that facilitated adolescents' engagement in physical activity were enjoyment, positive attitude towards physical activity, positive self-image, perceived personal competence (self-efficacy), and family and peer support.[90] These facilitators need to be considered when designing and implementing a physical activity program, and when counselling adolescents regarding their physical activity level.

Enjoyment and attitude towards physical activity become barriers when adolescents report negative experiences with physical activity, absence of friends, pressure to perform, and poor perception of competence.[90] It has been shown that when adolescents enjoy a physical activity, it is more likely they will adhere to the activity[91]; therefore, enjoyment must be a key feature to be considered when counselling adolescents on strategies to increase their physical activity. It is reasonable to think that consideration of enjoyment during physically activity is even more important to deliberate upon when participants may have already experienced negative associations with physical activity. Negative experiences may include exclusion from programs or teams, being mocked, or being considered by others as not being able to excel. Enjoyment is entangled with two other psychosocial barriers: self-image and perceived competence.

Self-image becomes a barrier to physical activity when adolescents develop discomfort moving in front of others, particularly in the presence of peers of the opposite gender or peers who they did not deem as friends.[90] Negative self-image was also identified as a barrier when adolescents reported feeling uncomfortable with their physical appearance due to the nature of exercise clothing or sportswear required, the presence of sweating, or body weight discomfort.[90] This is compounded by the societal belief that shaming people about their bodies will motivate them to make changes in their physical activity level.[34,35] Shaming people about their body weight often includes using language, such as “Your big butt can work harder than that”, or “If you move it, you’ll lose it!”. This shaming contributes to stigma towards people in larger body sizes, called weight bias.[34,35] It is assumed that people in larger body sizes are not fit or healthy.[32,36,92] Research suggests that weight bias in adolescents leads to further body dissatisfaction creating a negative self-image, adversely impacting participation in physical activity. Furthermore, a negative body image is associated with low self-esteem, anxiety, eating disorders, and depression.[33-35]

Adolescents experiencing weight bias may then find themselves in a cycle of weight bias, negative self-image, and worsening physical inactivity. Poor self-image may be exacerbated when it is added to personal perception of incompetence. Perceived incompetence with physical activity among adolescents may contribute to feeling fearful of being embarrassed in front of peers.[90] Weight bias, shaming, and feelings of incompetence are significant problems to be overcome among adolescents engaging in physical activity, sometimes for the first time since early childhood. In efforts to motivate people to work harder by shaming them, more problems are created then what was intended. When designing physical activity interventions that create long-term behaviour change, enjoyment, positive self-image, perceived competence, and family and peer support are key factors to consider in order to safeguard the psychosocial health of all participants.

1.3.1 A body positive approach

To ensure that these psychosocial barriers to adherence are addressed, a body positive approach may help. A body positive approach fosters body appreciation and taking care of one's body by promoting health behaviours rather than focusing on short-term weight loss. This approach encourages enjoyment of physical activity and fosters a positive self-image by ensuring a socially safe environment where there is no shaming or weight bias.[32-37] By taking a body positive approach when promoting physical activity, it diminishes the potential for unintended harm to participants.[32-37] Adolescents who have a positive self-image feel good about their body regardless of appearance, weight or shape, and are therefore are more likely to take care of their bodies by engaging in healthy behaviours.[32-37]

A body positive approach is evidence-based, by aligning with the compelling findings of studies and systematic reviews that show that physical activity (aerobic and resistance-based) not need change weight or BMI to improve insulin sensitivity.[10,12-21,29,31,80] An approach focusing on health rather than on physical appearance helps adolescents recognize that people can be healthy in different body shapes, sizes, and weights[32,36,64,92]; it is not necessary to achieve the 'thin ideal' that is often portrayed in the media to be healthy[32-36]. Some practical concepts when using a body positive approach are presented in Table 1.5. Details of this approach are presented in Appendix A. These concepts are those that are employed by the CDPP described in this thesis.

Table 1.5: Practical concepts when using a Body Positive Approach in physical activity programming

Practical Concepts	**Examples**
Recognize what health looks like	- Good health comes in many body shapes, sizes, and weights. - Weight does not equate directly with health.
Promote health	- Cardiorespiratory fitness is more predictive of health than weight. - Rather than focusing on obesity treatment or weight loss, design physical activity programs that promote healthy active living for all participants.
Educate yourself	- Be aware of your own assumptions, beliefs, and judgments about body weight and size, including assumptions made about a person's character/behaviours based on their weight. - Work toward changing your personal assumptions and biases. - Evidence shows that health is not directly correlated to weight. There are people who are naturally slim based on their genetics but engage in unhealthy behaviours; just as there are people with extra weight who are active and healthy.
Set health goals	- Do not make goals which are weight focused. Instead, set fitness or health goals with participants, such as "I will be able to run 5 kilometres in 12 weeks".
Provide a safe space	- Have clear guidelines around appropriate language, conversations, and behaviour. - Never make comments about participants' weight or appearance. - Do not enforce physical activity and dieting rules for the sole purpose of reducing participants' weight or changing their body shape. - Be responsive and supportive of participants needs. - Do not tolerate bullying of any kind. Address weight-based

	bullying when it occurs.
Be a good role model	- Do not make negative comments about your weight or body shape. - It is important that certain body types are not featured more visibly, such as putting dancers with extra weight on in the back row in a performance. - Program leaders need to model a respectful, inclusive attitude.
Be media smart	- Be mindful of program posters or brochures - show photographs of people of all body sizes being physically active.

1.4 CLINCAL CONCERNS REGARDING THE LIMITATIONS WITHIN CURRENT RESEARCH

As discussed, when examining the scope of research in this field, three main gaps have been identified. These include (1) a lack of well-controlled studies analyzing the effects of resistance exercise on insulin resistance in an adolescent population (compared to many more RCTs and clinical trials studying aerobic-based interventions), (2) published studies that have identified study participants based on BMI, not on a diagnosis of insulin resistance, and (3) no studies that have examined longer-term, beyond post-intervention, effects of resistance exercise on insulin resistance. Considering these limitations, some suggestions can be made to strengthen the current research and to gain a better understanding of the effects of resistance exercise on insulin sensitivity.

More well-controlled clinical trials (randomized or non-randomized) are needed to determine the impact of resistance exercise in the management of insulin resistance. When combined with other lifestyle interventions, it is difficult to decipher the ‘active’ ingredient. As stated, puberty and the process of maturation can result in a normal increase in insulin resistance during adolescence.[4,44,45] Careful attention to monitoring hormonal changes would be important in future study design, with trials that include a control ‘run-in’ period before baseline measurements to account for expected maturational changes.

Despite the fact that BMI is a poor predictor of insulin resistance in a pediatric population[33,54], participants in all studies[26-31] examining resistance exercise were recruited based on BMI and not by diagnosis of insulin resistance. So, in fact, some study participants may not have had insulin resistance. It is known in adult[92] and pediatric[64] populations that obesity on its own does not mean an individual has poor metabolic health. Therefore, more studies are needed that recruit participants based on a diagnosis of insulin resistance and not simply their BMI, especially if fasting insulin or glucose are the primary outcome measure. This may influence the external validity and effect sizes of the results.

Arguably, the limitation with the most clinical impact is a paucity of evidence around the use of physical activity (aerobic and resistance-based) in the long-term management of insulin resistance, as all published studies have only evaluated effects immediately post-intervention, with no long-term follow-up.[17,18,26-31] This raises a clinical concern, as there are no evidence-based methods to help support adolescents to make lifelong behaviour change. It has been reported in studies on adults that some of the effects of physical activity on insulin resistance only last approximately 48 hours, thus to maximize metabolic effects, regular physical activity is needed.[16,71] Despite demonstrating improvements in fasting glucose, fasting insulin, and insulin sensitivity immediately post-intervention[27,29-31], if there is no lifelong participation in daily physical activity by adolescents, the initial effects may not produce any long-term reduction in incidence of chronic disease. Future studies examining the long-term effects of resistance exercise on insulin resistance in combination with addressing barriers to long-term adherence to physical activity will provide invaluable information to healthcare professionals in order to help adolescents manage insulin resistance. It is reasonable to think that physical activity interventions that address barriers to promoting long-term adherence, rather than simply telling adolescents to be physical active, would have greater sustained benefit. To help adolescents manage their insulin resistance for life, we need to know details of the exercise prescription required to aid adolescents in making lifelong behaviour change.

1.5 CURRENT CLINICAL EFFORTS IN NEWFOUNDLAND AND LABRADOR TO ADDRESS INSULIN RESISTANCE IN ADOLESCENTS

As stated, there are at least 113 new cases of type 2 diabetes diagnosed in Canadian children annually, which may be exacerbated by the increasing incidence of obesity and insulin resistance in this cohort.[1,60] Not surprising, this concern is prevalent in the province of NL where the rates of insulin resistance are also rising[2], causing concern that adolescents in NL are at an increased risk to develop type 2 diabetes.

NL established a pediatric CDPP in 2006 to help address the metabolic health concerns in younger age groups. This family-based program is aimed at children and adolescents identified as having risk factors for the development of a chronic disease, including high cholesterol, high blood glucose, hypertension, nonalcoholic fatty liver disease, and obesity. The program states they focus on improving health behaviours, such as increasing vegetable and fruit intake, increasing physical activity time, decreasing sedentary activity time, and increasing self-esteem in efforts to avert the onset of chronic disease. This is based on available, clinical practice guidelines as well as the results of clinical research.[32,33,36,59,86,93]

In the CDPP, families meet with an interdisciplinary team consisting of a dietitian, pediatric endocrinologist, physiotherapist, psychologist, recreation therapist, and social worker. They attend an initial assessment clinic followed by a nine-week education program. Families receive education on how to eat well, be active, feel good, and live healthy. Participants are then followed every six months until they are 18 years old. During that time, they can be seen individually or invited to participate in a variety of groups depending on their needs (e.g., resistance exercise group for adolescents, physical literacy group for children, psychology-led coping group, or food skills group).

One of the main goals of the CDPP is to help participants increase their physical activity levels to improve their health. As mentioned, increasing levels of physical activity is important among the general population, but adherence is vital when trying to reduce risk factors for insulin resistance. By attempting to remove barriers to physical activity, the CDPP promotes physical activity as a lifelong commitment. In addition to the education adolescents receive about the benefits of physical activity on their health, all programming is offered using a body positive approach. As previously discussed, a body positive approach to lifestyle intervention targets and attempts to mitigate the psychosocial barriers to physical activity.

Combining a body positive approach with the knowledge of the benefits of resistance exercise to manage blood hemostasis, a resistance exercise program for adolescents with insulin resistance was developed to enrich the current education and programming offered by the CDPP. The aim of the resistance exercise program was to foster long-term compliance to regular physical activity, giving participants a chance to achieve a sustainable reduction in their risk factors for insulin resistance.

1.6 OBJECTIVES OF THESIS

The purpose of this thesis was to help address some of the limitations identified in the literature by designing a prospective cohort study that evaluated the effects, up to six months, of a 10-week, supervised resistance exercise program provided in the community on insulin resistance in adolescents. Importantly, this study recruited participants diagnosed with insulin resistance, provided an observational run-in control period to measure maturational changes in insulin resistance, and followed adolescents up to six months' post-intervention to assess changes in insulin sensitivity as well as secondary outcomes. The main objectives of this study were to:

1. assess changes in markers of insulin resistance, cardiorespiratory fitness, muscle strength, and anthropometric measures immediately following completion of a resistance exercise program and six months after the program ceased.
2. determine if adolescents with insulin resistance would continue to be physically active up to six months' after completion of a resistance exercise program.

We hypothesized that resistance exercise would improve primary (insulin sensitivity) and secondary outcomes immediately post-intervention; however, we anticipated that these benefits would begin to decline by six months.

1.7 CO-AUTHORSHIP STATEMENT

This research was conducted under the supervision of Drs. Michelle Ploughman and Tracey Bridger and with support of Dr. Laurie Twells. I was responsible for the design of the study, recruitment of participants, and data collection and analysis. Mr. Liam Kelly, exercise physiologist, completed the cardiorespiratory fitness testing and helped interpret these results. Dr. Tracey Bridger helped interpret the results of the OGTT. Mrs. Ashley Moore, recreation therapist, help design and implement the resistance exercise program. Ms. Laura King, recreation therapy student, helped supervise the resistance exercise program. I wrote the original drafts of the manuscripts that constitute the chapters of this thesis. The manuscripts were revised based on comments from Dr. Michelle Ploughman, Dr. Tracey Bridger, Dr. Laurie Twells, Ms. Megan Kirkland, and Ms. Elizabeth Wallack.

CHAPTER TWO

2.1 INTRODUCTION

Growing numbers of adolescents diagnosed with type 2 diabetes[1,8] has raised alarms among individuals and healthcare systems. In 2006, the annual incidence of type 2 diabetes in Canadian children (< 18 years) was 1.54 per 100 000. This translates into at least 113 new cases of type 2 diabetes diagnosed in Canadian children annually, a disease that in decades earlier was almost unheard of among this age group. Insulin resistance is believed to be a harbinger of future diabetes diagnosis, with 73% of adolescents diagnosed with type 2 diabetes showing early symptoms of insulin resistance.[1] Insulin resistance occurs when insulin sensitive cells, mainly skeletal muscle cells, have a muted response to the role of insulin in transporting glucose. In this state, insulin receptors fail to recognize circulating insulin, causing disruption in insulin binding to receptors, thus preventing glucose from being transported from the blood into cells.[38-40] Determining why many adolescents find themselves managing insulin resistance has become the critical work for chronic disease prevention programs (CDPP). CDPP aim to reduce risk factors, such as insulin resistance, that lead to the development of chronic diseases, through clinical services, research, government programming, and policy change.[8,33]

The startling rate of insulin resistance among adolescents is likely due to both non-modifiable (e.g., genetic abnormalities and ethnicity)[1,7,9] and modifiable (e.g., diet and physical activity level)[1,3,4,6,7,10-12] factors. Healthcare professionals focus their efforts on addressing modifiable factors, which include excess dietary intake of glucose and saturated fat, excess fat, physical activity, sedentary lifestyle, and lack of and/or interrupted sleep, in order to impede the transition from insulin resistance to type 2 diabetes.[1,4,6,12,40,57] The challenge when working with adolescents is that these poor lifestyle behaviours often overlap with typical adolescent behaviour. For example, many adolescents consume excess amounts of sugar[58], do not meet physical activity guidelines[22], spend excess amounts of time sedentary[22], and do not obtain adequate amounts of sleep[22]. Left unaddressed, these unhealthy lifestyle factors, combined with the natural increase in insulin resistance due to hormonal changes during this age[4,44,45], can precipitate the progression of insulin resistance and possible subsequent development of type 2 diabetes. Pediatric CDPPs employ multidisciplinary, patient and family-centered management in order to treat young people with impending metabolic dysfunction, with a focus on addressing modifiable lifestyle factors[33], of which physical activity is a consistent ingredient.

Clinical trials and systematic reviews with meta-analysis support that regular physical activity (both aerobic and resistance-based) can help improve insulin resistance in adolescents.[12-21] Emerging research suggests that because of exercise-induced physiological changes within skeletal muscle cells (e.g., increased density of glucose transporter type 4 (GLUT-4) proteins[78,84], enhanced insulin signaling[83], increased glycogen synthase activity[78], increased number and activity of mitochondrial enzymes that aid in glucose uptake[78]), resistance exercise, in particular, appears to have additional benefits in glycemic control.[29-31,69] Interestingly, the beneficial effects of resistance exercise on insulin sensitivity in adolescents were associated with an increase in muscle strength[26-31]; however, with[27,30] or without[26,28,29,31] changes in weight, BMI, waist circumference, and/or adiposity. Improvement in insulin sensitivity without concomitant alteration of anthropometric measures suggests that these traditional health measures may not be reliable metrics of metabolic health, at least in adolescents.

Since the goal of most CDPPs is to help patients adopt healthy behaviours to provide long-term protection from adverse health conditions, it is important that treatments are shown to be effective in the longer-term (months and years). Although the immediate benefits of resistance exercise on insulin resistance has been described[17,27,29-31], whether physical activity provides long-term reduction of insulin resistance is not known. Furthermore, previous studies examining the effects of physical activity among adolescents with insulin resistance recruited participants based on their BMI rather than a diagnosis of insulin resistance; this is surprising since it is well-established that meaningful improvements in blood levels of fasting insulin and glucose can occur with or without anthropometric changes. In addition, since insulin resistance can be perturbed during puberty, measurements of outcomes during a control period would help monitor for maturational changes.

The primary purpose of this study was to determine the effects, up to six months, of a supervised, 10-week resistance exercise (including an observational run-in control period) on markers of insulin resistance in adolescents, diagnosed with insulin resistance, participating in a pediatric CDPP. Secondary outcomes included cardiorespiratory fitness, muscle strength, physical activity level, and anthropometric measures. We hypothesized that resistance exercise would improve primary (insulin sensitivity) and secondary outcomes immediately post-intervention, however, these benefits would begin to decline by six months.

2.2 METHODS

This prospective cohort study took place within an established and publicly-funded pediatric CDPP. This family-based program was developed for children and adolescents who were identified as having risk factors for chronic disease, including insulin resistance. A repeated-measures design (with an observational run-in period) was used to determine the effects of resistance exercise on insulin resistance. Data from the observational run-in period was collected retrospectively up to 18 months prior to the study period.

2.2.1 Participants

Following approval by the local health research ethics committee (see Appendix B), participants involved with the CDPP were recruited. Participants were included if they were (1) between ages 13-18 years and (2) diagnosed with insulin resistance, which was based on results from oral glucose tolerance tests (OGTT) and the presence of physical markers, such as acanthosis nigricans. Participants were excluded if they (1) were taking prescription medication which would affect glucose or insulin metabolism, (2) had syndromic obesity (e.g., Prader-Willi syndrome), (3) had type 1 diabetes or other metabolic condition affecting glucose or insulin metabolism, and (4) were unable to commit to the 10-week resistance exercise program.

Potential participants were invited to an orientation session which explained details of the study (see Appendix C). Following consent, participants completed the *Physical Activity Readiness Questionnaire for Everyone* and the treating Paediatrician completed the *Physical Activity Readiness Medical Examination* (see Appendix D).[94] Only subjects who were declared safe to exercise proceeded.

2.2.2 Setting

The resistance exercise program took place in a community facility, equipped with free weights, kettle bells, resistance bands, weighted bars, medicine balls, full and half BOSU® balls, TRX® suspension training system, tractor trailer tire, and weighted ropes. During group sessions, no other patrons besides participants used the facility. There was no cost to participants to participate. A physiotherapist designed all the exercises and group sessions were supervised by a physiotherapist, recreation therapist, and university student, maintaining a 5:1 ratio of participants to supervisor. All personnel had knowledge of insulin resistance and effects of physical activity on maintaining blood hemostasis, had training and experience in teaching resistance exercise, and were competent in precautions, safety measures, and proper technique of resistance exercise. To safeguard against physical injury, supervisors ensured proper technique, provided supervision, used appropriate volume of work (number of repetitions and sets), and included a warm-up and cool down.

To minimize psychosocial barriers to exercise adherence, a body positive approach was taken. A body positive approach fosters body appreciation and taking care of one's body by promoting health behaviours rather than focusing on short-term weight loss.[32-37] To implement this approach, program supervisors received education regarding weight-based stigma and discrimination. Clear program guidelines around appropriate language, conversation, and behaviour were established and communicated to participants. Examples included, abstaining from making comments about participants' or supervisors' appearance or weight; avoiding language that suggested setting physical activity or dieting rules to reduce weight or change body shape; and, abstaining from shaming tactics in attempts to motivate participants to work harder. The physiotherapist assisted participants to set health and fitness goals.

All participants continued to be offered standard care by the CDPP; this consisted of attending follow-up clinic every six to eight months with the CDPP team and individual appointments with team members as required.

2.2.3 Intervention

The 10-week intervention consisted of three sessions per week (total of 30 sessions, 60 minutes each) on non-consecutive days divided into two components: community and home. Two supervised, community sessions per week (total of 20 sessions) took place at the training facility, while the third session was completed at home. Each session began with a light aerobic warm-up (five minutes), followed by resistance activities (50 minutes), and light stretching as a cool down (five minutes).

After assessing one-repetition maximum (1RM) at the pre-assessment, the amount of resistance in which participants used for weighted exercises was titrated using the following guide: weeks 1-4: 40-60% of 1RM; weeks 5-7: 60-80% of 1RM; weeks 8-10: 80-100% of 1RM. Other exercises were progressed as tolerated (e.g., throwing a 5-pound medicine ball up to throwing a 10-pound medicine ball). Resistance exercises were arranged in a circuit with six stations (two exercises per station) rotating between total, upper, and lower body exercises as outlined in Table 2.1. Participants spent two minutes completing each exercise for a total of four minutes per station; then, the entire circuit was repeated. There was no scheduled rest period between exercises or stations, however participants were advised to drink water as needed.

During the first three weeks, the focus was on technique and learning exercises. Participants' heart rate was monitored throughout sessions using a pulse oximeter to ensure a moderate intensity (50-70% of maximum heart rate) was maintained.

Table 2.1: Examples of resistance exercises by muscle group

Area	Muscle Group	Exercises
Upper Body	Pectoralis Major/Minor	Chest press with bar, free weights, or vipers; Flys with free weights; Reverse push-ups on TRX; Pull-ups on TRX
	Trapezius/Rhomboids	Seated rows with resisted bands; Bent over rows with resisted bands or free weights
	Triceps	Triceps dips on bench; Triceps extensions with free weights
	Biceps	Bicep curls with free weights
	Deltoids	Front raises with free weights or resisted bands; Lateral raises with free weights or resisted bands; Shoulder press with free weights or vipers
Lower Body	Quadriceps	Squats with/without kettle bells or barbell; Lunges with/without kettle bells; Wall squats
	Hamstrings	Dead lifts with kettle bells, barbell, or vipers; Hamstring curls on BOSU ball
	Gluteus maximus/medius	Bridges on BOSU ball; Hip extension while in 4-point; Hip flexion in standing with foot hooked into kettle bell; Hip abduction with resisted bands
	Gastrocnemius/Soleus	Calf raises holding free weights or kettle bells
Total Body	Abdominal	Side dips holding free weights or kettle bells; Bicycle crunches; Crunches on BOSU ball; V-sits while passing medicine ball
	Total Body	Tire flips; Front planks with/without feet on half BOSU; Side planks with/without feet on half BOSU; Waving or pulling weighed ropes; Walking ladder on hands; Superman (extend opposite arm and leg); Standing or kneeling on half BOSU while throwing medicine ball; Medicine ball slams; Kettle bell swings in squat; Walking while carrying frame (with or without weight added); Trunk rotation while pulling resisted bands or holding viper

Abbreviations: TRX: TRX® suspension training system; BOSU: BOSU® Balance Trainer

The home-based resistance sessions were structured in the same way as the community-based session (five-minute warm-up, 50-minute resistance activities, and five-minute cool down). Participants were provided with verbal and written instructions along with elastic tubing and small portable equipment (e.g., kettle bells, medicine balls, and free weights). They were instructed in how to monitor their own heart rate (at their carotid or radial arteries).

2.2.4 Outcome Measures

Participants were assessed at three time points: (1) prior to commencing the intervention (PRE), (2) after completion of the intervention (POST), and (3) 6-months following intervention (FOLLOW-UP). The primary outcome was insulin sensitivity as measured by an OGTT. Since there can be some fluctuation in OGTT with age, prior to the start of the study, there was an 18-month observational run-in period in which OGTT results were collected retrospectively. This measurement was used as a control period. Secondary outcomes included cardiorespiratory fitness, muscle strength, physical activity levels, and anthropometric measures. Age, gender, presence of acanthosis nigricans along back of neck, co-morbidities, and current medications were also recorded. Attendance was recorded at all community sessions. If a participant failed to attend a minimum of half the community sessions, their results were excluded from the study. Adherence to the home-based sessions was assessed weekly through self-report.

2.2.4.1 Oral glucose tolerance test

The primary outcome was insulin sensitivity as measured by an OGTT, which is a valid and reliable measure of insulin sensitivity in adolescents against the gold standard, euglycemic-hyperinsulinemic clamp.[41,55,56] Fasting samples of insulin and glucose were recorded. An OGTT was completed following consumption of 1.75g of glucose per kilogram (kg) of weight (maximal dose 75g). Blood samples were taken from antecubital vein at 60, 90, and 120 minutes recording insulin and glucose. From the OGTT, total area under the curve (AUC) for insulin was calculated using the trapezoid method and insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA-IR).

2.2.4.2 Cardiorespiratory fitness test

Cardiorespiratory fitness test was assessed using the Bruce Treadmill Protocol, recording heart rate, as per the standard care provided to participants by the CDPP (see Appendix E). In addition, a direct measure of maximal oxygen consumption (VO_2max) was assessed using a metabolic cart (MOXUS Metabolic Cart, AEI Technologies, Inc.; Pittsburgh, Pennsylvania). This metabolic cart was not available for follow-up assessments; therefore, a portable unit was used (VmaxST 1.0, AEI Technologies, Inc.; Pittsburgh, Pennsylvania). Participants were fitted with a face mask to measure expired gases while completing an incremental submaximal exercise test as per American College of Sports Medicine (ACSM) guidelines.[95] Resting blood pressure, sitting, was measured using a manual blood pressure cuff, according to ACSM guidelines.[96]

From the cardiorespiratory fitness test, time to exhaustion, VO_2max, maximal carbon dioxide production (VCO_2max), respiratory exchange ratio, breath frequency, tidal volume, ventilatory equivalent, and heart rate were collected. VO_2 and VCO_2 per kg were calculated. Data was smoothed using a moving cell average. VO_2peak was determined from the last 30 second average of the final stage. All other variables from cardiorespiratory fitness testing were considered at VO_2peak. VO_2max was achieved when a plateau was seen in VO_2 and VCO_2 or if secondary criteria was reached: within 10% of age-predicted maximum heart rate and if respiratory exchange ratio > 1.1.

2.2.4.3 Muscle strength and daily physical activity

Upper (chest press in supine) and lower (seated leg extension) body muscle strength was assessed using 1RM as per ACSM guidelines.[95] Physical activity level was assessed using accelerometry with a digital activity tracker, Garmin Vivofit (worn on wrist)[97,98], which collected daily step count over three consecutive days.

2.2.4.4 Anthropometric measures

Anthropometric measures were evaluated using ACSM guidelines.[96] Height was measured using a digital, wall-mounted stadiometer (Seca 264, Seca, Inc; Chinco, Califorina) to the nearest 0.1 centimetre (cm). The wall-mounted stadiometer was unavailable for FOLLOW-UP assessments thus a free-standing stadiometer (Eye Level Digital Scale with Adapter 500KLAD, Healthometer Professional Scales; McCook, Illinois) was used. Body weight was measured to the nearest 0.1 kg using an digital scale (Healthometer Pro+Plus, Healthometer Professional Scales; McCook, Illinois) and waist circumference was measured to the nearest 0.1cm using a non-elastic measuring tape from the top of the iliac crest or level of the last rib or narrowest point between these landmarks using the average of two measurements.[96] BMI was calculated by dividing body weight (in kg) by the square of the height (in metres(m)).[96] Percentiles for weight, BMI, waist circumference, and waist-to-hip ratio as well as BMI z-scores were determined based on World Health Organization's growth charts using an anthropometric calculator.[99,100]

2.2.5 Sample size calculation

A power calculation for a repeated-measures design was completed based on the primary outcome, insulin sensitivity, with the following parameters: power (1-β) 0.80; $\alpha < 0.05$; two-tailed; confidence interval 95%; effect size: 0.35; and three repetitions. Using effect size estimates from two meta-analyses reporting the effect of physical activity (aerobic and resistance-based) on insulin sensitivity[17,18], resulted indicated a required sample size of 15 participants. The CDPP sees approximately 300 children annually. All adolescents followed by the CDPP who met the selection criteria were invited to participate, resulting in 69 invitation letters being sent.

2.2.6 Statistical analysis

Data was entered into spreadsheets and statistical analysis was performed using Statistical Package for Social Science (SPSS) software version 24 (IBM, Chicago, IL, USA). All variables were continuous. Normality of distribution was checked for all variables using Kolmogorov-Smirnov and Shapiro-Wilk’s tests and homogeneity of variance ($p <0.05$) along with visual inspection of histograms and P-P plots. All variables were normally distributed. Mauchly's test indicated that the assumption of sphericity was not violated for any variable.

A repeated-measures ANOVA was used to compare outcomes at three assessment times (PRE, POST, FOLLOW-UP) and was followed by Least Significant Difference (LSD) correction, an adjustment for multiple comparisons, post-hoc test when a significant time effect was found. When a significant effect of time was found, it was important to consider each time period; between PRE and POST, POST, and FOLLOW-UP, and between PRE and FOLLOW-UP. This ANOVA was performed for each of the outcome measures: (1) OGTT (including fasting insulin and glucose, HOMA-IR, 2-hr insulin and glucose, and insulin AUC), (2) cardiorespiratory fitness testing (including time to exhaustion, VO_2max, VCO_2max, respiratory exchange ratio, breath frequency, tidal volume, ventilatory equivalent, and heart rate), (3) upper and lower body muscle strength, (4) step count, (5) waist circumference (mean and percentiles), (6) waist-to-hip ratio (mean and percentiles), (7) body weight (mean and percentile), and (8) BMI (mean, percentiles, and z-scores). For the OGTT only, data was collected from a control period (18 months prior to participants completing the PRE). This data was not included in the repeated-measures ANOVA since there was variability in the time in which participants' OGTT was taken (ranged from 4-18 months). Explanatory descriptive statistics were used to compare the control period to the PRE for the OGTT variables. Values were expressed as mean with standard deviation (SD) or mean with range. The level of significance was set at $p<0.05$. Effect sizes are calculated using partial eta squared (ηp^2) where 0.02 is considered a small effect, 0.13 a medium effect, and >0.26 a large effect.[101]

2.3 RESULTS

We recruited 13 (five males, eight females) adolescents (age 14.16 ± 1.19 years) with insulin resistance; this was a response rate of 19%. All participants were in puberty. Participants' height (1.68 ± 0.08m) did not change through the study period. Nine participants had acanthosis nigricans along the back of their necks. Co-morbidities among participants included: obesity (n=13), orthopedic issues (n=2), attention deficit disorder (n=1), processing disorder (n=1), and autism spectrum disorder (n=1). Participants attended 80% of community sessions (average 16.46 ± 2.47 sessions per participant). No participants were excluded for failing to attend the minimum number (<50%) of community sessions. All participants reported completing their weekly home-based session.

2.3.1 Improvements in insulin sensitivity and metabolic health

Repeated measures ANOVA demonstrated that there was an overall effect of time on fasting insulin [$F_{(2,22)}=7.54, p=0.003, \eta p^2=0.41$], fasting glucose [$F_{(2,22)}=3.58, p=0.045$, $\eta p^2=0.25$], and HOMA-IR [$F_{(2,22)}=7.60, p=0.003, \eta p^2=0.41$] (Table 2.2). Post-hoc analysis revealed significant improvements in fasting insulin (mean difference=30.17pmol/L,p=0.015), fasting glucose (mean difference=0.23mmol/L,p=0.043), and HOMA-IR (mean difference=0.49, p=0.019) from PRE to POST. As well, there was a significant improvement in fasting insulin (mean difference=50.00pmol/L,p=0.010) and HOMA-IR (mean difference=0.87,p=0.008) from PRE to FOLLOW-UP. HOMA-IR scores per participant (Figure 2.1) and overall group changes (Figure 2.2) are displayed.

Repeated measures ANOVA showed no effect of time on insulin or glucose measured at two hours into the OGTT. However, exploratory post-hoc analysis showed a significant decrease in insulin (mean difference=451.75pmol/L,p=0.024) measured at two hours into the OGTT from PRE to FOLLOW-UP. As well, there was a significant decrease in both insulin (mean difference=504.92pmol/L,p=0.045) and glucose (mean difference=0.87mmol/L,p=0.031) measured at two hours into the OGTT from POST to FOLLOW-UP (Table 2.2).

The observational run-in control period was not included in the repeated-measures ANOVA due to variability in the time in which participants' OGTT was taken, however explanatory descriptive statistics suggested a trend towards increasing fasting insulin and

HOMA-IR from the control period to the PRE. This suggests a worsening of insulin resistance before the intervention began, however not significantly so (Table 2.2; Figure 2.1; Figure 2.2). One participant's OGTT values were excluded from analysis due to changes indicative of failure to adhere to fasting protocol.

Table 2.2: Changes in outcomes from OGTT during the control period then PRE, POST, and FOLLOW-UP.

Outcomes	Control period	PRE	POST	FOLLOW-UP
Fasting insulin (pmol/L)	167.61 ± 94.76	203.33 ± 99.31	173.17 ± 84.47*	153.33 ± 67.81*
Fasting glucose (mmol/L)	4.92 ± 0.30	4.96 ± 0.50	4.73 ± 0.33*	4.77 ± 0.33
HOMA-IR	3.01 ± 1.64	3.62 ± 1.74	3.13 ± 1.50*	2.75 ± 1.19*
Insulin at 2 hrs (pmol/L)	1286.78 ± 652.57	1763.22 ± 797.25	1500.75 ± 1050.51	995.83 ± 527.12*#
Glucose at 2 hrs (mmol/L)	6.66 ± 1.39	6.66 ± 1.50	6.79 ± 1.44	5.93 ± 1.27#
Insulin AUC (pmol/L/min)	N/A	115.15 ± 78.18	109.95 ± 74.93	99.66 ± 64.65

*Values expressed as mean ± SD. p< 0.05. *difference from PRE p<0.05, #difference from POST p<0.05. Note: One participant's data excluded because evidence of inadequate fasting before blood collection (n=12). Abbreviations: n = sample size; pmol/L = picomoles per litre; mmol/L = millimoles per litre; HOMA-IR = Homeostasis model assessment of insulin resistance; hrs = hours; pmol/L/min = picomoles per litre per minute; AUC = area under the curve; N/A = not assessed.*

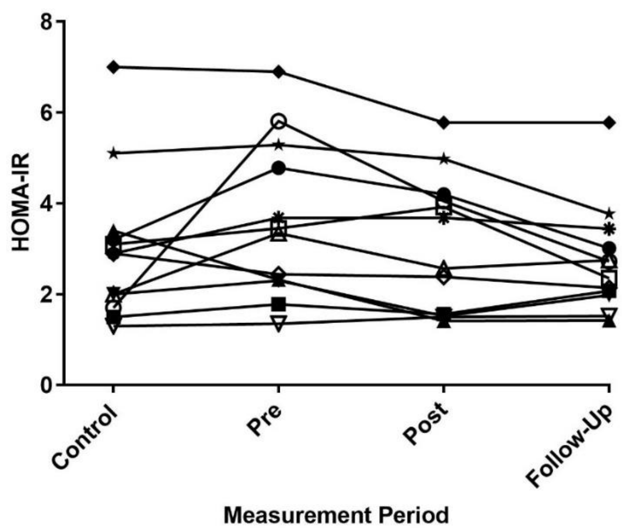


Figure 2.1: Individual changes in HOMA-IR score, a measure of insulin resistance, at each measurement period

Mean HOMA-IR scores for each participant (n=12) at each measurement period (control, PRE, POST, FOLLOW-UP). Each participant was given a separate symbol to mark their line.

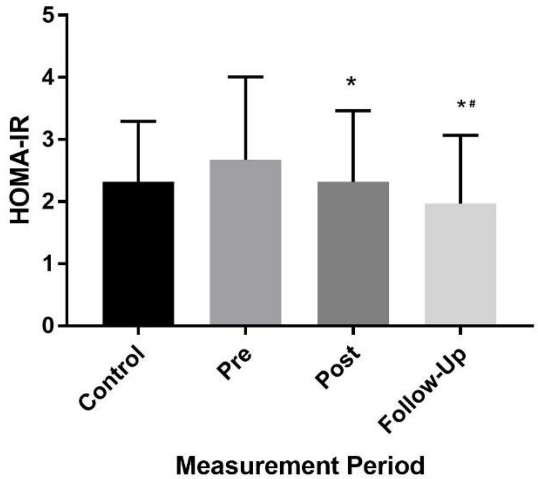


Figure 2.2: Overall changes in HOMA-IR score, a measure of insulin resistance, at each measurement period

*Mean HOMA-IR scores for all participants (n=12) each measurement period (control, PRE, POST, FOLLOW-UP). * p<0.05 compared to PRE, #p<0.05 compared to POST, error bars are SD.*

2.3.2 Improvements in measures of cardiorespiratory fitness

Repeated measures ANOVA demonstrated that there was an overall effect of time on VO_2max [$F_{(2,14)}=8.55, p=0.004, \eta p^2=0.55$], time to exhaustion [$F_{(2,14)}=5.08, p=0.022, \eta p^2=0.42$], and ventilatory equivalent [$F_{(2,14)}=5.54, p=0.017, \eta p^2=0.44$] from PRE to FOLLOW-UP, indicating an improvement in cardiorespiratory fitness (Table 2.3). Only eight participants completed the FOLLOW-UP cardiorespiratory fitness test, therefore, after confirming the normality of the data, repeated measures ANOVA for those participants was completed. Post-hoc analysis demonstrated a significant increase in VO_2max (mean difference= -3.18ml/min/kg, p=0.010), and subsequently an increase in time to exhaustion (mean difference= -1.47min, p=0.002), breath frequency (mean difference=-8.46bpm, p=0.003), and ventilatory equivalent (mean difference= -13.98L/min,p=0.004) from PRE to POST. Benefits were sustained or increased at FOLLOW-UP with an increase in VO_2max (mean difference= -3.37ml/min/kg, p=0.022), time to exhaustion (mean difference= 1.28min, p=0.041), and ventilatory equivalent (mean difference= -14.83L/min, p=0.033) from PRE to FOLLOW-UP (Table 2.3).

2.3.3 Changes in muscle strength and physical activity levels

Repeated measures ANOVA demonstrated that there was an overall effect of time on upper [$F_{(2,24)}=45.59, p<0.001, \eta p^2=0.79$] and lower [$F_{(2,24)}=28.78, p<0.001, \eta p^2=0.71$] body muscle strength (Table 2.3). Post-hoc analysis demonstrated a significant increase in upper (mean difference= -10.77kg,p<0.001) and lower (mean difference= -13.08kg,p<0.001) body muscle strength from PRE to POST; however, no significant effect from PRE to FOLLOW-UP, indicating that strength improvements were not maintained (Table 2.3).

Repeated measures ANOVA demonstrated that there was no effect of time on step count despite an increasing trend in mean step count throughout the study (Table 2.3). Data was incomplete due to technical failure (n=3 at PRE) and refusal to wear device (n=7 at FOLLOW-UP), thus, the repeated measures ANOVA represents only six participants.

Table 2.3: Changes in outcomes from cardiorespiratory fitness test, muscle strength, and daily physical activity level at PRE, POST, and FOLLOW-UP.

Outcomes	**PRE**	**POST**	**FOLLOW-UP**
Cardiorespiratory Fitness Test	**n=8**	**n=8**	**n=8**
Time to exhaustion (min)	8.88 ± 1.80	10.34 ± 1.88*	10.15 ± 2.11*
VO_2max (ml/min/kg)	24.15 ± 3.21	27.33 ± 1.76*	27.51 ± 2.68*
VCO_2max (ml/min/kg)	25.37 ± 5.29	29.03 ± 3.25	26.09 ± 5.46
Respiratory Exchange Ratio	1.04 ± 0.09	1.08 ± 0.05	0.94 ± 0.07*#
Breath frequency (breath/min)	37.96 ± 7.39	46.42 ± 7.83*	44.52 ± 10.78
Tidal Volume (L)	1.75 ± 0.35	1.74 ± 0.23	1.83 ± 0.29
Ventilatory equivalent (L/min)	65.89 ± 15.81	79.87 ± 14.44*	80.73 ± 20.16*
Heart rate, peak (beats/min)	182.33 ±15.44	190.21 ± 13.66	183.09 ± 17.38
Heart rate, rest (beats/min)	94.00 ± 7.07	95.88 ± 13.02	98.25 ± 14.42
Systolic blood pressure, rest (mmHg)	123.08 ± 7.72	123.85 ± 4.85	124.54 ± 6.15
Diastolic blood pressure, rest (mmHg)	74.38 ± 5.65	69.69 ± 9.91	75.31 ± 6.73
Muscle Strength	**n=13**	**n=13**	**n=13**
Upper body 1RM (kg)	10.99 ± 2.24	15.88 ± 2.45*	10.82 ± 1.89
Lower body 1RM (kg)	21.98 ± 5.27	27.91 ± 4.76*	21.98 ± 4.84
Physical Activity (Accelerometry)	**n=6**	**n=6**	**n=6**
Step Count (steps/day)	6120.13 ± 3621.72	7026.50 ± 2857.37	7829.00 ± 4962.45

*Values expressed as mean ± SD. *difference from PRE p<0.05, #difference from POST p<0.05. Abbreviations: n = sample size; min = minutes; VO_2max = maximal oxygen consumption; VCO_2max maximal carbon dioxide production; ml/min/kg = millilitres per kilogram per min; L = litres; mmHg = millimetres of mercury; 1RM = one-repetition maximum; kg = kilograms.*

2.3.4 Changes in anthropometric measures

Repeated measures ANOVA demonstrated that there was an overall effect of time on waist circumference [$F_{(2,24)}$=4.79,p=0.018,ηp^2=0.29] and waist-to-hip ratio [$F_{(2,24)}$=5.59,p=0.010,ηp^2=0.32]. Post-hoc analysis showed a significant reduction in waist circumference (mean difference=4.89cm,p=0.025) and waist-to-hip ratio (mean difference=0.03, p=0.021) from PRE to POST. As well, post-hoc analysis showed a significant reduction in waist-to-hip ratio (mean difference=0.03,p=0.032) from PRE to FOLLOW-UP and waist circumference (mean difference=5.18cm,p=0.051) nearing significance. There was no significant change in weight or BMI during the study periods (Table 2.4).

Table 2.4: Changes in participant characteristics between the PRE, POST, and FOLLOW-UP.

Outcome	**PRE**	**POST**	**FOLLOW-UP**
Weight (kg)	102.12 ± 18.95	103.13 ± 19.56	105.09 ± 19.40
Weight %, mean(range)	99.69 (99 to >99.9)	99.69 (99 to >99.9)	99.65 (98.1 to >99.9)
BMI (kg/m^2)	35.89 ± 5.14	36.17 ± 5.26	36.62 ± 4.70
BMI %, mean(range)	99.69 (99 to >99.9)	99.69 (99 to >99.9)	99.75 (99 to >99.9)
BMI z-score, mean(range)	3.41 (2.47 to >+3.00)	3.41 (2.38 to >+3.00)	3.56 (2.33 to >+3.00)
WC (cm)	113.23 ± 11.14	108.34 ± 10.32*	108.05 ± 10.57*
WC %, mean(range)	98.15 ± 0.69	97.46 ± 1.39*	96.75 ± 2.62*
Waist-to-hip ratio	0.67 ± 0.06	0.64 ± 0.05*	0.64 ± 0.05*
Waist-to-hip ratio %, mean(range)	97.61 (95 to >99.9)	96.31 (91 to 99)*	95.62 (86.2 to 98.4)*

*Values expressed as mean ± SD. n=13. *difference from PRE $p<0.05$, #difference from POST $p<0.05$. Abbreviations: n = sample size; m = metres; kg = kilograms; % = percentile; BMI = body mass index; kg/m^2 = kilograms per metre; WC = waist circumference; cm = centimetres.*

2.4 DISCUSSION

Insulin resistance is known to be a key risk factor in the development of type 2 diabetes in adolescents.[1] Interventions that can produce an improvement in insulin sensitivity are crucial, thus preventing the progression of diagnosis from insulin resistance to type 2 diabetes.[3-7] This study found that adolescents with insulin resistance who participated in a supervised, 10-week resistance exercise program, offered in a community setting, had significant improvement in their insulin sensitivity, lasting for up to six months. This was observed with a significant improvement in their cardiorespiratory fitness, waist circumference, and waist-to-hip ratio lasting for up to six months and with significant improvements in muscle strength immediately post-intervention.

2.4.1 Sustained improvements in insulin sensitivity

The most significant finding of this study was that adolescents had improvements in insulin sensitivity, observed as reduced fasting insulin, fasting glucose, and HOMA-IR, which were maintained and sometimes improved up to six months. Although there are no previous studies examining sustained effects of physical activity on insulin sensitivity in adolescents, among adults, exercise-induced improvements in insulin resistance are maintained for as little as 48 hours.[16,71] Considering that data collected during the control run-in period were suggestive of worsening health, these results are important and suggest that protection is possible even with a relatively short (10-week) intervention. The reduction in insulin resistance immediately post-intervention is consistent with other studies which provided a resistance-based intervention.[27,29-31] For example, we reported a 13.58% increase in insulin sensitivity, measured using the HOMA-IR, from pre- to post-assessments; this is comparable to other studies were the percent change ranged from 0.8 to 24%.[27,29-31] The results of the 6-month follow-up assessments are novel to this field of research and have meaningful clinical implications.

For adolescents, the continued reduction in insulin resistance recorded at six-month follow-up suggest that this population could help manage their insulin resistance by completing a 10-week resistance exercise program, maybe just twice a year. For adolescents who may find it difficult to commit to a physical activity program or may not naturally enjoy physical activity, the advice of committing to a 10-week program a couple of times a year may be sustainable. For healthcare professionals, it highlights that resistance exercise plays a significant role in the management of insulin resistance, with not just immediate effects observed, but benefits lasting up to six months.

Immediately post-intervention and at 6-month follow-up assessments, improvements in insulin sensitivity were not found in conjunction with a decrease in weight or BMI; this finding aligns with the conclusion of others in this field.[26,28,29,31] Our findings suggest that anthropometric measures, such as waist circumference or waist-to-hip ratio, were more responsive and better aligned with the metabolic outcomes measured. This finding is consistent with two of the four RCTs[27,30] which measured waist circumference, noting an increase in insulin sensitivity and a decrease in waist circumference. As well, in a cross-sectional study of 181 adolescents studying predictors of metabolic health, the authors noted a stronger correlation between waist circumference and insulin resistance compared with the correlation between BMI and insulin resistance.[64] Importantly, the disconnect between improvement in health without changes in body weight supports the notion that weight does not equate directly with health[53,89], and that health does come in many body sizes.[32,36,37,64,92] The evidence appears more controversial regarding the associations between anthropometric measures and the risk of developing cardiovascular disease in pediatrics.[102,103] Therefore, measurement of body weight and BMI should be considered with caution, pointing to the importance of completing direct measurements of insulin sensitivity or cardiorespiratory fitness as better outcomes to track change in this population.

Our criteria for participant selection differed from all other studies which selected participants based on BMI[26-31], in that we ensured that participants were diagnosed with insulin resistance prior to participating. It is not unexpected then that we showed robust effects on insulin resistance since all participants were known to have metabolic health concerns. The positive results from this study emphasize the need for adolescents with insulin resistance to receive a comprehensive, supervised, resistance exercise program to help them manage their health.

2.4.2 Sustained improvements in cardiorespiratory fitness

Improvement in insulin sensitivity was accompanied by an increase in cardiorespiratory fitness (seen as an average increase in VO_2max of 3ml/min/kg) among all participants which was maintained up to six months; this finding was surprising considering that aerobic training was not included in the intervention. Increase in cardiorespiratory fitness was only reported in one other study which employed a resistance-based intervention.[27] The reason for the improvement observed in cardiorespiratory fitness is unclear; however, we did promote heart rate as an intensity metric and minimized rest periods to increase the workload during the sessions. This intervention was designed similarly to previous RCTs and clinical trials completed on this cohort (60-90 minute supervised sessions, 2-3 x/week, 12-16 weeks).[26-31] By setting up our intervention in circuit format, as per the majority of studies using resistance-based interventions, likely muscle strength and aerobic capacity were both targeted.[14] The nature of circuit training means that there is a cardiorespiratory fitness element so although resistance exercise was the focus of the intervention, it is not possible to determine the isolated contribution from each component.[14] The degree and quality of supervision and the supervisors' attention to intensity may have also promoted safe progression of intensity and helped to motivate participants.[69,70] Another point to consider is that our participants were notably deconditioned with participants' cardiorespiratory fitness, reported as an average VO_2max of 24ml/min/kg, categorized as 'very poor', or 'poor'.[104] Our participants' VO_2max values were less (average 24ml/min/kg) than those reported of participants in similar studies (ranged from 24 to 31ml/min/kg).[27-29] All our participants were categorized as 'low active' or 'sedentary'[95,105] with a step count of less than 6100 steps per day.

Therefore, the attention to intensity may have been sufficient to increase cardiorespiratory fitness and, albeit insignificant, increase step count in this deconditioned group of adolescents.[16,24]

Importantly, we demonstrated that cardiorespiratory fitness improved without a significant change in weight or BMI; supporting previous research showing that regardless of changes in weight or BMI, participants' cardiorespiratory fitness and insulin sensitivity may increase.[10,12,15,16,54,73-75] This finding is important to consider in the context of providing physical activity within a CDPP. Healthcare professionals can assist adolescents in overcoming emotional barriers such as feelings of failure[90], when despite strong effort and compliance with exercise, weight loss is minimal or does not occur. By incorporating a body positive approach with knowledge of how resistance exercise can help manage blood hemostasis, the success of long-term compliance to regular physical activity can be optimized.[32-37]

2.4.3 Short-term benefits of resistance exercise on muscle strength

Immediately post-intervention, there were significant improvements in muscle strength; these improvements were anticipated given the direct relationship between muscle strength and resistance exercise.[26-31] Change in muscle strength is an important clinical outcome as it has been identified as a predictor of insulin resistance in adolescents.[73] Enhanced insulin signaling has been noted simply in response to muscle contractions.[83] Perhaps the more frequent muscle contractions, seen with adding resistance exercise to a weekly regime, enhanced insulin transport. By six months, most participants' muscle strength had returned to pre-assessment values, despite a continued reduction in insulin resistance, suggesting that other mechanisms beyond muscle strength may account for the finding. For example, higher levels of inflammatory markers are thought to play a role in the etiology of insulin resistance[106]; if resistance exercise reduces inflammatory markers it may improve insulin sensitivity regardless of changes in muscle strength or physiology.[107] Indeed, physiological changes within the skeletal muscle cell, the enhanced action of insulin, or the improvement cardiorespiratory fitness could account for the longer-term metabolic effects. It is compelling to think that such a relatively short (10-week) intervention of resistance exercise would have lingering effects up to six months afterwards.

2.4.4 Limitations

Although we provide evidence that supervised resistance exercise can provide sustained benefits to metabolic health and cardiorespiratory fitness, there are some limitations to consider. The study was completed as a cohort study, a less rigorous design than an RCT and not able to show evidence for a causal link between resistance exercise and improvements in insulin resistance (only an inverse association); however, data from the 18-month run-in period suggested that participants' health was worsening before the intervention, either due to hormonal changes during puberty[4,44-46] or worsening lifestyle habits[1,3,4,6,7,10-12]. We used a sample of convenience that was small and limited by 'volunteer bias', a common bias among studies with physical activity interventions, since more motivated people may naturally volunteer to participate. Only 13 of the 69 (19%) adolescents that were approached agreed to participate, likely representing the most motivated adolescents. Although we did not control participants' activity levels outside of the intervention, accelerometry data suggest there was no change over time; however, this is difficult to interpret as not all participants agreed to wear the activity trackers and there were technological malfunctions limiting the use of this data. Finally, we did not account for the dietary habits of the participants during the study period; dietary changes during the study period could contribute to over or underestimation of changes in outcomes.

Compliance was moderate, with participants attending 80% of community sessions. This is less than other studies in this field, which stated an attendance rate over 96%.[27-29] Despite moderate compliance, the impact on our results is felt to be minimal, as a significant reduction in insulin resistance was still noted. As in most physical activity programs, some adolescents put forward their maximum effort while others were difficult to engage at times. This introduces the topic of 'presenteeism' within physical activity interventions. A person may be present however they are putting very little effort forward or have low productivity.[108] The reasons for presenteeism in physical activity programs (e.g., stress, anxiety regarding exercise, or concern with competency of performance) have not been studied.

2.5 CONCLUSION

The findings of this study suggest that adolescents with insulin resistance, participating in a 10-week supervised resistance exercise program (60-minute duration, three times per week), may expect improved insulin sensitivity as well as improved cardiorespiratory fitness, waist circumference, and waist-to-hip ratio. Importantly, these benefits were maintained up to six months, suggesting that adolescents could help manage their insulin resistance by participating in a resistance exercise program even just two or three times a year. Furthermore, these benefits were observed among adolescents whose health was worsening even with the support of a CDPP; cementing the importance of physical activity as a key ingredient in the management of insulin resistance.

CHAPTER THREE

Insulin resistance is critical in the development of type 2 diabetes in adolescents[1] thus, interventions that result in an improvement in insulin sensitivity become paramount in disease prevention strategies. The primary purpose of this study was to evaluate effects, up to six months, of resistance exercise on insulin sensitivity in adolescents diagnosed with insulin resistance. Secondary outcomes that are known to be markers of metabolic health were also assessed; these included cardiorespiratory fitness, muscle strength, physical activity level, and anthropometrics. We hypothesized that resistance exercise would improve primary (insulin sensitivity) and secondary outcomes immediately post-intervention, but that, these positive benefits would begin to decline by six months. For most outcomes, the assumed trajectory moving back to pre-assessment values did not take place.

3.1 DISCUSSION OF RESULTS

As expected, based on other studies in this field[27,29-31], participants demonstrated a significant reduction in insulin resistance immediately following the 10-week intervention. But even more importantly, this reduction in insulin resistance was maintained up to six months. These findings are significant for adolescents with insulin resistance and healthcare professionals who work in the area of chronic disease prevention. The reduction in insulin resistance was observed with a significant improvement in waist circumference and waist-to-hip ratio but with no change in body weight or BMI at any measurement period. Furthermore, there was a significant improvement in cardiorespiratory fitness which was also maintained at six months follow-up. Our results concur with that of RCTs[27,29-31]and controlled trials[30,31] that a resistance exercise program can improve the metabolic health of adolescents with insulin resistance by increasing their insulin sensitivity, thus reducing their level of insulin resistance. This study adds new evidence to the field by providing follow-up beyond the immediate post-intervention testing period, showing that benefits of this relatively short (10-week) intervention were maintained up to six months. Since healthcare professionals are concerned with the longer-term effects of interventions on the management of insulin resistance, our findings help provide evidence for physical activity programming within CDPPs. The following sections will discuss in detail these findings, detailing the results immediately post-intervention as well as discussing the effects observed at six months.

3.1.1 Findings from the OGTT during the control period

The control run-in period included results of all participants' OGTT up to 18 months prior to the start of the study. Since an increase in insulin resistance can be expected due to hormonal changes during puberty[4,44,45], the control run-in period provided information on the stability of insulin resistance over time. Even though participants were being managed by an interdisciplinary team from control period to pre-assessment, there was an increase in fasting insulin and HOMA-IR, suggestive of increasing severity of insulin resistance among participants prior to commencing the intervention.

3.1.2 Improvements in OGTT outcomes

The most significant finding of this study is that improvements in insulin sensitivity, observed as reduced fasting insulin and HOMA-IR, were sustained up to six months. A reduction in fasting glucose was also noted immediately following the 10-week intervention. Furthermore, at follow-up there was a significant decrease in insulin and glucose measured at two hours into the OGTT compared to pre-assessment; indicating an improvement in glucose tolerance among participants, which also demonstrates a reduction in insulin resistance. An examination of individual level data showed that ten of the thirteen participants experienced a reduction in insulin resistance. As mentioned previously, this improvement occurred despite an apparent worsening of insulin resistance in the 18 months preceding the intervention.

Based on previous research[27,29-31], a reduction in insulin resistance following a resistance exercise is likely related to improvements in blood hemostasis, as cells within the body, mainly skeletal muscle cells[15,78], require more glucose from the blood resulting in reduced insulin production by the pancreas. Furthermore, physiological changes within the skeletal muscle fibres improve the metabolism of glucose and insulin with resistance exercise.[27,29,30,78,83] The results from this study, along with findings from similar studies, support the message that a moderate change in lifestyle, such as completing resistance exercise for one hour, two to three times per week, will have an impact on the metabolic health of adolescents. Our study was slightly shorter in duration (10-weeks) compared with other studies (12-16 weeks) published[27,29-31]; however, significant improvements in insulin resistance were still noted. This finding is important for adolescents who may find it difficult to participate in a physical activity program or may not naturally enjoy physical activity, committing to a 10-week program two or three times a year may be sustainable. Despite offering an intervention shorter in duration, we may have seen robust effects due to how the intervention was arranged. Our intervention may have, unintentionally, targeted both muscle strength and aerobic capacity in the effort to complete resistance exercises with minimal rest periods between stations, as will be discussed in the next section. Furthermore, it is felt that a main difference in our study, that may have contributed to an improvement in OGTT outcomes, was the selection criteria used to choose participants. Our selection criteria differed from all other studies, which selected participants based on BMI[26-31], compared to this study where adolescents were diagnosed with insulin resistance prior to participating. With known metabolic health concerns, these adolescents are the most clinically important patients to follow.

The results of the 6-month follow-up assessments are novel and begin to fill the gap in this research area pertaining to lack of long-term data. Our results highlight that resistance exercise plays a significant role in the management insulin resistance, with not just immediate effects observed but benefits lasting up to six months after cessation of the program. In our case, as part of a CDPP, participants had received education on the benefits of physical activity, nonetheless their metabolic health continued to improve from participating in a specific treatment tailored to met their needs. The positive results from this study emphasize the need for adolescents with insulin resistance to receive a comprehensive, supervised, resistance exercise program to help them manage their health.

3.1.3 Improvements in cardiorespiratory fitness while considering physical activity level

Sustained improvement in insulin sensitivity up to six months was accompanied by an increase in cardiorespiratory fitness, as detected by a significant rise in maximal oxygen consumption (VO_2max). We noted an improvement in cardiorespiratory fitness in all participants. This was surprising considering that the intervention did not include an aerobic component and there was no significant change in habitual physical activity level as measured by step count, up to six months. An improvement in cardiorespiratory fitness has been reported in only one of the three RCTs examining a resistance-based intervention and that measured cardiorespiratory fitness.[27-29]

We did ensure that the resistance exercises employed large muscle groups with minimal rest periods while monitoring heart rate to ensure that participants' efforts were between 50-70% of age-predicted values. By setting up our intervention in circuit format, as per the majority of studies using resistance-based interventions[14], likely muscle strength and aerobic capacity were both targeted. The nature of circuit training means that there is a cardiorespiratory fitness element so although resistance exercise was the focus of the intervention, it is not possible to determine the isolated contribution from each component.[14] If in fact aerobic capacity was targeted, inadvertently, our intervention may be similar to those offered by Damaso et al.[87] and Tulio de Mello et al.[88], who found that aerobic plus resistance-based interventions was more successful at reducing insulin resistance when compared to solely aerobic-based interventions.

Alternatively, the increase in cardiorespiratory fitness may be attributed to the considerable level of deconditioning when participants began the program. Participants had a very low cardiorespiratory fitness level based on their VO_2max values at pre-assessments (average 24ml/min/kg)[95,104] and were categorized as sedentary based on their step count (average 6100 steps per day)[105]. Janssen et al.[24] reported in their review of the benefits of physical activity among school-aged children and youth that even modest amounts of physical activity may have tremendous health benefits, such as increase cardiorespiratory fitness, in high-risk adolescents (e.g.; obese, insulin resistant). Furthermore, lower baseline values are an important predictor of greater magnitude of improvement in cardiorespiratory fitness.[16,24] Another point to consider for the 6-month follow-up assessments is that only eight participants completed the cardiorespiratory fitness test; these were likely the most motivated participants, and therefore, may have led to volunteer bias resulting in a higher average VO_2max among these participants.

Cardiorespiratory fitness could also improve if habitual levels of activity change over the course of the program. We employed accelerometry to determine whether there was a general change in daily physical activity which could account for the improvement in cardiorespiratory fitness. Following the intervention, there was a trend toward increasing (although not significant) average step count, suggestive of an improvement in habitual physical activity level. Davis et al.[109], in the only RCT measuring habitual physical activity with resistance exercise in adolescents, also found no significant difference in step count. The stability of these values suggests that the reduction in insulin resistance was likely attributable to the intensity of the intervention as opposed to widespread change in participants' daily physical activity outside of the study protocol. Although not significant, the slight increase in daily step count may have contributed to an improvement in cardiorespiratory fitness. It should be noted that due to technical difficulties and noncompliance, activity count data was incomplete at follow-up. First, some participants did not wish to wear the devices at follow-up and in some cases among those who did wear the units, there was evidence of device malfunction. Furthermore, step count was only measured for three days, chosen randomly on weekdays and weekends; whereas, Henderson et al.[12] suggested that the minimal accelerometer wear time should be 10 hours per day for at least four days to ensure valid data.

3.1.4 Changes in muscle strength

Along with the reduction in insulin resistance, there were significant improvements noted in upper and lower body muscle strength among all participants following the intervention. Strength improvements were anticipated given the direct relationship between muscle strength and resistance exercise, with this relationship being found in other studies.[26-31] It was not surprising that these beneficial effects on insulin sensitivity co-occurred with an increase in muscle strength[26-31], as muscle strength is a predictor of insulin resistance in adolescents, independent of body weight or cardiorespiratory fitness[73]. This improvement is physiologically important given the etiological links between changes in skeletal muscle cells (e.g., altered muscle fibre type (changing from type IIb to IIa)[69,70]), improved glucose metabolism (e.g., increased density of glucose transporter type 4 (GLUT-4) proteins[78,84]), and enhanced action of insulin (e.g., enhanced insulin signaling[83]) with resistance exercise. If improved muscle strength leads to increased insulin sensitivity, healthcare professionals may justifiably focus their efforts primarily on resistance exercise as a means of reducing insulin resistance among adolescents, as opposed to aerobic exercise only. Like other studies, we used exercises that targeted large muscle groups, where participants moved through stations in a circuit. Two studies by Lee et al.[27,28] used machine weights, while other controlled trials and RCTs used free weights[26,29-31]; we used a combination of resistance, such as participants' body weight, kettle bells, resisted bands, tractor trailer tires, and weighted ropes. This may have been novel for participants, helping to keep them interested during the sessions.

Of clinical interest, six months after the program was completed, most participants' muscle strength had returned to pre-assessment values, despite a continued reduction in insulin resistance. This result is somewhat contradictory, since previous research has implicated acute changes in skeletal muscle cell physiological and enhanced action of insulin as an important driver of improved insulin sensitivity.[27,29,30,78,83] The finding that muscle strength returned to pre-assessment values while insulin sensitivity was maintained suggests one of three things: (1) enhanced insulin action or glucose metabolism in cells not associated with muscle strength, (2) increased insulin sensitivity is due to some other mechanism, and (3) delayed effect of insulin sensitivity where, perhaps, if we had measured again in another three months, insulin benefit would have declined.

Despite a seemingly, obvious relationship between muscle strength and skeletal muscle glucose metabolism, our results suggest that possibly enhanced insulin action or glucose metabolism occurring in cells was not associated with only muscle strength. For example, Holten et al.[83] reported enhanced insulin signaling simply in response to muscle contractions. Perhaps the more frequent muscle contractions, seen with adding resistance exercise to a weekly regime, enhanced insulin transport regardless of changes in muscle strength. Increased insulin sensitivity may be due to another mechanism besides enhanced insulin action or skeletal cell glucose metabolism. For example, higher levels of inflammatory markers are thought to play a role in the etiology of insulin resistance.[106] If resistance exercise reduces inflammatory factors, such as C-reactive protein, in adolescents with insulin resistance (as it does in adults), it may improve their insulin sensitivity regardless of changes in muscle strength or physiology.[107] Although the 6-month follow-up was novel for this study, to continue to understand the relationship between insulin sensitivity and muscle strength in adolescents, further studies of longer duration are needed. It is possible that the reduction in muscle strength at six months follow-up may have indicated the beginning of a decline in metabolic health, suggesting a delayed decrease in insulin sensitivity.

3.1.5 Improvements in insulin sensitivity and cardiorespiratory fitness when considering anthropometric measures

One of the most important findings was that there were significant improvements in insulin sensitivity and cardiorespiratory fitness without reduction in body weight or BMI. If this physical activity program, like so many, had gauged its participants' success based on their body weight, it would have overlooked the significant improvement in health observed in reduced insulin resistance and an improvement in cardiorespiratory fitness.

The research examining the impact of resistance exercise on anthropometrics has detected metabolic benefits with[27,30] or without[26,28,29,31] changes in body weight, body mass index (BMI), waist circumference, and/or adiposity. Longitudinal studies on body weight lost in adults have noted that, despite maintaining lifestyle modifications such as increased physical activity or nutritional changes, the majority of adults regain the weight.[32] This may be true among adolescents as well, suggesting that a reduction in body weight and BMI may not be a realistic, modifiable factor to undertake. Behm at el. (2008)[69] noted in their review of resistance training among adolescents that studies suggested changes in body composition, such as an increase in muscle mass, may account for the less body weight loss; however, this supposition may be short-sighted in pediatrics since the reason for increased muscle strength following a resistance-based intervention is more likely due to neurological changes within the skeletal muscle fibres and not muscle hypertrophy.[69] Our anthropometric data supports the message that weight does not equate directly with health[53,89], that has led to the concept 'Health at Every Size'.[32-37] In this study other anthropometric measures, waist circumference and waist-to-hip ratio, seemed to better align with improvements in metabolic health, as reduction in waist circumference and waist-to-hip ratio among participants was retained up to six months from cessation of the program. Waist circumference and waist-to-hip ratio have been reported to be a better predictor of metabolic health than BMI or weight in adults, noting that a reduction in waist circumference is seen with a reduced risk of developing chronic disease.[110] As well, in a cross-sectional study of 181 adolescents studying predictors of metabolic health, the authors noted a stronger correlation between waist circumference and insulin resistance compared with the correlation between BMI and insulin resistance.[64] However, the evidence appears more controversial regarding the associations between anthropometric measures and the risk of developing cardiovascular disease in pediatrics.[102,103] Of the research examining resistance-based interventions among adolescents[26-31], only one study noted a reduction in waist circumference post-intervention[27]. Other researchers have suggested that a reduction in waist circumference without a decrease in body weight may imply a redistribution of abdominal fat or increase in abdominal tone.[54] Future research should consider a more direct anthropometric measure of abdominal fat and lean mass (such as using dual-energy x-ray absorptiometry (DXA)), following a resistance-based intervention.

As well, the improvements in cardiorespiratory fitness occurred without change in weight or BMI; supporting the current concept that cardiorespiratory fitness is a better predictor of insulin sensitivity than weight in adolescents.[10,12,15,16,54,73-75] In public and academic dissemination, this has given rise to the phrase 'fitness, not fatness'[10,12,15,16,54,73-75], a concept imperative for healthcare professionals working with adolescents with insulin resistance to appreciate directing healthcare professionals and adolescents away from the erroneous idea that excess weight is the only problem causing insulin resistance.

Refocusing of attention to health rather than body weight may assist in overcoming emotional barriers such as feelings of failure that may be experienced by adolescents[90] when, despite strong effort and compliance with exercise, weight loss is minimal or does not occur. Our findings also support the use of a body positive approach in physical activity programming, where the focus is shifted from short-term weight loss to long-term lifestyle modification.[32-37]

A summary of our results, with significant results noted with a *:

Immediately post-intervention	Retained up to six months
Reduced insulin resistance*	Yes*
Increased cardiorespiratory fitness*	Yes*
Increased muscle strength*	No returned to baseline*
Reduced waist circumference*	Yes*
Increased trend in step count	Yes
No change in weight or BMI	No change in weight or BMI

The results immediately post 10-week intervention are consistent with results found in other studies on adolescents with insulin resistance.[17,27-31,73] Low cardiorespiratory fitness and muscle strength in adolescents have all been shown to be associated with increased insulin resistance.[73] Given the potential modifiability of these factors, it is not unexpected that interventions focusing on improving these outcomes would demonstrate an immediate reduction in insulin resistance. The results of the 6-month follow-up assessments are novel, with a sustained reduction in insulin resistance and cardiorespiratory fitness found up to six months following cessation of the program. As healthcare professionals help adolescents manage their insulin resistance now, the loftier goal of reducing the burden of chronic disease on the healthcare system is the focus of all CDPPs. The following sections will examine how methodical design, participant selection and characteristics, compliance, intervention, and outcome measurement may have impacted these results.

3.1.6 Impact of methodical design on results

This study used a repeated-measures design (including a control run-in period) to determine effects of resistance exercise on insulin resistance. Initially, a RCT was planned which would have included 30 adolescents randomized to either an intervention or wait-list control group. Despite offering this physical activity program to 69 eligible adolescents, only 13 registered. Due to clinical service needs and program guidelines, the intervention had to be offered, thus, the study proceeded with those participants who were available. There is certainly a need within the current body of research for more rigorous studies in this field[17,18], but this limitation emphasizes the issues of balancing clinical-based, primary care research with ideal research methodology, such as randomization and a control group.

In lieu of RCT design, we included data from participants OGTT in the previous 18 months to establish a stable baseline. The time at which these laboratory tests were completed varied among participants, from 4-18 months (September 2014 – January 2016). The data from this period was used to provide information regarding progression of insulin resistance among participants; ideally, the timing of control period would have been more consistent among participants, such as 12-18 months, however testing times were at the discretion of the pediatric endocrinologist. The most important information from this period was that there was an increasing severity of insulin resistance among all participants.

3.1.7 Impact of participants' characteristics on results

There are aspects pertaining to participant characteristics and selection which need to be considered when discussing this study's results. These include previous history of care provided by the CDPP, participant selection criteria, baseline characteristics, and effects of puberty.

At recruitment, all participants had been a part of the CDPP for years (ranging from two to eight years), having participated in a 9-week education program, with individual clinic appointments to address concerns regarding lifestyle modification. Individual appointments with a physiotherapist were aimed at learning home-based physical activity programs and guidance on community-based physically activity opportunities. All participants had a similar history of care provided by the CDPP, so it is unlikely that variation would have impacted the findings of this study. This point does highlight, however, that even though adolescents were able to avail of a physiotherapist and a CDPP, they continued to experience improvements in their metabolic health from participating in a specific resistance exercise program. This suggests that a more targeted approach may be needed for adolescents with insulin resistance. The positive results from this study point to the success that can be achieved among adolescents with insulin resistance who participate in a comprehensive, supervised, resistance exercise program to help them manage their health.

A critical difference between our study and previous research on resistance exercise among adolescents at risk was participant selection criteria. This sample of adolescents were all diagnosed with insulin resistance, based on results from OGTT and presence of physical markers, prior to participating. As noted in the literature review, all studies recruited participants based on BMI, despite it being agreed in the literature that BMI was a poor predictor of insulin resistance in adolescents.[33,54] There is an assumption that excess body weight poses a significant increase in morbidity; however, once studies controlled for factors, such as physical activity level and nutrient intake, this risk of disease disappeared or was significantly reduced.[33,54] If we had selected participants on body weight alone (without confirmation of insulin resistance), we may have included participants that, despite having a high BMI, were metabolically healthy.

Apart from all participants being diagnosed with insulin resistance, they appeared to have similar baseline characteristics as participants in other studies completed in this field. All participants were defined as obese, as based on the WHO's growth charts.[49] All participants had a large waist circumference (> 97^{th} percentile). Nine of the thirteen (69%) participants had acanthosis nigricans along the backs of their necks, which is the most common clinical presentation associated with insulin resistance.[4,6,39,50] Importantly participants also presented with co-morbidities, such as orthopedic issues, attention deficit disorder, and autism spectrum disorder without impacting their ability to partake in the program. Furthermore, baseline characteristics for muscle strength and cardiorespiratory fitness were similar amongst participants, therefore, this group of participants could be considered reasonably uniform. When comparing our participants to standardized values, the adolescents were notably deconditioned. Our participants' VO_2max values (average 24ml/min/kg) were less than those reported of adolescents in similar studies (ranged from 24 to 31ml/min/kg).[27-29] Based on VO_2max, most participants' cardiorespiratory fitness was categorized as 'very poor', with three participants categorized as 'poor'.[104] As per ACSM guidelines, most participants were categorized as 'sedentary'[95], which was reinforced by step count data (average 6100 steps per day) which also categorized most participants as sedentary with a step count near or less than 5000[105]. No normative values could be found for muscle strength in adolescents; however, when participants were compared to other studies on adolescents, they were weaker (lower 1RM).[111] As mentioned previously, there was evidence from OGTT that our participants' health was in decline. The cardiorespiratory fitness measures corroborate that finding. As discussed in a review by Brambilla et al.[16], physical activity will help moderate the risk associated with poor metabolic health, such as very low levels of cardiorespiratory fitness, insulin resistance, and obesity.

Another patient characteristic that may have impacted the findings in this type of study was the adolescents' stage of development. Hormonal changes take place during puberty affect insulin response; insulin sensitivity naturally decreases at the onset of puberty and does not recover until the end of maturation.[4,44,45] These maturational effects may have impacted data collected during the control period, as some participants may have moved from a pre-pubertal stage to a pubertal stage of development. Therefore, they may have experienced a natural decrease in insulin sensitivity due to hormonal changes at this age, contributing to the increasing severity of insulin resistance. However, it was unlikely that puberty would have impacted our results between pre-, post-, and 6-months following intervention since this was a relatively short study period. Furthermore, all participants demonstrated signs of puberty by the beginning of the study. The natural decrease in insulin sensitivity seen in earlier stages of puberty would have already taken place and were unlikely to impact the study's results.

In summary, the participants' characteristics, including a diagnosis of insulin resistance, poor cardiorespiratory fitness, and sedentary behaviour, created opportunities for significant improvement in both the primary outcome of insulin sensitivity and secondary outcome of cardiorespiratory fitness. It is likely that the impact of pubertal changes on the results was insignificant.

3.1.8 Impact of compliance on results

We measured several indicators of compliance in the research which included participants' attendance and efforts in community sessions, completion of their weekly home program, and participation in assessments.

Compliance was moderate, with participants attending 80% of community sessions, an average of 16.46 ± 2.47 of 20 sessions per participant. Naturally, some participants completed more sessions than others, with the range between 11-20 community sessions. No participants were excluded for failing to attend the minimum number (<50%) of community sessions. Compliance was less than other studies in this field, which reported an attendance rate over 96%.[27-29] However, despite moderate compliance, a significant reduction in insulin resistance was still noted. This is worthy of consideration when planning physical activity programming; knowing that 100% compliance is not necessarily required to see improvement among participants will help in organization and planning.

During the community sessions, participants were encouraged to put their best effort forward. As in most physical activity programs, some adolescents put forward their maximum effort while others were difficult to engage at times. This introduces the topic of ‘presenteeism’ within physical activity interventions. Presenteeism is a concept presently being considered in research regarding work-place productivity. It refers to employees who present to the workplace but, because of illness or stress, perform at sub-optimal standards.[108] This concept may extend to other situations, such as participation in physical activity. There could be many reasons for presenteeism in physical activity programs, such as stress, anxiety regarding exercise, general feeling of unwell, or concern with competency of performance. There is no research in this field thus far, with most studies reporting compliance rate as a measure of attendance, with the goal of high attendance rates. For healthcare professionals providing physical activity interventions, measurement of attendance is likely somewhat superficial as a participant may be present however not actually participating in the intervention with enough effort to produce change in outcomes. We noted that for a couple of participants in this study, ‘presenteeism’ was an issue where they would attend sessions, however complete less work compared to their peers. This was noted with frequent breaks to get water, trips to the bathroom, or rests during the sessions. Some participants always chose lighter weights or resisted bands, requiring verbal cueing to encourage them to work at their maximum capacity. Future research could examine ways to manage presenteeism in physical activity interventions.

A measurement of compliance during the home-based sessions was provided by self-report; therefore, objectively this cannot be assured. For some participants, it appeared that they did not complete their home program as the details they provided regarding what was completed were very vague. Kelly et al.[26] employed a home-based resistance program to improve insulin resistance among adolescents; however, the program, unlike others that were supervised, did not alter insulin sensitivity. Our findings, along with others[26-31], suggest that supervision may be a key ingredient to ensure compliance, both in attendance and effort, to provide safe progression of intensity, monitor technique, and motivate participants, with these benefits being well established, particularly in children and adolescents.[69,70] Even though we could not be assured that participants completed the third, home-based session weekly, there was still a significant reduction in insulin sensitivity with two community-based sessions per week.

Compliance and presenteeism among adolescent participants in a physical activity program likely affects the measurement of outcomes as well as the intervention itself. It was interesting that all participants completed the primary outcome, OGTT, as well as anthropometrics at all measurement periods. We observed that measurements that involved physical activity were more challenging for participants and in fact five of the participants would not complete the cardiorespiratory fitness test stating ‘it is too hard’. Davis et al.[109] discussed this issue in their study, of the 64 participants who were pre-screened, 20 dropped out before the pretesting, reporting that they thought the cardiorespiratory fitness testing was too intense. These observations highlight the challenges in working with clinical populations who are sometimes unaccustomed to the physical efforts of exercise. In our study, it is likely that we were only able to complete cardiorespiratory fitness testing at six months with the most motivated participants, creating volunteer bias and opportunity for overestimation of VO_2max.

In summary, participants' attendance, and more importantly effort in community sessions, appeared to have little impact on results overall as the majority of participants attended most sessions and put forth their best effort. Compliance to the home-based sessions could not be assured, but likely had minimal impact on overall results. And finally, participants were quite compliant with laboratory testing and anthropometrics; however, they were less so with cardiorespiratory fitness testing at six months, which may have impacted those results.

3.1.9 Impact of the intervention on results

Although the benefits of resistance exercise had been examined previously, our intervention had two unique aspects. First, we emphasized a body positive approach and secondly, we monitored heart rate and minimized rest periods to maximize intensity.

The dosage of our intervention, in terms of frequency and duration, was arranged similarly to RCTs and clinical trials in this field.[26-31] All interventions offered 60-minute sessions except for Dias et al.[30] whose sessions were 30-40 minutes. The frequency of the sessions were between two and three times per week lasting 12-16 weeks.[26-31] As mentioned, our intervention was set-up in a circuit, like most studies in this area.[14] How intensity was determined and progressed varied among studies (e.g., time, repetitions or sets completed, percentage of 1RM).[14,26-31] All RCTs studied only one gender[26-29], whereas the controlled clinical trials recruited both males and females[30,31].

A body positive approach focuses on taking care of one's body by promoting health behaviours and long-term change[32-37] was taken. Ideally, another intervention group who received a non-body positive approach would have been included. The improvement in insulin sensitivity and cardiorespiratory fitness in this study are consistent with the evidence supporting this approach; there does not need to be a change in body weight or BMI to improve insulin sensitivity[10,12-21,80]. Previous research suggests that adolescents' daily physical activity amount is very low[22] and some of the barriers they identify include negative attitude towards physical activity, lack of enjoyment, negative self-image, lack of family or peer support, and lack of perceived competence.[90] A body positive approach helps to address these barriers affecting adherence to physical activity. During our intervention, it appeared that participants felt comfortable and supported during the community sessions. This was probably most evident when 11 of the 13 participants registered for and completed the same program when it was offered again, following their 6-month follow-up assessments. This information is vital for healthcare professionals working with this cohort, as it is not justifiable to develop a physical activity program where participants' success is based on their weight only; both the participants and facilitators will be disappointed.[32,36,37] By incorporating a body positive approach with knowledge that is known about how resistance exercise can help manage blood hemostasis, this ideally will optimize the success of long-term compliance to regular physical activity, giving participants a chance to see a sustainable reduction in their risk factors for insulin resistance through their clinical assessments of blood work, cardiorespiratory fitness, muscle strength, and daily physical activity levels.

These two features of the intervention, using a body positive approach and providing expert supervision with attention to intensity, may have impacted the results. The approach to the community-based sessions ensured activities were enjoyable yet challenging; observing that most participants were engaged and appeared comfortable to be active. By setting up the resistance exercises in a circuit format, paying attention to intensity by monitoring heart rate and minimizing rest periods, we likely influenced both improved muscle strength and cardiorespiratory fitness[14], which may have contributed to the robust effects.

3.1.10 Impact of outcomes measures on results

Outcomes were carefully chosen for this study; however, it is important to discuss their potential impact on results. The primary outcome was insulin sensitivity and secondary outcomes included cardiorespiratory fitness, muscle strength, physical activity levels, and anthropometric measures.

3.1.10.1 OGTT

It was essential for this research team to use a primary outcome which was a direct measure of metabolic health. Fortunately, participants complete the OGTT as part of the standard care they receive from the CDPP. The OGTT is a valid and reliable measure of insulin sensitivity in adolescents against the gold standard, euglycemic-hyperinsulinemic clamp.[41,55,56] In fact, we found that OGTT values were very consistent within an individual. When using laboratory tests, there is a risk with error within the blood collection process. This occurred for one participant in their 6-month follow-up assessment. They had a 111% change in HOMA-IR between post and 6-month assessments compared to a mean change of 20% among the group. This was likely due to error with blood collection or the participant not following fasting protocol; therefore, this participant's results were excluded from the study.

3.1.10.2 Cardiorespiratory fitness test

Cardiorespiratory fitness testing was assessed using the Bruce Treadmill Protocol, which participants completed as part of the standard care provided by the CDPP, along with a direct measure of VO_2max using a metabolic cart. It was unfortunate that only eight of the thirteen participants were agreeable to complete this outcome at the 6-month follow-up assessments. Any cardiorespiratory fitness test can be challenging; choosing a test that participants were very familiar with was thought to foster compliance. In fact, participants reported that the test was too difficult and that they did not like donning the face mask. Although measurement of cardiorespiratory fitness using a metabolic cart is the gold standard[95], it may have been more comfortable for participants to complete simply the Bruce Treadmill Protocol, obtaining estimated rates of exertion using heart rate as opposed to a direct measure of VO_2max. Choosing the direct measure of cardiorespiratory fitness strengthened the study methodology as it is a more rigorous outcome compared to estimation equations. However, the difficulty of this type of test is a limitation for participants.

Unfortunately, the metabolic cart was not available for 6-month follow-up assessments, therefore, a portable unit was used. Pre-testing of both units showed that the values obtained from the same individual were almost identical. The only impact this change appeared to have on results was the values measured for respiratory exchange ratio. There was a significant difference in respiratory exchange ratio between post- and 6-month follow-up assessments, with a higher value noted at six months. Respiratory exchange ratio is known to be higher when assessed using a portable unit, however, the portable unit is a reliable and valid against the metabolic cart.[112,113]

3.1.10.3 Physical activity level

Since changes in activity levels outside the intervention can impact results, we assessed physical activity levels using accelerometry, collecting step counts over three consecutive days. Of the studies completed in this field, only one RCT controlled for habitual change in physical activity during the study period[13], with most other studies stating it as a limitation. There are three points to consider when examining the impact of the step count data on the findings. Firstly, it would have been ideal to measure physical activity over seven days, however that was not possible secondary to scheduling. A longer measurement period would have provided a more realistic representation of participants' daily physical activity. Henderson et al.[12], reviewing 630 children, stated criteria for accelerometer data collection, suggesting that the minimal accelerometer wear time should be 10 hours per day for at least four days. It is thought that maybe the increase in step count was missed with only a three-day measurement. Secondly, several participants did not agree to wear the Garmin Vivofits and, even when they were agreeable, the data extracted suggested that they did not use it. It was interesting that all participants agreed to wear the activity trackers at the pre- and post-assessments, suggesting that perhaps participants found the device troublesome after a time. Audrey et al.[114] collected accelerometer data over seven days from 1000 students aged 12 to 13 years at baseline and follow-up. Adherence, which they defined as recording ≥ 600 minutes per day for ≥ three days, decreased from 75% at baseline to 56% at follow-up. They suggested that factors influencing adherence included the use and type of incentives, appearance, and discomfort in donning the device.[114] Furthermore, even during the pre-assessment, there were no steps recorded on three of the devices, suggestive of device failure or noncompliance. Unfortunately, this impacts the results, as it limits our understanding of change in daily physical activity, particularly at the 6-month follow-up assessments, and subsequently how that impacts change in cardiorespiratory fitness and insulin resistance. It also introduces volunteer bias with the most motivated participants willing to don the activity trackers, creating opportunity for overestimation of step count. Finally, the technology which supports the Garmin Vivofit also limited our ability to use the step count data to its potential. The Garmin Vivofits records total daily step count and step count in 15-minute blocks, allowing the researcher or user to obtain a measure of intensity. It was our intent to obtain daily amounts of sedentary, light, moderate, and vigorous activity, based on step count every 15 minutes, to acquire an overall picture of participants' daily physical activity level. This would have helped address the opinion posed by some experts that physical activity alone may not improve insulin sensitivity if amounts of sedentary behaviour are excessive.[12] However, despite help from Garmin's technical support team, the data in 15-minute intervals was unable to be downloaded from the website, leaving us only with the total daily step count amount for analysis. Clearly, there are opportunities for much more research and understanding about activity monitoring in special populations such as ours. We did not find a significant change in step count at either measurement period, which seems to clarify the results indicating that the reduction in insulin resistance was attributed to the intervention as opposed to participants increasing their daily physical activity. However, more questions are raised when looking at these results as without a significant increase in step count, it is unclear why there was a significant improvement in cardiorespiratory fitness.

3.1.10.4 Muscle strength

Muscle strength was assessed using 1RM, a valid and reliable method, as per ACSM guidelines.[95] Targeting key upper and lower body muscles, participants push as hard as they can against a resistance and force values are recorded. Despite reviewing technique and practicing, some participants found it difficult to complete the muscle strength testing during pre-assessments. Novelty was not a concern during the post- and 6-month follow-up assessments. Therefore, improvements in 1RM values between pre- and post-intervention assessments may have been related to improved acquisition of the tasks. Research on muscle strength improvements in a pediatric population suggests that increased muscle strength appears to be related to neurological adaptations such as increased coordination and learning which facilitates an improvement in recruitment of muscle fibres.[69] This is in contrast to adult physiology, in which an increase in muscle strength is directly associated with hypertrophy of the muscle.[69] It would have been ideal to employ a direct measure of body composition, such as DXA scan, particularly of learn muscle mass in order to decipherer whether an increase muscle strength through hypertrophy or neurological adaptions were associated with reduced insulin resistance in a pediatric population.

3.1.10.5 Anthropometric measures

Anthropometric measures are one of the outcomes reported by CDPPs to monitor health. Although we evaluated anthropometrics using ACSM guidelines[96], due to equipment unavailability, height was measured using a digital, wall-mounted stadiometer for pre- and post-assessments and a free-standing stadiometer for 6-month follow-up assessments. While an unfortunate occurrence, there was no significant difference in height between measurement periods, suggesting both methods are valid. As with measurement of lean muscle mass, a direct measure of body composition would have provided a valid measure of body fat distribution. Since this study took place in a clinical setting, we focused anthropometric measures that would be available to most healthcare professions using scales and tape measures. This focus, although less precise than DXA, may help healthcare professionals in outcome measure decision-making.

3.2 LIMITATIONS

Some study limitations have been previously discussed, such as the inability to follow through with a RCT design and limitations around the technology supporting the Garmin

Vivofits. Three other limitations warrant being mentioned, which include sample size, volunteer bias, and dietary change.

The first limitation was that our sample size (n=13) was small, which limits the generalizability of the results. Our sample size calculation indicated that a total of 15 subjects were required. Studies by Lee et al.[27,28] recruited 45 participants, with other RCTs and controlled trials recruiting between 12-26 participants.[26,29-31] This limitation is somewhat offset by using a precise, objective primary outcome in the OGTT. Due to the small sample size, we did not adjust for baseline difference among the group or between genders, as this may limit the statistical power of the results or be an over-adjustment for differences as many of our outcomes were intercorrelated.

Another limitation is that of volunteer bias. In studies examining physical activity interventions, more motivated people may naturally volunteer to participate, contributing to volunteer bias. Volunteer bias may possibly improve compliance and potentiate outcomes among study participants in comparison to patients trying to manage similar health concerns. In this study, 13 of the 69 adolescents invited to participate registered for the group; these participants likely represent the adolescents who were most motivated to make changes to their lifestyle. An important consideration of the healthcare professional when offering physical activity programs is the potential for lost opportunity among participants who choose not to come forward. Future research should examine the reasons for non-participation, which could range from socioeconomic to personal. When applying our results to clinical practice, it is important to recognize that patients do not just include those that are motivated to participate in studies or make change.

Perhaps the most important confounding variable in this study, which may or may not have influenced the results, is the impact of dietary changes outside of the study protocol. We did not account for the dietary habits of the participants during the study period. It would not be surprising if participants that were driven to increase their physical activity were also motivated to improve their eating habits. As well, participants may have felt hungrier and eaten more during the program because of their increase in physical activity. These factors could certainly contribute to over or underestimation of changes in primary or secondary outcomes resulting from the intervention.

When completing patient-orientated research within the primary care setting, it is difficult to maintain methodological rigor that is ideal in research. Despite its flaws, this study represents a practical ‘real world’ approach to studying the effects of resistance exercise in a special population.

3.3 FUTURE RESEARCH

It became apparent throughout the course of this study that there are areas which require further research. They include (1) an understanding of longer-term physiological changes within skeletal muscles and body composition, (2) changes in inflammatory markers or metabolic hormones following resistance exercise, (3) understanding the links between poor physical literacy, low cardiorespiratory fitness, and insulin resistance, and (4) to further study the concept of presenteeism.

The longer-term effects of resistance exercise on skeletal muscles in adolescents with insulin resistance could be measured using DXA or muscle biopsy. There are two reasons for including a direct measure of body composition, such as DXA. First, it may clarify changes, if any, in distribution of body fat. As stated, it is unlikely that this type of intervention will elicit changes in weight or BMI, however changes in waist circumference may be possible. A measure of body composition will clarify if this is due to increase abdominal tone or lean mass or redistribution of abdominal fat. Importantly, this knowledge would help patients understand how their body may change with resistance exercise. Secondly, a direct measure of body composition will begin to provide insight into changes in lean or muscle mass over the study period. It is known that the main reason for an increase in muscle strength in a pediatric population is due to neurological adaptations, not an increase in muscle mass[69], however a direct measure of body composition may begin to tell the story. Muscle biopsy is a very important tool to measure physiological changes within skeletal muscles, especially in terms of the role of skeletal muscle cells in the long-term management of blood hemostasis in adolescents. Holten et al.[83], evaluating muscle biopsies from adults, demonstrated that resistance exercise increased GLUT4 proteins and insulin receptors and enhanced glycogen synthase independent of an increase in muscle mass. Muscle biopsy has yet to be included in a clinical trial in this group. Whether such a relationship exists among adolescents is an area worthy of future research. Despite the invasive nature of the technique, the results could be compelling.

Another area of interest would be to examine the longer-term effects of resistance exercise on inflammatory factors, such as C-reactive protein, in adolescents with insulin resistance. For example, it has been noted that higher C-reactive protein concentrations indicate a low-grade whole-body inflammation in obese adolescents; higher levels of inflammatory markers are thought to play a role in the etiology of insulin resistance.[106] It may also be beneficial to map the longer-term effects resistance exercise on metabolic hormones, such as adiponectin and leptin, in adolescents with insulin resistance. It has been found that physical activity can improve levels of some metabolic hormones in adults, helping prevent the development of cardiovascular disease.[115] It would be interesting to complete similar research among adolescents.

We observed through the course of the study, as well as years of clinical practice in this field, that adolescents with insulin resistance also exhibit very low cardiorespiratory fitness along with limited physical literacy. A person is physical literate when they have the ability and confidence to move in a variety of physical activities in multiple settings.[116] To place this observation into context, during the first two to three weeks of our intervention, it became obvious that participants had difficulty navigating the sessions; instead of requiring one or two weeks to obtain competence in technique and safety, they required almost four weeks to become competent with training activities. For example, most participants were unfamiliar with almost all of the equipment and were unable to identify, independently, appropriate resistance exercises. Most participants had difficulty understanding even basic exercises, such as completing a squat with proper technique. For the first four weeks, participants required constant verbal and physical cueing to ensure proper technique, even as basic as remembering to stand with upright posture. Participants improved significantly over the 10-week intervention; with facilitators commenting that participants' transformation was astonishing. This led to many discussions which are not captured in the quantitative outcomes of this study, about these adolescents' past physical activity experience and the role it may have played in the risk of having low cardiorespiratory fitness and developing insulin resistance. A fascinating qualitative study would be to explore the associations between physical literacy, low cardiorespiratory fitness, and the development of insulin resistance. No studies could be found addressing this question.

A final suggestion would be to further study the idea of presenteeism and its role in physical activity research. As previously discussed, participants may have attended the sessions, however, in some cases their efforts were blunted. The reasons for presenteeism in physical activity programs, such as stress, anxiety regarding exercise, or concern with competency of performance, need to be examined. Knowledge about the sources of presenteeism and mitigation methods may help healthcare professionals address barriers preventing people from fully participating in physical activity programming.

3.4 CONCLUSION

In conclusion, the findings of this study suggest that adolescents participating in a supervised, 10-week resistance exercise program (60-minute duration, three times per week) may expect improved insulin sensitivity, cardiorespiratory fitness, waist circumference, and waist-to-hip ratio; with changes retained up to six months. The long-term benefits are especially novel to this field of research, addressing the gap identified in the literature that there are no studies analyzing the long-term benefit of physical activity on insulin resistance in adolescents. These results suggest that adolescents can help manage their insulin resistance by participating in a supervised 10-week (3 sessions of 60 minutes/week) resistance exercise program.

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APPENDICES

Appendix A: Body Positive Approach

BE ACTIVE

Body Positive Approach

What is a Body Positive Approach?

An approach which focuses on fostering body appreciation and taking care of one's body by promoting health behaviours rather than focusing on weight loss as the overall goal.

Why Use a Body Positive Approach?

A body positive approach diminishes the potential for unintended harm to the participants while participating in a physical activity program. There is a societal belief that shaming people about their bodies will motivate them to make changes such as, increasing their physical activity level. Focusing on weight, and not health, is ineffective at producing healthier people and can be damaging. A physical activity program which is weight-focused contributes to:

When only assessing weight as a measure of success, it is impossible to determine someone's cardiorespiratory fitness level or metabolic health; which are known to be stronger predictors of overall health. Someone may be categorized as obese, but be metabolically healthy and have a good cardiorespiratory fitness level; while a non-obese person may be the opposite. It is impossible to tell just by looking at their weight. In fact, if the focus is solely on weight, a large segment of the population at risk for chronic disease is missed.

When a physical activity program is offered using a body positive approach, it can foster a positive body image. A positive body image includes feeling good about one's body regardless of appearance, weight or shape. Children who have a positive body image are more likely to take care of their bodies by engaging in healthy behaviours. A negative body image is associated with many problems, including lower physical activity levels, low self-esteem, anxiety, eating disorders and depression. It is important that children recognize that people can be healthy in different body shapes, sizes and weights. It is not necessary to achieve the 'thin ideal' that is portrayed in the media in order to have a positive body image.

When children engage in active play and physical activity using a body positive approach, they:

- Learn fundamental movement skills
- Develop a positive body image
- Participate more in physical activity
- Have fun

With regular physical activity, children's cardiorespiratory fitness will improve thus preventing or delaying the onset of chronic disease. This is seen regardless of reductions in weight, BMI or waist circumference. Creating a safe social space for children to be active will support the development of healthy physical activity habits so that they can be active for life.

Janeway Lifestyle Program

Eastern Health

Good Health for EveryBODY

www.easternhealth.ca/OurServices

Key Concepts When Using a Body Positive Approach

- ✓ Recognize what health looks like
  - Good health comes in many body shapes, sizes and weights.
  - Weight ≠ Health

- ✓ Promote health
  - Cardiorespiratory fitness is more predictive of health than weight.
  - Rather than focusing on obesity treatment or weight loss, design physical activity programs that promote healthy active living for all participants.

- ✓ Educate yourself
  - Be aware of your own assumptions, beliefs and judgments about body weight and size; including assumptions made about a person's character/behaviours based on their weight.
  - Work toward changing your personal assumptions and biases.
  - Evidence shows that health is not directly correlated to body weight. There are people who are naturally slim based on their genetics but engage in unhealthy behaviours; just as there are people with extra weight who are active and healthy.

- ✓ Set health goals
  - Do not make goals which are weight focused. Instead, set a fitness or health goal (e.g. run 5 km in 12 weeks).

- ✓ Provide a safe space
  - Have clear guidelines around appropriate language, conversations and behaviour.
  - Never make comments about children's weight or appearance.
  - Do not enforce physical activity and dieting rules for the sole purpose of reducing children's weight or changing their body shape.
  - Be responsive and supportive of children's needs.
  - Do not tolerate bullying of any kind. Address weight based bullying when it occurs.

- ✓ Be a good role model
  - Do not make negative comments about your weight or body shape.
  - It is important that certain body types are not featured more visibly (e.g. putting dancers with extra weight on in the back row in a performance).
  - Program leaders need to model a respectful, inclusive attitude.

- ✓ Be media smart
  - Be mindful of program posters or brochures - show photographs of people of all body sizes being physically active.

Appendix B: Letter of approval from Health Research Ethics Authority

NEWFOUNDLAND AND LABRADOR
HREB
HEALTH RESEARCH ETHICS BOARD

Ethics Office
Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

March 07, 2016

Janeway
300 Prince Phillip Drive
St. John's, NL
A1B 3V6

Dear Ms. Critch:

Researcher Portal File # 20162013
Reference # 2016.009

RE: "The effects of resistance-based physical activity on insulin sensitivity in adolescents: a program evaluation"

This will acknowledge receipt of your correspondence.

This correspondence has been reviewed by the Chair under the direction of the Health Research Ethics Board (HREB). ***Full board approval*** of this research study is granted for one year effective **March 3, 2016**.

This is your ethics approval only. Organizational approval may also be required. It is your responsibility to seek the necessary organizational approval from the Regional Health Authority (RHA) or other organization as appropriate. You can refer to the HREA website for further guidance on organizational approvals.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

- Application, approved
- Bruce protocol, acknowledged
- Invitation letter to orientation session, approved
- Revised consent form, approved
- Letter from K. Pike Division Manager , acknowledged
- Letter from A Wareham Janeway Lifestyle Program, acknowledged
- Letter to Eastern Health Medical Records, acknowledged
- PARmed-X medical examination, acknowledged
- PAR-Q+ questionnaire, acknowledged
- Insulin Resistance Group Invitation, approved
- Orientation Session Telephone Script, approved
- Budget, acknowledged
- Physical Activity Questionnaire, approved
- Physical Activity Enjoyment Scale, approved

- Adolescent Sedentary Activity Questionnaire, approved
- Focus Group guide, approved

MARK THE DATE

This approval will lapse on March 3, 2017. It is your responsibility to ensure that the Ethics Renewal form is submitted prior to the renewal date; you may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an Event form.

If you do not return the completed Ethics Renewal form prior to date of renewal:

- ***You will no longer have ethics approval***
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*
- *Lapse in ethics approval* ***may result in interruption or termination of funding***

You are solely responsible for providing a copy of this letter, along with your approved HREB application form; **to Research Grant and Contract Services** should your research depend on funding administered through that office.

Modifications of the protocol/consent are not permitted without prior approval from the HREB. **Implementing changes without HREB approval may result in your ethics approval being revoked, meaning your research must stop**. Request for modification to the protocol/consent must be outlined on an amendment form (available on the Researcher Portal website as an Event form) and submitted to the HREB for review.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

You are responsible for the ethical conduct of this research, notwithstanding the approval of the HREB.

We wish you every success with your study.

Sincerely,

Dr Fern Brunger (Chair, Non-Clinical Trials Health Research Ethics Board)
Ms. Patricia Grainger (Vice-Chair, Non-Clinical Trials Health Research Ethics Board)

CC: M. Ploughman

Appendix C: Invitation Letter

Insulin Resistance Group invitation

The Janeway Lifestyle Program has identified the need to provide specialized services to youth with insulin resistance. One of the evidenced-based treatments for insulin resistance is physical activity, specifically strength training.

The Janeway Lifestyle Program would like to invite your child, ________________________________, to participate in a 10-week physical activity program for youth with insulin resistance. This will take place twice a week (Thursday and Sunday) after school at Power Conditioning in St. John's. As well, your child will complete one session at week at home (activities and equipment will be provided). There is no cost to participate in this program.

The program has been developed by the Janeway Lifestyle Program and will be supervised by team members. It is also part of a research study looking at the effects of physical activity on insulin resistance. This study has two phases. They are entitled *The effects of resistance-based physical activity on insulin sensitivity in adolescents: a program evaluation* and *The influence of removing weight stigma during a physical activity program on the enjoyment and motivation of adolescents with insulin resistance to be physically active: a program evaluation*. By participating in these studies your child will be required to complete some additional assessments such as, focus groups, wear a step counter and fitness testing with additional measures. The studies have been approved by the Health Research Ethics Board.

Please note that if you and your child do not wish to participate in the research studies, the 10-week physical activity program will still be offered to your child.

If you are interested in learning more, both parents and youth are invited to attend an orientation session. **Please call Ashley - 777-4870 or Sarah - 777-4309** to **REGISTER** for the program. A maximum of 15 participants can take part in the program at a time, they will be randomly selected from the list of registered participants. Those who are not initially selected will be placed on a waitlist for the next time the program is offered.
You <u>must</u> attend the orientation session in order to participate in the program. Orientation session details will be provided upon registration.

If you choose not to participate in this program, your child will continue to be followed by the Janeway Lifestyle Program through clinic appointments.

Appendix D: PARmed-X and PAR-Q

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

The PARmed-X is a physical activity-specific checklist to be used by a physician with patients who have had positive responses to the Physical Activity Readiness Questionnaire (PAR-Q). In addition, the Conveyance/Referral Form in the PARmed-X can be used to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. The PAR-Q by itself provides adequate screening for the majority of people. However, some individuals may require a medical evaluation and specific advice (exercise prescription) due to one or more positive responses to the PAR-Q.

Following the participant's evaluation by a physician, a physical activity plan should be devised in consultation with a physical activity professional (CSEP-Professional Fitness & Lifestyle Consultant or CSEP-Exercise Therapist™). To assist in this, the following instructions are provided:

PAGE 1: • Sections A, B, C, and D should be completed by the participant BEFORE the examination by the physician. The bottom section is to be completed by the examining physician.

PAGES 2 & 3: • A checklist of medical conditions requiring special consideration and management.

PAGE 4: • Physical Activity & Lifestyle Advice for people who do not require specific instructions or prescribed exercise.

• Physical Activity Readiness Conveyance/Referral Form - an optional tear-off tab for the physician to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

This section to be completed by the participant

A PERSONAL INFORMATION:

NAME ____________________

ADDRESS ____________________

____

TELEPHONE ____________________

BIRTHDATE ____________________ GENDER ________

MEDICAL No. ____________________

B PAR-Q: Please indicate the PAR-Q questions to which you answered YES

- ❑ Q 1 Heart condition
- ❑ Q 2 Chest pain during activity
- ❑ Q 3 Chest pain at rest
- ❑ Q 4 Loss of balance, dizziness
- ❑ Q 5 Bone or joint problem
- ❑ Q 6 Blood pressure or heart drugs
- ❑ Q 7 Other reason: ____________________

C RISK FACTORS FOR CARDIOVASCULAR DISEASE:

Check all that apply

- ❑ Less than 30 minutes of moderate physical activity most days of the week.
- ❑ Currently smoker (tobacco smoking 1 or more times per week).
- ❑ High blood pressure reported by physician after repeated measurements.
- ❑ High cholesterol level reported by physician.
- ❑ Excessive accumulation of fat around waist.
- ❑ Family history of heart disease.

***Please note:** Many of these risk factors are modifiable. Please refer to page 4 and discuss with your physician.*

D PHYSICAL ACTIVITY INTENTIONS:

What physical activity do you intend to do?

____

____

____

This section to be completed by the examining physician

Physical Exam:

Ht	Wt	BP i) /
		BP ii) /

Conditions limiting physical activity:

- ❑ Cardiovascular
- ❑ Respiratory
- ❑ Other
- ❑ Musculoskeletal
- ❑ Abdominal

Tests required:

- ❑ ECG
- ❑ Exercise Test
- ❑ X-Ray
- ❑ Blood
- ❑ Urinalysis
- ❑ Other

Physical Activity Readiness Conveyance/Referral:

Based upon a current review of health status, I recommend:

Further Information:
- ❑ Attached
- ❑ To be forwarded
- ❑ Available on request

- ❑ No physical activity
- ❑ Only a medically-supervised exercise program until further medical clearance
- ❑ Progressive physical activity:
  - ❑ with avoidance of: ____________________
  - ❑ with inclusion of: ____________________
  - ❑ under the supervision of a CSEP-Professional Fitness & Lifestyle Consultant or CSEP-Exercise Therapist™
- ❑ Unrestricted physical activity–start slowly and build up gradually

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

Following is a checklist of medical conditions for which a degree of precaution and/or special advice should be considered for those who answered "YES" to one or more questions on the PAR-Q, and people over the age of 69. Conditions are grouped by system. Three categories of precautions are provided. Comments under Advice are general, since details and alternatives require clinical judgement in each individual instance.

	Absolute Contraindications	Relative Contraindications	Special Prescriptive Conditions	ADVICE
	Permanent restriction or temporary restriction until condition is treated, stable, and/or past acute phase.	Highly variable. Value of exercise testing and/or program may exceed risk. Activity may be restricted. Desirable to maximize control of condition. Direct or indirect medical supervision of exercise program may be desirable.	Individualized prescriptive advice generally appropriate: • limitations imposed; and/or • special exercises prescribed. May require medical monitoring and/or initial supervision in exercise program.	
Cardiovascular	❑ aortic aneurysm (dissecting) ❑ aortic stenosis (severe) ❑ congestive heart failure ❑ crescendo angina ❑ myocardial infarction (acute) ❑ myocarditis (active or recent) ❑ pulmonary or systemic embolism—acute ❑ thrombophlebitis ❑ ventricular tachycardia and other dangerous dysrhythmias (e.g., multi-focal ventricular activity)	❑ aortic stenosis (moderate) ❑ subaortic stenosis (severe) ❑ marked cardiac enlargement ❑ supraventricular dysrhythmias (uncontrolled or high rate) ❑ ventricular ectopic activity (repetitive or frequent) ❑ ventricular aneurysm ❑ hypertension—untreated or uncontrolled severe (systemic or pulmonary) ❑ hypertrophic cardiomyopathy ❑ compensated congestive heart failure	❑ aortic (or pulmonary) stenosis—mild angina pectoris and other manifestations of coronary insufficiency (e.g., post-acute infarct) ❑ cyanotic heart disease ❑ shunts (intermittent or fixed) ❑ conduction disturbances • complete AV block • left BBB • Wolff-Parkinson-White syndrome ❑ dysrhythmias—controlled ❑ fixed rate pacemakers	• clinical exercise test may be warranted in selected cases, for specific determination of functional capacity and limitations and precautions (if any). • slow progression of exercise to levels based on test performance and individual tolerance. • consider individual need for initial conditioning program under medical supervision (indirect or direct).
			❑ intermittent claudication	progressive exercise to tolerance
			❑ hypertension: systolic 160-180; diastolic 105+	progressive exercise; care with medications (serum electrolytes; post-exercise syncope; etc.)
Infections	❑ acute infectious disease (regardless of etiology)	❑ subacute/chronic/recurrent infectious diseases (e.g., malaria, others)	❑ chronic infections ❑ HIV	variable as to condition
Metabolic		❑ uncontrolled metabolic disorders (diabetes mellitus, thyrotoxicosis, myxedema)	❑ renal, hepatic & other metabolic insufficiency	variable as to status
			❑ obesity ❑ single kidney	dietary moderation, and initial light exercises with slow progression (walking, swimming, cycling)
Pregnancy		❑ complicated pregnancy (e.g., toxemia, hemorrhage, incompetent cervix, etc.)	❑ advanced pregnancy (late 3rd trimester)	refer to the "PARmed-X for PREGNANCY"

References:

Arraix, G.A., Wigle, D.T., Mao, Y. (1992). Risk Assessment of Physical Activity and Physical Fitness in the Canada Health Survey Follow-Up Study. **J. Clin. Epidemiol.** 45:4 419-428.

Mottola, M., Wolfe, L.A. (1994). Active Living and Pregnancy, In: A. Quinney, L. Gauvin, T. Wall (eds.), **Toward Active Living: Proceedings of the International Conference on Physical Activity, Fitness and Health**. Champaign, IL: Human Kinetics.

PAR-Q Validation Report, British Columbia Ministry of Health, 1978.

Thomas, S., Reading, J., Shephard, R.J. (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). **Can. J. Spt. Sci.** 17: 4 338-345.

The PAR-Q and PARmed-X were developed by the British Columbia Ministry of Health. They have been revised by an Expert Advisory Committee of the Canadian Society for Exercise Physiology chaired by Dr. N. Gledhill (2002).

Disponible en français sous le titre «Évaluation médicale de l'aptitude à l'activité physique (X-AAP)»

Continued on page 3...

	Special Prescriptive Conditions	ADVICE
Lung	❑ chronic pulmonary disorders	special relaxation and breathing exercises
	❑ obstructive lung disease ❑ asthma	breath control during endurance exercises to tolerance; avoid polluted air
	❑ exercise-induced bronchospasm	avoid hyperventilation during exercise; avoid extremely cold conditions; warm up adequately; utilize appropriate medication.
Musculoskeletal	❑ low back conditions (pathological, functional)	avoid or minimize exercise that precipitates or exasperates e.g., forced extreme flexion, extension, and violent twisting; correct posture, proper back exercises
	❑ arthritis—acute (infective, rheumatoid; gout)	treatment, plus judicious blend of rest, splinting and gentle movement
	❑ arthritis—subacute	progressive increase of active exercise therapy
	❑ arthritis—chronic (osteoarthritis and above conditions)	maintenance of mobility and strength; non-weightbearing exercises to minimize joint trauma (e.g., cycling, aquatic activity, etc.)
	❑ orthopaedic	highly variable and individualized
	❑ hernia	minimize straining and isometrics; stregthen abdominal muscles
	❑ osteoporosis or low bone density	avoid exercise with high risk for fracture such as push-ups, curl-ups, vertical jump and trunk forward flexion; engage in low-impact weight-bearing activities and resistance training
CNS	❑ convulsive disorder not completely controlled by medication	minimize or avoid exercise in hazardous environments and/or exercising alone (e.g., swimming, mountainclimbing, etc.)
	❑ recent concussion	thorough examination if history of two concussions; review for discontinuation of contact sport if three concussions, depending on duration of unconsciousness, retrograde amnesia, persistent headaches, and other objective evidence of cerebral damage
Blood	❑ anemia—severe (< 10 Gm/dl) ❑ electrolyte disturbances	control preferred; exercise as tolerated
Medications	❑ antianginal ❑ antiarrhythmic ❑ antihypertensive ❑ anticonvulsant ❑ beta-blockers ❑ digitalis preparations ❑ diuretics ❑ ganglionic blockers ❑ others	NOTE: consider underlying condition. Potential for: exertional syncope, electrolyte imbalance, bradycardia, dysrhythmias, impaired coordination and reaction time, heat intolerance. May alter resting and exercise ECG's and exercise test performance.
Other	❑ post-exercise syncope	moderate program
	❑ heat intolerance	prolong cool-down with light activities; avoid exercise in extreme heat
	❑ temporary minor illness	postpone until recovered
	❑ cancer	if potential metastases, test by cycle ergometry, consider non-weight bearing exercises; exercise at lower end of prescriptive range (40-65% of heart rate reserve), depending on condition and recent treatment (radiation, chemotherapy); monitor hemoglobin and lymphocyte counts; add dynamic lifting exercise to strengthen muscles, using machines rather than weights.

*Refer to special publications for elaboration as required

The following companion forms are available online: http://www.csep.ca/forms.asp

The Physical Activity Readiness Questionnaire (PAR-Q) - a questionnaire for people aged 15-69 to complete before becoming much more physically active.

The Physical Activity Readiness Medical Examination for Pregnancy (PARmed-X for PREGNANCY) - to be used by physicians with pregnant patients who wish to become more physically active.

For more information, please contact the:

Canadian Society for Exercise Physiology
202 - 185 Somerset St. West
Ottawa, ON K2P 0J2
Tel. 1-877-651-3755 • FAX (613) 234-3565 • Online: www.csep.ca

Note to physical activity professionals...

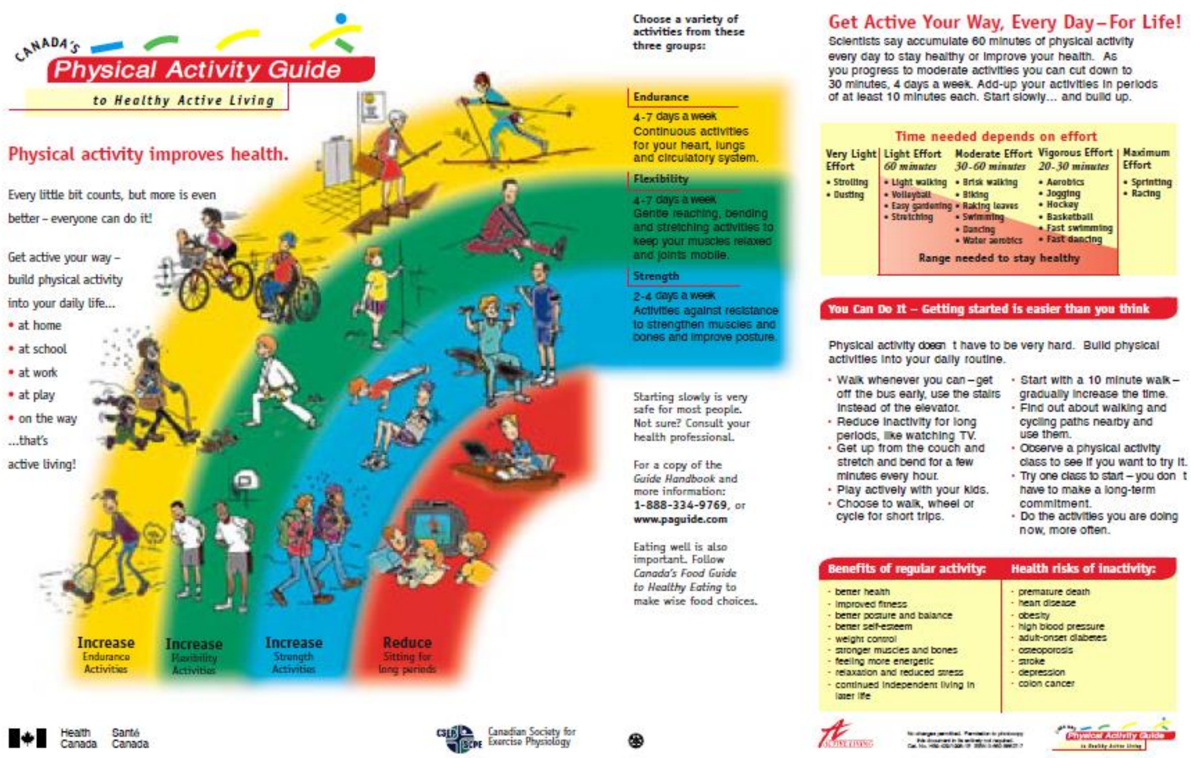
It is a prudent practice to retain the completed Physical Activity Readiness Conveyance/Referral Form in the participant's file.

Supported by: Health Canada Santé Canada

Continued on page 4...

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION



CANADA'S Physical Activity Guide

to Healthy Active Living

Physical activity improves health.

Every little bit counts, but more is even better – everyone can do it!

Get active your way – build physical activity into your daily life...

- at home
- at school
- at work
- at play
- on the way

...that's active living!

Increase Endurance Activities | Increase Flexibility Activities | Increase Strength Activities | Reduce Sitting for long periods

Choose a variety of activities from these three groups:

Endurance
4-7 days a week
Continuous activities for your heart, lungs and circulatory system.

Flexibility
4-7 days a week
Gentle reaching, bending and stretching activities to keep your muscles relaxed and joints mobile.

Strength
2-4 days a week
Activities against resistance to strengthen muscles and bones and improve posture.

Starting slowly is very safe for most people. Not sure? Consult your health professional.

For a copy of the *Guide Handbook* and more information: **1-888-334-9769**, or **www.paguide.com**

Eating well is also important. Follow *Canada's Food Guide to Healthy Eating* to make wise food choices.

Get Active Your Way, Every Day – For Life!

Scientists say accumulate 60 minutes of physical activity every day to stay healthy or improve your health. As you progress to moderate activities you can cut down to 30 minutes, 4 days a week. Add-up your activities in periods of at least 10 minutes each. Start slowly... and build up.

Time needed depends on effort

Very Light Effort	Light Effort *60 minutes*	Moderate Effort *30-60 minutes*	Vigorous Effort *20-30 minutes*	Maximum Effort
• Strolling • Dusting	• Light walking • Volleyball • Easy gardening • Stretching	• Brisk walking • Biking • Raking leaves • Swimming • Dancing • Water aerobics	• Aerobics • Jogging • Hockey • Basketball • Fast swimming • Fast dancing	• Sprinting • Racing
	Range needed to stay healthy			

You Can Do It – Getting started is easier than you think

Physical activity doesn t have to be very hard. Build physical activities into your daily routine.

- Walk whenever you can – get off the bus early, use the stairs instead of the elevator.
- Reduce inactivity for long periods, like watching TV.
- Get up from the couch and stretch and bend for a few minutes every hour.
- Play actively with your kids.
- Choose to walk, wheel or cycle for short trips.
- Start with a 10 minute walk – gradually increase the time.
- Find out about walking and cycling paths nearby and use them.
- Observe a physical activity class to see if you want to try it.
- Try one class to start – you don t have to make a long-term commitment.
- Do the activities you are doing now, more often.

Benefits of regular activity:	Health risks of inactivity:
- better health - improved fitness - better posture and balance - better self-esteem - weight control - stronger muscles and bones - feeling more energetic - relaxation and reduced stress - continued independent living in later life	- premature death - heart disease - obesity - high blood pressure - adult-onset diabetes - osteoporosis - stroke - depression - colon cancer

Health Canada Santé Canada

Canadian Society for Exercise Physiology

Source: Canada's Physical Activity Guide to Healthy Active Living, Health Canada, 1998 http://www.hc-sc.gc.ca/hppb/paguide/pdf/guideEng.pdf

PARmed-X Physical Activity Readiness Conveyance/Referral Form

Based upon a current review of the health status of ______________________________, I recommend:

- ❑ No physical activity
- ❑ Only a medically-supervised exercise program until further medical clearance
- ❑ Progressive physical activity
  - ❑ with avoidance of: ______________________________
  - ❑ with inclusion of: ______________________________
  - ❑ under the supervision of a CSEP-Professional Fitness & Lifestyle Consultant or CSEP-Exercise Therapist™
- ❑ Unrestricted physical activity — start slowly and build up gradually

Further Information:
- ❑ Attached
- ❑ To be forwarded
- ❑ Available on request

Physician/clinic stamp:

______________________________ M.D.

______________________________ 20______
(date)

NOTE: This physical activity clearance is valid for a maximum of six months from the date it is completed and becomes invalid if your medical condition becomes worse.

CSEP approved Sept 12 2011 version

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

SECTION 1 - GENERAL HEALTH

	Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO
1.	Has your doctor ever said that you have a heart condition OR high blood pressure?	☐	☐
2.	Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?	☐	☐
3.	Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4.	Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)?	☐	☐
5.	Are you currently taking prescribed medications for a chronic medical condition?	☐	☐
6.	Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer NO if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.	☐	☐
7.	Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity.

Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow the Canadian Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
- If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or CSEP Certified Personal Trainer® (CSEP-CPT).
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant – talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes – please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.

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SECTION 2 - CHRONIC MEDICAL CONDITIONS

Please read the questions below carefully and answer each one honestly: check YES or NO.			YES	NO
1.	Do you have Arthritis, Osteoporosis, or Back Problems?		☐ If yes, answer questions 1a-1c	☐ If no, go to question 2
	1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/ or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	☐	☐
	1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	☐	☐
2.	Do you have Cancer of any kind?		☐ If yes, answer questions 2a-2b	☐ If no, go to question 3
	2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and neck?	☐	☐
	2b.	Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?	☐	☐
3.	Do you have Heart Disease or Cardiovascular Disease? This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm		☐ If yes, answer questions 3a-3e	☐ If no, go to question 4
	3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	3b.	Do you have an irregular heart beat that requires medical management? (e.g. atrial fibrillation, premature ventricular contraction)	☐	☐
	3c.	Do you have chronic heart failure?	☐	☐
	3d.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer YES if you do not know your resting blood pressure)	☐	☐
	3e.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	☐	☐
4.	Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes		☐ If yes, answer questions 4a-4c	☐ If no, go to question 5
	4a.	Is your blood sugar often above 13.0 mmol/L? (Answer YES if you are not sure)	☐	☐
	4b.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?	☐	☐
	4c.	Do you have other metabolic conditions (such as thyroid disorders, pregnancy-related diabetes, chronic kidney disease, liver problems)?	☐	☐
5.	Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome)		☐ If yes, answer questions 5a-5b	☐ If no, go to question 6
	5a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	5b.	Do you also have back problems affecting nerves or muscles?	☐	☐

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	Please read the questions below carefully and answer each one honestly: check YES or NO.		YES	NO
6.	Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure		☐ If yes, answer questions 6a-6d	☐ If no, go to question 7
	6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	6b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	☐	☐
	6c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	☐	☐
	6d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	☐	☐
7.	Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia		☐ If yes, answer questions 7a-7c	☐ If no, go to question 8
	7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	7b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	☐	☐
	7c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	☐	☐
8.	Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event		☐ If yes, answer questions 8a-c	☐ If no, go to question 9
	8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	8b.	Do you have any impairment in walking or mobility?	☐	☐
	8c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	☐	☐
9.	Do you have any other medical condition not listed above or do you live with two chronic conditions?		☐ If yes, answer questions 9a-c	☐ If no, read the advice on page 4
	9a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months OR have you had a diagnosed concussion within the last 12 months?	☐	☐
	9b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	☐	☐
	9c.	Do you currently live with two chronic conditions?	☐	☐

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.

PAR-Q+

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

- It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually – 20-60 min. of low- to moderate-intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate-intensity physical activity per week.
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the follow-up questions about your medical condition:

- You should seek further information from a licensed health care professional before becoming more physically active or engaging in a fitness appraisal and/or visit a or qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise profesional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The Canadian Society for Exercise Physiology, the PAR-Q+ Collaboration, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.
- Please read and sign the declaration below:

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME ______________________________ DATE ______________________________

SIGNATURE ______________________________ WITNESS ______________________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ______________________________

For more information, please contact:
Canadian Society for Exercise Physiology
www.csep.ca

KEY REFERENCES

1. Jamnik VJ, Warburton DER, Makarski J, McKenzie DC, Shephard RJ, Stone J, and Gledhill N. Enhancing the eectiveness of clearance for physical activity participation; background and overall process. APNM 36(S1):S3-S13, 2011.
2. Warburton DER, Gledhill N, Jamnik VK, Bredin SSD, McKenzie DC, Stone J, Charlesworth S, and Shephard RJ. Evidence-based risk assessment and recommendations for physical activity clearance; Consensus Document. APNM 36(S1):S266-s298, 2011.

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or BC Ministry of Health Services.

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Appendix E: Bruce Protocol Worksheet

Bruce Treadmill Test Work Sheet

Name____________________ Date ____________________ Age ________

Gender _____

Time (min)	Stage	Speed (mph)	Grade (%)	Heart Rate (bpm)	Blood Pressure (mm Hg)
1	I	1.7	10	______	
2	I	1.7	10	______	
3	I	1.7	10	______	______
4	II	2.5	12	______	
5	II	2.5	12	______	
6	II	2.5	12	______	______
7	III	3.4	14	______	
8	III	3.4	14	______	
9	III	3.4	14	______	______
10	IV	4.2	16	______	
11	IV	4.2	16	______	
12	IV	4.2	16	______	______
13	V	5.0	18	______	
14	V	5.0	18	______	
15	V	5.0	18	______	______
16	VI	5.5	20	______	
17	VI	5.5	20	______	
18	VI	5.5	20	______	______
19	VII	6.0	22	______	
20	VII	6.0	22	______	
21	VII	6.0	22	______	______

Total treadmill test time: _____ min _____ s

13 Professional Fitness & Lifestyle Consultant Resource Manual • Work Sheets