Individuals with Down syndrome (DS) have less atherosclerosis than others with and without mental retardation (MR). Why individuals with DS do not develop atherosclerosis similarly to others is not known. The insulin resistance syndrome (IRS), a common neuroendocrine disorder underlying cardiovascular disease (CVD), has not been investigated in adults with DS to determine if adults with DS possess a more protective CVD risk factor profile than other adults with MR. The CVD risk factor components of the IRS were measured in 145 adults with mild MR (N=70) and DS (N=75) who reside in community settings. The overall mean values for the CVD risk factors were relatively high for all participants, especially for women with MR, who on average showed evidence of fasting hyperinsulinemia, abdominal obesity, and low high-density lipoprotein cholesterol. After adjusting for age, smoking status, residence type, and medication use, women with DS had lower fasting glucose, resting blood pressure, and abdominal fat than women with MR, indicating that women with DS may be somewhat protected against CVD due to lower IRS risk factors as compared to women with MR.

Adults with MR with abdominal obesity were approximately 2-10 times more likely than adults with MR without abdominal obesity to have
hyperinsulinemia, borderline high triglycerides, low HDL cholesterol and borderline hypertension (P<0.05). Furthermore, the associations between abdominal obesity and elevated CVD risk factors were independent of age, gender, presence of Down syndrome, smoking behavior, and medication use. Screening for abdominal obesity using simple anthropometric measures may be a cost-effective way to identify individuals with MR with an intermediate to high risk for a future CVD event. Adults with MR who participated in the recommended frequency (≥5 bouts/week) of moderate to vigorous physical activity or who consumed a below average dietary fat intake (≤35%) were approximately one third as likely to have hyperinsulinemia and abdominal obesity than adults with MR who participated in physical activity less than 5 times/week or who consumed more than 35% of their total caloric intake from fats (P<0.05). Increasing physical activity and reducing dietary fat may help lower the risk for a future CVD event in adults with MR.
Cardiovascular Disease Risk in Adults with Mental Retardation and Down Syndrome

by

Christopher Charles Draheim

A DISSERTATION

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

Presented May 5, 2000
Commencement June 2000

APPROVED:

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I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

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Christopher Charles Draheim, Author
ACKNOWLEDGEMENT

I would like to thank Dr. Jeffrey A. McCubbin for the support, guidance, and advice he has provided over the last four years. I would also like to thank Jeff for providing me the opportunity to study at Oregon State University, an experience that has prepared me to move on to the next step of academia, and an experience of which I am very grateful. Jeff has provided an excellent example of how to be a mentor. I will try to emulate Jeff's example while advising future students. I would also like to thank Dr. Daniel P. Williams for the guidance and advice he has provided over the last four years. The opportunities, which Dan has provided me, have been instrumental in developing a needed line of research, which I will likely continue to investigate in years to come.

I would like to thank the participants for their efforts and time. A special thanks also goes out to all the care providers and administrators who were involved in recruiting participants. I would also like to thank everyone who assisted in the data collection and analysis of the research project.

I would like to thank the Arc of Washington Trust Fund and the John C. Erkkila, M.D., Endowment for Health and Human Performance for funding the research project.
CONTRIBUTION OF AUTHORS

Christopher C. Draheim was involved with the design, data collection, analysis, and writing of each manuscript. Dr. Jeffrey A. McCubbin and Dr. Daniel P. Williams were involved with the design, analysis, and writing of each manuscript. The insulin assays were performed in the Endocrine and Metabolism laboratory of Dr. Daniel P. Williams.
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Cardiovascular Disease Risk in Adults with Mental Retardation and Down Syndrome

Chapter 1

Background and Significance

Cardiovascular disease (CVD) is a major health problem in the United States. CVD kills approximately one million men and women per year making it the leading cause of death in the United States (American Heart Association, 1997). The estimated direct cost of treating CVD in the United States is over $171 billion yearly (American Heart Association, 1997). The existing severity of CVD has led the American Heart Association to recognize the importance of primary prevention of CVD. A recent conference of health experts sponsored by the American Heart Association was convened with the sole purpose of developing strategies to identify patients at intermediate to high risk for a future CVD event who would likely benefit from primary prevention interventions (Smith, Greenland, Grundy, 2000). By identifying individuals at an intermediate to high risk for CVD, primary prevention strategies can be implemented, which may reduce the morbidity, mortality, and cost of treating CVD each year (Fletcher et al., 1996; Grundy et al., 1998; Smith et al., 1995).

The insulin resistance syndrome (IRS) is thought to proceed an acute CVD event and has been identified as a possible underlying cause of CVD events in industrialized societies (Despres, 1996). The IRS is comprised of a cluster of health factors, which include abdominal fat accumulation, insulin resistance, glucose intolerance, hypertriglyceridemia, increased number of small dense low-density lipoprotein (LDL) particles, hypertension, and decreased high-density lipoprotein (HDL) cholesterol concentration (Bjorntorp, 1997; Despres, 1996; Reaven, 1994).
Elevated CVD risk factor components of the IRS often are detectable earlier than traditional CVD risk factors in individuals who are at an intermediate to high risk for CVD (Reaven and Laws, 1990). Screening for elevated CVD risk factor components of the IRS may better identify those who are at an intermediate to high risk for CVD and those who will likely benefit greatly from primary prevention strategies aimed at reducing the risk for CVD. Preliminary results from a small sample in our laboratory indicate that adults with MR residing in community settings have a high prevalence of abdominal obesity and other CVD risk factor components of the IRS (67% had elevated fasting plasma insulin levels, 56% had low HDL-cholesterol levels, 17% had elevated fasting plasma triglyceride levels) (Draheim, Williams, Stanish, Wander, McCubbin, 1999). The IRS appears to be a severe health concern for adults with MR residing in community settings.

Adults with Down syndrome (DS) have consistently been reported to have significantly low atherosclerosis formation (Brattstrom, England, and Brun, 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989). In fact, autopsy findings, which indicate greatly reduced atherosclerosis in the coronary, aortic, femoral, iliac, carotid, and cerebral arteries, have led individuals with Down syndrome to be labeled as "atheroma free" (Brattstrom et al., 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989). The underlying mechanisms for decreased atherosclerosis in adults with DS have not been identified and are not understood. Individuals with DS typically have a very low blood pressure and low cortisol levels, which are both associated with a lower risk for a CVD event (Anwar, Walker, and Frier, 1998; Murdoch et al., 1977; Salo et al., 1979; Yla-Herttuala et al., 1989). Interestingly, the clustering of the CVD risk factor components of the IRS and abdominal obesity have not been investigated in adults with DS or adults with MR. Adults with DS may have a protective profile of CVD risk factor components of the IRS, which in turn, may slow the rate of atherosclerotic plaque formation. Studying the CVD risk factor components of the IRS in adults with DS may provide a unique view into the workings of CVD risk and the CVD risk factor components of the IRS.
The prevalence of atherosclerosis, elevated CVD risk factors, obesity, and overall mortality in all adults with mental retardation (MR) are greater than those found in the general population (Beange et al., 1995; Chaney, 1987). Two categories of adults with MR have been identified to have the highest risk for CVD of all adults with MR; 1) adults with mild to moderate MR and 2) adults with MR residing in community settings (Fox and Rotatori, 1882; Kelly et al., 1986; Janicki and Jacobson, 1986; Janicki and MacEachron, 1984; Strauss and Kastner, 1996; Rimmer et al., 1993; Rimmer et al., 1994; Rimmer et al., 1995). The elevated prevalence of CVD in adults with MR may be due to adults with MR living longer than they have in the past coupled with more adults with MR residing in community settings with less nutritional and health behavior guidance (Braddock, 1999; Carter and Jancar, 1983; Day and Jancar, 1994; Janicki et al., 1999; Mercer and Eckvall, 1992; Pitetti, et al., 1993). The CVD risk factor components of the IRS have not been studied in adults with MR. Identification of elevated CVD risk factors components of adults with MR may help focus program resources designated for improving the health of adults with MR (Martin, Roy, Wells, 1997). Furthermore, identification of behavioral risk factors for CVD, which are significantly associated with the CVD risk factor components of the IRS, may be used to develop recommendations for decreasing the risk for CVD and increasing the health of adults with MR residing in community settings.

The importance of screening for adults with MR who are at an intermediate to high risk for disease has recently emerged as a necessary step to identify and quantify needed health and nutrition services (Blyler and Lucas, 1992; Day and Jancar, 1994; Rimmer, 1999; Wells, Turner, Martin, Roy, 1997). Identification of individuals who are at risk for CVD and implementing primary prevention strategies aimed at reducing CVD risk is an extremely important concept for adults with MR and DS for the following three major reasons: 1) to reduce the cost of treating adults with MR for CVD, 2) to decrease the importance of adults with MR to
recognize and communicate symptoms of a CVD event to their care provider or physician, and 3) to help ensure continued participation in the community.

Primary prevention is important to reduce the economic cost of treating CVD for all individuals and especially for those with MR. We know that the economic burden of treating CVD every year is extremely high in the United States (American Heart Association, 1997). When considering that adults with MR have an elevated CVD prevalence above those without MR (Beange et al., 1995; Kapell et al., 1998) and when considering the fact that the majority of health care of individuals with MR is provided by government funded agencies (McDermott, Platt, Krishnaswami, 1997), the economic burden on society due to CVD treatment for the population of adults with MR may be even greater than a similar population of adults without MR (Braddock, 1999).

The ability to communicate the early signs and symptoms of CVD to physicians and care providers is impaired in adults with MR, which may be leading to an under-diagnosis of health conditions by physicians and may decrease the chances of getting early treatment (Beange et al., 1995; McDonald 1985; Reis and Szysko, 1983). Identifying those with an intermediate to high risk for CVD and slowing the progression of CVD through primary prevention strategies may decrease the importance of adults with MR to recognize and communicate signs and symptoms of a CVD event to their care provider or physician.

Because adults with MR often do not possess the cognitive abilities to drive automobiles or work in mentally challenging employment settings, adults with MR rely on their functional physical capacity for transportation and employment. Due to the reliance on physical ability for transportation and employment, the physical health of adults with MR is extremely important for successful integration into the community. Early identification of individuals with MR who are at a high risk for CVD and implementation of primary prevention strategies will help ensure continued participation in the community.
This study identifies the magnitude of the CVD risk factor components of
the IRS and the traditional CVD risk factors in adults with MR and DS residing in
community settings. This study also identifies which CVD risk factor components
of the IRS may differ between adults with DS and MR. Identification of differences
in CVD risk between adults with MR and DS may point to possible underlying
mechanisms for the reduced development of atherosclerosis in adults with DS.
Studying abdominal visceral fat and the clustering of the CVD risk factor
components of the IRS in adults with MR and DS may also point to specific risk
factors which are likely leading to the high prevalence of CVD and high mortality
rates in all adults with MR.

The present study identifies simple anthropometric indices of abdominal
obesity, which are associated with elevated CVD risk factor components of the IRS
in adults with MR. Anthropometric assessment of abdominal obesity may be used
as a cost-effective screening tool to identify adults with MR with an intermediate to
high risk for CVD who would benefit most from primary prevention strategies
aimed at reducing their elevated risk for CVD. This study also identifies health
behaviors that are associated with elevated CVD risk factor components of the IRS
to provide preliminary information regarding the eventual development of behavioral
recommendations aimed at reducing CVD risk in adults with MR. The resulting
recommendations for behavioral primary prevention strategies will focus on realistic
behavioral changes, which can be made by the individuals themselves, or with the
assistance of direct care providers with the intent of reducing the metabolic risk for
CVD. A reduction in the metabolic risk for CVD, in turn, would likely increase the
overall health and well being of adults of MR, thereby increasing their likelihood for
more complete and successful integration into community settings (Hatton et al.,
1996; Pitetti et al., 1993). Also, direct care providers of adults with MR living in
community settings likely need more specific, relevant, and realistic evidence to
encourage more healthful physical activity and dietary behaviors for adults with MR.
Chapter 2

Differences in Cardiovascular Disease Risk between Non-Diabetic Adults with Mental Retardation and Down Syndrome

Christopher C. Draheim, Jeffrey A. McCubbin, and Daniel P. Williams
Adults with Down syndrome (DS) have been reported to have less atherosclerosis despite having mostly similar risk factors for cardiovascular disease (CVD) as compared to other adults with mental retardation (MR) without DS (Brattstrom, England, Brun, 1987; Murdoch, Rodger, Rao, Fletcher, Dunnigan, 1977; Yla-Herttuala, Luoma, Nikkari, and Kivimaki, 1989). In general, adults with MR have an elevated prevalence of CVD (Beange et al., 1995; Chaney, 1987;). Despite the high prevalence of CVD in adults with MR, autopsy findings have consistently indicated a very low prevalence of atherosclerosis in the coronary, aortic, femoral, iliac, carotid, and cerebral arteries in individuals with DS (Brattstrom et al., 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989). Why adults with DS do not develop atherosclerosis in a similar way as others with MR is not known. Adults with DS may have lower blood pressure than others with MR. However, adults with DS appear to be have similar total and low-density lipoprotein (LDL) cholesterol levels as other adults with MR (Kapell et al., 1998; Murdoch et al., 1977; Yla-Herttuala et al., 1989). Specifically, adults with mild MR and adults with MR who reside in community settings tend to have a higher prevalence of CVD, possess a greater risk for CVD, and have a higher overall mortality rate than those with severe to profound MR or those who live in institutional settings (Beange et al., 1995; Janicki and MacEachron, 1984; Janicki and Jacobson, 1986; Kapell et al., 1998; Rimmer et al., 1994; Rimmer et al., 1995; Strauss and Kastner, 1996).

A cluster of health problems, known as the insulin resistance syndrome (IRS), is becoming increasingly recognized as a common neuroendocrine disorder underlying CVD in industrialized nations (Despres, 1996). A lesser expression of the IRS may also play a critical role for the decreased atherosclerosis in adults with DS. The IRS, which typically develops long before the clinical onset of CVD, includes such CVD risk factor components as abdominal obesity, hyperinsulinemia, elevated fasting glucose, hypertriglyceridemia, increased number of small dense LDL particles, hypertension, decreased HDL cholesterol concentration, and steroidal and growth hormone abnormalities (Bjorntorp, 1997; Despres, 1996;
Mann and Bjomtorp, 1993; Reaven, 1994). Unfortunately, the components of the IRS were not examined or compared between individuals with DS and MR in the previous studies which reported low atherosclerosis in adults with DS (Brattstrom et al., 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989). Lower CVD risk factor components of the IRS in individuals with DS as compared to individuals with MR may have explained the decreased atherosclerosis in individuals with DS as compared to individuals with MR in the previous reports. Other studies which have compared the IRS components, such as blood pressure, insulin levels, triglyceride levels, and HDL levels between individuals with DS and MR typically had very small sample sizes and did not control for confounding factors in the analysis (Nishida et al., 1977; Pueschel and Haddow, 1992; Salo et al., 1979; Serrano-Rios et al., 1973; Yasuda et al., 1979). Also, the studies, which reported the low atherosclerosis in adults with DS (Brattstrom et al., 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989), did not control for potential confounding variables, which may have contributed to differences in atherosclerosis formation between individuals with DS and MR.

Adults with DS have been reported to have low blood pressure, normal insulin levels, and normal glucose levels (Serrano-Rios et al., 1973; Yasuda et al., 1979), indicating adults with DS may possess a protective IRS risk factor profile against atherosclerosis (Reaven, 1995; Reaven, Lithell, Landsberg, 1996). The previous reports used traditional, less specific insulin assays to measure insulin levels (Serrano-Rios et al., 1973; Yasuda et al., 1979). However, a recent meta-analysis suggests that stronger associations between insulin and CVD events are detectable when a more specific insulin assay is used to measure insulin as compared to using the traditional, less specific insulin assay to measure insulin (Ruige et al., 1998).

The purpose of the present study is to compare the CVD risk factor components of the IRS between adults with DS and MR to determine if adults with DS may have lower CVD risk factor components of the IRS, independent of potential confounding factors.
Method

Participants

This study focused on adults with mild MR residing in community settings, who are considered to be at the highest risk for CVD of all adults with MR (Beange et al., 1995; Janicki and MacEachron, 1984; Janicki and Jacobson, 1986; Rimmer et al., 1994, Rimmer et al., 1995; Strauss and Kastner, 1996). Seventy adults with mild MR (40 men, 30 women) and 75 adults with DS with mild MR (34 men, 41 women) were recruited into the study and completed all of the assessments. The prevalence of individuals over 40 years of age, male vs. female gender, Down syndrome presence, cigarette smoking, and medication use in all participants are listed in Table 3.1. Identification of participants was facilitated through the local Arc chapters and its network of agencies throughout Oregon and Washington and through each county's Office of Developmental Disabilities Services. Participants were selected on a volunteer basis. Individuals were considered to have mental retardation based on the definition of the American Association on Mental Retardation (Luckasson et al., 1992). Individuals previously diagnosed with diabetes mellitus or prior CVD event, such as a myocardial infarction or stroke, were excluded from the study. A fasting glucose level of 126 mg/dL or above is considered to be a provisional diagnosis of diabetes mellitus according to the clinical standards established by the American Diabetes Association (American Diabetes Association, 1997). Any individual with a fasting glucose level of 126 mg/dL or above was excluded from the study. Five individuals with MR (2 men and 3 women) were excluded from the study due to a provisional diagnosis of diabetes mellitus. Only ambulatory individuals were included in the study.

Prior to the day of data collection, care providers and/or parents of the participants were instructed to explain all procedures to each participant and to answer any questions or concerns that arose. On the day of the data collection, one
of the researchers read through the consent form and explained all procedures to each participant. All participant questions and concerns were addressed prior to asking the participant to sign an informed consent form. All participants (and parents or guardians when needed) then signed an informed consent form. The participants and the direct care staff were each compensated for their time, effort, and contributions to the study with a $15.00 personal check.

**Blood Collection**

All blood draws were made in the morning after an overnight fast (12 hours). Participants were called the night prior to testing to remind them to fast overnight and again in the morning prior to the testing session. Venous blood samples were collected through venipuncture by a trained phlebotomist using sterile procedures (National Committee for Clinical Laboratory Standards, 1991). The samples were collected in vacutainers containing EDTA to inhibit clotting. Blood samples were placed in an ice bath until separation. After separation of the plasma from the blood cells by centrifugation, the plasma was aliquoted into specific, labeled vials for each analyte and stored frozen at $-70^\circ$ C for subsequent lipid, lipoprotein cholesterol, insulin, and glucose analysis. Plasma samples that could not be immediately frozen in the $-70^\circ$ C freezer were frozen and kept on dry ice until transportation to the $-70^\circ$ C freezer could be completed. A portable centrifuge and dry ice was used for plasma separation and storage for the participants that lived more than approximately 60 miles from Oregon State University.

**Fasting Plasma Glucose, Lipid, Lipoprotein, and Insulin Determination**

The clinical laboratory at Good Samaritan Hospital measured the fasting plasma glucose, lipid, and lipoprotein cholesterol concentrations of all samples. The hospital clinical laboratory used Boehringer Mannheim reagents (Indianapolis, IN) and an automated Boehringer Mannheim/Hitachi 917 clinical chemistry analyzer to
Table 2.1 Mean age and prevalence of group home residence, cigarette smoking, and medication use in women and men with MR and DS.

<table>
<thead>
<tr>
<th></th>
<th>Men with MR (N=40)</th>
<th>Men with DS (N=34)</th>
<th>P</th>
<th>Women with MR (N=30)</th>
<th>Women with DS (N=41)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean and SD)</td>
<td>37.1(10.1)</td>
<td>34.5(10.0)</td>
<td>0.267</td>
<td>41.4(11.2)</td>
<td>36.3(9.3)</td>
<td>0.037*</td>
</tr>
<tr>
<td>Reside in Group Home</td>
<td>52.5%</td>
<td>47.1%</td>
<td>0.525</td>
<td>30.3%</td>
<td>48.8%</td>
<td>0.009*</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>22.5%</td>
<td>2.9%</td>
<td>0.006*</td>
<td>10.0%</td>
<td>2.4%</td>
<td>0.107</td>
</tr>
<tr>
<td>Anti-hypertension Med.</td>
<td>12.5%</td>
<td>5.9%</td>
<td>0.243</td>
<td>16.7%</td>
<td>7.3%</td>
<td>0.107</td>
</tr>
<tr>
<td>Psychogenic Med.</td>
<td>27.5%</td>
<td>11.8%</td>
<td>0.039*</td>
<td>40.0%</td>
<td>17.1%</td>
<td>0.003*</td>
</tr>
<tr>
<td>Thyroid Med.</td>
<td>2.5%</td>
<td>32.4%</td>
<td>0.000*</td>
<td>10.0%</td>
<td>39.0%</td>
<td>0.000*</td>
</tr>
<tr>
<td>Seizure Med.</td>
<td>15.0%</td>
<td>5.9%</td>
<td>0.137</td>
<td>40.0%</td>
<td>12.2%</td>
<td>0.000*</td>
</tr>
<tr>
<td>Lipid Lowering Med.</td>
<td>7.5%</td>
<td>8.8%</td>
<td>0.770</td>
<td>6.7%</td>
<td>2.4%</td>
<td>0.275</td>
</tr>
<tr>
<td>Anti-inflammatory* Med.</td>
<td>12.5%</td>
<td>8.8%</td>
<td>0.517</td>
<td>10.0%</td>
<td>19.5%</td>
<td>0.042*</td>
</tr>
<tr>
<td>Vitamin and Mineral Supl.</td>
<td>17.5%</td>
<td>29.4%</td>
<td>0.068</td>
<td>23.3%</td>
<td>41.5%</td>
<td>0.006*</td>
</tr>
<tr>
<td>HRT</td>
<td>N/A</td>
<td>N/A</td>
<td>---</td>
<td>16.7%</td>
<td>7.3%</td>
<td>0.107</td>
</tr>
<tr>
<td>Oral Contraceptive Use</td>
<td>N/A</td>
<td>N/A</td>
<td>---</td>
<td>23.3%</td>
<td>22.0%</td>
<td>0.838</td>
</tr>
</tbody>
</table>

MR = mental retardation, DS = Down syndrome, SD = Standard Deviation, P = probability, Med. = medications, N/A = Not applicable, HRT = Hormone replacement therapy
* Non-steroidal anti-inflammatory medications
assess the following: plasma glucose with a hexokinase method (Peterson and Young, 1958), plasma total cholesterol with a cholesterol esterase/oxidase method (Allain et al., 1974), plasma triglycerides with an peroxidase-coupled enzymatic method (Fossati and Prencipe, 1982), and high-density lipoprotein (HDL) cholesterol with a direct homogeneous enzymatic method (Sugiuchi et al., 1995). Low-density lipoprotein (LDL) cholesterol was calculated from the Friedwald equation (Friedwald et al., 1972). The measurement error, expressed as coefficients of variation, for the clinical laboratory was 1.8% for plasma glucose, 1.3% for plasma total cholesterol, 2.0% for plasma triglycerides, and 1.5% for plasma HDL cholesterol.

Fasting plasma insulin concentration was determined with a human insulin-specific double-antibody radioimmunoassay (RIA) (Linco Research, Inc., St. Charles, MO) (Morgan and Lazarow, 1963). The insulin specific Linco assay is a highly specific insulin assay, which does not cross-react with other insulin-like molecules secreted by the pancreas. A recent meta-analysis reported that stronger associations were observed between elevated insulin levels and risk for a CVD event when the more specific insulin assay was used to measure insulin as compared to the less specific insulin assay (Ruige et al., 1998). In the present study, the interassay coefficient of variation was 4.6% for a low-level serum insulin control that ranged from 10.6 to 11.7 μU/mL and 1.9% for a high-level serum insulin control that ranged from 41.2 to 42.9 μU/mL.

**Blood Pressure Determination**

Auscultatory blood pressure was measured with Diagnostix 920 series calibrated portable mercury sphygmomanometer (American Diagnostic Corporation, Hauppauge, New York) according to the guidelines established by the American Heart Association (Perloff et al., 1993) and the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Joint...
National Committee, 1997). An adult-sized cuff was used for all blood pressure measurements. A seated blood pressure was measured after a five-minute rest. A practice blood pressure was first performed followed by three measured blood pressures separated by approximately two-minute rest periods.

**Anthropometric Measurements**

Weight was measured with a portable, calibrated, electronic load-cell scale to the nearest 0.5 kilogram with participants dressed in lightweight clothing. Height was measured to the nearest 0.5 centimeter with a portable wall-mounted measuring tape. Body Mass Index (BMI) was calculated by dividing the weight in kilograms by the height in meters squared (BMI = kg body weight/height in meters^2). Total body fat and regional body fat was assessed with anthropometric measurements. Total body fat was estimated from anthropometric prediction equations developed by Durnin and Womersley (1974) for women and Jackson, Pollock, and Ward (1980) for men. Both equations were previously validated for use in adults with mental retardation (Rimmer, Kelly, Rosentsweig, 1987). Skinfolds and body circumferences were measured according to previously described procedures (Behnke and Wilmore, 1974). Skinfolds were measured to the nearest 0.1 millimeter with a Lange Skinfold Caliper (Cambridge Scientific Industries Inc., Cambridge, MD) at six sites: biceps, triceps, subscapular, suprailiac, abdomen, and thigh. Circumferences were measured to the nearest 0.1 centimeter with a cloth measuring tape at four sites: abdomen, hip, thigh, and waist. Waist circumference can be used to identify individuals with excess abdominal visceral fat (Lemieux et al., 1996), which has been associated with elevated risk factors for a future CVD event (Despres et al., 1990). The abdominal sagittal diameter was measured to the nearest 0.1 centimeter according to previously described techniques (Williamson et al., 1993) with a caliper manufactured by Holtain Ltd. (Dyfed, Wales, United Kingdom). The mean of two measurements was used for all anthropometric measurements. If the first two skinfold measurements were not within ten percent
agreement, a third measurement was made. The mean of the two closest measurements was used in the analysis. If the second circumference or sagittal diameter measurement was not within one centimeter of the first measurement, then a third measurement was made. The mean of the two closest circumference or diameter measurements was used. To eliminate inter-observer measurement error, the same technician made all anthropometric measurements.

**Analysis of Data**

Each variable was screened for missing data, outliers, and normal distribution. Fasting insulin, fasting glucose, and fasting triglycerides were all found to be positively skewed and were logarithmically transformed for the analysis. All assumptions of normality were met for the statistical tests following the logarithmic transformation of fasting insulin, glucose, and triglycerides. Significance was set at $\alpha \leq 0.05$ for all statistical comparisons.

The data were also analyzed to detect any potential confounding variables, which would need to be controlled for prior to making comparisons between those with MR and DS. To identify differences in potential confounders between adults with DS and adults with MR, independent Chi square tests were conducted on the prevalence of cigarette smoking, medication use, and group home residence. To identify the amount of variation in the CVD risk factor outcomes explained by potential confounders within each group simple correlations were also calculated between potential confounding variables and the CVD risk factors outcomes within each of the gender and disability groups. The Chi square tests and the correlation analysis were used to determine which confounders to include in the multivariate analysis. Each individual was coded for the presence or absence (i.e., 0,1) of each of the following medications: anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, lipid lowering medications, anti-inflammatory medications, and vitamin use. The prevalence of lipid lowering
medications was very low and was not found to significantly correlate with any of the CVD risk factor outcomes, so they were not included in the multivariate analysis.

Means and standard deviations of all the CVD risk factor components of the IRS, and the traditional CVD risk factors were calculated for men with MR, men with DS, women with MR, and women with DS. Independent t-tests were used to detect differences between adults with MR and DS in the CVD risk factor components of the IRS and the traditional CVD risk factors prior to adjusting for the potential confounding variables. An analysis of covariance, was then done to determine whether the CVD risk factor differences were independent of age, cigarette smoking, residence type, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, oral contraceptive use, and hormone replacement therapy. Separate t-tests and analyses of covariance were conducted for men and women. Oral contraceptive use and hormone replacement therapy were not included in the analysis for men.

**Results**

**CVD Risk Factor Components of the IRS**

The unadjusted and adjusted means and standard deviations of the CVD risk factor components of the IRS along with the probability of adults with MR differing from adults with DS are listed in Table 2.2. With or without statistical adjustment for age, residence type, cigarette smoking, and medications use, fasting glucose, systolic blood pressure, diastolic blood pressure, waist circumference, and abdominal sagittal diameter were all significantly higher for women with MR than for women with DS. By contrast statistical adjustment for age, residence type, cigarette smoking, and medication use was needed to detect that HDL cholesterol was lower in women with MR than women with DS. The unadjusted and adjusted systolic and diastolic blood pressures were significantly higher in the men with MR.
than the men with DS. Besides blood pressure none of the other CVD risk factor components of the IRS differed between men with MR and DS before or after adjusting for age, residence type, cigarette smoking, and medication use.

**Traditional CVD Risk Factors and Overweight**

The unadjusted and adjusted means and standard deviations of the traditional CVD risk factors and overweight along with the probability of adults with MR differing from adults with DS are listed in Table 2.3. None of the traditional CVD risk factors differed between men with MR and DS before adjusting for age, residence type, cigarette smoking, and medication use. After adjusting for age, residence type, cigarette smoking, and medication use BMI was significantly higher in women with MR than in women with DS and total body fat was significantly lower in men with MR than in men with DS.

**Discussion**

The mean fasting insulin, mean estimates of abdominal fat, mean total cholesterol, and mean body fat percentage for all participants (especially for women) were close to or above established clinical cutoffs (NIH/NHLBI, 1998; National Center for Health Statistics, 1987; National Cholesterol Education Program, 1994), indicating that men and women with MR and DS have an intermediate to high risk for a future CVD event due to elevated fasting insulin, abdominal fat, total cholesterol, and body fat percentage. The mean HDL cholesterol for women with MR (48.2 mg/dL) and women with DS (45.4 mg/dL) was below the established clinical cutoff for women (<50 mg/dL) indicating that a high proportion of women with MR and DS have an increased risk for a future CVD event due to low HDL cholesterol levels (Miller Bass et al., 1993). As the risk for dying from a CVD event is almost twice as high in women with insulin resistance as compared to men with insulin resistance (Barrett-Connor et al., 1991), women with MR and DS may be at a much greater risk for a future CVD event than men with MR and DS.
Table 2.2. Unadjusted and adjusted mean and standard deviation of cardiovascular disease risk factor components of the insulin resistance syndrome (IRS) in women and men with MR and DS.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Fasting Insulin (μU/mL)</td>
<td>16.5 (1.6)</td>
<td>14.8 (1.6)</td>
<td>0.359</td>
<td>17.3 (1.2)</td>
<td>14.3 (1.2)</td>
<td>0.054</td>
</tr>
<tr>
<td>Fasting Glucose (mg/dL)</td>
<td>98.4 (1.1)</td>
<td>92.3 (1.1)</td>
<td>0.016*</td>
<td>99.8 (1.0)</td>
<td>92.7 (1.0)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Fasting HDL Cholesterol (mg/dL)</td>
<td>48.8 (17.8)</td>
<td>45.4 (12.2)</td>
<td>0.338</td>
<td>46.0 (7.5)</td>
<td>47.5 (5.1)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Fasting Triglycerides (mg/dL)</td>
<td>133.8 (1.8)</td>
<td>116.4 (1.7)</td>
<td>0.311</td>
<td>128.5 (1.3)</td>
<td>119.7 (1.2)</td>
<td>0.065</td>
</tr>
<tr>
<td>Resting Systolic BP (mmHg)</td>
<td>123.1 (16.1)</td>
<td>107.4 (11.8)</td>
<td>0.000*</td>
<td>121.4 (7.7)</td>
<td>108.7 (5.1)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Resting Diastolic BP (mmHg)</td>
<td>84.1 (13.4)</td>
<td>72.7 (10.7)</td>
<td>0.000*</td>
<td>80.9 (5.1)</td>
<td>75.0 (3.5)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Abdominal Fat Estimates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>104.8 (19.6)</td>
<td>91.3 (15.6)</td>
<td>0.002*</td>
<td>101.6 (10.0)</td>
<td>93.6 (6.8)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Abdominal Sagittal Diameter (cm)</td>
<td>26.2 (5.5)</td>
<td>23.4 (4.7)</td>
<td>0.024*</td>
<td>25.4 (0.8)</td>
<td>24.0 (0.6)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IRS Component</th>
<th>Men with MR (N=40)</th>
<th>Men with DS (N=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Insulin (μU/mL)</td>
<td>12.7 (1.6)</td>
<td>13.9 (1.9)</td>
</tr>
<tr>
<td>Fasting Glucose (mg/dL)</td>
<td>95.6 (1.1)</td>
<td>97.4 (1.1)</td>
</tr>
<tr>
<td>Fasting HDL Cholesterol (mg/dL)</td>
<td>42.5 (13.6)</td>
<td>40.7 (11.7)</td>
</tr>
<tr>
<td>Fasting Triglycerides (mg/dL)</td>
<td>141.3 (1.8)</td>
<td>134.9 (1.6)</td>
</tr>
<tr>
<td>Resting Systolic BP (mmHg)</td>
<td>126.7 (12.8)</td>
<td>111.4 (13.6)</td>
</tr>
<tr>
<td>Resting Diastolic BP (mmHg)</td>
<td>86.9 (12.3)</td>
<td>73.2 (10.2)</td>
</tr>
<tr>
<td>Abdominal Fat Estimates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>97.9 (18.5)</td>
<td>97.5 (14.8)</td>
</tr>
<tr>
<td>Abdominal Sagittal Diameter (cm)</td>
<td>23.2 (6.1)</td>
<td>23.3 (4.9)</td>
</tr>
</tbody>
</table>

IRS insulin resistance syndrome, MR = mental retardation, DS = Down syndrome, HDL = high-density lipoprotein, BP = blood pressure, * = significant at the alpha < 0.05 level, a = adjusted for age, smoking status, resident type, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, oral contraceptive use and hormone replacement therapy.
Table 2.3. Unadjusted and adjusted total cholesterol, LDL cholesterol, body fat percentage, and Body Mass Index in women and men with MR and DS.

<table>
<thead>
<tr>
<th>CVD Risk Factor</th>
<th>Women with MR (N=30)</th>
<th>Unadjusted</th>
<th>Probability</th>
<th>Women with DS (N=41)</th>
<th>Unadjusted</th>
<th>Probability</th>
<th>Women with MR (N=30)</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Probability&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Women with DS (N=41)</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Probability&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>191.7 (35.6)</td>
<td>182.4 (56.8)</td>
<td>0.431</td>
<td>182.6 (101.9)</td>
<td>189.1 (69.5)</td>
<td>0.234</td>
<td>182.6 (101.9)</td>
<td>189.1 (69.5)</td>
<td>0.234</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>111.0 (34.9)</td>
<td>106.9 (33.1)</td>
<td>0.613</td>
<td>106.2 (54.8)</td>
<td>110.5 (37.4)</td>
<td>0.897</td>
<td>106.2 (54.8)</td>
<td>110.5 (37.4)</td>
<td>0.897</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Total Body Fat (%)</td>
<td>31.1 (4.9)</td>
<td>29.3 (5.6)</td>
<td>0.151</td>
<td>30.8 (1.2)</td>
<td>29.5 (0.8)</td>
<td>0.175</td>
<td>30.8 (1.2)</td>
<td>29.5 (0.8)</td>
<td>0.175</td>
<td></td>
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<tr>
<td>Body Mass Index (kg/m²)</td>
<td>32.9 (10.2)</td>
<td>31.6 (7.5)</td>
<td>0.555</td>
<td>32.2 (2.6)</td>
<td>32.2 (1.8)</td>
<td>0.005*</td>
<td>32.2 (2.6)</td>
<td>32.2 (1.8)</td>
<td>0.005*</td>
<td></td>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>CVD Risk Factor</th>
<th>Men with MR (N=40)</th>
<th>Unadjusted</th>
<th>Probability</th>
<th>Men with DS (N=34)</th>
<th>Unadjusted</th>
<th>Probability</th>
<th>Men with MR (N=40)</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Probability&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Men with DS (N=34)</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Probability&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>181.4 (44.0)</td>
<td>183.8 (40.6)</td>
<td>0.805</td>
<td>177.4 (54.6)</td>
<td>188.6 (65.1)</td>
<td>0.415</td>
<td>177.4 (54.6)</td>
<td>188.6 (65.1)</td>
<td>0.415</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>104.8 (31.1)</td>
<td>113.3 (33.9)</td>
<td>0.267</td>
<td>101.6 (29.0)</td>
<td>117.0 (35.2)</td>
<td>0.073</td>
<td>101.6 (29.0)</td>
<td>117.0 (35.2)</td>
<td>0.073</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Total Body Fat (%)</td>
<td>25.3 (7.5)</td>
<td>25.1 (5.7)</td>
<td>0.865</td>
<td>24.4 (0.9)</td>
<td>26.2 (1.1)</td>
<td>0.000*</td>
<td>24.4 (0.9)</td>
<td>26.2 (1.1)</td>
<td>0.000*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.7 (6.7)</td>
<td>29.6 (7.6)</td>
<td>0.085</td>
<td>25.8 (1.5)</td>
<td>30.6 (1.9)</td>
<td>0.354</td>
<td>25.8 (1.5)</td>
<td>30.6 (1.9)</td>
<td>0.354</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MR = mental retardation, DS = Down syndrome, LDL = low-density lipoprotein, CVD = cardiovascular disease
* = significant at the alpha < 0.05 level.
<sup>a</sup> = adjusted for age, smoking status, residence type, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, oral contraceptive use (in women only), and hormone replacement therapy (in women only).
In the previous studies, which reported an absence of atherosclerosis in individuals with DS, the autopsied individuals resided in institutional settings (Brattstrom et al., 1989; Murdoch et al., 1977; Yla-Herttuala et al., 1989). In the present study, it appears that on average adults with MR (including adults with DS) residing in community settings have an elevated CVD risk factor profile that puts them at a high risk for developing CVD. Individuals with MR and DS residing in community settings may have greater unhealthy behaviors than adults residing in institutional settings, which may have resulted in elevated CVD risk factor components of the IRS. Future research should investigate if adults with DS residing in community settings who have elevated CVD risk factor components of the IRS have reduced atherosclerosis formation. Safe, noninvasive technology, such as B-mode ultrasound, has been developed to estimate subclinical atherosclerosis and would likely be useful for investigating the relationship between the IRS and atherosclerosis in adults with DS and MR (Chambless et al., 1996). Future studies should also investigate possible mechanism for the elevated CVD risk factor components of the IRS in adults with MR and DS.

The CVD risk factor components of the IRS were not reported for the individuals examined in the previous studies, which indicated that adults with DS do not develop atherosclerosis as extensively as other adults with MR (Brattstrom, et al., 1987; Murdoch et al., 1977; Yla-Herttuala et al., 1989). It was hypothesized that adults with MR alone would have a higher risk for CVD than adults with DS due to more highly elevated CVD risk factor components of the IRS. In the present study, women with MR did have more highly elevated estimates of abdominal fat, elevated fasting glucose, elevated systolic and diastolic blood pressure, lower HDL cholesterol, and elevated fasting insulin (borderline significance) than women with DS. Elevated abdominal fat (Seidell et al., 1994; Zamboni et al., 1992), elevated fasting glucose (Gertein, 1997), elevated blood pressure (Kannel et al., 1986), elevated fasting insulin (Despres et al., 1996; Ruige et al., 1998), elevated fasting triglycerides (Hokanson and Austin, 1996), and lower HDL cholesterol (Miller Bass...
et al., 1993) are all independently associated with greater atherosclerosis
development and/or future CVD events, indicating that women with DS may be
somewhat protected against atherosclerosis as compared to women with MR.

There were no significant differences (other than higher blood pressure in
men with MR) in the CVD risk factor components of the IRS between men with
MR and DS independent of age, smoking status, and residential type, indicating that
the overall IRS severity may not be greater in men with MR as compared to men
with DS. Other factors, which have been identified as potential markers for CVD,
such as plasminogen activator inhibitor-1, hyperuricaemia, C-reactive protein, and
tissue plasminogen activator should also be investigated in individuals with DS to
identify possible mechanisms for the lower atherosclerosis in individuals with DS
(Greenland et al., 2000; Hamsten et al., 1985; Reaven et al., 1994).

Men and women with DS had significantly lower systolic and diastolic blood
pressure than men and women with MR. This finding is consistent with other
reports of blood pressure differences between adults with DS and adults with MR
(Kapell et al., 1998; Murdoch et al., 1977; Yla-Herttuala et al., 1989). Low blood
pressure may play a significant role in the low prevalence of atherosclerosis in adults
with DS (Brattstrom et al., 1987; Chad et al., 1990; Murdoch et al., 1977; Yla-
Herttuala et al., 1989). Elevated blood pressure may play a significant role in the
initial damage of the vascular endothelium and the associated injury response to the
endothelial damage, which both give rise to the initiation and progression of
atherosclerosis (Ross, 1999; Vanhoutte and Boulanger, 1995). Future research
should investigate whether the relationship between low blood pressure among
adults with DS persists throughout the aging process and whether it is a primary
causal factor for the reduced development of atherosclerosis in adults with DS.
Chapter 3

Physical Activity, Dietary Intake, and the Insulin Resistance Syndrome in Non-Diabetic Adults with Mental Retardation

Christopher C. Draheim, Daniel P. Williams, and Jeffrey A. McCubbin
A common neuroendocrine disorder, referred to as the insulin resistance syndrome (IRS), is becoming increasingly recognized as a possible underlying cause of cardiovascular disease (CVD) (Despres, 1996). The CVD components of the IRS frequently develop sooner than traditional CVD risk factors during the development of CVD (Reaven and Laws, 1990). The American Heart Association (AHA) recommends that the CVD risk factor components of the IRS should be used in screenings to identify individuals with an intermediate to high risk for a future CVD event (Grundy et al., 2000). The CVD risk factor component of the IRS include elevated abdominal visceral fat accumulation, elevated fasting insulin, elevated fasting glucose, hypertriglyceridemia, increased number of small dense low-density lipoprotein (LDL) particles, hypertension, decreased high-density lipoprotein (HDL) cholesterol concentration, and steroidal and growth hormone abnormalities (Bjorntorp, 1997; Despres, 1996; Marin and Bjorntorp, 1993; Reaven, 1994).

Identifying individuals with elevated CVD risk factor components of the IRS at an earlier stage in the progression of CVD may allow for earlier implementation of primary prevention strategies and a more positive prognosis. Simple anthropometric measures, which estimate abdominal obesity, have been shown to be highly associated with elevated CVD risk factor components of the IRS in adults without mental retardation (MR) (Avellone et al., 1994; Despres, 1993; Jern, 1992; Pouliot et al., 1994; Rissanen et al., 1997). Using these simple anthropometric measurements to estimate abdominal obesity may be a cost-effective screening tool, which may identify individuals with MR who have a high risk for a CVD event (Hauner et al., 1990; Peiris et al., 1989).

The prevalence of atherosclerosis, elevated CVD risk factors, obesity, and overall mortality in adults with mental retardation (MR) is greater than found in the general population (Beange et al., 1995; Chaney, 1987). Two categories of adults with MR have been identified to have the highest risk for CVD of all adults with MR; 1) adults with mild to moderate MR and 2) adults with MR residing in
community settings (Fox and Rotatori, 1882; Kelly et al., 1986; Janicki and Jacobson, 1986; Janicki and MacEachron, 1984; Strauss and Kastner, 1996; Rimmer et al., 1993; Rimmer et al., 1994; Rimmer et al., 1995). Since the deinstitutionalization of adults with MR, there has been a greater proportion of adults with mild MR living in community settings (Braddock, 1999; Kraus and Seltzer, 1986). With less direct supervision and less nutritional guidance, adults with MR living within the community likely have more freedom to make recreation and dietary choices compared to adults residing in institutional settings, whose dietary intakes and recreational activities are frequently determined by care providers and administrators (Golden and Hatcher, 1997; Litchford and Wakefield, 1985; Mercer and Ekvall, 1992). Similar to the national population without MR (Crespo et al., 1996; Ernst et al., 1997), adults with MR residing in community settings have likely chosen lifestyles consisting of low physical activity levels and a dietary intake consisting of a high percentage of fat (Beange et al., 1995; Chad et al., 1990; Mercer and Ekvall, 1992; Rimmer et al., 1994; Rimmer et al., 1995).

Programs or interventions designed at increasing the physical activity levels and improving cardiovascular fitness of adults with MR would likely improve their overall CVD risk profile. One of the major modifiable behavioral risk factors for preventing CVD is physical activity (Pate et al., 1995; Surgeon General's Report, 1996). High physical activity levels and endurance exercise training are associated with reductions in insulin resistance and reductions in glucose intolerance (Goodyear and Kahn, 1998; Ivy, 1997; Mayer-Davis, 1998; Rankinen et al., 1997; Wojtaszewski et al., 1998). High physical activity levels have also been associated with reductions in other CVD risk factor components of the IRS including, low abdominal fat (Anderssen et al., 1998; Tremblay et al., 1990), low triglyceride levels (Crouse et al., 1997), high HDL cholesterol levels (Wood and Haskell, 1979), low blood pressure (Blair et al., 1984; Leon, 1991), and a reduced incidence of non-insulin dependent diabetes mellitus (James et al., 1998; Krista, Blair, and Pereira, 1994) in adults without MR. The Centers for Disease Control and Prevention
(CDC) and the American College of Sports Medicine (ACSM) have recommended that individuals participate in moderate to vigorous physical activity at least five or more times per week to decrease their risk for CVD (Pate et al., 1995; Report of the Surgeon General, 1996). No previous studies have investigated the association between the recommended frequency (≥5 times/week) of physical activity and the components of the IRS in adults with MR.

Another major modifiable behavioral risk factors for CVD is dietary intake. Reducing total dietary fat intake and increasing fruit and vegetable intake may also lower the risk for CVD by reducing the CVD risk factor components of the IRS, such as lowering fasting insulin, fasting glucose, fasting triglycerides, blood pressure, and abdominal visceral fat (Anderssen et al., 1998; Hatton et al., 1996; McCarron et al., 1997; Ravussin and Gautier, 1999; Renaud and Lorgeril, 1994; Rimm et al., 1996; Schaefer et al., 1996; Shrapnel et al., 1992; Wolk et al., 1999). The National Cholesterol Education Program (NCEP) and the AHA recommend that less than 30% of the total caloric intake should be from dietary fat and at least five or more fruits and vegetable should be consumed per day to reduce the risk for CVD (AHA, 1997; NCEP, 1994). No studies have investigated the association between the recommended dietary intake and the CVD risk factor components of the IRS.

The primary purpose of this study is to identify the association between the recommended behaviors (physical activity, dietary fat intake, and fruit and vegetable intake) and elevated CVD risk factor components of the IRS in adults with MR. The second purpose of this study is to identify the association between abdominal obesity and elevated CVD risk factor components of the IRS in adults with MR.

**Method**

The design of the research project was a cross sectional evaluation of the CVD risk factor components of the IRS and the behavioral risk factors of adults with MR. The CVD risk factor components of the IRS measured include fasting
insulin, fasting glucose, HDL cholesterol, fasting triglycerides, resting systolic and diastolic blood pressure, and estimates of abdominal fat (estimated through abdominal sagittal diameter and waist circumference). The behavioral CVD risk factors of interest included frequency of moderate to vigorous leisure time physical activity, dietary fat intake, and daily fruit and vegetable intake.

**Participants**

This study focused on those adults with mild MR and adults with DS with mild MR residing in community settings, who are considered to be at the highest risk for CVD of all adults with MR (Beange et al., 199; Janicki and MacEachron, 1984; Janicki and Jacobson, 1986; Rimmer et al., 1994, Rimmer et al., 1995; Strauss and Kastner, 1996). Seventy adults with mild MR (40 men, 30 women) and 75 adults with DS with mild MR (34 men, 41 women) were recruited into the study and completed all of the assessments. Participants were selected on a volunteer basis. Prevalence of individuals over 40 years of age, male vs. female gender, Down syndrome presence, cigarette smoking, and medication use in all participants are listed in Table 3.1. Individuals previously diagnosed with diabetes mellitus or prior CVD event, such as a myocardial infarction or stroke, were excluded from the study. A fasting glucose level of 126 mg/dL or above is considered to be a provisional diagnosis of diabetes mellitus according to the clinical standards established by the American Diabetes Association (American Diabetes Association, 1997). Any individual with a fasting glucose level of 126 mg/dL or above was excluded from the study. Five individuals with MR (2 men and 3 women) were excluded from the study due to a provisional diagnosis of diabetes mellitus. Only ambulatory individuals were included in the study.

Prior to the day of data collection, care providers and/or parents of the participants were instructed to explain all procedures to each participant and to answer any questions or concerns that arose. On the day of the data collection, one of the researchers read through the consent form and explained all procedures to
each participant. All participant questions and concerns were addressed prior to asking the participant to sign an informed consent form. All participants (and parents or guardians when needed) then signed an informed consent form. The participants and the direct care staff were each compensated for their time, effort, and contributions to the study with a $15.00 personal check.

**Blood Collection**

All blood draws were made in the morning after an overnight fast (12 hour). Participants were called the night prior to testing to remind them to fast overnight and again in the morning prior to the testing session. Venous blood samples were collected through venipuncture by a trained phlebotomist using sterile procedures (National Committee for Clinical Laboratory Standards, 1991). The samples were collected in vacutainers containing EDTA to inhibit clotting. Blood samples were placed in an ice bath until separation. After separation of the plasma from the blood cells by centrifugation, the plasma was aliquoted into specific, labeled vials for each analyte and stored frozen at −70° C for subsequent lipid, lipoprotein cholesterol, insulin, and glucose analysis. Plasma samples that could not be immediately frozen in the −70° C freezer were frozen and kept on dry ice until transportation to the −70° C freezer could be completed. A portable centrifuge and dry ice was used for plasma separation and storage for the participants that lived more than approximately 60 miles from Oregon State University.

**Fasting Plasma Glucose, Lipid, Lipoprotein, and Insulin Determination**

The clinical laboratory at Good Samaritan Hospital measured the fasting plasma glucose, lipid, and lipoprotein cholesterol concentrations of all samples. The hospital clinical laboratory used Boehringer Mannheim reagents (Indianapolis, IN) and an automated Boehringer Mannheim/Hitachi 917 clinical chemistry analyzer to assess the following: plasma glucose with a hexokinase method (Peterson and Young, 1958), plasma triglycerides with an peroxidase-coupled enzymatic method
Table 3.1. Prevalence of individuals over 40 years of age, male vs. female gender, Down syndrome presence, cigarette smoking, and medication use in all participants.

<table>
<thead>
<tr>
<th>Potential Confounding Factor</th>
<th>Prevalence</th>
<th>(N=145)</th>
</tr>
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<tbody>
<tr>
<td>Participants Over 40 Years of Age</td>
<td>36.6%</td>
<td></td>
</tr>
<tr>
<td>Female Gender</td>
<td>49.0%</td>
<td></td>
</tr>
<tr>
<td>Presence of Down Syndrome</td>
<td>51.7%</td>
<td></td>
</tr>
<tr>
<td>Residential Settings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>4.1%</td>
<td></td>
</tr>
<tr>
<td>Semi-Independent</td>
<td>33.8%</td>
<td></td>
</tr>
<tr>
<td>Group Home</td>
<td>45.5%</td>
<td></td>
</tr>
<tr>
<td>With Family Member</td>
<td>16.6%</td>
<td></td>
</tr>
<tr>
<td>Current Cigarette Smoker</td>
<td>9.7%</td>
<td></td>
</tr>
<tr>
<td>Anti-hypertension Medications</td>
<td>10.3%</td>
<td></td>
</tr>
<tr>
<td>Psychogenic Medications</td>
<td>23.4%</td>
<td></td>
</tr>
<tr>
<td>Thyroid Medications</td>
<td>21.4%</td>
<td></td>
</tr>
<tr>
<td>Seizure Medications</td>
<td>17.2%</td>
<td></td>
</tr>
<tr>
<td>Lipid Lowering Medications</td>
<td>6.2%</td>
<td></td>
</tr>
<tr>
<td>Anti-Inflammatory Medication</td>
<td>13.1%</td>
<td></td>
</tr>
<tr>
<td>Vitamin and Mineral Supplements (any type)</td>
<td>28.3%</td>
<td></td>
</tr>
<tr>
<td>Hormone Replacement Therapy</td>
<td>11.0% (% of women only)</td>
<td></td>
</tr>
<tr>
<td>Oral Contraceptive Use</td>
<td>22.0% (% of women only)</td>
<td></td>
</tr>
</tbody>
</table>

DS = Down syndrome
(Fossati and Prencipe, 1982), and high-density lipoprotein (HDL) cholesterol with a
direct homogeneous enzymatic method (Sugiuchi et al., 1995). The measurement
error, expressed as coefficients of variation, for the clinical laboratory was 1.8% for
plasma glucose, 2.0% for plasma triglycerides, and 1.5% for plasma HDL
cholesterol.

Fasting plasma insulin concentration was determined with a human insulin-
specific double-antibody radioimmunoassay (RIA) (Linco Research, Inc., St.
Charles, MO) (Morgan and Lazarow, 1963). The insulin specific Linco assay is a
highly specific insulin assay, which does not cross-react with other insulin-like
molecules secreted by the pancreas. A recent meta-analysis reported that stronger
associations were observed between elevated insulin levels and risk for a CVD event
when the more specific insulin assay was used to measure insulin as compared to the
less specific insulin assay (Ruige et al., 1998). In the present study, the interassay
coefficient of variation was 4.6% for a low-level serum insulin control that ranged
from 10.6 to 11.7 μU/mL and 1.9% for a high-level serum insulin control that
ranged from 41.2 to 42.9 μU/mL.

**Blood Pressure Determination**

Auscultatory blood pressure was measured with a Diagnostix 920 series
calibrated portable mercury sphygmomanometer (American Diagnostic Corporation,
Hauppauge, New York) according to the guidelines established by the American
Heart Association (Perloff et al., 1993) and the Joint National Committee on
Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Joint
National Committee, 1997). An adult-sized cuff was used for all blood pressure
measurements. The seating blood pressure was measured after a five-minute rest.
A practice blood pressure was first performed followed by three measured blood
pressures separated by approximately two-minute rest periods.
Anthropometric Measurements

Weight was measured with a portable, calibrated, electronic load-cell scale to the nearest 0.5 kilogram with participants dressed in lightweight clothing. Height was measured to the nearest 0.5 centimeter with a portable wall-mounted measuring tape. Body Mass Index (BMI) was calculated by dividing the weight in kilograms by the height in meters squared (BMI = kg body weight/height in meters\(^2\)). Waist circumference was measured to the nearest 0.1 centimeter with a cloth measuring tape according to methods described by Benke and Wilmore (1974). The abdominal sagittal diameter was measured to the nearest 0.1 centimeter according to previously described techniques (Williamson et al., 1993) with a caliper manufactured by Holtain Ltd. (Dyfed, Wales, United Kingdom). The mean of two measurements was used for all anthropometric measurements. If the second circumference or sagittal diameter measurement was not within one centimeter of the first measurement, then a third measurement was made. The mean of the two closest measurements was used in the analysis. To eliminate inter-observer measurement error, the same technician made all anthropometric measurements with a female assistant present as needed.

Physical Activity Assessment

The National Health and Nutrition Examination Survey III, Physical Activity Survey was used to assess the participants' regular physical activity habits (National Center for Health Statistics, 1994). The physical activity survey was administered through an interview with the participant and the participant's direct care provider to assist with the questions as needed. The participant and direct care providers were instructed to provide the most accurate information. The energy expenditure of each specific activity was estimated using the Ainsworth Compendium for Physical Activities (Ainsworth et al., 1993). The Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) have recommended that individuals participate in moderate to vigorous LTPA at least five
or more times per week to decrease their risk for CVD (Pate et al., 1995; Report of the Surgeon General, 1996). Moderate to vigorous intensity leisure time physical activity (LTPA) was defined as any physical activity greater than or equal to 3.5 metabolic equivalents (METS) (Crespo, Keteyian, Heath, Sembros, 1996). Participants were coded as to whether or not they were participating in the recommended frequency of 5 or more times per week of moderate to vigorous LTPA (Pate et al., 1995; Report of the Surgeon General, 1996).

**Dietary Assessment**

The Block Screening Questionnaire for Fat Intake (Block et al., 1989) was used to estimate the percent of dietary fat intake of the total dietary intake. The Behavioral Risk Factor Surveillance System (BRFSS), Fruit and Vegetable Module (Serdula et al., 1993) was used to estimate the mean number of fruits and vegetables eaten per day and the grams of fiber consumed per day. The food frequency questionnaires were administered as an interview with the participant and the participant's direct care provider present to assist with the questions as needed. The participant and direct care providers were instructed to provide the most accurate information. The participants were also given three questions to determine their cigarette smoking habits.

**Clinically Significant Cutoff Points**

Established cutoff points, which are associated with an intermediate to high risk for a future CVD event, were used to identify individuals who possessed an increased risk for CVD due to elevated CVD risk factor components of the IRS and recommended health behaviors for reducing CVD risk. The prevalence of participants with elevated CVD risk factor components of the IRS and with the recommended health behaviors are listed and defined in Table 3.2.
Analysis of Data

Each variable was screened for missing data, outliers, and multicollinearity. Dichotomous variables were made using the clinically unhealthy cutoff points for the CVD risk factor components of the IRS and the healthy behavioral risk factors. The data were first evaluated for expected cell frequencies to determine suitability for all logistic regression derived estimates of odds ratios (OR). The prevalence of the recommended dietary fat intake (< 30%) was less than 8% and did not meet the minimal requirements for expected cell frequencies when stratified by the presence or absence of elevated CVD risk factors (Tabachnick and Fidell, 1996). The next highest category provided by the Block Screening Questionnaire for Fat Intake (1989), which is ≤ 35% fat of total intake, was used to determine the odds ratio of elevated CVD risk factor components of the IRS in those reporting fat intake of 35% or above verse those reporting a fat intake less than 35%. The Block Screening Questionnaire for Fat Intake (1989) was developed to identify individuals consuming fat intakes above and below the average fat intake. As the average fat intake in the Block (1989) sample was approximately 35% of the total dietary intake, and the national average for daily fat intake is also approximately 35% of the total dietary intake (Ernst et al., 1997), thus the 35% fat intake threshold may be a realistic, generalizable, and appropriate way to assess the association between a lower fat intake (≤ 35%) and a lower occurrence of the CVD risk factor components of the IRS. Significance was set at $\alpha < 0.05$ for all statistical comparisons.

The prevalence for individuals above 40 years old, gender, presence of Down syndrome, cigarette smoking, and medication use are listed in Table 3.1. Individuals were coded for more mature age (above and below 40 years old), gender, presence of Down syndrome, cigarette smoking, and medication use. The medications were grouped into the following groups and each individual was coded for the presence of taking medications in each grouping (0,1); anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications,
lipid lowering medications, anti-inflammatory medications, and vitamin use. The prevalence of lipid lowering medications was very low and not adjusted for in the analysis.

Logistic regression was used to detect the separate associations of overweight, abdominal obesity, recommended physical activity, and the dietary recommendations with each of the elevated CVD risk factor components of the IRS, both with and without adjusting for potential confounding variables. The potential confounding variables included each of the following: age, gender, presence of Down syndrome, cigarette smoking, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, oral contraceptive use, and hormone replacement therapy.

**Results**

**Overweight and Abdominal Obesity**

The unadjusted and adjusted odds ratio and 95% confidence intervals for elevated CVD risk factor components of the IRS are presented by overweight and abdominal obesity presence verse absence in Table 3.3. Prior to adjusting for the potential confounding variables, individuals who were overweight were 2 to 7 times more likely to have hyperinsulinemia, borderline high triglycerides, and borderline hypertension than those who were not overweight. After adjusting for age, gender, presence of Down syndrome, smoking status, and medication use, overweight individuals were 3 to 9 times more likely to have hyperinsulinemia, borderline high triglycerides, and borderline hypertension. Prior to adjusting for potential confounding variables, individuals with abdominal obesity (estimated by waist circumference or abdominal sagittal diameter) were 2 to 10 times more likely to have hyperinsulinemia, borderline high triglycerides, low HDL cholesterol, and borderline hypertension than those without abdominal obesity. After adjustment for age, gender, presence of Down syndrome, smoking status, and medication use,
individuals with abdominal obesity were 2 to 16 times more likely to have hyperinsulinemia, borderline high triglycerides, low HDL cholesterol, and borderline hypertension than those without abdominal obesity.

**Behavioral Risk Factors**

The unadjusted and adjusted odds ratios and 95% confidence intervals for elevated CVD risk factor components of the IRS are presented by recommended health behavior presence versus absence in Table 3.4. Individuals with the recommended LTPA (≥5 times per week) were approximately two-fifths as likely to have hyperinsulinemia as compared to individuals with lower LTPA (<5 times per week). After adjusting for age, gender, presence of Down syndrome, smoking status, and medication use, individuals with the recommended LTPA were less than one-third as likely to have hyperinsulinemia as compared to individuals with lower LTPA. Individuals who reported dietary intakes at or below 35% fat were one-third to two-fifths as likely to have hyperinsulinemia, abdominal obesity, and borderline hypertension as compared to individuals reporting dietary intakes above 35% fat. After adjusting for age, gender, presence of Down syndrome, smoking status, and medication use, individuals who reported dietary intakes at or below 35% fat were approximately one-third as likely to have hyperinsulinemia and abdominal obesity as compared to individuals reporting dietary intakes above 35% fat. No odds ratios for high and low fruit and vegetable intake were significant before or after adjusting for age, gender, presence of Down syndrome, smoking status, and medication use.

**Discussion**

Participating in moderate to vigorous LTPA five or more times per week is recommended by the CDC and the ACSM to reduce the risk for a future CVD event and developing obesity (Pate et al., 1995; Surgeon General's Report, 1996). Higher physical activity levels are associated with lower CVD risk factor components of the IRS, including lower fasting insulin, lower triglycerides, lower blood pressure, and
Table 3.2. Prevalence and established cutoff points used to identify prevalence of elevated CVD risk factor components of the IRS, overweight, abdominal obesity, and behavioral risk factors in adults with mental retardation.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence (N=145)</th>
<th>Established Cutoff Point (Reference for Intermediate to High Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular Disease Risk Factor Components</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperinsulinemia</td>
<td>42.1%</td>
<td>≥15 μU/mL (Despres et al., 1996)</td>
</tr>
<tr>
<td>Borderline High Triglycerides</td>
<td>20.7%</td>
<td>≥200 mg/dL (NCEP, 1994)</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>45.5%</td>
<td>&lt;35 mg/dL-men, &lt;50 mg/dL-women (NCEP, 1994; Miller Bass et al., 1993)</td>
</tr>
<tr>
<td>Borderline Hypertension</td>
<td>24.8%</td>
<td>Diastolic BP ≥90 mmHg or Systolic BP ≥140 mmHg (JNC, 1997)</td>
</tr>
<tr>
<td><strong>Overweight and Abdominal Obesity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>56.6%</td>
<td>BMI ≥27.8 kg/m² for men, ≥27.3 kg/m² for women (NCHS, 1987)</td>
</tr>
<tr>
<td>Abdominal Obesity (WC)</td>
<td>52.4%</td>
<td>WC ≥102 cm for men or ≥88 cm for women (NIH/NHLBI, 1998)</td>
</tr>
<tr>
<td>Abdominal Obesity (ASD)</td>
<td>37.9%</td>
<td>ASD &gt;25 cm (Pouliot et al., 1994)</td>
</tr>
<tr>
<td><strong>Recommended Health Behaviors for Reducing Cardiovascular Disease Risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended LTPA</td>
<td>44.1%</td>
<td>≥5 times/week (Pate et al., 1995)</td>
</tr>
<tr>
<td>Recommended Dietary Fat Intake</td>
<td>7.6%</td>
<td>&lt;30% of total intake (NCEP, 1994)</td>
</tr>
<tr>
<td>Below Average Fat Intake</td>
<td>35.9%</td>
<td>≤35% of total intake (Block et al., 1992)</td>
</tr>
<tr>
<td>Recommended Fruit and veg. Intake</td>
<td>36.6%</td>
<td>≥5 per/day (NCEP, 1994)</td>
</tr>
</tbody>
</table>

CVD = cardiovascular disease, IRS = insulin resistance syndrome, NCEP = National Cholesterol Education Program, HDL = high-density lipoprotein, BP = blood pressure, JNC = Joint National Committee, BMI = Body mass index, NCHS = National Center for Health Statistics, WC = waist circumference, NIH/NHLBI = National Institute of Health/National Heart Lung Blood Institute, ASD = abdominal sagittal diameter, LTPA = moderate to vigorous leisure time physical activity.
Table 3.3. Odds ratios for elevated CVD risk factor components of the IRS for adults with MR who are overweight or who have abdominal obesity as compared to those who are not overweight or do not have abdominal obesity.

<table>
<thead>
<tr>
<th>OR (95% C.I.)</th>
<th>Hyperinsulinemia</th>
<th>Borderline High Triglycerides</th>
<th>Low HDL&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Borderline Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overweight</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>7.39 (3.36-16.23)*</td>
<td>3.11 (1.24-7.84)*</td>
<td>2.16 (1.10-4.24)*</td>
<td>2.07 (0.93-4.63)</td>
</tr>
<tr>
<td>Adjusted&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>9.04 (3.77-21.63)*</td>
<td>4.16 (1.42-12.21)*</td>
<td>2.01 (0.99-4.25)</td>
<td>3.27 (1.09-10.14)*</td>
</tr>
<tr>
<td><strong>Abdominal Obesity (estimated by waist circumference)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>10.46 (4.56-22.56)*</td>
<td>3.11 (1.28-7.55)*</td>
<td>2.61 (1.33-5.12)*</td>
<td>3.07 (1.35-6.97)*</td>
</tr>
<tr>
<td>Adjusted&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>16.34 (6.27-42.60)*</td>
<td>3.65 (1.28-10.35)*</td>
<td>2.59 (1.25-5.38)*</td>
<td>2.14 (0.81-5.66)</td>
</tr>
<tr>
<td><strong>Abdominal Obesity (estimated by abdominal sagittal diameter)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>10.25 (4.68-22.45)*</td>
<td>4.57 (1.94-10.77)*</td>
<td>2.29 (1.16-4.54)*</td>
<td>5.03 (2.24-11.29)*</td>
</tr>
<tr>
<td>Adjusted&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.19 (4.13-25.16)*</td>
<td>6.40 (2.02-20.26)*</td>
<td>1.93 (0.92-4.08)</td>
<td>11.15 (3.03-41.02)*</td>
</tr>
</tbody>
</table>

N = 145, OR = odds ratios calculated from logistic regression. C.I. = confidence interval.
CVD = cardiovascular disease, IRS = insulin resistance syndrome, MR = mental retardation, HDL = high-density lipoprotein
<sup>a</sup> = adjusted for age, gender (except when indicated otherwise), smoking status, resident type, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, and oral contraceptive and hormone replacement medications.
<sup>b</sup> = not adjusted for gender because of gender specific cutoff points.
* P < 0.05.
Table 3.4. Odds ratios for elevated CVD risk factor components of the IRS for adults with MR with the recommended LTPA, below average dietary fat intake, and recommended fruit and vegetable intake per day compared to those with lower than recommended LTPA, above average dietary fat intake, and low fruit and vegetable intake.

<table>
<thead>
<tr>
<th>OR (95% C.I.)</th>
<th>Hyperinsulinemia</th>
<th>Borderline High TG</th>
<th>Low HDL$^b$</th>
<th>Borderline Hypertension</th>
<th>Abdominal Obesity$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended LTPA (≥5 times per week)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.44 (0.22-0.88)*</td>
<td>0.68 (0.30-1.55)</td>
<td>0.77 (0.38-1.57)</td>
<td>1.37 (0.64-2.92)</td>
<td>0.94 (0.49-1.81)</td>
</tr>
<tr>
<td>Adjusted$^a$</td>
<td>0.29 (0.13-0.66)*</td>
<td>0.55 (0.21-1.46)</td>
<td>0.51 (0.22-1.20)</td>
<td>1.03 (0.40-2.70)</td>
<td>0.67 (0.25-1.75)</td>
</tr>
<tr>
<td><strong>Below Average Fat Intake (≤35% of total intake)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.41 (0.20-0.86)*</td>
<td>0.47 (0.19-1.19)</td>
<td>0.56 (0.28-1.13)</td>
<td>0.34 (0.14-0.85)*</td>
<td>0.40 (0.19-0.86)*</td>
</tr>
<tr>
<td>Adjusted$^a$</td>
<td>0.35 (0.15-0.82)*</td>
<td>0.54 (0.19-1.60)</td>
<td>0.70 (0.33-1.49)</td>
<td>0.51 (0.17-1.54)</td>
<td>0.32 (0.13-0.80)*</td>
</tr>
<tr>
<td><strong>Recommended Fruit &amp; Vegetable Intake (≥5 per day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.67 (0.33-1.33)</td>
<td>0.84 (0.36-1.95)</td>
<td>0.87 (0.44-1.73)</td>
<td>0.49 (0.21-1.15)</td>
<td>1.44 (0.72-2.87)</td>
</tr>
<tr>
<td>Adjusted$^a$</td>
<td>0.65 (0.28-1.50)</td>
<td>1.15 (0.45-3.29)</td>
<td>1.03 (0.48-2.23)</td>
<td>0.55 (0.18-1.65)</td>
<td>1.74 (0.73-4.18)</td>
</tr>
</tbody>
</table>

N= 145, OR = odds ratios calculated from logistic regression, C.I. = confidence interval.  
CVD = cardiovascular disease, IRS = insulin resistance syndrome, MR = mental retardation, TG = triglycerides, LTPA = moderate to vigorous leisure time physical activity, HDL = high-density lipoprotein, BP = blood pressure  
$^a$ = adjusted for age, gender (except when indicated otherwise), smoking status, resident type, anti-hypertension medications, psychogenic medications, thyroid medications, seizure medications, and oral contraceptive and hormone replacement medications (in women only).  
$^b$ = not adjusted for gender because of gender specific cutoff points.  
$^c$ = Abdominal obesity estimated through abdominal sagittal diameter >25cm (Pouliot et al., 1994)  
* probability < 0.05.
higher HDL cholesterol levels (Goodyear and Kahn, 1998; Ivy, 1997; Mayer-Davis, 1998; Rankinen et al., 1997; Wojtaszewski et al., 1998) in adults without MR. In the present study, adults with MR residing in community setting participating in moderate to vigorous LTPA five times per week or greater, as assessed by the NHANES III Physical Activity Survey, were less than one-third as likely to have hyperinsulinemia than those participating in less than the recommended LTPA, independent of age, gender, presence of Down syndrome, smoking status, and medication use. As hyperinsulinemia is an independent predictor of a future CVD event (Despres et al., 1996), reducing the prevalence of hyperinsulinemia may lower the morbidity rates due to CVD in adults with MR. A similar but nonsignificant CVD “protective” trend was also observed between recommended LTPA frequencies and lower prevalence of borderline high triglycerides, borderline hypertension, low HDL cholesterol, and abdominal obesity. The protective findings of LTPA against hyperinsulinemia suggest that all adults with MR residing in community settings should participate in moderate to vigorous LTPA at least five times per week to potentially lower their risk for CVD regardless of age, gender, presence of Down syndrome, smoking status, and medication use. Physician’s approval should be obtained prior to initiating a physical activity program (American College of Sports Medicine, 1995).

In the present study adults with MR who reported a fat intake at or below 35% were approximately one-third as likely to have hyperinsulinemia and abdominal obesity than those who reported a fat intake above 35%, independent of age, gender, presence of Down syndrome, smoking status, and medication use. A similar but nonsignificant CVD “protective” trend was also observed between lower dietary fat intakes and a lower prevalence of borderline high triglycerides, borderline hypertension, and low HDL cholesterol. The present findings suggest that adults with MR residing in community settings should consume less than 35% of their total calories from fat to potentially lower their risk for hyperinsulinemia and abdominal obesity. Adults with MR, who are consuming very high fat intake, may initially need
to target a dietary fat intake of 35% or less of the total intake. To be consistent with the American Heart Association (1997) and the National Cholesterol Education Program (1994) all adults with MR should have the long-term goal of lowering their risk for CVD by consuming a diet that consists of less than 30% of the calories from fat. Stronger associations between dietary intake and the components of the IRS may have been detected if more specific types of dietary fat intake were assessed, such as saturated, polyunsaturated, and monounsaturated fatty acids (Gordon et al., 1982; Illingworth, Harris, and Conner, 1984; Mattson and Grundy, 1985; Mensink and Katan, 1989; Mensink and Katan, 1990). Further research should focus on the relationship between more specific types of fat intake and the CVD risk factor components of the IRS in adults with MR.

It is likely that a larger sample size would have provided the power to identify more significant protective findings for the recommended LTPA, daily fat intake, and the recommended daily fruit and vegetable intake (Tabachnick and Fidell, 1996). Also, the estimated energy expenditures from the Ainsworth Compendium for Physical Activity may have overestimated the intensity for the specific physical activities reported by the adults with MR or care providers in the present study. The compendium was not designed for use in populations with MR. Generally, upon watching individuals with MR participating in physical activity, the perceived effort given by the participants with MR often will not appear to equal an intensity similar to others without MR. An overestimation of physical activity intensity for certain physical activities may have resulted in an overestimation of the frequency of actual moderate to vigorous LTPA, which is required to meet the requirements for the LTPA recommendations (Pate et al., 1995). Including less intense physical activity (or less frequent “true” moderate to vigorous physical activity) in the analysis may decrease the association between LTPA and the CVD risk factor components of the IRS (Mayer-Davis et al., 1998), making it more difficult to detect lower prevalences of elevated CVD risk factor components of the IRS in those participating at or above the recommended LTPA. The nutrition
assessment tools used in the present study were designed to screen for individuals without MR who consumed a high or low fat intake or a high or low fruit and vegetable intake (Block et al, 1989; Serdula et al., 1993) rather than detecting those consuming above and below the recommended dietary intakes. The Block Screening Questionnaire for Fat Intake (1989) was reported to correctly identify 62-82% of the individuals who consumed either a high or low percent fat. More expensive, elaborate, and time consuming methods to quantify LTPA and dietary intake, such as using pedometers, or multiple day food diaries may have resulted in more significant findings than by using the frequency questionnaires as used in the present study. The present protective findings of regular LTPA and low fat intake are still important because they provide a starting point for the development of recommendations aimed specifically at improving CVD risk in adults with MR who reside in community settings regardless of age, gender, and presence of Down syndrome.

The high prevalence of hyperinsulinemia (42.1%), low HDL cholesterol (45.5%), and abdominal obesity (37.9-52.4%) indicate that, overall, adults with MR residing in community settings have an intermediate to high risk for a future CVD event. Together, the high prevalence of hyperinsulinemia, low HDL cholesterol, and abdominal obesity indicate that the clustering of the IRS is a major concern for adults with MR residing in community settings. The overall high prevalence of behavioral risk factors for CVD of adults with MR in the present study was also alarming, as more than 55% reported participating in moderate to vigorous LTPA less than five times per week, more than 92% reported dietary fat intakes at or above 30% of the total diet, and more than 63% reported consuming less than the recommended 5 or more fruit or vegetable servings per day. The high prevalence of the behavioral risk factors for CVD have likely played a major role in the development of the elevated prevalence of CVD risk factor components of the IRS in adults with MR residing in community settings (Anderssen et al., 1998; Blair et al., 1984; Crouse et al., 1997; James et al., 1998; Krista, Blair, and Pereira, 1994;
Lamarche et al., 1992; Leon, 1991; Mayer-Davis et al., 1998; Tremblay et al., 1990). The high prevalence of the CVD risk factor components of the IRS in adults with MR have likely led to the increased CVD morbidity and mortality of adults with MR reported in previous studies. Future research should focus on the benefits of the behavioral risk factors on the CVD risk factor components of the IRS. Programs, which focus on increasing LPTA and decreasing dietary fat intake, would be helpful for potentially reducing the overall risk for CVD in adults with MR residing in community settings. Upon improving the behavioral risk for CVD, it is also likely that the prevalence of CVD risk factor components of the IRS would be reduced, thereby lowering the overall risk for a future CVD event in adults with MR.

Adults with MR with abdominal obesity (as estimated by a high waist circumference or a high abdominal sagittal diameter) were 2-16 times more likely to have elevated CVD risk factors components of the IRS than those without abdominal obesity independent of age, gender, presence of Down syndrome, smoking status, and medication use. Similar to previous research on adults without MR (Peiris et al., 1989; Pouliot et al., 1994; Rissanen et al., 1997), both measures of abdominal obesity were better at identifying individuals with elevated CVD risk factors of the IRS than being classified as overweight. Waist circumference or abdominal sagittal diameter should be used to identify adults with MR who are at an intermediate to high risk for a future CVD event due to elevated CVD risk factor components of the IRS independent of age, gender, presence of Down syndrome, smoking status, and medication use.

Using the simple anthropometric measures of abdominal sagittal diameter and waist circumference to identify adults with MR who may have abdominal obesity may be a cost-effective screening tool for identifying those adults with the greatest risk for elevated CVD risk factor components of the IRS. Adults with MR with abdominal obesity may potentially have the greatest to gain from behavioral (diet and exercise) interventions. Thus, due to the limited personnel and financial
resources, individuals with abdominal obesity should be targeted for intervention. The CDC, ACSM (Pate et al., 1995; Surgeon General’s Report, 1996), National Cholesterol Education Program (1994) and the American Heart Association’s (1997) recommend that adults should participate in moderate to vigorous physical activity 5 or more times per week, consume a diet that contains less than 30% fat, and consume at least five servings of fruits and vegetables per day. As supported by the results of the present study, all adults with MR should also be encouraged to participate in moderate to vigorous LTPA five or more times per week, to consume a diet that contains 35% fat or less of the total calories (likely below 30%), and to consume five or more fruit and vegetable servings per day to protect against elevated CVD risk factor components of the IRS.
Chapter 4

Summary and Conclusions

Comparison between Adults with MR and DS

Because adults with DS have been reported to not develop atherosclerosis as extensively as other adults with MR (Brattstrom, et al., 1987; Chad et al., 1990; Murdoch et al., 1977; Yla-Herttuala et al., 1989), it was hypothesized that adults with MR alone would have a higher risk for CVD than adults with DS due to more highly elevated CVD risk factor components of the IRS. In the present study, women with MR did have more highly elevated estimates of abdominal fat, elevated fasting glucose, elevated systolic and diastolic blood pressure, lower HDL cholesterol, and elevated fasting insulin (borderline significance) than women with DS, indicating that women with DS may be somewhat protected against atherosclerosis as compared to women with MR.

There were no significant differences (other than higher blood pressure in men with MR) in the CVD risk factor components of the IRS between men with MR and DS independent of age smoking status, and residential type, indicating that the overall IRS severity may not be greater in men with MR as compared to men with DS.

Men and women with DS had significantly lower systolic and diastolic blood pressure than men and women with MR. This finding is consistent with other reports of blood pressure differences between adults with DS and adults with MR (Kapell et al., 1998; Murdoch et al., 1977; Yla-Herttuala et al., 1989). Low blood pressure may play a significant role in the low prevalence of atherosclerosis in adults with DS (Brattstrom et al., 1987; Chad et al., 1990; Murdoch et al., 1977; Ross, 1999; Vanhoutte and Boulanger, 1995; Yla-Herttuala et al., 1989). Future research should investigate whether the relationship between low blood pressure among adults with DS persists throughout the aging process and whether it is a primary
causal factor for the reduced development of atherosclerosis in adults with DS. Other factors, which have been identified as potential markers for CVD, such as plasminogen activator inhibitor-1, hyperuricaemia, C-reactive protein, and tissue plasminogen activator should also be investigated in individuals with DS to identify possible mechanisms for the lower atherosclerosis in individuals with DS (Greenland et al., 2000; Hamsten et al., 1985; Reaven et al., 1994).

Prevalence and Magnitude of CVD Risk Factors in Adults with MR and DS

In the present study, the high prevalence of hyperinsulinemia (42.1%), low HDL cholesterol (45.5%), and abdominal obesity (37.9-52.4%) were relatively high for adults with MR residing in community settings. Also, the mean fasting insulin, mean estimates of abdominal fat, mean total cholesterol, and mean body fat percentage for all participants (especially for women) were close to or above established clinical cutoffs (NIH/NHLBI, 1998; National Center for Health Statistics, 1987; National Cholesterol Education Program, 1994), indicating that men and women with MR and DS have an intermediate to high risk for a future CVD event due to elevated fasting insulin, abdominal fat, total cholesterol, and body fat percentage. The mean HDL cholesterol for women with MR (48.2 mg/dL) and women with DS (45.4 mg/dL) was below the established clinical cutoff for women (<50 mg/dL) indicating that the majority of women with MR and DS have an increased risk for a future CVD event due to low HDL cholesterol levels (Miller Bass et al., 1993). As the risk for dying from a CVD event is almost twice as high in women with insulin resistance as compared to men with insulin resistance (Barrett-Connor et al., 1991), women with MR and DS may be at a much greater risk for a future CVD event than men with MR and DS.

Behavioral Risk Factors and the CVD Risk Factor Components of the IRS

In the present study, adults with MR residing in community setting participating in moderate to vigorous LTPA five time per week or greater, as
assessed by the NHANES III Physical Activity Survey, were less than one-third as likely to have hyperinsulinemia than those participating in less than the recommended LTPA independently of age, gender, presence of Down syndrome, smoking status, and medication use. Also in the present study, adults with MR who reported a fat intake at or below 35% were approximately one-third as likely to have hyperinsulinemia and abdominal obesity than those who reported a fat intake above 35%, independent of age, gender, presence of Down syndrome, smoking status, and medication use. As hyperinsulinemia is an independent predictor of a future CVD event (Despres et al., 1996), reducing the prevalence of hyperinsulinemia may lower the morbidity rates due to CVD in adults with MR. The protective findings of LTPA and lower fat intake against hyperinsulinemia suggest that all adults with MR residing in community settings should participate in moderate to vigorous LTPA at least five times per week and consume a diet of 35% or less to potentially lower their risk for CVD regardless of age, gender, presence of Down syndrome, smoking status, and medication use. The present protective findings of regular LTPA and low fat intake are important because they provide a starting point for the development of recommendations aimed specifically at improving CVD risk in adults with MR who reside in community settings regardless of their age, gender, and presence of Down syndrome.

**Abdominal Obesity and the CVD Risk Factor Components of the IRS**

Adults with MR with abdominal obesity (as estimated by a high waist circumference or a high abdominal sagittal diameter) were 2-16 times more likely to have elevated CVD risk factors components of the IRS than those without abdominal obesity independent of age, gender, presence of Down syndrome, smoking status, and medication use. Waist circumference or abdominal sagittal diameter should be used to identify adults with MR who are at an intermediate to high risk for a future CVD event due to elevated CVD risk factor components of the IRS. Using the simple anthropometric measures of abdominal sagittal diameter and
waist circumference to identify adults with MR who may have abdominal obesity may be a cost-effective screening tool for identifying those adults with the greatest risk for elevated CVD risk factor components of the IRS.

Future research should focus on the development of primary prevention intervention strategies aimed at lowering the risk for CVD due to the CVD risk factor components of the IRS. Longitudinal investigations designed to study the effects of physical activity and low fat dietary intakes on abdominal obesity and the CVD risk factor components of the IRS may help strengthen the protective relationship between the recommended LTPA or low fat diets and the decreased risk for CVD in adults with MR residing in community settings. Physical activity programs and dietary counseling programs may help reduce the risk for CVD events in adults with MR residing in the community.
Bibliography


Appendix
Literature Review

Cardiovascular Disease Risk

The term cardiovascular disease (CVD) encompasses the major cardiovascular diseases, which include coronary heart disease, hypertensive disease, rheumatic fever/rheumatic heart disease, and cerebral vascular disease and other cardiovascular diseases. The other cardiovascular diseases include arrhythmias, peripheral vascular disease, bacterial endocarditis, cardiomyopathy, congenital heart disease, congestive heart failure, and valvular heart disease (AHA, 1997). CVD kills approximately one million men and women per year making it the leading cause of death in the United States (AHA, 1997). The estimated cost of treating CVD and cost from lost productivity due to morbidity and mortality related to CVD in the United States was over $274,000,000,000 for 1998 (AHA, 1997). The severity of CVD is evidenced by the high prevalence of CVD and the associated high mortality rates along with the extremely high cost of treating CVD in the United States. The existing severity of CVD has led the American Heart Association (AHA) to recognize the importance of primary prevention of CVD. A recent conference of health experts sponsored by the AHA was convened with the sole purpose of developing strategies to identify patients with an intermediate to high risk for CVD for primary prevention purposes (Smith, Greenland, Grundy, 2000). By identifying individuals with an intermediate to high risk for CVD, primary prevention strategies can be implemented, which may reduce the morbidity, mortality, and cost of treating CVD each year (Grundy et al., 2000; Fletcher et al., 1998; Smith, Greenland, Grundy, 2000).

The American Heart Association and the National Cholesterol Education Program recognize a set of traditional physiological risk factors and a set behavioral risk factors that influence the initiation and progression of CVD (AHA, 1997; NCEP, 1994). The traditional physiological risk factors include elevated total cholesterol, elevated low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein
cholesterol (HDL), elevated blood pressure, family history of CVD, and diabetes mellitus status (AHA, 1997; NCEP, 1994). The behavioral risk factors include low physical activity levels, high dietary fat intake, low fruit and vegetable intake, smoking status, and elevated psychosocial stress (AHA, 1997; NCEP, 1994).

Even though the development of CVD typically progresses with age (Berenson et al., 1987) and there is evidence of a genetic disposition for CVD (Despres, Moorjani, and Jupien, 1992; Goldbourt and Neufeld, 1986), the behavioral risk factors for CVD negatively affect the physiological risk factors for CVD and play an important role in the progression of CVD. The negative influence of the behavioral risk factors on the physiological risk factors accelerate the progression of the disease and may result in a CVD related death (Lindahl, Asplund, and Hallmans, 1993; Reaven, 1995; Report of the Surgeon General, 1996; Yusuf et al., 1998). As an individual's number of positive CVD risk factors increase the risk of developing coronary heart disease, the risk of having a stroke, and overall mortality risk also increases (Yusuf et al., 1998).

Obesity, while not presently considered to be an independent risk factor for CVD, is highly associated with elevated blood pressure, elevated total cholesterol, diabetes, elevated insulin, and elevated glucose, which all, in turn, increase the overall risk for CVD (Denke et al., 1993; Report of the Surgeon General, 1996). Obesity, however, has recently been shown to independently increase the risk for CVD (Yusuf et al., 1998) and is becoming increasingly recognized as an independent risk factor for CVD (Eckel and Krauss, 1998). Elevated abdominal fat, often seen in groups of adults with a high risk for CVD (Folsom et al., 1989; Lemieux et al., 1994; Rissanen et al., 1997; Van Gaal, Vansant, and Leeuw, 1989; Zamboni et al., 1992), has been shown to be closely associated with a cluster of health conditions related to CVD (Avellone et al., 1994; Despres, 1993; Hauner et al., 1990; Jern, 1992; Peiris et al., 1989). The cluster of health conditions, known as the insulin resistance syndrome (IRS), is becoming increasingly recognized as a possible underlying cause of CVD in industrialized nations (Despres, 1996).
IRS, which typically precedes CVD, includes CVD risk factor components, which include elevated abdominal visceral fat accumulation, elevated fasting insulin, elevated fasting glucose, hypertriglyceridemia, increased number of small dense LDL particles, hypertension, decreased HDL cholesterol concentration, and endocrine abnormalities (Bjorntorp, 1997; Despres, 1996; Marin and Bjorntorp, 1993; Reaven, 1994). The combination of insulin resistance, elevated abdominal visceral fat, and the endocrine abnormalities lead to elevated insulin levels, elevated glucose levels, increased number of small dense LDL particles, hypertriglyceridemia, hypertension, and decreased HDL cholesterol concentration, which accelerate atherosclerotic plaque formation and may increase the risk for CVD events (Bjorntorp, 1997; Despres, 1996; Lindahl, Asplund, and Hallmans, 1993; Reaven, 1994; Ross et al., 1999; Vanhoutte and Boulanger, 1995).

The Insulin Resistance Syndrome and Cardiovascular Disease Risk

The development and progression of the IRS is not completely understood, but the main component of the IRS, insulin resistance, along with visceral fat accumulation and the endocrine abnormalities may perpetuate the syndrome (Bjorntorp, 1997; Despres, 1996; Marin and Bjorntorp, 1993; Reaven, 1994). The components of the IRS may also lead to an elevated CVD risk profile, increasing the risk for a CVD event (Despres, 1996). Elevated plasma insulin levels stimulate FFA and triglyceride uptake by the liver, which lead to elevated apolipoprotein B and VLDL production and secretion resulting in an increase in total cholesterol levels (Despres, 1996; Lindahl et al., 1993; Reaven, 1996). The elevated VLDL cholesterol levels within the circulation are often converted to LDL cholesterol, increasing the number of circulating small dense LDL particles (Tchernof et al., 1996) and decreasing HDL2 cholesterol levels (Despres, 1989). Elevated small dense LDL cholesterol particles have been associated with an increased risk for a CVD event (Tchernof et al., 1996), while low HDL cholesterol levels are associated with an elevated risk for CVD (Bass Miller et al., 1993). Elevated insulin and
glucose levels also adversely affect many of the CVD risk factors and may lead to other conditions, such as insulin resistance, glucose intolerance, NIDDM (Gerstein, 1997; Haffner, 1996; Lindahl, Asplund, and Hallmans, 1993), peripheral vascular resistance (Jern, 1992), elevated blood pressure (Swislocki, 1990), hypertriglyceridemia (Gerstein, 1997), and dyslipidemia (Lindahl et al., 1993; Reaven, 1996).

Visceral adipocytes have an increased lipid turnover as compared to other lipid stores within the body (Despres, Ferland, and Moorjani, 1989; Hoffstedt, Wahrenberg, Thorne, and Lonnqvist, 1996). As visceral fat accumulates there is an increase in free fatty acid (FFA) flux to the liver via the hepatic portal vein (Carey et al., 1996; Ivy, 1997; Jensen, et al., 1989; Kooner et al., 1998). An increase in FFA flow to the liver can lead to a decreased hepatic insulin extraction, an increase in hepatic triglyceride production, increased hepatic VLDL production and secretion, increased apolipoprotein B production and secretion, and increased hepatic glucose output (Carey et al., 1996; Despres et al., 1989; Hoffstedt et al., 1996; Kooner et al., 1998), resulting in elevated plasma insulin levels and glucose levels (Bjorntorp, 1997). The elevated glucose levels further stimulate the pancreas to secrete insulin, which further increase the plasma insulin levels. Prolonged elevated plasma insulin levels may also result in many cells to become resistant to insulin (Ivy and Kuo, 1998). Insulin also stimulates the FFA uptake in the adipocytes causing the adipocytes to enlarge, making the adipocytes more resistant to insulin, which leads to a greater lipid turnover and a continued FFA flux to the liver, which may further perpetuate the insulin resistance and visceral fat accumulation (Carey et al., 1996; Despres, 1993; Laws et al., 1997).

It is not known for sure what initiates the visceral fat accumulation. It has been proposed to be the result of elevated testosterone levels in women, decreased testosterone levels in men, low growth hormone levels (or low insulin-like growth factor 1), and elevated cortisol levels (Bjorntorp, 1997; Haffner, 1996; Marin and Bjorntorp, 1993; Phillips, Pinkernell, and Jing, 1997). Psychosocial stress may
increase cortisol levels, which may result in elevated abdominal obesity and increased insulin resistance (Marin et al., 1992; Bjorntorp, 1993; Bjorntorp, 1997). Psychosocial stress has also been associated with increased CVD risk and CVD events (Linden et al., 1996). An abnormal response to stress may also increase cortisol levels, which may lead to an abdominal fat distribution and the clustering of the IRS components (Bjorntorp, 1993). Elevated abdominal visceral fat, through its affects the liver and through insulin resistance is the likely mediator of the clustering of the CVD risk factor components of the IRS, such as elevated insulin, elevated blood pressure, elevated triglycerides, elevated small dense LDL particle numbers, and the low HDL cholesterol levels (Reaven, 1993; Swislocki, 1990). An abdominal fat distribution has frequently been associated with insulin resistance, high fasting insulin levels, glucose intolerance, high free fatty acid levels, high triglyceride levels, high apolipoprotein B levels, low HDL cholesterol levels, and high blood pressure levels (Carey et al., 1996; Folsom et al., 1989; Hoffstedt et al., 1996; Jensen et al., 1989; Peiris et al., 1989; Rissanen et al., 1997; Van Gaal 1989; Zamboni et al., 1992). An abdominal fat distribution has also been reported to be associated with high fibrinogen levels, and high plasminogen activator inhibitor levels, other fibrinolytic markers for CVD risk (Avellone et al., 1994).

**Energy Balance and the Insulin Resistance Syndrome**

A balance between energy consumed and energy used during the day is very important to reduce the risk of developing high amounts of total body fat or abdominal visceral fat (Eckel and Crouse, 1998; Leon, 1989; Ravussin and Gautier, 1999). Body fat and abdominal visceral fat may increase when the amount of energy consumed is greater than the amount of energy used during the day (Eckel and Crouse, 1998; Leon, 1989; Ravussin and Gautier, 1999). Individuals with particular endocrine profiles, such as elevated testosterone in women, low testosterone in men, elevated cortisol, low growth hormones, may be more prone to distribute adipose tissue in the abdominal region (Bjorntorp, 1997; Marin and Bjorntorp, 1993).
Elevated body fat and elevated abdominal visceral fat can lead to many health conditions including, diabetes mellitus, insulin resistance, elevated cholesterol profiles, and orthopedic impairments (Leon, 1989; Pouloit et al, 1994; Zamboni et al., 1992). Decreasing the amount of energy consumed and increasing the amount of energy used during the day through participating in physical activity and reducing the total caloric intake are two ways to equalize the daily energy balance and reduce the risk of developing obesity or abdominal obesity (Dausch, 1992; Leon, 1989; Leon et al., 1979; Tremblay, 1995). Lowering the amount of calories consumed through reducing the total fat intake and increasing daily energy expenditure through regular physical activity may also decrease the progression of atherosclerosis and risk for CVD (Schuler et al., 1992). High levels of physical activity are also beneficial in reducing the risk for CVD due to the CVD risk factor components of the IRS (Despres, 1996; Goodyear and Kahn, 1998; Ivy and Kuo, 1998; Wojtaszewski and Richter, 1998)

Total dietary caloric intake is also very important for balance between energy consumed and energy used, as an elevated total dietary intake may cause increases in body fat and abdominal visceral fat (Anderssen et al., 1998; Leon, 1989; Tremblay, 1995). A high total fat intake, which may increase total caloric intake, may also increase total body fat (Dausch, 1992; Shrapnel et al., 1992; Tremblay, 1995). A high total fat intake has also been positively associated with elevated fasting insulin levels, elevated total body fat, and elevated abdominal visceral fat (Anderssen et al., 1998, Rankinen et al., 1997). An elevated fat intake and low fruit and vegetable intake may also results in elevated total and LDL cholesterol levels and an increased risk for a CVD event or CVD death (Rimm et al., 1996; Schaefer et al., 1996; Shrapnel et al., 1992; Wolk et al., 1999). A reduction in the total fat intake would likely lower the risk for obesity and likely lower the risk for developing abdominal fat accumulation (Wing et al., 1998).
Physical Activity and Exercise and Cardiovascular Disease Risk

One of the major modifiable behavioral risk factors for CVD is physical activity (Pate et al., 1995; Surgeon General’s Report, 1996). Physical activity and exercise can improve insulin resistance, positively effect the other components of the IRS, and improve the overall CVD risk profile (Bjorntorp, Jounge, Sjolstrom, Sullivan, 1970; Goodyear and Kahn, 1998; Ivy, 1997; Ivy and Kuo, 1998; King et al., 1995; Mayer-Davis et al., 1998; Report of the Surgeon General, 1996). High physical activity levels and endurance exercise training have been shown to be associated with reductions in insulin resistance and reductions in glucose intolerance (Goodyear and Kahn, 1998; Ivy, 1997; Mayer-Davis, 1998; Rankinen et al., 1997; Wojtaszewski et al., 1998), low total cholesterol (Leon, 1991), low triglyceride levels (Crouse et al., 1997), lower total body fat (Ching et al., 1996), low abdominal fat Anderssen, Holme, Urdal, and Hjermann, 1998; Tremblay et al., 1990), low blood pressure (Blair et al., 1984; Leon, 1991) and reduced incidence of NIDDM (James et al., 1998; Krista, Blair, and Pereira, 1994).

Total HDL cholesterol levels may also increase with regular endurance exercise (Eriksson et al., 1998; Wood and Haskell, 1979) and often there is an increase in the HDL2 subfraction (Crouse et al., 1997; Lamarche et al., 1992). The HDL2 subfraction plays an important role in the complex process of delivering cholesterol from the body to the liver for conversion to bile acids, which may lower the total cholesterol levels within the body (Berne and Levy, 1993).

Many of the CVD related health improvements due to physical activity and exercise can be attributed to improvements in insulin regulation and its subsequent effects on the components of the IRS and CVD risk factors (Bjorntorp et al., 1970; Bjorntorp, 1997; Despres, 1996; Reaven 1995). During exercise, the skeletal muscle cells have an increased sensitivity to insulin and glucose uptake, which allows for greater glucose uptake by the skeletal muscle cells and increased binding of insulin to the receptors (Ivy and Kuo, 1998). The increased insulin sensitivity and glucose uptake temporarily lowers the glucose and insulin levels (Ivy and Kuo,
The increased insulin sensitivity continues after exercise and results in a temporary increase in insulin sensitivity of the skeletal muscles cells that may last up to seven to ten days after a session of vigorous exercise (Ivy, 1997; Ivy and Kuo, 1998; Goodyear and Kahn, 1998, King et al., 1998). The increase in insulin sensitivity due to an acute exercise bout even occurs in adults with known insulin resistance (Goodyear and Kahn, 1998). Regular low intensity physical activity also increases insulin sensitivity and reduces fasting insulin levels (Mayer-Davis, 1998; Rankinen, et al., 1997). There appears to be a strong direct relationship between the intensity and amount of physical activity and the level of insulin sensitivity (Mayer-Davis, 1998; Rankinen, et al., 1997). Low physical activity levels represent one important behavioral risk factor, which may be increased to be protective against CVD.

**Dietary Intake and Cardiovascular Disease Risk**

Another major modifiable behavioral risk factors for CVD is dietary intake. Elevated fat intake and low fruit and vegetable intake may results in elevated serum cholesterol levels and an increased risk for CVD (Renaud and Lorgeril, 1994; Schaefer et al., 1996; Shrapnel et al., 1992). Lowering total fat intake, saturated fatty acid (SFA) intake, trans fatty acid (TFA) intake, cholesterol intake, and substituting monounsaturated fatty acids (MUFA) or polyunsaturated fatty acids (PUFA) for SFA may all decrease the risk for CVD (Grundy and Vega, 1988; Mattson and Grundy, 1985; Mensink and Katan, 1989; Mensink and Katan, 1990). Higher fiber intake through fruit and vegetable intake is also associated with a decreased risk for CVD events and CVD deaths (Renaud and Lorgeril, 1994; Rimm et al., 1996; Wolk et al., 1999).

Since diet has a great influence on serum cholesterol levels it is essential to target diet as one of the main combatants against CVD (Grundy and Vega, 1988; Mattson and Grundy, 1985; Mensink and Katan, 1989; Mensink and Katan, 1990). The relationship between serum cholesterol levels and coronary heart disease (CHD)
risk appears to be a strong, continuous, graded relationship over the entire range of cholesterol levels (Renaud and Lorgeril, 1994; Shrapnel et al., 1992). Shrapnel et al. (1992) stated that high serum cholesterol levels are causally related to CHD and that “the mean level of serum cholesterol is the most significant determinant of population risk for CHD.”

The equation developed by Keys, Anderson, and Grande (1965), which predicts the change in serum cholesterol levels with changes in dietary fat intake, suggests changes in dietary SFA result in the greatest change in serum cholesterol levels. The trend of a decreasing dietary fat and cholesterol intake coupled with the trend of decreasing serum cholesterol and lipid levels over the last three National Health and Nutritional Examination Surveys supports the positive association between dietary fat intake and serum cholesterol levels (Ernst et al., 1997). Population reductions in percent of total energy intake from total fat, SFA, MUFA, and cholesterol, along with increases in dietary PUFA, also coincided with reductions in population total cholesterol levels (Graves et al., 1993). Reductions in total dietary fat intake would likely reduce the risk for CVD through lowering total and LDL cholesterol levels.

A high total fat intake may also affect CHD indirectly by possibly increasing SFA intake, increasing total caloric intake, and increasing total body fat (Shrapnel et al., 1992). A high total fat intake has also been positively associated with elevated fasting insulin levels, elevated total body fat, and elevated abdominal visceral fat (Anderssen, Holme, Urdal, Hjermann, 1998, Rankinen et al., 1997). A reduction in the total fat intake would likely lower the overall risk for CVD due to the influence of the CVD risk factor components of the IRS. A low calorie, low fat diet aimed at reducing total body weight resulted in reductions in serum total cholesterol, LDL cholesterol, HDL cholesterol, blood pressure, fasting insulin levels, and fasting glucose levels (Wing et al., 1998).

Even though each individual’s change in serum cholesterol levels widely vary with changes in dietary fat intake (McNamara et al., 1987), the type of fat that
is consumed in the diet greatly influence the risk for CVD (Grundy and Vega, 1988; Hatton et al., 1996; McCarron et al., 1997; Mattson and Grundy, 1985; Mensink and Katan, 1989; Mensink and Katan, 1990). Reduction of the energy intake due to SFA may represent the single most effective dietary modification to lower serum cholesterol levels (Shrapnel et al., 1992). Reducing total dietary fat intake and SFA intake may also lower the risk for CVD by reducing many of the CVD risk factor components of the IRS and the traditional CVD risk factors (Hatton et al., 1996; McCarron et al., 1997) and may also reduce the risk of CVD deaths (Renaud and Lorgeril, 1994). Serum total cholesterol levels, LDL cholesterol levels, triglyceride levels, blood pressure, weight, fasting glucose levels, and fasting insulin levels, were all reduced in individuals with elevated CVD risk or general CVD through a low total fat and SFA diet (Hatton et al., 1996; McCarron et al., 1997). With a more severe reduction of total dietary fat (≤10% of total caloric intake) along with a recommended physical activity program, the narrowing of coronary arteries was reversed and the number of heart attacks were significantly lower than controls in adults with previous severe CVD diagnosis (Ornish et al., 1998).

The exchange of other types of fatty acids for SFA in the diet have been shown to lower serum cholesterol levels and decrease the risk for CVD (Gordon, Slaz, Roggenkamp, and Franklin, 1982; Mensink and Katan, 1989; Renaud et al., 1986; Schaefer et al., 1996). Mensink and Katan (1989) reported decreases in total cholesterol levels, LDL cholesterol levels, and apolipoprotein B levels after SFA were replaced by PUFA in the diet. The consumption of n-6 PUFA instead of SFA has also been shown to lower the LDL and HDL cholesterol levels (Gordon et al., 1982). Decreased platelet aggregation and clotting activity has also been associated with substituting PUFA for SFA in the diet (Renaud et al., 1986). The replacement of SFA with n-3 PUFA within the diet has been shown to decrease the risk for CHD by lowering total cholesterol, lowering VLDL cholesterol, lowering serum triglyceride levels, decreasing platelet aggregation, decreasing blood pressure,
increasing bleeding time, and altering lipoprotein metabolism (Illingworth, Harris, and Conner, 1984; Schaefer et al., 1996).

MUFA traditionally have been reported to have a neutral effect on serum cholesterol levels (Shrapnel et al., 1992). Replacing dietary SFA with MUFA, however, has been shown to reduce serum total cholesterol levels, LDL cholesterol levels, and apolipoprotein B levels (Mattson and Grundy, 1985; Mensink and Katan, 1989). An increase in dietary trans fatty acids (TFA) have been shown to increase total cholesterol levels, increase LDL cholesterol levels, increase triglyceride levels, increase apolipoprotein B levels, and decrease HDL cholesterol (Mensink and Katan, 1990; Willett et al., 1993). An high intake of TFA has also been directed associated with an elevated risk for CVD independently of traditional, established CVD risk factors (Willett et al., 1993).

Changes in dietary cholesterol intake were also associated with changes in CHD risk (Gartside and Glueck, 1995). High intakes of dietary cholesterol may raise serum total and LDL cholesterol, but to a lesser extent than SFA (Shrapnel et al., 1992). A high dietary cholesterol intake has also been reported to be associated with elevated fasting insulin levels (Rankinen et al., 1997).

Diets aimed at reducing the total energy intake and the total fat intake may result in reducing total body weight, serum total cholesterol, LDL cholesterol, blood pressure, fasting insulin levels, and fasting glucose levels (Wing et al., 1998). Unfortunately HDL cholesterol may also be reduced through low fat diets (Wing et al., 1998). As high levels of physical activity or exercise may increase HDL levels (Eriksson et al 1998; Wood and Haskel, 1979), the reduction of HDL cholesterol through diet may be counteracted by the addition of physical activity to a low fat diet program (Schuler et al., 1992; Wood et al., 1991). Reducing total dietary fat intake and saturated fatty acid intake may also lower the risk for CVD by reducing many of the CVD risk factor components of the IRS (Hatton et al., 1996; McCarron et al., 1997; Schuler et al., 1992). Fasting insulin levels, fasting glucose levels, triglyceride levels, blood pressure, and weight were all reduced in individuals with
elevated CVD risk or general CVD through a low total fat and saturated fatty acid diet (Hatton et al., 1996; McCarron et al., 1997; Schuler et al., 1992).

**Psychosocial Stress and Cardiovascular Disease**

High levels of psychosocial stress have been associated with increased risk for CVD and CVD events (Jain, Burg, Soufer, Zaret, 1995; Jiang et al., 1996, Linden et al., 1996). Specifically, the anger, anxiety, hostility, and depression areas of stress have been associated with increased risk for CVD (Barefoot et al., 1983; Embroski et al., 1985; Fasure-Smith, 1995). Psychosocial stress is thought to contribute to the risk of CVD independently (NHLBI Review Panel, 1981) and also through its affects on the risk factors for CVD, such as, elevated blood pressure, elevated cholesterol levels, and elevated heart rate (Linden et al., 1996). Psychosocial stress may also increase the risk for CVD due to the CVD risk factor components of the IRS and abdominal obesity through increasing cortisol levels (Marin et al., 1992; Rosmond and Bjorntorp, 1998). Psychosocial stress may also elevate cortisol levels, which may increase heart rate, blood pressure, insulin resistance, total and LDL cholesterol levels, and abdominal fat distribution (Becker et al., 1988; Marin et al., 1992; Rosmond and Bjorntorp, 1998; Rosmond, Dallman, Bjorntorp, 1998). The addition of psychosocial treatments to traditional treatments of CVD has also been shown to decrease the overall morbidity and mortality of CVD, decrease blood pressure, and decrease total and LDL cholesterol in patients with CVD (Barefoot et al., 1983; Blumenthal et al., 1997; Linden et al., 1996). Further investigation into the mechanisms of psychosocial stress and CVD need to be examined.

**Cardiovascular Disease in Adults with Mental Retardation**

There has been a progressive decline in CVD deaths over the last thirty years in the United States (AHA, 1994). This decline in the proportion of all deaths due to CVD and the decline in risk factors associated with CVD are likely due to the
improvements in the understanding of CVD risk factors and the public’s knowledge of the importance of healthier living. This is evidenced by an overall decrease in the average American’s total serum cholesterol levels over the last 30 years (Ernst, et al., 1997). The reductions in total cholesterol and LDL cholesterol are indicators that the American public has reduced its total fat intake and saturated fat intake, which reduces the risk for CVD (Ernst et al., 1997). Unfortunately, for individuals with mental retardation (MR) there has not been a decrease in the proportion of overall deaths due to CVD, but instead, a steady increase in the proportion of deaths due to CVD from 1930 to 1980 (Carter and Jancar, 1983) with a leveling off of CVD deaths from 1984 to 1993 (Janicki, Dalton, Henderson, Davidson, 1999). Why this phenomenon has occurred has not been studied and is not well understood.

The American Heart Association recognizes the importance of screening for risk factors for CVD in individuals who may be at a high risk for CVD (Grundy et al., 2000; Smith et al., 2000). The importance of screening for adults with MR who are at a high risk for disease has also emerged as a necessary step to identify needed health and nutrition services (Blyler and Lucas, 1992; Day and Jancar, 1994; Wells, Turner, Roy, 1997). Identification of individuals who are at a high risk for CVD and implementing primary prevention strategies aimed at reducing CVD risk is an extremely important concept for adults with MR and DS for three major reasons.

1.) Primary prevention is important to reduce the economic cost of treating CVD for all individuals and especially for those with MR. We know that the economic burden of treating CVD every year is extremely high in the United States (American Heart Association, 1997). When considering that adults with MR have an elevated CVD prevalence above those without MR (Beange et al., 1995; Janicki and MacEachron, 1984; Janicki and Jacobson, 1986) and when considering the fact that the majority of health care of individuals with MR is provided by government funded agencies (McDermott, Platt, Krishnaswami, 1997), the economic burden on society due to CVD treatment for the population of adults with MR may be even greater than a similar population of adults without MR (Braddock, 1999).
with MR are now living longer than in the past and possess a high risk for CVD the number of individuals needing government funded health care and services will increase, especially for those without preventative CVD strategies (Janicki et al., 1999; Janicki and MacEachern, 1984). 2.) The ability of adults with MR to communicate the early signs and symptoms of CVD to their physicians and care providers is impaired (McDonald et al., 1985; Reis and Szysko, 1983), which may decrease their chances of getting early treatment and reduce their likelihood of avoiding or fully recovering from a CVD event. Identifying those at a high risk for CVD and slowing the progression of CVD through primary prevention strategies may decrease the importance of adults with MR to recognize and communicate signs and symptoms of a CVD event to their care provider or physician. Physician diagnosed chronic conditions and health behaviors in adults with MR were recently reported to be less prevalent than in those without MR (McDermott, Platt, Krishnaswami, 1997). McDermott et al., (1997) concluded that adults with MR truly had less chronic conditions than adults without MR (McDermott, Platt, Krishnaswami, 1997). The less frequent diagnosis of chronic conditions, however, is more likely due to a diagnosis bias by the physicians and not actually the result of less health conditions in adults with MR (McDonald 1985; Reis and Szysko, 1983). Under diagnosis of health conditions in adults with MR is supported by Beange et al. (1995), who reported that approximately one half of the medical conditions, which were detected in a health screening, were not previously diagnosed in adults with MR. 3.) Because adults with MR often do not possess the cognitive abilities to drive automobiles or work in mentally challenging employment settings, adults with MR rely on their functional physical capacity for transportation and employment, such as walking, biking, and using public transportation systems, and working in physical labor type jobs. Due to the reliance on physical ability for transportation and employment, the physical health of adults with MR is extremely important for successful integration into the community. Early identification of individuals with
MR who are at a high risk for CVD and implementation of primary prevention strategies will help ensure continued participation in the community.

One possible explanation of the increased proportions of deaths due to CVD in adults with MR over the last 60 years may be due to a greater proportion of adults with MR living longer and living in communities with less direct supervision, allowing for sedentary lifestyles and high fat dietary intakes, similar to many Americans (Carter and Jancar, 1983; Pitetti, 1993). Since the de-institutionalization of adults with MR there has been a greater proportion of adults with mild MR living in small group homes, with families, or independently within their communities (Kraus and Seltzer, 1986). With less direct supervision and less nutritional guidance, adults with MR living within the community likely have adversely changed their health behaviors.

Unfortunately, complete CVD risk profiles have not been reported for adults with MR residing in institutional or community settings. Previous research groups have only reported subsets of traditional physiological and behavioral CVD risk factors. The traditional physiological risk factors for CVD which have been reported include cholesterol profiles (Eastham and Jancar, 1969; Rimmer, Braddock, and Fujiura, 1994; Rimmer, Braddock and Marks, 1995), hypertension (Beange et al., 1995; Rimmer et al., 1994), and obesity (Beange, McEllduff, and Baker, 1995; Fox and Rotatori, 1983; Kelly, Rimmer, and Ness, 1986; Rimmer, Braddock, and Fujiura, 1993). The behavioral risk factors for CVD that have been reported for adults with MR include nutritional intake (Chad, Jobling, and Frail, 1990; Cunningham, Gibney, Kevay, and Mulchaney, 1990; Litchford and Wakefield, 1985; Mercer and Ekvall, 1992; Wilton and Irvine, 1983), exercise or physical activity level (Compton, Eisenman, and Henderson, 1989; Fernhall, 1993; Fernhall, Tymeson, and Webster, 1988; Fernhall et al., 1996; Moon and Renzaglia, 1982; Pitetti, Rimmer, and Fernhall, 1993), smoking status (Beange et al., 1995; Rimmer et al., 1994; Rimmer et al., 1995), and alcohol intake (Beange et al., 1995; Rimmer et al., 1995). No studies have examined the clustering of the CVD risk factors
components of the IRS in adults with MR. No studies have evaluated the relationships between behavioral risk CVD factors and the CVD risk factor components of the IRS in adults with MR residing in community settings.

The reported cholesterol levels of adults with MR in different living settings over the last 30 years support an adverse change in health behaviors since the de-institutionalization movement in the 1970's. Eastham and Jancar (1969) reported that serum cholesterol levels of adults with mental retardation residing in a large institutional setting were considerably lower than the general public. Rimmer et al. (1994) later reported individuals with MR residing in group homes or family settings had considerably higher total cholesterol levels, LDL cholesterol levels, and serum triglyceride levels than individuals residing in larger institutions. The CVD risk profiles of adults with MR residing in the community settings were also reported to be similar to the CVD risk profiles of adults without MR (Rimmer et al., 1994). Rimmer et al. (1995) later reported that adults with MR residing in group home or family settings exercised less frequently, smoked more frequently, drank alcohol more frequently, and drank coffee more frequently than adults with MR residing in institutional settings. Adults residing in family settings also had the highest percent body fat (Rimmer et al., 1995). The elevated CVD risk factors of adults with MR residing in community settings are likely due to elevated behavioral risk factors, such as low physical activity levels and high dietary fat intake, which may potentially be modified to decrease the overall risk for CVD.

The increases in elevated CVD risk profiles since the institutional era have likely lead to the increase in CVD mortality for adults with MR living in community settings. Strauss and Kastner (1996) reported that after adjusting for age, gender, and motor skills adults with MR residing in community settings have a 72% higher overall mortality risk than adults with MR residing in institutional settings. Adults with MR residing in community settings also had a higher prevalence of CVD (42%) than adults with MR residing in institutions (32%) (Janicki and MacEachron, 1984; Janicki and Jacobson, 1986). Beange et al. (1995) reported that adults with MR
have a higher mortality rate with significantly greater prevalence of no physical activity, obesity, and hypertension, above national standards for adults without MR in Australia. It is likely that adults with MR residing in community settings in the United States would have similar mortality risk and CVD risk as the adult with MR in Australia due to the majority of adults with MR from Australia residing in similar community settings (Beange et al., 1995).

Because of their cognitive capacity and physical abilities to perform the necessary skills to live on their own, adults with mild MR are more likely to live in community settings than adults with severe/profound MR (Kraus and Seltzer, 1986). Adults with mild/moderate MR also have been reported to have a higher prevalence (55%) of CVD than adults with severe/profound MR (26%) (Janicki and MacEachron, 1984; Janicki and Jacobson, 1986). The high mortality rates, CVD prevalence, and obesity rates in adults living in community settings and adults with mild MR are likely related to modifiable behavior risk factors for CVD, such as low physical activity levels, high dietary fat intake, and low fruit and vegetable intake, which lead to adverse health conditions. Adults with mild MR and adults residing in community settings likely have more freedom to make recreation and dietary choices compared to adults with severe/profound MR and adults residing in institutional settings, whose dietary intakes and recreational activities are determined by care providers and administrators. Similar to the national population without MR (Crespo et al., 1996; Ernst et al., 1997), adults with MR residing in community settings have likely chosen lifestyles consisting of low physical activity levels and a dietary intake consisting of a high percentage of fat.

Obesity typically results from an uneven balance between energy consumed through dietary intake and energy expended throughout the day through physical activity and resting energy requirements (Leon et al., 1989). Low physical activity levels and high dietary fat intakes would contribute to an uneven energy balance, which may result in high levels of total body fat. As assessed by skinfold prediction equations, which were validated for individuals with MR (Rimmer et al., 1987),
Kelly et al. (1986) reported that 45.2% of the men with MR and 50.5% of the women with MR residing in a state school were classified as obese. The frequency of obesity was lowest in adults with severe and profound MR and greatest in adults with mild and moderate MR. Fifty-six percent of the men with mild MR were obese and 74% of the women with mild MR were obese (Kelly et al., 1986). Rimmer et al. (1993) examined percent body fat through the skinfold equations (Rimmer et al., 1987) in adults with MR residing in different living settings. Adults with MR residing in the institutional settings had the lowest levels of body fat and the lowest frequency of obesity among men and women with MR living in all residential settings. The individuals with mild (46.5%) and moderate MR (53.2%) also had a considerably higher frequency of obesity than adults with severe MR (29.4%) (Rimmer et al., 1993). Regardless of living setting, men and women with MR both have a higher prevalence of obesity as compared to men and women without MR (Fox and Rotatori, 1982; Rimmer et al. 1993). Fox and Rotatori (1982) also investigated obesity prevalence in adults with MR and reported that the prevalence of obesity increased considerably with age for both men and women with MR. The high obesity levels of adults with mild MR or adults with MR residing in community settings are likely due to some combination of low physical activity levels and elevated energy intakes, which likely contain high dietary fat intakes.

Few studies have reported the dietary intake of adults with MR. Most studies investigating the nutritional status in individuals with MR have focused on the malnutrition of adults with severe/profound MR residing in institutional settings, who often are underweight (Hals, Ek, Svalastog, and Nilsen, 1996; Kennedy et al., 1997). Considering that adults with mild MR and adults with MR residing in community settings have a such a high prevalence of obesity, it seems likely that nutritional differences exist between adults residing in institutional and community settings (Fox and Rotatori, 1982; Kelly et al., 1986; Rimmer et al., 1993). Adults with mild MR residing in community settings consumed diets with relatively high total energy intakes (Mercer and Ekvall, 1992), possibly due to high fat intakes.
Chad et al. (1990) reported that adults with MR were consuming diets in which over 42% of the calories consumed were from fat intake. The national average percent fat for adults without MR for the same time period was only about 34% (Ernst et al., 1997). The elevated fat intake has likely contributed to the high prevalence of obesity in adults residing in community settings. A reduction in total dietary fat and saturated fat intake reduced the weight, serum triglyceride levels, and serum cholesterol levels in obese adults with MR, indicating that elevated fat intakes may play an important role in the high prevalence of obesity and CVD risk factors in adults with MR (Antal et al., 1988). The dietary intake of individuals with MR residing in institutions are positively influenced by the paraprofessionals that work with the residents allowing for a closer evaluation of the type of diet consumed (Litchford and Wakefield, 1985). Without direct daily supervision it is likely that adults with MR residing in the community have a greater opportunity for higher dietary fat intakes than they would with more nutritional supervision. Dietary fat intake is another important behavioral risk factor for CVD, which can be modified to improve the overall health and risk for CVD. Unfortunately, the dietary at intakes and the influence of elevated dietary fat intakes on the CVD risk factor components of the IRS, traditional CVD risk factors, and obesity have not been closely examined in adults with MR residing in community settings.

Another possible explanation for the overall increase in CVD prevalence and the elevated mortality risk for adults with adults with MR may be due to the fact that adults with MR are living longer now than they have in the past 60 years (Braddock, 1999; Carter and Jancar, 1983; Janicki et al., 1999). Considering that CVD is a progressive disease that starts early in life and progresses with age (Berenson et al., 1987), it is likely that there would be an increase in deaths due to CVD in adults with MR who are living longer and potentially have an increased CVD risk profile (or more progressive state of CVD). Janicki and Jacobson (1986) reported that CVD was the most prevalent chronic disease condition that increased the greatest with age (over any other disease) in older adults with MR. The
increased average age of death has likely resulted in the increased proportion of
deaths over the last 60 years due to myocardial infarctions and cerebral vascular
accidents in adults with MR (Carter and Jancar, 1983; Day and Jancar, 1994).

No studies have examined the relationship of low physical activity levels
with the risk for CVD in adults with MR. Beange et al., (1995) reported that adults
with MR engaged in significantly less vigorous physical activity than other adults
without MR. Cardiovascular fitness of adults with mental retardation (MR) have
also been consistently reported to be lower than adults without mental retardation
(Compton, Eisenman, and Henderson, 1989; Fernhall, 1993; Fernhall, Tymeson, and
Webster, 1993; Fernhall et al., 1996; Moon and Renzaglia, 1982; Pitetti, Rimmer,
and Fernhall, 1993). Even though measuring cardiovascular fitness may include
genetic determinants of aerobic fitness it also provides an indication of the physical
activity or exercise habits of the participants. Typically, cardiovascular fitness
increases with the amount or intensity of physical activity or exercise. Individuals
with high physical activity levels typically have higher cardiovascular fitness levels
than individuals with low physical activity levels. The low cardiovascular fitness
levels of adults with MR likely indicate low physical activity levels, a behavioral risk
factor for CVD that could be increased to improve CVD risk. The cardiovascular
fitness levels of adults with MR have been reported to improve with exercise
training (Croce, 1990; Fernhall, 1993; Pommering et al., 1994) and have even been
shown to equal individuals without MR in highly trained runners with MR (Frey et
al., 1999). Programs or interventions designed at increasing their physical activity
levels and improving cardiovascular fitness of adults with MR would likely improve
their overall CVD risk profile.

**Cardiovascular Disease Risk in Adults with Down Syndrome**

The manifestation of Down syndrome (DS), which is caused by a trisomy of
chromosome 21, typically includes mental retardation of varying degrees, muscular
hypotonia, short stature, high body fat, typical facies, delayed or incomplete sexual
development, and congenital heart defects (Bronks and Parker, 1985; Chumlea and Cronk, 1981; Tolksdorf and Weidemann, 1981). Interestingly, adults with DS have been reported to have less CVD even though they possess similar low physical activity levels and elevated dietary fat intakes of other adults with MR (Brattstrom, England, Brun, 1987; Chad et al., 1990; Murdoch, Rodger, Rao, Fletcher, Dunnigan, 1977; Yla-Herttuala, Luoma, Nikkari, and Kivimaki, 1989). Murdoch et al. (1977) conducted postmortem artery examinations on five adults with DS and five adults with MR (non-DS) that resided in an institutional setting (aged 40-66). Atherosclerosis in aorta, femoral, carotid, and coronary arteries was absent in all five adults with DS, while two of the younger adults with MR had mild atherosclerosis and the three older adults with MR had severe atherosclerosis in the same arteries. Though the control group (adults with MR without DS) was not age matched with the adults with DS it is very likely that adults with DS have considerably lower atherosclerosis than adults with MR because older and younger adults with MR had considerably greater atherosclerosis than adults with DS. A determination of cholesterol levels and blood pressure of other residents within the same institution where the subjects of the postmortem examinations resided, revealed that the adults with DS generally had similar cholesterol levels, but lower blood pressure than adults with MR (Murdoch et al., 1977). Other postmortem studies reported similar results. Yla-Herttuala et al. (1989) also reported that adults with DS had significantly less area of the coronary arteries covered by raised atherosclerosis, lower mean arterial calcium concentration, and lower mean arterial esterified cholesterol than age-matched adults with MR and normal controls. Brattstrom et al. (1987) also reported a decreased incidence of atherosclerosis and atheromas in a group of older adults (aged 42-66) with DS. Why adults with DS do not develop atherosclerosis in a similar way to others with MR is not known. There appears to be similar traditional CVD risk factors in adults with MR and DS other than hypertension (Murdoch et al., 1977; Yla-Herttuala et al., 1989). No
researchers have investigated the clustering of the IRS in adults with DS to determine if adults with DS may have a protective IRS risk factor profile.

Similar cholesterol levels between adults with MR and DS along with higher triglyceride levels in adults with DS than adults with MR have been consistently reported (Lacko et al., 1983; Nishida, Akaoka, Nishizawa, Maruka, Maruka, 1977; Pueshel, Craig, Haddow, 1992; Salo, Solakivi-Jaakkola, Kivimaki, Nikkari, 1979). Nishida et al. (1977) reported that children with DS had elevated plasma triglyceride levels as compared to children with MR without DS but similar plasma cholesterol, phospholipid, and free fatty acids levels. Salo et al. (1979) reported that adults with DS did not have different total cholesterol, LDL, or HDL cholesterol levels than other adults with MR that resided at the same institution, however, triglyceride levels were significantly higher for adults with DS. Pueshel, Craig, and Haddow (1992) also reported young adults with DS had higher serum triglyceride levels and lower HDL and apolipoprotein A1 levels than the control group, which consisted of siblings of the participants with DS, but there were no differences in total cholesterol, LDL, and apolipoprotein B levels. Lacko et al. (1983) also reported that there were no differences in cholesterol or lipid levels between adults with DS and other adults with MR residing at the same institution.

Adults with DS have also been shown to have similar percent total body fat than adult with MR (Bronks and Parker, 1985; Chumlea and Cronk, 1981). Somewhat different than adults with MR, however, adults with DS typically develop high levels of total body fat during adolescence and maintain a high level throughout adulthood without significant increases with age (Bronks and Parker, 1985; Chumlea and Cronk, 1981). Abdominal fat distribution has not been compared between adults with MR and DS. The consistent finding of similar total cholesterol levels and total body fat in adults with MR and DS indicate that total cholesterol or total body fat is likely not an important factor for the reduced atherosclerotic plaque formation in adults with DS. Examining abdominal visceral fat and the clustering of
the CVD risk factor components of the IRS may provide some insight for the reduced development of atherosclerosis in adults with DS.

Research has been done examining individual components of the CVD risk factor components of the IRS in individuals with DS, which includes insulin and glucose regulation, and endocrine levels. Children and adults with DS had normal insulin and glucose response to an oral and intravenous glucose tolerance test (Serrano-Rios, Gayon, Soro, Rodriguez-Minon, 1973). Yashuda et al. (1979) also reported that adults with DS had normal fasting glucose and insulin levels along with normal glucose tolerance and insulin response to a glucose load. Previous research has been conducted examining individual components of the CVD risk factor components of the IRS in individuals with DS. Along with low blood pressure, adults with DS appear to have normal insulin and glucose regulation (Serrano-Rios, Gayon, Soro, Rodriguez-Minon, 1973; Yashuda et al., 1979). A few endocrine abnormalities, which may influence health and CVD risk (Reaven, 1995; Bjorntorp, 1992), have been assessed in adults with DS (Hestes et al., 1991; Kennedy et al., 1992; Murdoch, Giles, Grant, and Ratcliffe, 1979; Murdoch, Gray, McLarty, and Ratcliffe, 1978; Rooney and Rooney and Walsh, 1997). Basal cortisol levels, basal ACTH levels, and pituitary function in adults with DS appear to be normal (Murdoch, Giles, Grant, and Ratcliffe, 1979; Murdoch, Gray, McLarty, and Ratcliffe, 1978). Adults with DS had an abnormally low cortisol response to synacthen, a cortisol releasing stimulator similar to ACTH, and a high prevalence of low thyroid levels (Karlsson et al., 1998; Murdoch, Giles, Grant, and Ratcliffe, 1979; Rooney and Rooney and Walsh, 1997). Elevated cortisol is associated with elevated abdominal visceral fat and often leads to insulin resistance, two of the main components of the IRS (Reaven, 1995; Reaven, Lithell, Landsberg, 1996; Bjorntorp, 1992). Low cortisol levels in adults with DS may provide protection against CVD by reducing the likelihood of developing abdominal obesity and insulin resistance, therefore reducing the likelihood for the clustering of the CVD risk factor components of the IRS and reducing the risk for CVD (Reaven, 1995;
Reaven, Lithell, Landsberg, 1996; Bjorntorp, 1992). The low thyroid levels in adults with DS may also influence the risk for CVD (Aronow, 1995; Gomberg-Maitland and Frishman, 1998; Saadi, 1997; Williams, 1997). Low thyroid may lower cardiac output, decrease contractility, lower myocardial oxygen demand, and increase HDL cholesterol, which all may decrease the risk for CVD or a CVD event (Aronow, 1995; Gomberg-Maitland and Frishman, 1998). Low thyroid also increases total cholesterol, increases LDL cholesterol, increases triglycerides, slightly increases blood pressure, and may increase atherosclerosis development and progression, (Saadi, 1997; VanHaelst et al., 1967. Williams, 1997). The overall affect of low thyroid in adults with DS would indicate a increased risk for CVD and appears not to be protective against CVD due the CVD risk factor components of the IRS.

The reviewed research indicates that adults with DS have very similar traditional physiological CVD risk factors and total body fat as adults with MR (Bronks and Parker, 1985; Chumlea and Cronk, 1981; Lacko et al., 1983; Murdoch et al., 1977; Nishida, Akaoka, Nishizawa, Maruka, Maruka, 1977; Pueshel, Craig, Haddow, 1992; Salo, Solakivi-Jaakkola, Kivimaki, Nikkari, 1979; Yla-Herttuala et al., 1989). The clustering of the CVD risk factor components of the IRS has not been examined in adults with MR and DS. Individual factors of the IRS have been studied and have shown that individuals with DS have low blood pressure, normal insulin and glucose regulation, and low cortisol levels in response to an ACTH analog (Serrano-Rios et al., 1973; Murdoch et al., 1979; Murdoch et al., 1978; Yashuda et al., 1979), which all indicate adults with DS may possess a protective CVD related IRS profile (Reaven, 1995; Reaven, Lithell, Landsberg, 1996; Bjorntorp, 1992). Low thyroid levels in adults with DS, however, would likely increase the risk for CVD and CVD events (Vanhaelst et al., 1967). A more complete investigation of the CVD risk factor components of the IRS, the traditional CVD risk factors, and the behavioral risk factors of adults with MR and
DS may provide additional insight into the underlying mechanisms for low CVD in adults with DS.

Summary

Cardiovascular disease is the leading cause of death in the United States (AHA, 1997). The behavioral risk factors for CVD include low physical activity, smoking, psychosocial stress, and adverse dietary intake, while the physiological risk factors for CVD include unfavorable cholesterol levels, high blood pressure, age, family history of CVD, and diabetes mellitus (American College of Sports Medicine, 1995; Report of the Surgeon General, 1996). As an individual’s number of CVD risk factors increase the risk of developing CVD and having a cardiovascular event increases (Yusuf et al., 1998). The behavioral risk factors for CVD also may negatively affect the physiological risk factors for CVD, which accelerate the progression of the disease and can lead to CVD related death (Lindahl, Asplund, and Hallmans, 1993; Reaven, 1995; Report of the Surgeon General, 1996; Yusuf et al., 1998). The IRS, which typically proceeds CVD, includes health factors such as visceral fat accumulation, insulin resistance, glucose intolerance, hypertriglyceridemia, increased number of small dense LDL particles, hypertension, decreased HDL cholesterol concentration, and endocrine abnormalities (Bjorntorp, 1997; Despres, 1996; Marin and Bjorntorp, 1993; Reaven, 1994). The major behavioral risk factors, physical activity level and dietary intake, along with the components of the IRS may have the greatest influence on overall CVD risk and should be targeted for future interventions aimed at reducing CVD risk (Bjorntorp, 1997; Despres, 1996; Lindahl, Asplund, and Hallmans, 1993; Reaven, 1994; Report of the Surgeon General, 1996; Shrapnel et al., 1992).

The prevalence of CVD in adults with MR is greater and apparent earlier in life than that found in the general population (Janicki and Jacobson, 1986; Janicki and MacEachron, 1984; Rimmer, Braddock, and Fujiura, 1994; Rimmer, Braddock and Marks, 1995). Two categories of adults with MR have been identified to have
the highest risk for CVD; 1) adults with mild to moderate MR and 2) adults with MR residing in community settings (Fox and Rotatori, 1882; Kelly et al., 1986; Janicki and Jacobson, 1986; Janicki and MacEachron, 1984; Strauss and Kastner, 1996; Rimmer et al., 1993; Rimmer et al., 1994; Rimmer et al., 1995). Along with the already high prevalence of CVD in adults with MR, there is a continuing trend of an increasing proportion of total deaths due to CVD (Carter and Jancar, 1983). The trend of increasing deaths due to CVD over the last 50 years is likely related to adults with MR living longer (Carter and Jancar, 1983) combined with a greater proportion of adults living within community settings who have adverse health behaviors (Kraus and Seltzer, 1986). Adults with DS have been reported to have significantly less CVD than adults with MR even though they have relatively similar CVD risk profiles as adults with MR (Brattstrom, England, and Brun, 1987; Murdoch et al., 1977; Murdoch et al., 1978; Murdoch et al., 1979; Nishida et al., 1977; Pueshel et al., 1992; Salo et al., 1979; Serano-Rios et al., 1973; Yashuda et al., 1979; Yla-Herttuala et al., 1989). The underlying mechanisms for decreased CVD in adults with DS have not been identified and are not understood.

None of the previous studies have investigated the relationships between the modifiable behavioral risk factors or the components of the IRS with the physiological risk factors for CVD in adults with MR or DS (Fox and Rotatori, 1882; Kelly et al., 1986; Janicki and Jacobson, 1986; Janicki and MacEachron, 1984; Strauss and Kastner, 1996; Rimmer et al., 1993; Rimmer et al., 1994; Rimmer et al., 1995). By determining the relationships between physical activity, dietary intake, and the components of the IRS with the physiological CVD risk factors, specific, effective, and efficient intervention programs aimed at decreasing the risk for CVD and increasing the overall health of adults with MR and DS may be developed and implemented. Furthermore, identifying possible underlying causes of the elevated CVD risk profile for adults with MR and DS may provide new information on why there is elevated CVD risk in adults with MR and lower CVD in adults with DS.
References


