Are the Initiation and Maintenance of a Resistance Training Program Associated with Changes to Dietary Intake and Non-Resistance Training Physical Activity in Adults with Prediabetes?

Tanya M. Halliday

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Brenda M. Davy, Chair

Richard A. Winett

J. Tina Savla

Matthew W. Hulver

Andrew P. Neilson

Kevin P. Davy

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ABSTRACT (Academic)

Prediabetes is associated with an elevated risk for developing type 2 diabetes (T2DM) and associated cardiovascular complications. Lifestyle factors such as physical activity (PA) and dietary intake are strongly implicated in the development of metabolic disease, yet few Americans meet PA and dietary recommendations. Middle-aged and older adults are at increased risk for developing prediabetes and T2DM due to age-related muscle loss, increased fat mass, and alterations in glucose handling. In addition, this segment of the population is least likely to meet PA guidelines, particularly the resistance training (RT) recommendation of completing a whole body routine 2x/week. Ideally, individuals would alter their lifestyle in order to meet PA guidelines and habitually consume a healthy diet, to decrease disease risk. However, behavior change is difficult and optimal strategies to promote and maintain changes have yet to be determined. Furthermore, behavior change interventions tend to be time-, cost-, and resource-intensive, limiting the ability for efficacious programs to be translated into community settings and broadly disseminated. Evidence suggests that health-related behaviors, particularly diet and exercise habits, tend to cluster together. Thus, intervening on one behavior (e.g. PA) may elicit a spillover effect, promoting alterations in other behaviors (e.g. diet), though findings to date are conflicting. The purpose of this dissertation was to determine if participation in a social cognitive theory-based RT program targeting the initiation and maintenance of RT exerts a spillover effect and is associated with alterations in dietary

intake and/or non-RT PA in a population at risk for T2DM. Data from the 15-month Resist Diabetes study was analyzed to evaluate this possibility. Sedentary, overweight/obese (BMI 25-39.9 kg/m^2), middle-aged and older (50 -69 years) adults with prediabetes (impaired fasting glucose and/or impaired glucose tolerance) completed a 3 month initiation phase where they RT 2x/week in a lab-gym with an ACSM-certified personal trainer. Participants then completed a 6-month faded contact maintenance phase, and a 6-month no-contact phase during which they were to continue RT on their own in a public facility. No advice or encouragement was given to participants to alter dietary intake or non-RT PA habits. At baseline, and months 3, 9, and 15, three non-consecutive 24-hour diet recalls were collected to evaluate dietary intake and quality, the Aerobics Institute Longitudinal Study Questionnaire was completed to evaluate non-RT PA, and body mass, body composition, and strength (3 repetition maximum on leg and chest press) were measured. At months 3, 9, and 15 social cognitive theory (SCT) constructs were assessed with a RT Health Beliefs Questionnaire. In the first study, dietary intake was assessed at baseline and after 3 months of RT. Using paired sample t-tests, reductions in intake of energy (1914 ± 40 kcal vs. 1834 ± 427 kcal, p = 0.010), carbohydrate (211.6 ± 4.9 g vs. 201.7 ± 5.2 g, p = 0.015), total sugar (87.4 ± 2.7 g vs. 81.5 ± 3.1 g, p = 0.030), glycemic load (113.4 ± 3.0 vs. 108.1 ±3.2, p= 0.031), fruits and vegetables (4.6±0.2 servings vs. 4.1±0.2 servings, p= 0.018), and sweets and desserts (1.1 ± 0.07 servings vs. 0.89 ± 0.07 servings, p = 0.023) were detected from baseline to month 3. No changes in other dietary intake variables were observed. These findings supported additional investigation in this area. The second study assessed changes in overall diet quality (Healthy Eating Index [HEI]-2010 scores) and non-RT PA over the initiation,

maintenance, and no-contact phases using mixed effects models. Demographic, physiological, and psychosocial factors that may predict alterations to diet quality and non-RT PA were also explored. Energy and carbohydrate intake decreased with RT (β= -87.9, p=.015 and β= -16.3, p<.001, respectively). No change in overall dietary quality (HEI-2010 score: β= -0.13, p=.722) occurred, but alterations in HEI-2010 sub-scores were detected. Maintenance of RT was accompanied by an increase in MET-min/week of total non-RT PA (β=153.5, p=0.01), which was predicted by increased self-regulation for RT (β=78.1, p=0.03). RT may be a gateway behavior leading to improvements in other health-related behaviors among adults with prediabetes. These results support the use of single-component vs. multi-component interventions. This may have broad translational potential for the development of time-, resource-, and cost-efficient lifestyle interventions which can improve multiple health-related behaviors and decrease disease risk.

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GENERAL AUDIENCE ABSTRACT

The potential for an intervention to result in spontaneous changes to other behaviors is often referred to as the "spillover" effect. The spillover effect can be supportive, meaning that engagement in one beneficial behavior (e.g. physical activity [PA]) is accompanied by another behavior occurring in a similar direction (e.g. intake of a healthier diet), or the spillover effect can be compensatory, meaning that engagement in the one beneficial behavior is accompanied by a behavior that negates the expected effects of the first (e.g. consuming a less healthful diet). In the nutrition, exercise, and weight loss literature, the majority of research has been conducted on the ability of aerobic exercise interventions to influence dietary intake, and results are mixed. Therefore, the spillover effect in response to resistance training (RT) deserves examination. Since RT is a more challenging health behavior to initiate and maintain, success with doing so may result in increased self-confidence. This may increase participants' confidence in their ability to improve their diet. Furthermore, RT is associated with different physiological responses than aerobic exercise (e.g. increased strength and functional ability) that may increase the likelihood of participants engaging in aerobic PA as well. The current study was conducted to determine if participation in an RT intervention was accompanied by alterations to dietary intake and non-RT PA in middle-aged and older, overweight and obese, men and women that were considered at high risk of developing type 2 diabetes mellitus (T2DM). Findings from the first analysis indicate that successful completion of a 3-month,

supervised RT program is associated with a reduction in caloric intake. Specifically participants reported consuming less carbohydrates and sugar due to decreased intake of sweets and desserts, and fruits and vegetables. The second analysis found that the reductions in calorie and carbohydrate intake persist with maintenance of RT. No change in overall diet quality (measured as adherence to national dietary guidelines) occurred with RT initiation and maintenance, but changes to sub-categories of the diet quality index used were noted. In addition, participants reported engaging in greater amounts of non-RT PA with maintenance of the RT program. This research suggests that health-related behavior change interventions that focus on changing only a single behavior (e.g. resistance training) may result in other beneficial lifestyle changes. Since interventions that encourage changes in just one behavior tend to be less costly and resource-intensive than interventions which directly intervene on multiple health-related behaviors, use of programs focusing on one behavior should be encouraged, particularly when resources are limited.

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project within the Resist Diabetes (RD) trial, involving me in other RD study analyses, and always providing valuable and detailed feedback on abstract and manuscript drafts. ***Dr. Matthew Hulver*** is deserving of many thanks, for not only serving on my committee, but also for providing me with multiple opportunities for professional growth during my graduate career. As the Human Nutrition, Foods, and Exercise (HNFE) Department Head, Dr. Hulver allowed me to participate in the ***College of Agriculture and Life Sciences (CALS) Graduate Teaching Scholars (GTS) program***, travel to Scandinavia to take a course with ***East Carolina University on Exercise for the Prevention and Treatment of Metabolic Disease at the Karolinska Institute and the GIH***, and offered financial support for conference presentations through the HNFE Travel Fund. The contribution these experiences had to my development cannot be quantified. Thanks is also extended to ***Dr. Kevin Davy*** for allowing me to develop skills and knowledge in vascular physiology. In addition to my dissertation work, with the guidance and expertise of Drs. Kevin and Brenda Davy, I was able to obtain funding for, and carry out a cross-sectional study examining the relationship between added sugar intake and arterial stiffness. I am very appreciative of the additional research experience and the insights during this process that Dr. Davy provided me with. Finally, I am grateful to ***Dr. Andrew Neilson*** for the support and encouragement he provided with during prelims and my proposal. Furthermore, I was fortunate enough to be given the opportunity to work on a project of his examining the influence cocoa intake has on metabolic health. Being involved in that project taught me a lot about study organization, development of controlled feeding trials, gastrointestinal physiology, and metabolism. In sum, the expertise of my committee members and the various opportunities they provided me with

have all contributed to the breadth and depth of my graduate school experience. Thank you all!

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For those I forgot, or did not name – I beg your forgiveness!

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Attributions

Manuscript 1: *Dietary intake modification in response to participation in a resistance training program for sedentary older adults with prediabetes: Findings from the Resist Diabetes study*

Brenda Davy, Richard Winett and Jyoti Savla were all involved in the original design of the Resist Diabetes study and responsible for obtaining funding. Tanya Halliday and Brenda Davy designed the current study. Tanya Halliday, Adrienne Clark, Mary Elizabeth Baugh, Valisa Hedrick, Elaina Marinik, and Kyle Flack were involved in the data collection. Sheila Winett was responsible for the study website development and maintenance, and data management. Tanya Halliday, Jyoti Savla and Brenda Davy analyzed the data. Tanya Halliday, Brenda Davy, and Richard Winett developed the manuscript. All authors approved the final version of the manuscript.

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Manuscript 2: Resistance Training is associated with Spontaneous Changes in Aerobic Physical Activity but not Overall Diet Quality in Adults with Prediabetes

Brenda Davy, Richard Winett and Jyoti Savla were all involved in the original design of the Resist Diabetes study and responsible for obtaining funding. Tanya Halliday and Brenda Davy designed the current study. Tanya Halliday, Valisa Hedrick, and Elaina Marinik collected the data. Jyoti Savla was responsible for data management. Tanya Halliday and Jyoti Savla analyzed the data. Tanya Halliday and Brenda Davy developed the manuscript. This manuscript is currently being reviewed by all authors, and will be submitted for publication when finalized.

Chapter 1 – Introduction

Type 2 Diabetes Mellitus & Prediabetes Background

Type-2 diabetes mellitus (T2DM) is a chronic, non-communicable disease characterized by elevated blood glucose levels, resulting from progressively worsening insulin resistance and defects in insulin secretion[1]. In the US alone, approximately 12-14% of the population has diabetes, and it is estimated that 1 out of every 3 people will develop T2DM in their lifetime[2,3]. A state of intermediate hyperglycemia, known as "prediabetes" with blood glucose levels above normal, but below the thresholds for diabetes diagnosis, has been recognized for several years[4]. While the classification criteria have been revised several times, and differ slightly between professional organizations[5-7] prediabetes prevalence is also alarmingly high. It is estimated that 86 million, or greater than 1 out of 3, US adults fall in to this stage of abnormal glucose homeostasis[2,3]. Prediabetes is associated with an elevated risk of frank diabetes diagnosis, with up to 70% of individuals with prediabetes expected to progress to T2DM[8]. The aberrant metabolic profile observed in individuals with T2DM and prediabetes is associated with increased macro- and micro-vascular complications[9-12], namely cardio and cerebral vascular disease, retinopathy, nephropathy and specific neuropathies. Because metabolic disease progression represents a substantial individual and societal cost[13] targeted lifestyle interventions, specially focusing on the prediabetic stage, are of great importance.

The primary physiological defects causing the hyperglycemic stage of T2DM and prediabetes are increased hepatic glucose production, impaired insulin secretion by the β-cells of the pancreas, and decreased peripheral glucose uptake by skeletal muscle[1,5],

though other organs and factors (e.g. adipose tissue[1,14], GI tract[1,15,16], pancreas[17],kidney[18], and brain[19]) are also implicated in the intermediate states of abnormal glucose regulation and overt T2DM diagnoses. However, arguably more important than these complex proximal contributors to disease progression are the more distal risk factors that set in motion the pathophysiological chain of events, which often lead to T2DM and its associated consequences. Specifically, obesity and physical inactivity are well-established and powerful risk factors for T2DM and prediabetes. Approximately 25% of overweight adults between the ages of 45 – 74 have prediabetes[20]. However, the negative influence excess adiposity has on insulin and glucose homeostasis likely occurs while individuals are still classified as exhibiting normal glucose tolerance[1]. It has been argued that the metabolically healthy, but obese phenotype is simply a transitional stage to impaired glucose regulation and T2DM[21-23]. Therefore, habitual dietary intake that achieves and maintains a healthy body mass and composition is an important lifestyle factor involved in the prevention and treatment of prediabetes and T2DM[5,24-26]. Physical activity (PA) and exercise [used interchangeably from this point forward] habits also contribute to risk for these conditions. Appropriate levels of PA are involved in promoting energy balance, and thus can be important to weight loss and maintenance efforts[5,26,27]. In addition to the effect on body weight and composition, PA exerts additional benefits on blood glucose control, both acutely and chronically (discussed below)[27]. Thus, lifestyle modifications to promote healthy dietary intake patterns and sufficient levels of PA are important in the prevention and treatment of metabolic disease.

Importantly, these modifiable risk factors of obesity and PA contribute to the association of the non-modifiable risk factors with prediabetes and frank T2DM[5,28]. For

instance, aging is associated with reductions in skeletal muscle mass, which decreases peripheral glucose uptake, and contributes to T2DM development. However, regular muscle-strengthening exercise can help to attenuate the decline in muscle mass and subsequent insulin resistance[27,29-31]. Similarly, males typically display android-pattern obesity, which contributes to their increased risk for metabolic abnormalities[32]. Yet, proper diet and exercise to prevent excess adipose tissue accumulation can overcome the risk associated with being of male sex[28].

Dietary Intake Recommendations for T2DM Prevention

Current dietary recommendations from the ADA and the Academy of Nutrition and Dietetics (AND) strongly endorse (Ratings: Grade A[Footnote-1]; Strong and Imperative[Footnote-2], respectively) that individualized medical nutrition therapy (MNT) be provided to individuals at high risk for diabetes (e.g. those with prediabetes and/or the metabolic syndrome), as well as individuals with T2DM[5,24,33]. MNT provision in prediabetic populations has been shown to be an efficacious treatment strategy for decreasing fasting and postprandial blood glucose values (by 2-9 mg/dL, and 9-16 mg/dL, respectively) and decreasing waist circumference (by 3.8-5.9 cm)[24]. Specific recommendations from the ADA to prevent the progression to T2DM in individuals with prediabetes include: weight loss of ~7% for those who are overweight or obese (Grade A); dietary fiber intake of 14g/1,000 kcals and for whole grains to comprise at least half

[1] ADA evidence grading system for clinical practice recommendations descriptions: **Grade A** – Clear evidence from well-conducted, generalizable RCTs that are adequately powered, compelling nonexperimental evidence, i.e., "all or none" rule developed by the Center for Evidence-Based Medicine at the University of Oxford, and/or supportive evidence from well-conducted RCTs that are adequately powered. **Grade B** – Supportive evidence from well-conducted cohort studies and/or supportive evidence from a well-conducted case-control study. **Grade C** – Supportive evidence from poorly controlled or uncontrolled studies and/or conflicting evidence with the weight of the evidence supporting the recommendation. **Grade E** – Expert consensus or clinical experience.

[2] See Appendix A for information related to the Academy of Nutrition and Dietetics rating system.

of all grain intake (Grade B) (which is consistent with guidelines from the USDA for general adult populations); limiting intake of sugar sweetened beverages (Grade B); controlling carbohydrate intake (Grade B); limiting saturated fat intake to less than 7% of total energy intake (Grade B); and limiting *Trans* fat intake (Grade E)[5,33].

The AND also recommends that overweight and obese individuals at high risk for T2DM be prescribed a weight-reducing diet (Rating: Strong, Conditional)[24]. Weight loss achieved via lifestyle modifications results in decreases in fasting glucose levels (2-9 mg/dL) and more extreme weight loss achieved via bariatric surgery has been shown to produce even greater improvements in fasting and post-prandial glucose levels (16-21 mg/dL and 16 mg/dL, respectively)[24]. In addition, both the ADA and AND recognize that a variety of dietary strategies can be utilized (e.g., low carb, low fat, etc.) and effective for short term weight loss, but suggest additional research is needed to determine what dietary patterns are most effective for sustained weight loss and glycemic control[5,24,34]. Like the ADA, recommendations from the AND for individuals with prediabetes also encourage that fiber and whole grain intake meet levels set by the USDA for the general adult population (Ratings: Fair, Imperative and Weak, Imperative, respectively)[24].

Additional recommendations from the AND on specific types of macronutrients and food groups for preventing the progression to T2DM exist, but the evidence is limited and the strength of their recommendation ratings is lower. For instance, regarding fat, sugar, fruit and vegetable intake and glycemic index/load, the AND states that there is limited evidence on the impact specific types of fat, limiting sugar intake, increasing fruit and vegetable intake, and lowering glycemic index/load will have on progression from prediabetes to T2DM in the absence of weight loss (Ratings: Fair, Imperative;

Insufficient Evidence, Conditional; Insufficient Evidence, Conditional; and Weak, Conditional, respectively)[24]. However, dietary fat intake recommendations from the AND for the general adult population do call for saturated fat intake to be limited to 7-10% of total energy intake, and for *Trans* fat intake to be as low as possible[35]. In addition, the AND suggests that Americans limit their intake of added sugars, as higher intake may contribute to increased total energy intake, and thus weight gain, which is a risk factor for T2DM (Rating for prevention of T2DM: Insufficient Evidence, Conditional) [24,36].

Regarding fruit and vegetable intake, there is a lack of evidence to directly support the commonly held belief that increased consumption will decrease risk for chronic diseases, including T2DM[24,37-40]. This is because most studies focus on total dietary patterns or on intake of specific nutrients, not food groups, and/or use clinical biomarkers related to T2DM risk as outcome measures, not disease incidence[39,40]. The few trials which considered solely fruit and vegetable intake on T2DM incidence produced underwhelming results. For instance, a meta-analysis by Hamer et al. included 5 prospective cohort studies assessing baseline fruit and vegetable intake and incident T2DM at follow-up found no protective effect of consuming 3+ or 5+ servings of fruits and vegetables on T2DM risk[40]. A more recent meta-analysis including 10 prospective cohort studies found increased fruit and green leafy vegetable intakes were associated with a lower risk of T2DM (RR: 0.93, 95% CI: 0.8-0.99 and RR: 0.87, 95% CI: 0.81-0.93, respectively), but neither total vegetable intake nor combined fruit and vegetable intake was associated with a lower risk of T2DM[39].

However, most of these trials rely on food frequency questionnaires (FFQs) to determine fruit and vegetable intake, which is not the preferred method for assessment[41],

and included primarily overweight/obese subjects, which is a stronger risk for T2DM than can likely be overcome with increased intake of fruits and vegetables. Thus, these analyses should not be taken as evidence to not promote intake of fruits and vegetables in groups at risk for T2DM. The high fiber, antioxidant, and phytochemical content and low energy density of fruits and vegetables may elicit health benefits and improve weight loss/maintenance efforts (when combined with reduced energy intake from other sources[42]) and thus, contribute to decreased risk for T2DM. In addition, most all studies which examine overall dietary intake patterns associated with risk for T2DM show that diets high in fruits and vegetables (as well as low-fat dairy, lean meats, fish, and whole grains) and at an appropriate total energy intake are related to lower risk than more "westernized" diets (e.g.- those high in refined grains, sugar-sweetened beverages, high-fat red meats, and processed foods)[37,38,43,44]. In sum, the available evidence supports the role habitual dietary intake has on risk for progression to T2DM, and as such dietary intake modifications are most always warranted in individuals with prediabetes.

Physical Activity Recommendations for T2DM Prevention

Skeletal muscle insulin resistance is the primary defect associated with the manifestation of T2DM[45,46]. Regular physical activity and exercise training represent efficacious therapeutic interventions that significantly increase insulin sensitivity in skeletal muscle and attenuate the onset of T2DM in prediabetic individuals[47,48]. PA recommendations from the US government as well as the American College of Sports Medicine (ACSM) and the American Diabetes Association (ADA) are similar for the general US adult population, older adults, and individuals with and at-risk for, T2DM[5,27,29,49]. The guidelines call for individuals to: engage in at least 150 minutes/week

of moderate-intensity PA or 60-75 minutes of vigorous-intensity PA or a combination in order to obtain a total volume of 500-1,000 MET-minutes per week; and to RT at least two times per week[5,27,29,49]. The principle of specificity related to exercise training states that alterations in function and phenotype are dependent upon the specific modes of exercise which are done[50]. Typically, we view the adaptations to exercise as resulting from two ends of the spectrum, endurance training (e.g. low load-high repetition) and strength training (high load-low repetition), though overlap occurs between the two modes, and both are considered important for prevention of T2DM.[27,29,50].

Aerobic Exercise

Aerobic exercise can result in beneficial effects on blood glucose control, and thus is an effective treatment option for individuals with prediabetes and frank T2DM. During an acute bout of exercise, contracting skeletal muscle causes an increased uptake of blood glucose in to the working muscle, which can result in a decline in blood glucose levels[27]. This occurs even in the presence of skeletal muscle insulin resistance because the pathways involved in glucose uptake differ at rest and during exercise[51,52]. At rest uptake of blood glucose in to skeletal muscle is primarily dependent upon insulin to activate a complex signaling cascade which results in mobilization of the glucose transporter, GLUT4, to the plasma membrane[52]. Impairments in insulin-stimulated translocation of GLUT4 to the plasma membrane are seen in individuals progressing towards, and with, T2DM[52-54], thus contributing to hyperglycemia. During exercise, however, skeletal muscle contractions are able to mobilize GLUT4 from its intracellular location to the plasma membrane via a different signaling cascade involving AMPK[52,55-

[57]. Fortunately, this pathway is not impaired in individuals who demonstrate insulin resistance at rest and postprandially[55].

For individuals with T2DM, the ADA and ACSM recommend that in addition to obtaining at least 150 min/week of moderate-intensity PA that individuals spread this volume over at least 3 days, and have no more than 2 consecutive days without PA. This is because the acute benefit of exercise on insulin action and blood glucose control is transient and does not seem to persist beyond a maximum of 72 hours[27,58,59].

In addition to the acute effects of aerobic exercise, improvements in insulin action (and thus, blood glucose control) are also realized through adaptations resulting from chronic exercise training. Several mechanisms and pathways are implicated in the training adaptation, and are beyond the scope of this proposal. In brief, the training effect occurs due to cumulative effects realized through each acute session which ultimately results in increased maximal oxygen consumption (VO_2max) due to alterations to the cardiovascular system and skeletal muscle[50,56]. A single bout of exercise elicits a rapid, but transient, increase in transcription rate and/or mRNA content of specific genes involved in metabolism [e.g. growth factors, enzymes, contractile proteins, mitochondrial proteins, etc.][56,60,61]. Ca+ signaling and AMPK sensing of energy status have been identified as the primary initiators of the endurance training stress-induced signaling cascades which ultimately converge and stimulate PGC-1α transcription, which is considered one of the main coordinators of the skeletal muscle response to endurance training[56,60,61].

With chronic training, increases in protein content occur, leading to skeletal muscle remodeling and enhanced insulin sensitivity and insulin action[56,61-63]. Specifically,

aerobic exercise training has been shown to increase Akt2 and GLUT4 protein content[56,60,62,64,65], mitochondrial volume[50,56,60,61], capillary density[56,66,67], and enhance glycogen synthase activity[5,64]. These alteration in skeletal muscle morphology and metabolism result in increased insulin-mediated glucose uptake and storage as glycogen within skeletal muscle. Aerobic exercise also improves lipid oxidation due to increased mitochondrial density[56] and protein expression of uncoupling protein (UCP) 3, diacylglycerol kinase (DGK) δ, and peroxisome proliferator-activated receptor (PPAR) δ[68]. DGKδ is known to be downregulated in skeletal muscle of T2DM individuals[69], which results in increased accumulation of diacyl-glycerol [an intracellular lipid metabolite], known to impair insulin signaling by serine phosphorylation of insulin receptor substrate-1 (IRS-1) and block glucose uptake and inhibit beta-oxidation[70]. Thus, exercise interventions which increase expression of related intracellular regulators and improve fatty acid oxidation[71] may improve insulin and glucose homeostasis.

Furthermore, aerobic exercise has been shown to reduce central adiposity[27,72,73]. Obesity is associated with a low-grade chronic inflammatory state which contributes to insulin resistance. For instance, macrophage infiltration associated with excess adiposity results in increased secretion of cytokines. These inflammatory cytokines can act upon peripheral tissues, initiating signaling cascades activated by stress kinases (such as Jnk), which result in serine phosphorylation of IRS-1 and thus inhibit insulin action on glucose uptake[74]. The role of inflammation in the development of insulin resistance has also been implicated as an underlying cause of adverse vascular remodeling, which explains the link between chronic hyperglycemia and the associated cardiovascular consequences[9,75]. Thus, if aerobic exercise is able to decrease adipose tissue, resulting in lower levels of

circulating FFA and adipokines, improvements in whole body insulin resistance are likely to occur and decrease the risk for T2DM and associated co-morbidities.

Resistance Exercise

In addition to aerobic exercise, physical activity guidelines also recommend incorporation of RT as it has been shown to decrease risk of T2DM and associated complications[5,27,49,50]. Like aerobic exercise, skeletal muscle contractions associated with RT also promote insulin-independent uptake of glucose into working muscle via translocation of GLUT4 to the plasma membrane[27,30,76]. The acute effects of a bout of RT on blood glucose levels and insulin action post exercise, particularly in individuals with prediabetes or T2DM, have not been examined as thoroughly as aerobic exercise[27,77-79]. However, studies conducted to date suggest that an acute bout of RT can result in transient decreases in blood glucose and improvements in insulin sensitivity, to a similar degree experienced with a bout of aerobic exercise[77,79].

Like aerobic training, the influence of chronic RT on improvements in glucose homeostasis is the result of the cumulative effect of the stimulus from each bout, eventually resulting in skeletal muscle adaptations. Glycemic control and insulin sensitivity with RT are thought to occur via some of the similar pathways as described above for aerobic training (e.g. increases in GLUT-4, glycogen synthase activity, and decreased low-grade inflammation), but not all (e.g.- RT does not alter capillary density or mitochondrial volume)[27,30,56,60,61,80,81]. Importantly RT induces additional benefits beyond those seen from AT as strength training leads to skeletal muscle fiber growth and increases in strength[27,29,50,82]. Specifically, RT results in the stimulation of several mechanosensory and energy status signaling cascades which eventually converge to

activate mammaliam target of rapamycin (mTOR), which integrates these signals and drives the translational process responsible for protein accretion[56,60,83]. These transient increases in contractile and myofibrillar protein synthesis occur following each bout of RT. Over time, the activation of the mTOR/serine kinase 6 (S6K) leads to increased skeletal muscle mass[56,60,83]. Since skeletal muscle is the primary site of glucose disposal, increases in lean body mass from RT can improve glucose control[27,30]. Additionally, lean mass is a more metabolically active tissue than fat mass, so increased fiber size and muscle cross sectional area will result in increased resting energy expenditure, which could help contribute to improvements in body composition[27,30]. Finally, RT results in improvements in functional capacity, which can increase quality of life and ability to engage in other activities (discussed more in Chapter 2), and thus total daily energy expenditure, further contributing to reduced T2DM risk[29,84]. However, the evidence to date on RT as an efficacious and effective intervention (as well as the underlying mechanisms) for diabetes prevention is lacking in comparison to AT and warrants further investigation[27].

Recent work has highlighted a number of questions which need to be addressed regarding RT and its ability to influence T2DM. For instance, 7 weeks of resistance training was found to only improve insulin sensitivity in women with normal body fat, and not those with elevated levels of fat mass in a study by Malin and colleagues[85]. This indicates that RT alone may be insufficient to overcome the deleterious effects of obesity leading to an insulin resistant state. Furthermore, the subjects in this study were young, and evidence also shows that the response to resistance training differs between younger and older adults[82,86,87]. While RT is known to help combat the age-related decline in

skeletal muscle mass, known as sarcopenia, greater volume may be needed in order to overcome the hypertrophic resistance seen in older adults compared to younger[82,86-88]. However, with increased volume of exercise, there is a chance that adherence to protocols may be lower[82,89,90], so practicality needs to be considered with development of 'optimal' resistance training prescriptions.

Combined AT and RT

While both aerobic and RT are known to confer substantial health benefits, these modes differ in their specific metabolic and molecular responses, and thus in the functional and phenotypic outcomes associated with chronic training. Therefore, incorporation of both aerobic and resistance exercise is likely to be more effective than either modality alone for reducing insulin resistance and improving metabolic health, as combined training will capitalize on the beneficial adaptations each provide. For example, resistance training is expected to lead to an increase in muscle fiber size and muscle cross sectional area, but not capillary density, while aerobic training is expected to lead to an increase in capillary and mitochondrial density, but not skeletal muscle size[60,81]. Most exercise trials to date have examined aerobic training or RT separately on their ability to either delay the progression from prediabetes to T2DM or improve glucose control in individuals with T2DM. For instance, Bacchi and colleagues recently compared the effect of aerobic training or RT to improve metabolic risk in individuals with T2DM, and found similar improvements in both groups for HbA1c, fat mass, insulin sensitivity[91]. Trials which have investigated a combination of the training modalities, have shown that inclusion of both aerobic and RT results in greater improvements in relevant outcomes (e.g. HbA1c, fasting blood glucose, postprandial blood glucose, and

insulin sensitivity)[92-94], though this is not always the case[95]. Yet, in the majority of these trials, total volume of exercise was higher in the combined training group than in the singular modality exercise groups. Thus, researchers are unable to conclude if increased volume of exercise or combination of modalities is the reason for greater benefits in the combined groups. Further complicating the ability to compare outcomes across trials is that some interventions also include a dietary intervention, often with the goal of producing weight loss (such as the landmark Diabetes Prevention Program (DPP))[26,93,96,97]. Therefore, improvements seen in glucose control may be due to dietary manipulation and decreased body/fat mass, and not specifically the PA intervention.

Recently, Church and colleagues published findings from the HART-D trial, which attempted to address the exercise volume vs. modality question in a RCT that did not include a dietary intervention[98]. This 9-month intervention consisted of 3 exercise groups (aerobic training only, RT only, and combined aerobic and RT) which were matched on total exercise time (~150 min/week, consistent with PA guidelines from most organizations), and a sedentary control group. The combined exercise group experienced a modest decrease (0.34%) in HbA1c (the main outcome of the trial) compared to the control group, but there was no difference between either of the singular exercise mode groups and the control group[98]. Furthermore, no changes were detected in fasting insulin nor glucose in any of the exercise groups[99]. Importantly, reductions in HbA1c in the combined group occurred while glycemic control medications use decreased compared to increased reliance on drug treatment in the control group. This trial provides support for the efficacy of a combination of aerobic and RT to decrease HbA1c in individuals with diabetes, and suggests incorporation of both may provide the greatest benefit to

individuals with prediabetes who are at increased risk for T2DM. However, trials conducted to date examining the ability of exercise to decrease risk for T2DM have employed different intensities and volume, and a range in individual responses to exercise stimuli have been seen in participants[27,81,100-103]. In addition, concern has been voiced regarding the potential for concurrent training protocols to interfere at the molecular level and thus lessen the expected benefits associated with each specific mode of training[60,104]. As such, optimal protocols have yet to be established, and likely differ based upon individual characteristics, such as prediabetes phenotype (e.g. IFG, IGT, or both)[105,106], but it is generally agreed that some exercise is better than none for achieving health-related benefits, and that individuals should engage in both AT and RT[27].

Benefits of Combined Exercise and Dietary Interventions

The greatest improvements in blood glucose control seem to occur when individuals make positive changes to both their dietary habits and PA regimens. The most well-known and widely cited trial showing the efficacy of lifestyle interventions on prevention of T2DM is the DPP[26]. This large (n = 3,234) RCT compared the ability of an intensive lifestyle intervention (diet and aerobic PA) vs. metformin to prevent the onset of T2DM in individuals with IFG or IGT. While both treatments reduced the incidence of T2DM more than the placebo, the intensive lifestyle intervention was more effective than metformin; reducing the incidence by 58% compared to the 31% reduction seen in the metformin group[26]. These findings that lifestyle interventions can substantially reduce the progression from prediabetes to diabetes and also result in regression from prediabetes to normoglycemia have been reported in other trials, such as the Finnish Diabetes

Prevention Study[107], the Da Quing IGT and Diabetes Study[48], and the Indian DPP[108], to name a few of the large RCTs.

Evidence for the strong benefits of lifestyle modifications on metabolic health is best summarized by this quote from the ACSM/ADA Joint Position Statement on Exercise and Type 2 Diabetes: "Diet and PA are central to the management and prevention of T2DM because they help treat the associated glucose, lipid, BP control abnormalities, as well as aid in weight loss and maintenance. ***When medications are used to control T2DM, they should augment lifestyle improvements, not replace them***" [emphasis added][27]. This view is echoed by the American Heart Association (AHA) related to CV health. In their 2015 Heart Disease and Stroke Statistical Update, they state that of the 7 metrics of CV health in the AHA's 2020 goals (smoking, body mass index, physical activity, healthy diet score, total cholesterol, blood pressure, and fasting plasma glucose), "the metrics with the greatest potential for improvement are health behaviors, including diet quality, PA, and body weight"[109]. A similar report on the "Status of CV Health in US Adults" says that "it is likely that these unfavorable CV behaviors [poor diet, inactivity, and high BMI] are substantially responsible for the coinciding unfavorable state of CV health factors in the US adult population"[110]. Recently the Community Preventive Services Task Force conducted a thorough systematic review and economic analysis of combined diet and PA programs for T2DM prevention[111-113]. Their findings support the use of combined diet and PA programs for reducing the incidence of T2DM and associated cardiometabolic risk factors in at-risk individuals.

However, the combination of dietary interventions with increases in both aerobic PA and RT on the ability to decrease risk for T2DM has received considerably less

attention. Most trials investigating the combination of diet and PA include only aerobic exercise[96]. A recent review by Aguiar and colleagues was conducted specifically to assess the efficacy of interventions which include all three components on T2DM prevention in at risk populations[96]. In evaluating the eight studies which met their inclusion criteria, it was determined that these combined interventions are effective and support exists for the incorporation of all three behaviors for prevention of T2DM[96].

Prevalence of Meeting Diet and PA Recommendations

Healthful dietary intake patterns and sufficient levels of PA have been established as key factors in the prevention of T2DM and treatment for it. Unfortunately, a minority of US adults meet national physical activity and dietary guidelines[49,114,115]. Only 49.9% of US adults report meeting aerobic exercise guidelines of 150 min/week of moderate-intensity or 75 min/week of vigorous intensity, or a combination of both, and even fewer (24.1%) report performing muscle-strengthening activities on 2 or more days/week[115]. The prevalence of meeting PA recommendations decreases with increasing age. The latest data from Healthy People 2020 indicate that ~44% of adults aged 55-64 years old and 35.8% of adults >65 years of age report meeting aerobic activity recommendations and less than 20% of adults over the age of 55 report meeting muscle-strengthening recommendations[115]. However, these rates are likely to be an overestimation since they are based upon self-reported data. Additionally, the questions related to "muscle-strengthening" activities on national surveys are very general, and so it is more likely that an even smaller number of US adults consistently engage in appropriate levels of RT.

More concerning is that individuals at greater risk for, or diagnosed with, T2DM report lower participation in PA than the general population[116,117]. In the Medical

Expenditure Panel Survey, self-reported participation in an average of 30 min or more of moderate or vigorous-intensity PA at least 3x/week, was 58% in adults without T2DM, compared to only 39% in individuals with, or at high risk for T2DM[116]. However, using an objective assessment [accelerometers], Steeves, et al. did not find a difference in PA between individuals with prediabetes and normogylycemia, but did note lower rates of PA in those with T2DM[117].

In regards to dietary intake, several indices have been developed to assess overall diet quality. These various indices are inversely related to risk for chronic disease, with lower scores indicating increased disease risk[38,118-122]. Not surprisingly, scores on these indices are suboptimal in general US populations[109,110,123]. For instance: less than 1 in 5 US adults reports meeting fruit and vegetable intake recommendations[124]; less than 1% achieve "ideal" [e.g. meeting ≥4 out of 5 primary goals related to intake of: fruits and vegetables, fish, whole grains, sodium, and sugar-sweetened beverages] Healthy Diet Scores[109,110]; and the average Healthy Eating Index (HEI)-2010 score for US adults is estimated at 49.8 out of 100, indicating "poor" dietary quality[123,125]. Although older adults tend have slightly higher quality dietary intake than younger age groups, dietary quality is still generally inadequate in this segment of the population as well[109,110,115,123].

Like the PA data, some evidence, but not all[126] suggests that adherence to healthful dietary patterns may be lower in individuals at high risk for, and with, T2DM than among individuals demonstrating normoglycemia[120,127]. However, it is important to note that this area of research is limited by discrepancies in methods used to assess dietary intake (e.g. FFQs v. food recalls) and different operational definitions of "dietary quality" (e.g. various indices of diet quality and/or using specific food or nutrient intake

such as fruit and vegetables only, saturated fat only, etc. as a proxy for overall dietary quality). Furthermore, it may be expected that individuals with T2DM would demonstrate higher levels of dietary quality and PA than individuals without T2DM, as they are likely receiving education and counseling on disease management which includes lifestyle modifications. Thus, even if no difference exists between diet quality and PA levels of those with and without diabetes, that is concerning, as overall diet quality and PA prevalence is low in the United States, and those with or at high risk for a chronic disease would benefit from following specific MNT and PA recommendations.

Barriers to Meeting Physical Activity and Dietary Intake Recommendations

As demonstrated in preceding sections, the benefits of diet and exercise on risk for T2DM are well-established, yet few adults meet established guidelines. This suggests that several barriers exist which prevent intake of a healthful diet and engagement in sufficient levels of PA. Individual level factors interact with social environments/networks, and the physical environment, as well as the macro-level setting in ways which can either help to facilitate or otherwise inhibit healthy dietary or physical activity habits[128-133]. Specific influences/barriers of lifestyle behaviors include: individual demographic characteristics such as age, race/ethnicity, sex, socioeconomic status; physiological and biological characteristics such as genetic make-up, physical and cognitive function, hunger/satiety signals, and circadian rhythm; psychological characteristics such as beliefs, attitudes, values, self-efficacy, motivations, body-image; skills and time (both perceived and actual); social and cultural factors such as support, norms, and modeling; characteristics of the physical environment such as food availability and marketing, access to safe and attractive recreational facilities and spaces,

healthcare services, level of pollution, and community infrastructure and design; as well as policy-driven factors at the organizational (e.g. worksite), community, town, state, and national level which influence availability of products, services, practices, and programs[128,130,131,133-135]. All these, and likely others not included in that list, interact in complex ways to ultimately influence individual PA and dietary habits[128,130,131,133,136,137].

For overweight/obese and older adults, particularly those with or at risk for chronic diseases, such as T2DM, these barriers may be more difficult to overcome[131,133,138]. Excess fat mass and low lean mass can decrease mobility and work capacity, increase the degree of discomfort experienced when performing PA, and also increase concerns over teasing and embarrassment when exercising[139]. Furthermore, certain chronic conditions and medications used to treat them can alter the typical response to exercise or otherwise be another challenge to overcome[139]. For instance, abnormal heart rate, blood pressure, ventilation, and localized inflammatory responses to exercise are specific condition/medication specific concerns which could result in a person choosing sedentary activities over PA[27,29,50,139]. Combination of these barriers may translate into decreased self-esteem and self-efficacy for PA, and thus less participation[139]. Self-efficacy is a critical psychological trait (and hallmark feature of the social cognitive theory [SCT], discussed below) identified as the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations[140]. It is considered an important determinant of health-related behaviors[140,141]. Older adults specifically report that self-efficacy (aka perceived confidence) in their ability to make effective diet and PA behavior changes is an important predictor of their likelihood to successfully initiate and maintain these beneficial changes[142]. Additionally,

Dutton and colleagues have shown that increases in PA amongst individuals with T2DM are mediated by improvements in self-efficacy[143].

Since RT guidelines are met less frequently than aerobic exercise, this suggests that it is more difficult to overcome the above mentioned barriers in order to participate in RT and that perhaps, additional barriers to adoption and maintenance of this mode of exercise exist[138,144]. These include: perceived complexity of RT programs[145]; concern over safety of RT protocols (particularly in older adults)[29]; incorrect perceptions that RT will lead to undesirable levels of hypertrophy (e.g.-women may fear they will get "too big and bulky")[144]; access to facilities to perform RT program, including cost of membership, distance from home/work, transportation to facility, and times facility is open[144,146]; and comfort in the exercise facility[138,144], to name a few. In recent evaluations of self-reported barriers to not maintaining a RT program, individuals with T2DM commonly endorse time, work commitments, illness/injury, poor weather (snow, heat/humidity, etc), vacation, boredom, access to facilility, cost of facility membership, and lack of social support as barriers to continued RT following initial adoption in a supervised research setting[146,147]. Several of these barriers associated with RT clearly have ties to self-efficacy and other SCT constructs, suggesting that those are key aspects to target in interventions designed to overcome barriers for RT participation.

Evidence-based Recommendations to Overcome Barriers

Policy and environmental changes will no doubt be needed to promote improvements in health-related behaviors and decrease the risk for chronic disease[128], but interventions which act more proximally will also be important to improve lifestyle and health-related outcomes, particularly in older adults at risk for diabetes. The importance

of focusing on behavior modification at the individual level has been strongly recommended for decreasing the risk of T2DM by both the ADA and the AND (Grade A[Footnote-3], Rating: Strong and Imperative[Footnote-4], respectively)[5,24]. The AND notes that interventions focused on decreasing risk of T2DM should focus on skill-building, problem-solving, and confidence-boosting. Specific techniques to incorporate include: goal setting, relapse prevention, self-monitoring, social support, and ability to practice the new behaviors[24]. Recommendations from the AHA for improving health behaviors endorses those of the AND, and offer additional evidence-based approaches. They call for interventions/programs to include: goal setting; self-monitoring (specifically via web-based tracking); follow-up (e-monitoring specifically mentioned); provision of feedback; motivational interviewing (Class I, Level of Evidence: A[Footnote-5]); provide long-term support (Class I, Level B); and use a multi-component approach [e.g. 2+ of previous] in behavior change efforts (Class I, Level A)[109]: In addition, the AHA provides recommendations for evidence-based healthcare systems approaches to support and

[3] ADA evidence grading system for clinical practice recommendations descriptions: **Grade A** – Clear evidence from well-conducted, generalizable RCTs that are adequately powered, compelling nonexperimental evidence, i.e., "all or none" rule developed by the Center for Evidence-Based Medicine at the University of Oxford, and/or supportive evidence from well-conducted RCTs that are adequately powered. **Grade B** – Supportive evidence from well-conducted cohort studies and/or supportive evidence from a well-conducted case-control study. **Grade C** – Supportive evidence from poorly controlled or uncontrolled studies and/or conflicting evidence with the weight of the evidence supporting the recommendation. **Grade E** – Expert consensus or clinical experience.

[4]See Appendix A for information related to the Academy of Nutrition and Dietetics rating system.

[5] AHA Evidence-Based Scoring System - *Classification of Recommendations:* **Class I**-Conditions for which there is evidence, general agreement, or both that a given procedure or treatment is useful and effective. **Class II**- Conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/efficacy of a procedure or treatment. **Class IIa**-Weight of evidence/opinion is in favor of usefulness/efficacy. **Class IIb**-Usefulness/efficacy is less well established by evidence/opinion. **Class III**-Conditions for which there is evidence, general agreement, or both that the procedure/treatment is not useful/effective and in some cases may be harmful. *Level of Evidence:* **A-** Data derived from multiple randomized clinical trials. **B-** Data derived from a single randomized trial or nonrandomized studies. **C-** Consensus opinion of experts.

facilitate improvements in health factors which are important for interventionists and program leaders to incorporate. These include: E-Systems for scheduling, tracking visits and follow-up for behavior change; e-records to assess, track, and report on health behaviors and factors, as well as to provide feedback; and E-Systems to facilitate provision of feedback to patients on their progress and efforts.[No class or evidence level given][109].

These evidence-based guidelines from esteemed organizations all include aspects specific to the SCT. This theoretical framework is frequently applied to health-related behaviors as it focuses on the interaction between personal, behavioral, and environmental factors which each influence the other, bidirectional and reciprocally[140] and ultimately determine if a person initiates and continues a certain habit (e.g.- PA, specific dietary intake, etc). The main constructs of the SCT are self-efficacy, self-regulation (e.g. planning, self-monitoring, goal setting, and self-incentives), and outcome expectancy (e.g. consequences-both positive and negative associated with participation in the behavior)[140,144]. These components interact with environmental factors to influence PA and other health-related behaviors[142,143,148,149].

As RT is likely a more difficult behavior to adopt and maintain, and much attention has previously been spent on interventions and programs designed specifically for AT, it is important for effective and efficacious programs targeting RT to be developed, tested, and refined[144]. For example, RT interventions which are theory-based, focus on increasing self-efficacy and self-regulation, and address barriers to adoption and maintenance of RT (such as the Resist Diabetes study[90]; see Methods section) are needed. Examples of specific program components include: opportunities for mastery of RT in

order to increase self-efficacy to perform the task, and a focus on planning for slips and strategies to get back on track in order to increase self-regulatory skills[89,90,150]. In addition, consideration for interventions which are easily deliverable and scalabale (e.g.- on-line) should also be taken in to account.

Clustering of Health-Related Behaviors

Health-related behaviors (e.g. physical activity, dietary intake, alcohol use, cigarette smoking, etc.) tend to cluster together. Individuals who engage in or abstain from one health-related behavior tend to also engage in or abstain from other health-related behaviors[109,123]. For instance, individuals with poor dietary habits, also generally fail to meet PA guidelines[151]. Cross-sectional examinations have noted that more physically active individuals tend to consume more fiber, fruits and vegetables, low-fat dairy products and certain vitamins and minerals, and less meat, fried foods, sweets, full-fat milk, total fat and saturated fat than less active individuals[151-153]. However, due to variations in data collection methodologies used to assess PA and dietary intake, as well as participant characteristics, this is not always observed[154]. Recently, Monfort-Pire and colleagues examined the relationship between diet quality and PA in a group of prediabetic Brazilian adults[155]. When adjusting for age and BMI, their analysis revealed that individuals who participated in >150 min/week had higher HEI [adapted for Brazilian populations] scores than those participating in <150 min/week. Importantly, this study utilized three 24-hour food recalls to calculate HEI, which is the gold standard criterion for assessing self-reported dietary intake[41].

These cross-sectional associations between dietary intake and PA lead to important questions related to changing multiple health-related behaviors. Specifically, is

it more effective to target each health-related behavior alone (e.g.- a single behavior change strategy), perhaps in a sequential order, or several at once in a simultaneous, multiple behavior change strategy? Furthermore, since these behaviors tend to cluster together, will targeting one result in "spontaneous" changes to others? If so, which behavior should be the focus of interventions? For instance, if someone initiates an exercise program, are they then more likely to make changes to their dietary intake, or vice-versa? If so, this phenomenon (often referred to as the "spillover effect") could be capitalized on in order to develop effective, yet time-, cost-, and resource-efficient interventions focusing on alterations of a single health behavior, rather than multiple.

Therefore, the primary aims of the current dissertation were to determine if initiation and maintenance of an RT intervention exerts a "spillover" effect, resulting in changes to 1. dietary intake and quality, and 2. non-RT PA. It is hypothesized that initiation and maintenance of a RT intervention will be associated with beneficial alterations to dietary intake and quality, and increased participation in non-resistance training physical activity among individuals with prediabetes from baseline to months 3, 9, and 15. An exploratory aim was to evaluate potential factors (physiological, psychological, and demographic) that influence whether or not participation in an RT intervention is associated with changes in dietary intake and quality, and non-resistance training physical activity. To complete these aims, data from the ***Resist Diabetes*** Study was utilized. Resist Diabetes is a 15-month phase II clinical trial focusing on initiation and maintenance of RT in older, overweight, inactive adults with prediabetes. The main aim of this trial is to demonstrate the efficacy and effectiveness of a high fidelity Social Cognitive Theory (SCT)-based intervention for initiating and maintaining RT in older

adults with prediabetes to improve glucose homeostasis[90]. As participants were not instructed or encouraged to change dietary habits or non-RT PA, this trial provided an opportunity to address the potential of a RT intervention to result in a spillover effect, and be associated with changes to dietary intake and quality, and non-RT PA. The initial analysis, determining if initiation of RT is associated with changes to dietary intake is presented in Chapter 3. The follow-up analyses examine if initiation and maintenance of RT are associated with changes to dietary quality, and non-RT PA, which is presented in Chapter 4.

Chapter 2 – Literature Review on the Spillover Effect of Exercise

Overview

No activity or behavior is truly an isolated event. Our behaviors are linked together, as shown by the clustering of health-related behaviors[151]. Thus, it is likely that our behaviors have the ability to influence future behaviors. This phenomenon, often referred to as the "spillover" effect, can be thought of visually as a series of dominoes or ripples on a pond, where one behavior influences subsequent behaviors[156]. These can be "supportive", meaning that engagement in one behavior leads to another behavior occurring in the same direction[156] (e.g. a decision to make a healthy breakfast at home instead of having a drive-thru biscuit is then followed up by taking a walk at lunch), or they can be "compensatory", meaning that engagement in one positive behavior leads to engagement in other negative health behaviors[157] (e.g. taking a dietary supplement with perceived health benefits leads to decreased PA and less healthy diet preferences[158]) which may negate the expected effects of the initial behavior[156,157]. Interventions can have unintended, and possibly unmeasured consequences/other effects. These can be positive and lead to additional health-related benefits, or negative. This concept is broadly applicable to a variety of health-related behaviors and settings from individual level decisions (e.g. antioxidant use increasing number of cigarettes smokers have)[158] up to the influence policies and taxes may have on an individual's behaviors (e.g. taxes on sugary beverages leading to increased beer purchases)[159]. The ensuing discussion will be narrow in scope, focusing specifically on the possibility for PA interventions to influence dietary intake and other PA. Evidence exists for both supportive and compensatory spillover effects, and further investigation is warranted[157].

Rationale for Studying the Spillover Effect

Ideally individuals would meet both AT and RT guidelines, and consume a healthful dietary pattern in line with evidence-based recommendations in order to promote healthy living and decrease risk for chronic disease, and it has been suggested that interventions focus on all three (refer to section 1.5). However, multi-component interventions can become excessively burdensome for participants, leading to ego-depletion, less adherence, more barriers, and greater susceptibility to relapse[160-163]. As an example, in a group of individuals with T2DM who were randomized to either AT, RT, or an AT + RT intervention, those assigned to the combination group reported time, work commitments, and boredom to be barriers to protocol adherence more so than either of the single-component intervention groups[147]. Furthermore, multi-component interventions can become too burdensome for interventionists due to increased strains on resources (time, financial, personnel, space, etc.), which then limits the number of individuals who can be enrolled[163]. In their systematic review and economic evaluation, the Community Preventive Services Task Force determined that intensive combined diet and exercise programs were more effective than less intensive programs at preventing T2DM and that overall, combined interventions are to be considered cost-effective[111-113]. However, limited evidence is available on the cost-effectiveness of these interventions, and intensive programs such as the DPP cost $5,881 (in 2013 U.S. dollars) per participant[111]. In 2005, the CDC funded five states to translate diabetes primary prevention trials (such as the DPP) into real-world settings (known as the Diabetes Primary Prevention Initiative Interventions Focus Area [DPPI-IFA]). Early evaluation of these programs revealed that "implementing the DPP curriculum as designed was too burdensome" and that "adapting the DPP curriculum was also a challenge in terms of

time and resources required"[164]. As such, there is a need to develop interventions with improved cost-benefit ratios. Interventions which are less intensive and focus on the alteration of only a single health-related behavior (such as the Resist Diabetes trial) have lower associated costs per participant and possibly greater translational potential[89]. If the spillover effect is observed and results in beneficial alterations in dietary intake and non-RT PA, the cost-benefit ratio of these single-behavior change interventions could far exceed that of more intensive programs.

Evidence for Spillover Effect between PA and Dietary Habits

The majority of evidence on the spillover effect comes from the literature on weight loss interventions showing that they do not result in as much weight loss as expected[154,157,165]. Exercise interventions are generally considered inadequate to produce changes in body weight unless done at a high level, often leading to incorrect assumptions about its importance in weight management efforts and the concept of energy balance[50,84]. Since increased PA should alter the energy balance equation in the direction of an energy deficit and result in weight loss, it suggests that when weight loss does not occur, it is because compensation occurs to restore energy balance by individuals increasing energy intake, decreasing level of other PA, or a combination of both. However, portrayal of only compensatory changes occurring resulting in little to no weight loss are not completely accurate as a wide variation in individual responses to exercise interventions designed to result in weight loss are observed. Some individuals lose substantial amounts of weight, some lose a lesser amount, some do not change their weight, and some gain weight[154,157,165]. Thus, it is possible that in some situations, a PA

intervention serves as a gateway behavior to improve dietary intake and/or increase other forms of PA[166-168].

Exercise Exerting a Spillover Effect on Dietary Intake

A recent meta-analysis by Donnelly sought to determine if increased exercise or PA alters energy intake or dietary macronutrient composition[154]. This comprehensive review found that the majority of cross-sectional, acute, short-term, and long-term trials found no effect of an exercise intervention on total energy or macronutrient intake[154]. However, these findings must be interpreted within the context of the many limitations associated with the literature on this topic. First, most studies have not been conducted specifically to determine the influence of exercise on dietary intake, and often times participants are instructed to not alter diet or other PA. Second, assessment of dietary intake has typically been via self-reported measures such as FFQs, or food records/recalls. Studies which have directly assessed energy intake are generally focused on the influence a single bout of exercise has on acute energy intake during a buffet meal in the laboratory. This is likely not representative of habitual intake and dietary alterations which may occur following chronic exercise participation. Third, most studies have not assessed dietary changes beyond energy or macronutrient intake, and it is possible that alterations in specific food groups/nutrients do occur despite no changes to total caloric intake and macronutrient composition. Fourth, most studies have been conducted in young populations (and the review by Donnelly included only studies in healthy adults) and thus may not be indicative of the influence exercise interventions may have on older adults and/or those with, or at risk for, chronic diseases. Finally, differences in intervention characteristics (group vs individual setting; theory-based vs

not; main outcomes of behavior change vs physiological adaptations; mode, intensity, frequency, volume, and supervision of exercise component, etc.) are likely important determinants of whether or not the spillover effect is seen. Given these limitations, and recent estimates from RCTs utilizing objective measures of PA and dietary intake showing that mean weight loss from exercise studies is up to 55-64% less than that which would be expected after accounting for metabolic compensation (e.g. decreased resting metabolic rate), it is clear that behavioral compensation does occur in some individuals, and that increased energy intake is likely involved[165].

Trials conducted in older and/or more at-risk adults have also yielded conflicting results[167-172]. For example, Hughes and colleagues randomized 18 older, previously sedentary adults with impaired glucose tolerance to one of two 12-week supervised aerobic exercise conditions: Moderate intensity (50% of maximal heart rate reserve) or high intensity (75% of maximal heart rate reserve), and did not detect differences in energy or macronutrient intake in response to training[62]. However, this study was conducted with the purpose of evaluating a physiological outcome (e.g. changes in skeletal muscle GLUT4 content), not a behavioral outcome. It is likely that interventions which target behavior change and are theoretically-based would be more likely to result in maintenance of the targeted behavior as well as spillover to influence other behaviors[168,173]. Findings from "The Coach Approach" study by Annesi and colleagues support that view. Obese adults were enrolled in an SCT-based exercise intervention designed to result in weight loss were randomized to receive either standard nutrition education or an SCT-based nutrition intervention as well. Both treatments were associated with increased fruit and vegetable consumption and self-efficacy and self-

regulation skills, though the SCT-nutrition group experienced a greater increase in fruit and vegetable intake, and also increased their self-regulation for eating[171]. While promising, this study utilized a less reliable measure of dietary intake (e.g. a fruit and vegetable screener) and nutrition education was provided to both groups. Therefore more research is needed in order to assess the potential for an exercise intervention to influence other dietary choices. Furthermore, like most of the literature in the field, these studies only examined the potential for a spillover effect from AT, and a focus on the potential for RT to alter dietary intake has been suggested[157].

Trials which have focused specifically on RT have provided promising preliminary evidence that successful adoption and maintenance of a RT regimen may be a keystone, or gateway behavior leading to alterations in dietary intake. In a group of overweight/obese adults with dyslipidemia, Bales and colleagues reported a decrease in total fat intake from baseline to post 8 months of a RT intervention[172]. Since reduced fat intake is a recommendation for the treatment of hyperlipidemia[174], it is plausible that dietary modifications associated with successful initiation of an exercise intervention will be specific to the disease state individuals are at risk for. Furthermore, Avila et al. reported a reduction of ~50 kcals/day of energy intake in a group of relatively healthy overweight/obese adults from baseline to week 10 of a RT intervention[167]. While this difference was not statistically significant, they had a small sample size (n=15) which may have inhibited the detection of modest decreases in energy intake in response to RT. While preliminary, these findings suggest that mode of exercise, intervention components, and participant characteristics are likely important factors in determining if the spillover effect occurs in response to an exercise intervention.

Exercise Exerting a Spillover Effect on Other Forms of Physical Activity

In addition to increased caloric intake being suggested as a reason for less weight loss occurring than expected with initiation of an exercise regimen, it is also likely that individuals compensate for the increased energy expenditure by decreasing other forms of PA[157,165]. A session chaired by Dr. Barry Braun at the 2012 American College of Sports Medicine Annual Meeting and a subsequent review published by the presenters focused on compensatory adaptations resulting in resistance to exercise-induced weight loss sought to address this issue. Short (2-10 days) and longer (8+ weeks)-term studies produced equivocal results, with some showing increased non-exercise PA, non-exercise activity thermogenesis (NEAT), and total daily energy expenditure (TDEE) and others finding decreases in those variables in response to exercise training[157]. The authors note that the conflicting results are likely due to variations in exercise mode/intensity, duration, participant characteristics, and the methods used to measure non-exercise PA/energy expenditure (e.g. – self-report, activity monitors, doubly-labeled water, etc). Interestingly, while no study compared these populations directly, their review indicates that older adults are more likely than younger adults to be prone to compensatory changes in NEAT and non-Ex PA[157]. As reductions in NEAT and non-exercise PA will likely lower TDEE and thus the degree of weight loss experienced, this has important implications for the design of effective exercise interventions for older adults who are at greater risk for chronic disease and loss of independence associated with the aging process. While concerning, it is important to note that the majority of studies have used endurance training in their intervention, not strength-training, and it is possible that RT may be more likely to promote increased non-exercise PA[157,175,176].

To date, only a few trials have examined changes in non-exercise PA in response to an RT intervention. Unsurprisingly, results are mixed, and variations in study design, participant characteristics, assessment of PA, etc. limit our ability to generate overarching conclusions. Church et al. saw no change in step counts outside of supervised exercise in the RT and combination (AT + RT) groups in the 9 month HART-D trial which was designed to examine the influence of exercise mode on HbA1c in a group of adults with T2DM[98], suggesting that no spillover effect occurs. However, this trial did not include a behaviorally-focused theoretical approach and all exercise sessions were supervised, which may decrease the potential for an exercise intervention to promote changes to other forms of PA. In addition, the location (Baton Rouge) and study population (~44% African American, diagnosed with T2DM for ~7 years, etc) may be important factors related to the potential for RT to result in a spillover effect[133,147,177]. Conversely, a study by Hunter and colleagues in overweight, premenopausal women found that the group assigned to RT during an energy-restricted diet increased non-exercise PA more than the AT group and no-exercise group[84]. This trial relied on objective measures of various components of energy expenditure (indirect calorimetry and doubly labeled water) and noted that the increase in PA seen in the RT group was related to increased ease of locomotion (e.g. decreased VO2 of walking), providing important mechanistic data which may explain why RT could be effective at increasing non-RT PA. However, this study was conducted in young (20-44 years old) women, and results cannot be generalized to older men and women. A recent analysis from Dr. Fielding's lab examined the hypothesis that increased functional ability due to a RT intervention could be responsible for increasing non-RT PA in a group of previously sedentary elderly adults

(70-85 years old). Physical function improved over the 6-month RT intervention, but non-RT PA (assessed via accelerometry) did not increase[178]. While lacking a control group and relying on secondary data analysis, their findings suggest that improvements in muscular strength and functional ability are insufficient to increase non-RT PA in elderly adults and that additional determinants of PA (e.g. psychosocial factors) may need to be addressed.

To date, findings related to the potential for exercise interventions to result in changes to dietary intake and other forms of PA are inconclusive and the potential for RT specifically to exert a spillover effect on other health-related behaviors has not been thoroughly examined, resulting in investigators citing it as a priority research area[157]. Preliminary results, while mixed, provide encouraging evidence that this mode of PA may be unique in its ability to influence dietary intake and non-RT PA. Further research, particularly in at risk populations, utilizing theoretically-based lifestyle interventions, and examining mechanisms and determinants of the spillover effect in response to RT are warranted.

Mechanisms Related to the Spillover Effect

In addition to trials providing evidence on if –and in what direction - spillover effects occur in response to an exercise intervention, mechanistic data can also be found to explain both compensatory and supportive behavioral adaptations, which likely leads to more confusion. Potential mechanisms include physiological, metabolic, functional, and psychosocial reasons for alterations in dietary intake and other forms of PA in response to initiation of exercise programs. For instance, exercise likely results in alterations in production of gut peptides (e.g. PYY, ghrelin, and leptin) which may blunt

appetite and thus decrease food intake. However, data are mainly from acute studies involving AT, and conflicting, so a consensus has not been reached regarding the ability of exercise to alter GI hormones in a manner than influences long-term caloric intake[179-183]. Furthermore, the changes seen in these appetite-regulating hormones are likely dependent upon exercise intensity, as more intense exercise typically decreases appetite more than low intensity exercise[125,182], and as such blunting of appetite post exercise is less likely in older, overweight, previously sedentary adults participating in lower-intensity exercise programs. Similarly, conflicting data exist on psychosocial mechanisms which may explain the presence or absence, and direction of observed spillover effects. For instance evidence for supportive changes to other health-related behaviors following successful initiation of an exercise program suggest that self-efficacy will be enhanced, which is then transferable to other health-related domains (e.g. dietary intake)[140,150,166,171]. Conversely, participation in an exercise intervention may lead to decreased self-control for other health-related behaviors, resulting in a compensatory spillover effect. Some data suggest that self-control may be a limited resource, and a source of glucose depletion, which then leads to less ability to exert self-regulatory skills to another task[160,161,184]. As these select examples show, the mechanisms underpinning the spillover effect are not well elucidated. They are likely to be multi-factorial, complex, and integrated. Thus, this is another area of investigation related to the spillover effect that deserves focused attention, specifically as it relates to RT.

In addition to some of the mechanisms discussed previously specific to RT (e.g. – more challenging behavior to initiate, so improvements in self-efficacy may be greater and spillover to other health-related behaviors; and improved physical function increasing

non-RT PA), others may also support the rationale for focusing on RT as the "gateway" behavior in single-component interventions. For instance, RT may be a more 'exciting' and enjoyable mode of exercise than AT. Tulloch and colleagues found adults with T2DM randomized to a RT or combination (RT + AT) group in an exercise trial reported greater enjoyment and adherence to the exercise prescription than those randomized to the AT only group[147]. One participant in the combination group commented, "The weight training is not the problem, but I don't like the treadmill…it's incredibly boring". A similar theme emerged in a study by Wycherly et al. In their 1 year follow-up interviews with subjects who previously completed a 16-week lifestyle intervention involving an energy-restricted diet with or without supervised RT, several participants indicated that participation in the RT intervention helped them to adhere to the dietary prescription[146]. A sample interview transcript read as follows: "Without exercise, I probably would have got bored with the programme". Therefore, RT may be a novel mode of exercise for adults, which is impetus enough for increased adherence to PA and dietary prescriptions.

Another rationale for focusing on RT is because overweight/obese adults are often limited in their ability to perform PA, particularly weight-bearing, aerobic activities such as jogging due to the increased effort required to move a larger body[139]. Participation in RT may be a more comfortable form of PA for these people to participate in, which overtime improves economy and comfort of AT participation (as suggested by the findings of Hunter et al[84]). Interestingly, in the same study by Wycherly et al mentioned above, while 33% of participants assigned to the 16-week diet + RT group were no longer participating in RT after 1 year, 13% had since taken up other forms of PA (walking and hiking). Along the same lines, in addition to RT improving functional ability, it is able to

increase skeletal muscle mass, which is more metabolically active than adipose tissue[145]. Overweight/obese adults who embark on weight loss plans focusing on caloric restriction or AT only, are likely to lose lean mass as well as fat mass. Loss of FFM, may predispose individuals to weight regain due to lower basal metabolic rate. As such, intervening on RT first in an effort to increase lean mass before initiating caloric restriction and/or AT may be a more effective intervention sequence for decreased chronic disease risk.

Finally, and while speculative in nature, it is plausible that overcoming the barriers associated with RT (see Chapter 1), such as getting to the gym, lowers the "activation-energy" needed to also participate in AT. Most fitness facilities with weight machines and equipment will also have treadmills, bikes, and aerobic-based fitness classes. Since those engaged in RT are already at the exercise facility for one purpose they may simply extend their time there a bit in order to also participate in AT. Tying a new behavior (AT) in to an established behavior (RT), might make it easier for this additional behavior to be adopted and maintained. More research focused specifically on measuring the spillover effect related to RT, and potential mechanisms responsible, are clearly needed. Thus, this dissertation also addresses this gap in the literature.

Chapter 3 – Manuscript 1 -Dietary intake modification in response to participation in a resistance training program for sedentary older adults with prediabetes: Findings from the Resist Diabetes study

Abstract:

Engagement in one type of health behavior change may exert a "spillover" effect resulting in other behavior changes. Few studies have examined dietary intake following prolonged training, and none have evaluated spontaneous dietary changes beyond alterations in energy or macronutrient intake following initiation of strength/resistance training (RT). The purpose of this observational investigation was to determine if spontaneous dietary intake modifications occur in response to initiation of an RT program, among older adults. Previously sedentary adults with prediabetes (n = 134, age = 59 ± 1 years) were enrolled in a supervised 12-week RT program. Participants were not given dietary advice or encouraged to change eating behaviors. Three non-consecutive 24-hour dietary recalls were collected at baseline and after 12 weeks of RT. Reductions in intake of energy (1914 ± 40 kcal vs. 1834 ± 427 kcal, p = 0.010), carbohydrate (211.6 ± 4.9 g vs. 201.7 ± 5.2 g, p = 0.015), total sugar (87.4 ± 2.7 g vs. 81.5 ± 3.1 g, p = 0.030), glycemic load (113.4 ± 3.0 vs. 108.1 ±3.2, p= 0.031), fruits and vegetables (4.6±0.2 servings vs. 4.1±0.2 servings, p= 0.018), and sweets and desserts (1.1 ± 0.07 servings vs. 0.89 ± 0.07 servings, p = 0.023) were detected over time. No changes in other dietary intake variables were observed. Mode of exercise and disease state may be important factors in determining whether dietary modifications occur with exercise initiation, among previously sedentary adults. Successful initiation of RT may represent an opportunity for health care professionals to promote beneficial changes in dietary habits, among older adults with prediabetes.

Introduction:

Less than 20% of middle-aged and older adults meet national physical activity and dietary guidelines[1-3], yet optimal strategies for behavior change remain uncertain. Engagement in one type of health-related behavior (e.g. exercise) may exert a "spillover" effect resulting in changes to another (e.g. diet)[4]. Additionally exercise may influence dietary intake by altering gut peptides that influence appetite and satiety[5-7]. Although findings are conflicting, aerobic exercise generally reduces appetite and/or energy intake while resistance training (RT) does not[5,8,9].

To date, most investigations have focused on the influence of an acute exercise bout on reported hunger/satiety and alterations in gut peptides, rather than longer term trials with comprehensive analyses of dietary intake. The few studies which have examined dietary intake following prolonged (10+ weeks) RT have not evaluated dietary changes beyond energy or macronutrient intake[8,9]. Due to the importance of consuming specific nutrients, food components and food groups for optimal health and disease prevention[2,10,11], more comprehensive investigations are warranted.

RT is recommended for the treatment and prevention of type 2 diabetes[12,13], yet, only 13.7% of older US adults regularly engage in RT[14]. Exercise in general may be a more challenging behavior to adopt compared to dietary changes, particularly when dietary change is already underway[15], and it is possible that successful adoption of an exercise program first may increase self-efficacy for other beneficial lifestyle changes, such as improving dietary habits[4,15]. The purpose of this observational trial was to determine if sedentary, overweight individuals with prediabetes who complete an intervention targeting a single health behavior, initiating RT, spontaneously alter their dietary intake.

Methods and materials:

Participants

This investigation utilized data from the "Resist Diabetes" clinical trial in which participants engaged in a supervised 12-week RT program, but were not provided with personalized dietary advice or recommendations to alter eating habits. Overweight/obese (BMI 25–39.9 kg/m2), middle-aged and older (50–69 years), weight-stable (±2 kg in past year), sedentary or minimally active (i.e., b120 min/week of moderate intensity physical activity) adults with prediabetes (impaired fasting glucose ≥95 and b126 mg/dl and/or impaired glucose tolerance ≥140 and b200 mg/dl)[16-18] were eligible. The Virginia Tech Institutional Review Board approved the study protocol and participants provided written informed consent prior to enrollment.

Measurements and resistance training protocol

Detailed methods for the "Resist Diabetes" trial are published elsewhere[19]. The current analysis utilized dietary intake and anthropometric results from baseline and week 12 (post-intervention initiation). Baseline dietary intake was assessed during the two-week period following initial eligibility screening for prediabetes status, and after 12 weeks of RT, using the average of three multiple-pass 24-h recalls collected on nonconsecutive days (one weekend day included) by trained research dietitians/technicians. This method is able to determine energy intake to within 8–10% of actual energy intake[20,21]. To exclude potential under-reporters, participants (n = 25) that reported an energy intake b80% of estimated resting metabolic rate (Mifflin-St. Joer equation[22]) were excluded from final analysis.

Average daily servings using recommendations from the USDA[23] (when available) or FDA[24] of specific food groups were calculated for: drinking water; no/low-

calorie beverages; sugar-sweetened beverages; fruits and vegetables (FV); FV excluding juices; savory snacks; high/medium-fat meats; and sweets/desserts. Recommendations from the Dietary Guidelines for Americans 2005 and the USDA Food Guide Pyramid guided decisions regarding the inclusion of foods within the NDSR NCC Food Group Serving Count System[25].

Participant's height and weight were determined without shoes, in light clothing to the nearest 0.1 cm and 0.1 kg, respectively using a wall-mounted stadiometer and a digital scale. Body fat percent, fat mass (FM) and fat-free mass (FFM) were assessed using dual energy X-ray absorptiometry (DXA — GE Lunar Prodigy, software version 11.40.004, Madison, WI).

Following baseline assessments, participants completed a 12-week RT program, 2 sessions per week, supervised by American College of Sports Medicine (ACSM)-certified personal trainers. Additionally, an information packet was provided to participants, which contained their anthropometric measurements and dietary intake analysis compared to national dietary reference intakes (DRI). No dietary advice or encouragement to alter eating behaviors was given.

Statistical analyses

Statistical analyses (SPSS v. 12.0, SPSS Inc., Chicago, IL) included descriptive statistics, paired-sample t-tests to assess changes from baseline to week 12 for anthropometric and dietary variables, and independent sample t-tests to assess sex differences in mean change from baseline to week 12. Effect size was determined by calculating Cohen's d (d = paired differences mean/paired differences standard deviation)

and conventional interpretation was utilized[26]. Continuous data are expressed as mean ± SEM. Alpha was set at 0.05.

Results and Discussion:

Participant characteristics, RT session and recall completion

Participants (n = 134; age = 59.8 ± 0.5 years, 70% female, 94% white) completed 90% of sessions during the RT program. No change in body weight occurred (93.1 ± 1.2 kg vs. 93.1 ± 1.2 kg, p = 0.975) from baseline to week 12, respectively. FM declined (40.0 ± 0.7 kg vs. 39.4 ± 0.7 kg, p b0.001) and FFM increased (52.5 ± 0.9 kg vs. 53.0 ± 0.9 kg, p = 0.001). Most participants completed all three possible dietary recalls (pre: 96%, post: 86%). Self-reported energy intake was within 8% of estimated energy needs (Mifflin-St. Joer × 1.3 activity factor) (pre: 6%, post: 10%), suggesting minimal underreporting.

Energy, macronutrient and food group intake

Table 1 summarizes energy, macronutrient, selected micronutrients and food group intake at baseline and week 12. Reductions in intake of total energy (p= 0.010, Cohen's d effect size [d]= 0.22), carbohydrate (p= 0.015, d= 0.21), total sugar (p= 0.030, d= 0.19), glycemic load (p= 0.031, d = 0.19), FV excluding juices (p= 0.018, d = 0.21), and sweets/desserts (p = 0.023, d = 0.20) were observed from baseline to week 12. Although the effect size is small, reduced intake of sweets/desserts in this population following initiation of an exercise program is a beneficial dietary modification consistent with the recommendation to reduce dessert consumption in the Dietary Guidelines for Americans (DGA) 2010[2]. No changes in percent of energy intake from macronutrients (carbohydrate: 43.3 ± 0.7% vs. 42.8% ± 0.8%; fat: 37.0 ± 0.6% vs. 37.0 ± 0.6%; protein:

17.6 ± 0.3% vs. 18.0 ± 0.3%, p N 0.05) or other dietary intake variables were observed. No sex differences (p N 0.06) in dietary changes were noted (data not shown).

Table 1
Reported energy, macronutrient, micronutrient and food group intake at baseline and after 12 weeks of supervised resistance training among previously sedentary, older, prediabetic adults.

	Baseline	Week 12
Total energy, kcal*	1914 ± 40	1834 ± 37
Energy density, kcal/g	0.7 ± 0.02	0.7 ± 0.02
Macronutrients		
Carbohydrates, g*	211.6 ± 4.9	201.7 ± 5.2
Total sugar, g*	87.4 ± 2.7	81.5 ± 3.1
Added sugar, g	56.7 ± 2.6	52.3 ± 2.7
Total fiber, g	19.2 ± 0.6	18.3 ± 0.6
Fat, g	81.9 ± 2.5	77.9 ± 2.0
Saturated fat, g	27.2 ± 0.8	25.4 ± 0.8
Monounsaturated fat, g	29.9 ± 1.1	28.6 ± 0.9
Polyunsaturated fat, g	18.3 ± 0.7	17.4 ± 0.2
Trans fat, g	3.2 ± 0.2	2.9 ± 0.1
Protein, g	81.8 ± 2.0	79.9 ± 1.8
Animal protein, g	56.2 ± 1.7	54.5 ± 1.6
Vegetable protein, g	25.6 ± 0.8	25.4 ± 0.8
Alcohol, g	6.2 ± 1.0	6.3 ± 1.1
Micronutrients		
Calcium, mg	815 ± 22	781 ± 22
Iron, mg	14.7 ± 0.4	13.8 ± 0.4
Sodium, mg	3364 ± 86.1	3317 ± 84
Vitamin A, IU	7261 ± 395	7351 ± 492
Vitamin B_{12}, mcg	4.8 ± 0.2	4.7 ± 0.2
Vitamin C, mg	78.1 ± 4.1	75.8 ± 3.9
Vitamin E, IU	14.0 ± 0.7	13.5 ± 0.7
Food group servings		
Drinking water, servings	3.7 ± 0.2	3.8 ± 0.2
No-and low-calorie beverages, servings	6.7 ± 0.3	6.7 ± 0.2
Sugar sweetened beverages, servings	0.5 ± 0.07	0.6 ± 0.08
Total fruits and vegetables, servings	4.9 ± 0.19	4.5 ± 0.2
Fruits and vegetables excluding juices, servings*	4.6 ± 0.2	4.1 ± 0.2
Savory snacks, servings	0.14 ± 0.03	0.14 ± 0.03
High-and medium-fat meats, servings	2.2 ± 0.16	2.3 ± 0.15
Sweets and desserts*	1.1 ± 0.07	0.89 ± 0.07

* Significant change from baseline to week 12, $p < 0.05$.

Although the reduction in FV intake is contrary to DGA 2010 recommendation for weight management, participants' intake remained within that recommended (i.e., 4-4.5 servings of FV for an 1800–2000 kcal eating pattern)[2]. Further dietary modifications, including replacement of sweets/desserts with FV could be warranted, in order to

increase dietary fiber intake and reduce total fat intake to DGA 2010 recommendations (22–28 g and 20–35% of total calories, respectively)[2].While speculative, it is possible that participants reduced fruit consumption based upon media coverage of research portraying fructose as harmful, without understanding the differences between amount of fructose naturally present in fruit and that present in foods as added sugars, and the amounts of fructose associated with adverse metabolic effects[11,27].

Research is inconsistent, but accumulating evidence suggests that the glycemic response as well as the effect on blood pressure, blood lipids, and inflammation differ between added and naturally occurring sugars[11,27,28]. Food labels currently do not distinguish between naturally occurring and added sugar content, making it difficult for consumers to differentiate the two. While decreases in glycemic load and total sugar intake were noted, the American Diabetes Association currently does not have specific recommendations for these dietary components for type 2 diabetes prevention, due to inconsistent and insufficient information[12,29].

These findings are contrary to previous reports that RT does not result in decreased energy intake[8,9]. A similar study by Bales and colleagues of overweight/obese adults with dyslipidemia reported a reduction in total fat intake from baseline to post-RT (8 months)[9]. Reductions in total and saturated fat intake are components of the Therapeutic Lifestyle Change diet recommended for treatment of hyperlipidemia[30, 31] whereas controlled carbohydrate intake is recommended for management of type 2 diabetes[12]. Avila and colleagues saw no significant decrease in energy intake in a group of relatively healthy overweight/obese subjects following ten weeks of RT[8]. However, given their small sample size (n = 15), we would suggest that their reported ~50 kcal

reduction in energy intake is comparable to the ~80 kcal reduction noted in the current study and supportive of our finding that initiation of RT may cause modest decreases in energy intake.

Strengths and limitations

To our knowledge, this is the first investigation to include a comprehensive analysis of dietary intake changes in response to initiation of an exercise program, among previously sedentary adults. Dietary intake was collected using recommended methods[31,32], with a high recall completion rate and low degree of potential underreporting. This investigation provides novel information on changes in food choices which may spontaneously occur in a prediabetic population, upon participation in an RT initiation program. Nevertheless, we acknowledge several limitations. This investigation was observational, lacked a control group and focused specifically on initiating RT. Thus, we cannot determine if dietary changes observed result from exercise mode, prediabetes status, and/or educational information provided in baseline feedback packets. However, most participants were aware of their prediabetes status prior to enrollment, since being at high-risk for diabetes was listed in study recruitment materials. Additionally, participants were informed of their OGTT results (i.e., prediabetes status) the day of the assessment clinic yet food recalls were completed in the 2 weeks following the OGTT. If prediabetes diagnosis alone was an impetus for dietary modifications, they likely would have occurred in that two-week time frame, before completion of the baseline dietary records and prior to beginning RT. Thus it is unlikely that dietary changes occurring from baseline to week 12 could be attributed to knowledge of prediabetes status, as this was communicated to participants prior to completion of the baseline dietary records.

Although trained research staff collected dietary data and potential under-reporters were excluded prior to analyses, reliance on self-reported dietary intake rather than objective measures is a limitation[33]. However, accuracy is likely relatively high as predictable social desirability changes, such as a large increase in reported FV intake, did not occur (rather a small decrease was noted). Providing subjects with result packets following baseline testing containing their anthropometric measurements and dietary intake compared to DRIs may be sufficient to prompt some to initiate dietary behavior changes. However, dietary behavior change is a difficult process that may not occur with education alone[34] and is unlikely to occur with the provision of passive educational materials and information[35]. Finally, the duration of our initial supervised training phase does not provide information on whether changes persisted beyond 12 weeks; however future investigations should address this possibility.

Findings from this observational trial suggest a "spillover" effect of health-related behavior change may exist as successful initiation of an exercise program may result in spontaneous dietary modifications. This information may be meaningful to health professionals, as successful initiation of an RT program may represent an opportunity to encourage and support beneficial changes in dietary habits, among older, previously sedentary clients and patients with prediabetes. Future studies should investigate timing and sequence of changing health behaviors, and include assessments of changes in health behavior constructs (i.e., self-efficacy), in order to develop lifestyle intervention strategies for health promotion and disease prevention.

Conclusions:

Previously sedentary, prediabetic individuals who completed 12 weeks of RT without receiving dietary counseling reported decreasing total energy and carbohydrate (g) intake. Reduction in FV and sweets/ desserts likely explains the reduction in energy and carbohydrate intake. To the best of our knowledge, this is the first investigation to assess spontaneous dietary changes in response to RT beyond energy and macronutrient intake. Mode of exercise (aerobic vs. RT) and disease state may be important factors in determining whether dietary modifications occur with exercise initiation. Additional research assessing success of exercise programs when coupled with dietary modifications, and the timing and sequence of initiating these changes, is warranted.

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Chapter 4 – Manuscript 2 - Resistance Training is associated with Spontaneous Changes in Aerobic Physical Activity but not Overall Diet Quality in Adults with Prediabetes

Abstract:

This study aims to determine if initiation and maintenance of resistance training (RT) is associated with spontaneous changes in dietary quality and non-RT physical activity (PA) in adults with prediabetes. Sedentary to recreationally-active, overweight/obese adults (n=170, BMI= 32.9±3.8 $kg \cdot m^{-2}$, age=59.5±5.5, 73% female) with prediabetes were enrolled in the 15-month Resist Diabetes trial. Participants completed a supervised 3-month RT (2x/week) initiation phase followed by a 6-month maintenance phase and a 6-month no-contact phase. Participants were not encouraged to change eating or non-RT PA behaviors. At baseline, and months 3, 9, and 15, three non-consecutive 24-hour diet recalls were collected to evaluate dietary intake and quality, the Aerobics Institute Longitudinal Study Questionnaire was completed to evaluate non-RT PA, and body mass (BM), body composition (DXA), and strength (3 repetition maximum [RM] on leg and chest press) were measured. At months 3, 9, and 15, social cognitive theory (SCT) constructs were assessed with a RT Health Beliefs Questionnaire. Mixed effects models were used to assess changes in dietary intake and non-RT PA over the 15-month study period. Energy and carbohydrate intake decreased with RT (β= -87.9, p=.015 and β= -16.3, p<.001, respectively). No change in overall dietary quality (HEI-2010 score: β= -0.13, p=.722) occurred, but alterations in HEI-2010 sub-scores were detected. Maintenance of RT was accompanied by an increase in MET-min/week of total non-RT PA (β=153.5, p=0.01), which was predicted by increased self-regulation for RT (β=78.1, p=0.03). Initiation and maintenance of RT may be a gateway behavior leading to

improvements in other health-related behaviors. These results provide rationale for single-component lifestyle interventions as an alternative to multi-component interventions, when resources are limited.

Introduction:

Type-2 diabetes mellitus (T2DM) and prediabetes prevalence have increased in recent decades, reaching epidemic levels[1]. These states of hyperglycemia are associated with increased risk of macro- and micro-vascular complications[2] and medical costs[3]. Physical inactivity, obesity, and poor dietary quality have been established as key factors in the progression to many chronic diseases, including T2DM[4]. Middle-aged and older adults are at increased risk for developing prediabetes and T2DM due to age-related muscle loss, increased fat mass, and alterations in glucose handling[5]. In addition, this segment of the population is least likely to meet physical activity (PA) guidelines, particularly the resistance training (RT) recommendation of completing a whole body routine 2x/week[6]. Thus, interventions that improve the initiation and maintenance of multiple health-related behaviors and decrease metabolic disease progression in this population are needed[7].

Improving health-related behaviors is challenging, and optimal strategies to promote and maintain changes have yet to be determined. Furthermore, effective behavior change interventions tend to be time-, cost-, and resource-intensive, limiting the ability for efficacious programs to be broadly translated into community or clinical settings[8]. In addition, multi-component interventions can be burdensome for participants, leading to increased barriers, reduced adherence, and greater susceptibility to relapse[8-10]. Evidence suggests that health-related behaviors, particularly diet and exercise habits, tend

to cluster together; individuals that do not meet PA guidelines, also generally have poor dietary habits[11]. Thus, intervening on one behavior (e.g. PA) may lead to a "spillover effect" and result in alterations to other behaviors (e.g. dietary intake)[12,13]. If so, this phenomenon could be utilized in order to develop effective, yet time-, cost-, and resource-efficient interventions focusing on alterations of a single (vs. multiple) health behavior.

To date, findings related to the potential for exercise interventions to produce changes in dietary intake and other forms of PA are mixed, and have focused primarily on aerobic exercise. The potential for RT to exert a spillover effect on other health-related behaviors has received little attention[14,15]. Preliminary results have provided encouraging evidence that RT may be a unique mode of exercise in its ability to influence dietary intake and non-RT PA[13,16-19]. We have previously reported that initiation of a RT intervention (e.g. Initiation Phase of the Resist Diabetes study[20]) was associated with a reduction in reported energy, carbohydrate, total sugar, fruit and vegetable, and sweets and dessert intake over a 3 month period[13]. Similarly, Bales and colleagues have shown that an 8 month RT program is associated with decreased self-reported fat intake in overweight/obese adults with dyslipidemia[17]. This suggests that dietary modifications associated with successful initiation of an exercise intervention may be specific to the disease state individuals are at risk of developing. Supporting the notion that RT may increase non-RT PA, using objective measures of PA energy expenditure, Hunter et al. reported that free living PA increased in a group of women assigned to RT during a calorie-restricted weight loss intervention, but not in those assigned to an aerobic training[18]. However, the participants were young and relatively healthy, and it is currently

unknown if RT would alter non-RT PA in older, less healthy adults, or among those with prediabetes.

To date, no evaluation of changes to overall diet quality in response to exercise interventions have been conducted. The objective of this investigation was to determine if participation in a social cognitive theory (SCT)-based RT program targeting the initiation and maintenance of RT exerts a spillover effect on other health behaviors. Specifically, we aimed to determine if RT initiation and maintenance are associated with alterations in overall diet quality (HEI-2010 scores), and total non-RT PA in a population at risk for T2DM. A secondary aim was to explore demographic, physiological, and psychosocial factors which may be predict spontaneous changes in health behaviors, with RT adoption.

Methods:

Participants

Overweight/obese (BMI: 25 – 39.9 kg/m^2), middle-aged (50-69 years) adults who were sedentary to recreationally active and had not engaged in RT for the previous year were recruited from the Roanoke, Virginia area. Detailed inclusion and exclusion criteria have previously been published[20]. Briefly, eligible individuals had prediabetes, defined as impaired fasting glucose (IFG; fasting plasma glucose between 95-125 ml/dl[21]) and/or impaired glucose tolerance (IGT; blood glucose between 140-199 mg/dl 2-hours following a 75 gram oral glucose tolerance test [OGTT]) and received clearance from their personal physician. Individuals were excluded if they had a diagnosed cardiovascular, metabolic, pulmonary, liver, or kidney disease. In addition, current smokers, individuals taking medications known to influence energy metabolism or body weight or composition, and individuals with conditions that restricted their ability to be

physically active and engage in RT (e.g. orthopedic limitations) were also excluded. Prior to enrollment, individuals were fully informed about the study procedures and provided written informed consent.

Design

Resist Diabetes was a 15-month randomized controlled trial focusing on the initiation and maintenance of meeting RT guidelines (training all major muscle groups 2x/week). All study procedures were approved by the Virginia Tech Institutional Review Board (see Marinik et al for detailed methods[20]). Following baseline testing, all participants followed the same 3-month Initiation Phase that consisted of 2x/week supervised RT with an ACSM-certified personal trainer in a lab-gym using Nautilus Nitro Plus resistance training equipment. The progressive RT protocol consisted of a whole-body routine targeting major muscle groups, with twelve exercises per session. Participants completed one set of each exercise to concentric failure, which is consistent with RT guidelines from the ACSM for sedentary, older adults, and has been shown to result in skeletal muscle hypertrophy and increased strength[22], while being time efficient (~35-45 minutes per session). Training records of each RT session were maintained.

Participants who successfully completed the initiation phase (e.g. completed ≥70% of scheduled RT sessions) entered the 6-month Maintenance Phase and were randomly assigned to one of two different intervention maintenance conditions: a social cognitive theory (SCT)-based intervention involving more frequent and personalized contact with study staff and enhanced RT-tracking features and tailored feedback on the Resist Diabetes website; or a standard, usual care condition involving minimal contact with study staff (STD) and limited RT-tracking features and generic feedback on the

Resist Diabetes website. While less intensive, the STD condition was informed by the SCT (i.e. ability to schedule and track RT sessions are a form of self-regulation). During the maintenance phase, participants were to continue the RT program on their own in a community/public workout facility. Finally, participants in both conditions completed a 6-month No Contact Phase in which they did not interact with study staff, but were expected to continue the 2x/week RT protocol. Participants retained access to the same website features associated with their intervention conditions (SCT or STD) during this phase.

Outcome Assessments

Assessment clinics occurred at baseline, and following the initiation, maintenance, and no-contact phases (e.g. months 3, 9, and 15, respectively). Testing occurred over 2 days. Following completion of each assessment clinic, participants were mailed a packet containing their results (body mass and composition, blood glucose, blood pressure, strength, and a summary report of their dietary intake). In addition, a brief description of each measurement and categorical chart of normative or ideal results (for body composition and mass, blood glucose, and blood pressure) was provided. An educational handout containing standard nutrition information from the 2010 Dietary Guidelines for Americans[23] was also included. Participants were not encouraged to make alterations to their dietary intake or non-RT PA by study staff.

Dietary Intake. Habitual dietary intake was assessed using the average of three multiple-pass 24-hr recalls[24] collected at each assessment time point by a research dietitian/technician. The first recall was completed in-person at the assessment clinic, using 2D food models to aid in serving size estimations. The 2nd and 3rd recall were

unannounced, and completed by phone within 2 weeks, and included 1 weekend day. Previous trials have found no difference in reported energy intakes between 24-hr food recalls completed in-person or via telephone[25,26]. Food recalls were analyzed using the Nutrition Data System for Research software (NDS-R 2010, University of Minnesota, Minneapolis, MN). Healthy Eating Index (HEI)-2010 total and component scores[27] were calculated from NDSR output files following established protocols[28]. The HEI-2010 total score is a measure of overall diet quality as determined by adherence to the 2010 Dietary Guidelines for Americans (DGA)[23,27]. The HEI-2010 total score is the sum of 12 component scores, each reflecting intake of specific food groups or nutrients. Nine components (total fruit, whole fruit, total vegetables, dark-green vegetables and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acid ratio) are included in the adequacy category, meaning individuals should eat enough of these foods/nutrients. Three components (refined grains, sodium, and empty calories [e.g. – solid fats, alcohol, and added sugar (SoFAAS)]) are included in the moderation category, meaning individuals should limit consumption of foods containing these nutrients[27]. Component scores range from 0 – 5 (total fruit, whole fruit, total vegetables, dark-green vegetables and beans, total protein foods, and seafood and plan proteins), 0 – 10 (whole grains, dairy, and fatty acid ratio), or 0 – 20 (empty calories), and an HEI-2010 total score of 100 indicates perfect conformity to 2010 DGA[23]. HEI-2010 scores can be divided into three categories based on dietary quality: good (>80), needs improvement (51-80), or poor (<51)[27].

Non-RT PA. Prior to each scheduled assessment clinic, PA over the previous 3 month period was assessed online via the Aerobics Center Longitudinal Study

Questionnaire[29]. This questionnaire consists of questions on type, frequency, and intensity of PA participants may have performed. To assess non-RT PA, responses to the RT specific question were not included in the calculations of total non-RT PA. Non-RT PA were categorized as low (< 3 METs), moderate (3-6 METs), or vigorous-intensity (>6 METs)[30]. Total MET-minutes/week of all non-RT PA, moderate-intensity PA, and vigorous-intensity PA were calculated by multiplying the number of frequency (sessions/week) * duration (the number of minutes/session) * intensity (assigned MET-value) for each activity in order to determine if participants were meeting U.S. physical activity guidelines of 500-1,000 MET-minutes/week[31].

Anthropometrics. Height was measured without shoes to the nearest 0.1 cm using a wall-mounted stadiometer. Body mass was measured in light clothing, without shoes, to the nearest 0.1 kg using a digital scale (Healthometer ProPlus, Pelstar, McCook, IL). BMI was calculated as weight (kg)/height (m^2). Fat mass (FM), fat free mass (FFM) were assessed via dual energy X-ray absorptiometry (DXA; GE Lunar Prodigy, software version 11.40.004, Madison, WI).

Muscular Strength. Three repetition maximum (3RM) on the chest press and leg press were used to evaluate upper and lower body strength, respectively. Testing was conducted in accordance with ACSM guidelines[32]. Briefly, following orientation and familiarization with movements, participants completed warm-up sets. Participants rested between 3RM trials and resistance was increased until rate of perceived exertion on the last repetition was rated as a 9 or 10 and participants were unable to perform 3 or more repetitions using proper form.

Prediabetes Status. Following an overnight fast, blood samples were collected from the antecubital vein in the fasting state and 120 minutes following consumption of a 75 g orange-flavored glucose beverage (Fisherbrand, Fisher Scientific, Hanover Park, IL). Plasma was collected in EDTA BD vacutainers and immediately placed on ice until centrifuged at 2000 g for 15 minutes (Model 5702R, Eppendorf, Hauppauge, NY) for sample separation. Plasma glucose concentrations were determined using an YSI 2700 Select glucose analyzer (YSI Life Sciences, Yellow Springs, OH) on the day of the assessment clinic. Participants were classified according to pre-diabetes phenotype status as 1. IFG only, 2. IGT only, or 3. IFG and IGT.

RT Health Beliefs. Following the initiation phase, but prior to randomization to intervention maintenance conditions, as well as prior to the 9- and 15-month assessment clinic visits, participants completed the RT Health Beliefs survey[33]. Measures included: outcome expectancies; behavioral resolve (e.g. self-efficacy for overcoming barriers); and self-regulation related to RT. The scales have demonstrated adequate internal consistency ($\alpha = 0.729 – 0.925$) and moderate predictive validity of self-reported RT participation ($r = 0.296 – 0.506$)[33].

The outcome expectancy scale is scored as the mean of all positive items and negative items (separately) with a scale of 1-7 as well as the mean of the outcome expectancy scale times the outcome value (for both positive and negative items separately), which has a scale of 1-49. For the positive scale, a higher score indicates more positive outcome expectancies. For the negative scale, a higher score indicates more negative outcome expectancies associated with RT. The behavioral resolve scale is scored as the mean of all items with a scale of 1-100. A higher score indicates a greater

perceived ability to overcome barriers associated with RT. The self-regulation scale is scored as the mean of all items with a scale of 1-7. A higher score indicates a greater number of strategies are often used in order to maintain a regular RT regimen.

Adherence to RT Protocol. A timeline follow back (TLFB) approach was used to assess RT adherence at the 9 and 15 month assessment clinics[20]. At the assessment clinic visits participants were provided with a paper calendar in which they were to indicate each day a RT session occurred within the past 30 days. Since the purpose of the Resist Diabetes intervention was to initiate and maintain a 2x/week RT protocol, 8 completed sessions per 30 day period were expected.

Statistical Analysis

A Monte Carlo approach was used for sample size/power calculation estimations for the main outcomes of the Resist Diabetes trial[20]. Statistical analyses were performed with STATA, version SE 14 (StataCorp LP, College Station, TX). Analyses included descriptive statistics (means, standard deviations, and frequencies) for demographic characteristics. Mixed effects models, controlling for intervention group and sex, were used to assess changes in dietary intake and non-RT PA across assessment clinic time points, as well as to explore potential predictors of changes to dietary intake and non-RT PA. Missing data were addressed by using full information maximum likelihood estimation, a default in STATA routines. Alpha was set *a priori* as $p<0.05$. Continuous data are presented as mean±S.D.

Results:

Participant Characteristics. Participant characteristics are presented in Table 1. The majority of participants were Caucasian (94%) and female (73%). Forty-eight percent of

participants were classified as having IFG only, 12% as having IGT only, and 40% as having both IFG and IGT at baseline. Detailed glycemic outcomes of the Resist Diabetes trial will not be addressed as they are presented in the main outcomes analysis (Davy et al, in preparation[34]). Retention was considered high; 76% of participants who entered supervised training completed the month 15 assessment clinic visit.

Table 1. Participant Characteristics

	Baseline	**Month 3**	**Month 9**	**Month 15**
Total number of participants, n	170	159	138	129
Male, n (%)	46 (27%)	44 (28%)	38 (28%)	37 (29%)
Female, n (%)	124 (73%)	115 (72%)	100 (72%)	92 (71%)
Age, years	59.5±5.5	59.6±5.4	59.8±5.4	60.2±5.3
BMI, kg/m^2	32.9±3.8	33.0±3.9	32.8±3.9	32.7±4.0
Fat Mass				
%	43.8±7.0	43.2±6.8	43.0±6.8	42.8±6.8
Kg	40.6±8.4	39.9±8.3	39.4±8.4	39.2±8.5
Fat Free Mass				
%	56.2±7.0	56.8±6.8	57.0±6.8	57.2±6.8
Kg	52.1±10.4	52.7±10.7	52.3±10.0	52.1±10.0
Chest press, 3 RM, kg	33.7±11.6	42.9±14.9	43.0±16.1	43.0±16.2
Leg Press, 3 RM, kg	141.3±36.0	166.7±39.4	165.6±39.4	164.9±39.7

Note: BMI = body mass index; 3 RM = 3 repetition maximum

Dietary Intake. Most participants completed all three 24-hr dietary recalls at each time point (baseline: 96%, month 3: 90%, month 9: 92%, and month 15: 90%), and average energy intake was 113±29% of estimated energy needs (Mifflin-St. Joer equation[35]) across time points, suggesting reasonably accurate reporting. Energy, macronutrient, fiber, and HEI-2010 (total and sub-scores) are presented in Table 2. Energy intake decreased from baseline to month 9 (e.g. with the initiation and

maintenance phases of the intervention; β= -87.9, p=.015) and was maintained through the no-contact phase (month 9 to 15; β= 1.3, p=.973). No differences over time were detected from either gender or intervention condition (both p>0.05), though women did report lower energy intakes than men at all time points (p<0.05 for all). The decrease in energy intake detected could be explained by the reduction in absolute carbohydrate intake (baseline to month 9, β= -16.3, p<.001).

The mixed effects model showed no change in total HEI-2010 score across intervention time points (β= -0.13, p=.722). Probing for changes in dietary quality by gender and intervention groups also revealed no change in total HEI-2010 scores within groups (p>0.05 for all). Despite no change to overall HEI-2010 score, the mixed model analysis of specific HEI-2010 component scores revealed alterations to specific food groups. Initiation of RT was accompanied by a reduction in scores for the whole fruit, whole grains, and refined grains components (baseline to month 3: β= -0.52, p=0.003; β=-0.66, p=0.039; and β= -0.64, p=0.019, respectively). The whole fruit and refined grain scores returned to baseline during the RT maintenance phase (baseline to month 9: β= -0.31 , p=0.087 and β=0.31, p=0.279), but the reduction in whole grain score persisted for the remainder of the intervention (baseline to month 15: β= -0.78, p=0.023). Maintenance of RT was accompanied by an increase in scores for the total vegetable and greens and beans components (month 3 to 9: β= 0.45, p=0.002 and β=0.7, p<0.001, respectively), which returned to baseline during the no-contact phase (baseline to month 15: β=0.19, p=0.123 and β=0.3, p=0.157, respectively). Over the 15-month study period, the fatty acid ratio component score increased (baseline to month 15: β= 0.70, p=0.036). Finally, the sodium component score decreased over the initiation and maintenance phases

(baseline to month 9: β= -0.59, p=0.048), but returned to baseline during the no-contact phase (baseline to month 15: β= -0.2, p=0.515).

Table 2. Reported energy, macronutrient, fiber, and HEI-2010 total and sub-scores.

	Baseline	**Month 3**	**Month 9**	**Month 15**
	Initiation Phase	*Maintenance Phase*	*No Contact Phase*	
Energy, kcal	1803±514	1743±462	1727±454*	1736±500*
Macronutrients				
Carbohydrate				
%	44±8	43±8	42±9	43±10
g	201±63	192±62*	185±61*	191±64*
Fat				
%	37±7	37±6	37±7	36±7
g	76±30	74±24	75±25	73±28
Protein				
%	18±4	19±4	18±5	19±5
g	78±23	78±21	78±23	78±24
Fiber, g	19±7	18±6	18±7	19±7
HEI-2010 Scores				
Total HEI-2010	61.2±12.0	59.5±13.1	61.7±10.4	60.6±12.8
Total Fruit[a,d]	2.3±1.6	2.0±1.7	2.2±1.7	2.2±1.6
Whole Fruit[a,d]	3.0±1.8	2.5±1.9*	2.7±2.0	2.9±1.9
Total Vegetables[a,d]	3.6±1.3	3.6±1.3	4.0±1.1*	3.8±1.3
Greens and Beans[a,d]	2.9±2.1	2.7±2.1	3.4±2.0*	3.2±2.1
Whole Grains[b,d]	5.2±3.5	4.5±3.7*	4.3±3.5*	4.4±3.3*
Dairy[b,d]	5.5±2.7	5.5±2.6	5.3±2.8	5.1±2.6
Total Protein Foods[a,d]	4.8±0.6	4.8±0.5	4.8±0.7	4.8±0.6
Seafood and Plant Proteins[a,d]	3.0±2.0	2.9±2.1	3.2±2.0	3.1±2.0
Fatty Acids[b,d]	4.6±3.0	5.0±3.2	5.2±3.1	5.4±3.1*
Refined Grains[b,e]	7.7±2.6	7.0±3.2*	8.0±2.4	7.4±2.7
Sodium[b,e]	3.3±3.0	3.1±3.0	2.7±2.6*	3.0±3.0
Empty Calories[c,e]	15.4±3.6	15.8±3.7	15.9±3.1	15.7±3.8

*Indicates significant difference from baseline ($p<0.05$).
[a]Score ranges from 0-5, [b] Score ranges from 0 – 10, [c] Score ranges from 0 – 20.
[d]Adequacy component. Higher score indicates higher consumption
[e]Moderation component. Higher score indicates lower consumption.

To explore physiological and psychosocial factors which may predict the reduction in energy intake reported, baseline prediabetes status (IFG, IGT, or IFG + IGT), fat mass (kg), leg press, outcome expectancies, behavioral resolve, and self-regulation were added to the model. None of these factors predicted the reduction in

energy intake (all p>0.05). Additionally, RT adherence at months 9 and 15 did not predict changes in energy intake (β= -107.1, p=0.158).

Non-RT Physical Activity. Prevalence of meeting aerobic activity guidelines of 500-1,000 MET-min/week[31] was 65% at baseline, 71% at month 3, 79% at month 9, and 83% at month 15. Reported engagement (n, % of participants) and average MET-minutes/week of those reporting participation in low, moderate, and/or vigorous-intensity non-RT PA at each study phase is presented in Table 3. Of participants reporting engagement in non-RT PA, walking and lawn and garden work were the most common modes of low and moderate-intensity PA, and running was the most common mode of vigorous-intensity PA reported, although very few participants reported engaging in vigorous-intensity PA (Table 3).

Table 3. Reported Engagement in Low-, Moderate-, and Vigorous-Intensity Non-RT PA

	Baseline (n=170)	**Month 3** (n=159)	**Month 9** (n=138)	**Month 15** (n=129)
Total PA				
n (%)	155 (91%)	146 (92%)	120 (87%)	97 (75%)
MET-min/week	752.5±721.6	786.7±590.9	928.8±825.8	906.1±864
Low-Intensity PA				
n (%)	138 (82%)	122 (77%)	98 (71%)	78 (61%)
MET-min/week	382.5±257.9	358.7±222.7	368.7±252.3	368.8±264.2
Moderate-Intensity PA				
n (%)	109 (64%)	122 (77%)	107 (78%)	83 (64%)
MET-min/week	561.3±633.8	576.9±565.4	662.3±698.7	690.6±779.5
Vigorous-Intensity PA				
n (%)	8 (5%)	4 (3%)	11 (8%)	9 (7%)
MET-min/week	333.5±236.7	176.8±187.2	405.3±523.9	200.2±172.1

MET-min/week presented as mean±SD for participants reporting participation at each stage

Of participants reporting participation in any non-RT PA at each study phase, total MET-min/week of non-RT PA increased during the RT maintenance phase (month 3 to month 9; β=153.5, p=0.01) and was maintained through the no-contact phase (month 9 to month 15; β=18.0, p=0.791). Changes in non-RT PA were not different according to gender or group assignment and were trimmed from the mixed effects model. To explore

physiological and psychosocial factors which may predict the increase in non-RT PA seen from month 3 to months 9 and 15, baseline prediabetes status (IFG, IGT, or IFG + IGT), fat mass (kg), leg press 3RM, outcome expectancies, behavioral resolve, and self-regulation were added to the model, controlling for gender. Increases in RT self-regulation (β=78.1, p=0.03) predicted the increase in non-RT PA. Prediabetes status, leg press 3RM, and behavioral resolve for RT were not predictive of the increase in non-RT PA. Trends were noted for decreases in fat mass (β= -9.7, p=0.096) and decreases in negative outcome expectancies of RT [e.g. participants were less likely to expect that RT would be accompanied by negative outcomes, such as "Make me feel embarrassed while I am resistance training"[33]] (β= -68.7 p=0.05) to predict an increase in non-RT PA. Adherence to the RT protocol at months 9 and 15 did not predict engagement in non-RT PA (β=19.4, p=0.890).

Discussion:

The major findings of the present study are that participation in an SCT-based RT program was accompanied by decreased energy and carbohydrate intake, alterations to HEI-2010 sub-scores, and increased non-RT PA in previously inactive, older, overweight/obese adults with prediabetes. Self-regulation for RT predicted the increase in non-RT training PA, and trends were noted for decreased fat mass and decreased negative outcome expectancies to be predictive of increased reported engagement in non-RT PA. Prediabetes phenotype, strength, and behavioral resolve for RT did not predict the increase seen in non-RT PA. None of our hypothesized predictors explained the alterations in dietary intake. This is likely due to the specific focus on RT in the psychosocial questionnaires utilized, which did not capture changes to these outcomes

specific for dietary intake and non-RT PA. However, the predictive analysis was exploratory in nature and provides preliminary data for future work in this area (e.g., interventions could target these as possible mediators). Overall our findings add to the body of literature on health-related behavior change by showing that RT is a mode of exercise which may result in changes to dietary intake and increased participation in non-RT PA.

Previous trials evaluating changes to dietary habits in response to exercise interventions have produced conflicting results, and have primarily focused on aerobic exercise and examined only changes to total energy and macronutrient intake[14]. Studies which have assessed overall diet quality have been cross-sectional in nature, showing an association between increased HEI scores and increased participation in PA[36,37]. To our knowledge, no prior studies have evaluated changes in overall dietary quality with adoption of PA programs, particularly RT. While no change in overall HEI-2010 scores occurred with initiation or maintenance of RT in the current trial, energy and carbohydrate intake decreased and alterations in sub-component scores were detected, suggesting that adoption and maintenance of RT may influence the dietary habits of adults at risk for type 2 diabetes. We previously reported that initiation of RT was accompanied by reductions in energy, carbohydrate, fruit and vegetable, and sweets and dessert intake[13]. The current, longer-term analysis indicated that reductions in energy and carbohydrate intake are maintained with continued RT participation. This has important implications for overall diabetes risk, as decreased energy and carbohydrate intake are key recommendations from the American Diabetes Association[38]. Since exercise, particularly RT, is a challenging behavior to initiate[39], successful adoption may increase

self-efficacy for additional health-related behavior changes and result in changes to dietary habits[12]. A study by Wycherly and colleagues provides supportive evidence for this hypothesis. While dietary intake was not measured, in one-year follow-up interviews with subjects who previously completed a 16-week lifestyle intervention involving an energy-restricted diet with or without supervised RT, several participants indicated that participation in the RT intervention helped them to adhere to the dietary prescription[40]. A sample interview transcript read as follows: "Without exercise, I probably would have got bored with the programme". Therefore, RT may be a novel mode of exercise for adults, which is impetus enough for increased adherence to provided dietary prescriptions.

In addition to energy and carbohydrate intake, we detected other longer-term changes to dietary intake, some beneficial (e.g. increased sub-scores) and some negative (e.g. decreased sub-scores). Specifically a reduction in the whole grains component score and an increase in the fatty acid ratio component score from baseline values existed at the 15 month assessment clinic. Increased scores for total vegetable and dark green vegetables and beans components and decreased scores for whole fruit, refined grain, and sodium components were noted over the course of the RT program, but returned to baseline values by the conclusion of our intervention. Furthermore, average total HEI-2010 score in our sample was ~60 (out of 100), indicating "needs improvement" in dietary intake quality. This is comparable to dietary quality reported by older US adults (60.5±0.6) in population-wide investigations[41], and indicates that theoretically-based behavior change nutrition education and intervention is warranted in conjunction with, or after successful adoption of, RT.

Previous studies examining the spillover effect of exercise interventions to other forms of PA, while conflicting, suggest that older adults are prone to decreased engagement in non-exercise PA[15]. Similar to the literature regarding spontaneous changes to dietary intake, the majority of trials evaluating spontaneous changes to non-exercise PA have used endurance training interventions. Our study provides evidence that maintenance of an established RT program may promote increased PA outside of the prescribed RT intervention exercise bout. Tying a new behavior (aerobic PA) in to an established behavior which is more difficult (RT)[39], might make it easier for this additional behavior to be adopted and maintained. As such, intervening on RT first before initiating caloric restriction and/or aerobic exercise may be a more effective intervention sequence for improved health-related behaviors and decreased chronic disease risk. Furthermore, it is important to note that that increase in non-RT PA in the current trial (~140 MET-minutes/week) is clinically relevant for individuals at risk for T2DM. Glycemic-outcomes improve in a dose-dependent manner as PA volume increases, which could prevent the progression from prediabetes to overt diabetes diagnosis, or result in regression to normoglycemia[4,42]. In addition, increased non-RT PA increases total daily energy expenditure, which can lead to weight loss, which further reduces the risk for T2DM[32,43].

Related to the potential for RT to influence other forms of PA, our findings add to the limited and inconclusive body of literature on this topic. In agreement with Hunter and colleagues, participation in RT by our participants was also accompanied by increases in non-RT PA[18]. Hunter et al's findings provide evidence that increased ease of aerobic activity following RT explains the increased participation in non-RT PA. While

economy of movement was not measured in the current study, detection of a trend for decreased fat mass to predict the increase in non-RT PA may be considered a similar explanatory mechanism, as ease of locomotion increases with loss of fat mass[44]. Contrary to our results, Church et al. saw no change in step counts outside of supervised exercise in the RT and combination (AT + RT) groups in the 9 month HART-D trial[45]. Similarly, a secondary analysis from Fielding and colleagues found that despite increases in muscular strength and functional ability following a 6-month RT program in elderly adults, non-RT PA did not increase[46]. While these studies suggest no spillover effect occurs when older individuals engage in RT, neither trial included a behaviorally-focused theoretical approach. In our analysis, increased leg press 3RM was not predictive of the increase in non-RT PA, but self-regulation for RT was. Therefore, psychosocial factors are likely an important determinant of PA that should be addressed in interventions, particularly for older, inactive adults at risk for chronic diseases, as they have been shown to improve health-related behaviors[47].

To our knowledge, this is the first investigation which examines spontaneous alterations to overall diet quality in response to RT, and one of the few to date which evaluates if RT is associated with increased non-RT PA in previously inactive adults. Strengths of our study include a large sample size, minimal attrition, high dietary recall completion rates, and use of validated methods and instruments for assessing dietary intake[24], non-RT PA[29], and psychosocial factors[33]. Our focus on HEI-2010 scores extends previous findings[13-15] by providing novel information on alterations to specific dietary patterns which may spontaneously occur with RT adoption and maintenance in adults with prediabetes. Our study is not without limitations. The observational nature and lack

of a control group diminishes our ability to determine if changes observed are the result of participation in RT, or instead due to knowledge of prediabetes status, interaction with study staff, and/or health-related information provided in the feedback packets. However, being at risk for diabetes was listed in study recruitment material and most participants were aware they had prediabetes prior to enrollment. Furthermore, if knowledge of prediabetes status was impetus enough for changes to dietary intake and increases in non-RT PA, changes would have occurred during the baseline testing period and not detected as different with initiation of RT, or occurring during the initiation phase only and not the maintenance phase. Although validated instruments and trained staff were utilized to assess dietary intake and non-RT PA, the reliance on self-reported rather than more objective measures is a limitation. Despite this, we are confident reporting areas due to social desirability biases were minimal, as not all dietary changes detected were beneficial (e.g. decreased whole fruit and whole grain scores) and only a small number of participants reported engagement in vigorous-intensity PA. Finally, completion of the non-RT PA questionnaire was not captured as intended in the on-line database, so we are only able to present average participation from participants who reported engaging in specific intensity levels at each time point. However, this limitation will be addressed by verifying paper copies kept of PA questionnaire completion for follow-up analysis.

Conclusion:

Findings from this observational trial suggest that RT may be a unique mode of PA in its ability to influence non-RT PA and dietary intake among previously inactive, overweight/obese adults with prediabetes. As single-component interventions are generally less costly and resource-intensive than multi-component interventions, our

results support the use of single-component interventions, focused on RT, when time and resources are limited. Further research, particularly in at risk populations, utilizing theoretically-based lifestyle interventions, and examining mechanisms and determinants of the spillover effect in response to RT are warranted.

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Chapter 5 – Conclusions & Future Directions

The main findings from this dissertation are that initiation and maintenance of a SCT-based RT intervention is associated with changes to dietary intake and non-RT PA in previously inactive, overweight/obese adults with prediabetes. In the first analysis (Chapter 3), which examined changes in energy, macronutrient, and food group intake with initiation of RT (e.g. baseline to month 3 of the Resist Diabetes trial), decreases in reported energy intake of ~80 kcals/day as well as decreases in carbohydrate, total sugar, fruit and vegetable, and sweets and dessert intake from baseline to week 12 were noted[185]. Reductions in energy, carbohydrate, and sweets and dessert intake are in line with recommendations from multiple professional organizations for the prevention and treatment of prediabetes and T2DM[5,24,25,121]. Importantly, the decreased sweets and desserts intake noted in our study (1.1 servings/day to 0.89 servings/day) is comparable to long term (1-5 years post randomization) decreases in consumption of sweets noted via FFQ in the intensive DPP trial[186]. The DPP trial had a large focus on nutrition changes in the lifestyle intervention, and was more costly than the Resist Diabetes trial[89,111]. Therefore, it is exciting that our single-component intervention which did not intervene on dietary intake was associated with a similar beneficial change.

Results from the first analysis provided rationale for continued investigation in this area. The second analysis examined changes in diet quality and non-RT PA across the 15-month Resist Diabetes. No change in overall diet quality (HEI-2010 scores) occurred with RT, but energy and carbohydrate reductions were maintained throughout the RT intervention, and changes to specific HEI-2010 sub-scales were noted. An increase in non-RT PA, of ~140 MET-minutes/week occurred with maintenance of RT,

and was maintained through the no contact phase. This has clinically relevant implications, as a dose-response relationship exists between increased exercise volume and improvements in glycemic control[5,27,187]. Thus, even though our participants reported engaging in above 500 MET-minutes/week of non-RT PA at baseline, increasing their volume of PA is expected to further decrease risk for progression to T2DM. In addition to being the first trial (to my knowledge) to investigate dietary modifications in response to RT beyond energy and macronutrient intake, and one of the few to investigate changes to non-RT PA, the second analysis (Chapter 4) also added to the literature on the spillover effect by exploring potential demographic, physiologic, and psychosocial factors which may predict changes to dietary intake and non-RT PA. None of our hypothesized predictors explained the decrease in energy intake. Increases in RT self-regulation predicted the increase in non-RT PA, and trends were noted for decreases in fat mass and decreased negative outcome expectancies of RT to predict the increase in non-RT PA.

This dissertation has provided preliminary evidence for future health-related interventions to focus on improving one (i.e., single-component interventions) "keystone" or "gateway" health behavior, instead of intervening on multiple health-related behaviors. This approach could make lifestyle interventions and programs more cost-, resource-, and time-efficient, while leading to clinically relevant improvements in health, particularly risk for T2DM and its associated adverse CV outcomes. T2DM has reached levels of epidemic proportion with approximately 347 million diabetic individuals (~9% of population) worldwide[188,189]. While diabetes is the 7th leading cause of death in the U.S., this is often considered an underestimation of the true mortality risk associated with the disease. Due to damage of the vascular endothelium and cardiac tissue from prolonged

hyperglycemia, the majority of individuals with diabetes eventually die from cardiovascular disease (CVD). The risk of CVD death in adults with diabetes is 1.7 times greater than in adults not afflicted with diabetes[3]. In addition, the total cost of diagnosed T2DM in the U.S. is approximately 245 billion dollars (72% due to direct medical costs and 28% due to reduced productivity)[13]. While less evidence exists on the associated morbidity, mortality and financial cost of the prediabetes stage, it is known that micro- and macrovascular damage occurs during this stage as well. For instance, chronic kidney disease prevalence is higher[10], coronary atherosclerosis and plaque vulnerability are more advanced[11], and markers of sub-clinical inflammation (such as CRP) are elevated in individuals with prediabetes compared to those displaying normoglycemia[12]. Therefore, metabolic disease progression represents a substantial individual and societal cost. Targeted lifestyle interventions, specially focusing on modifiable risk factor (e.g. diet and exercise) at the prediabetic stage, which are feasible to implement in to community, are of great importance.

In addition to providing support for single-component interventions that can have a broad public health impact, the findings of this dissertation also provide preliminary data for future research on the spillover effect associated with RT, as studies with stronger designs are warranted to confirm these findings. First, studies using objective and more accurate measures of PA (and the various components of total energy expenditure) and dietary intake would be needed. Second, randomized controlled trials (RCTs) to determine what "keystone" or "gateway" behavior (e.g.- specific exercise modality, intensity, frequency, and gym settings or dietary recommendation(s)) exerts the greatest spillover effect to promote alterations of other health-related behaviors would be

justified. To our knowledge, the possibility for dietary interventions to result in changes to PA has not been adequately explored, and warrants investigation as well. Third, interventions which compare altering levels of contact with participants and modes of communication (e.g. completely internet based vs mixed-methods approaches) would be of interest. Fourth, there is strong interest in the individual variability seen in response to exercise and diet interventions. While this has mainly been examining non-responders and responders from a physiological standpoint, evaluation of variability seen in the spillover effect is of interest. Why do some people seem prone to beneficial and supportive behavioral adaptations, while others are more prone to compensatory behavior changes (e.g. increased energy intake and/or decreased non-exercise energy expenditure upon initiation of an exercise program)? Examination of physiological, psychological, and neurological traits of participants and alterations of these with an intervention, as well as components of the intervention to predict responders v. non-responders v. negative responders could be used to tailor interventions to be the most effective for each individual.

Another avenue of research to pursue related to our work, would be test the potential for RT to exert a spillover effect in individuals with other pre-clinical diagnoses such as dyslipidemia and pre-hypertension, as well as in individuals who are currently metabolically healthy but are sedentary and/or obese. Furthermore, measures of CV fitness, functional capabilities and satiety hormones, as well as psychosocial measures of self-efficacy, self-regulation, and stage of change related to dietary intake and non-RT PA should be added to future trials. These variables will allow understanding of the

proposed mechanisms related to the spillover effect we expect to observe following successful adoption of an RT program.

Furthermore, as initiation and maintenance of RT did not result in alterations to overall diet quality in the current study, follow-up work examining the timing for shifting focus to an additional health-related behavior is warranted. For instance, how long should individuals have successfully maintained RT before intervening on a new behavior such as dietary quality? If too many health-related behaviors are focused on at once, it could lead to fatigue and burnout, causing participants to abandon all changes. Therefore, it is important to know when the addition of another behavior change would result in the greatest adoption of that behavior, while not compromising the ability of the individual to continue with the previously initiated behavior. Likely, the timing would relate more so to the person's current level of self-efficacy than to a specific length of time in the maintenance phase, but that question currently remains unanswered.

Overall, there is a need for development and refinement of effective interventions and treatment programs that promote positive lifestyle improvements which can be disseminated broadly and implemented in a variety of settings (e.g. community fitness centers, worksites, etc.). The findings of this research and the additional research questions which have been generated from it will provide valuable information that clinicians, fitness-center managers, extension agents, and other who interact directly with the public can utilize in order to improve the health and well-being of their clients and patients.

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Appendices

Appendix A – Academy of Nutrition and Dietetics EAL Rating System

Criteria for Recommendation Ratings

Strong: A Strong recommendation means that the workgroup believes that the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), and that the quality of the supporting evidence is excellent/good (grade I or II), In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the names. Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.

Fair: A Fair recommendation means that the workgroup believes that the benefits exceed the harms (of that the harms clearly exceed the benefits in the case of a negative recommendation), but the quality of the evidence is not as strong (grade II or III). In some clearly identified circumstances, recommendation may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms. Practitioners should generally follow a Fair recommendation, but remain alert to new information and be sensitive to patient preferences.

Weak: A Weak recommendation means that the quality of evidence that exists is suspect of that well-done studies (grades I, II, or III) show little clear advantage to one approach versus another. Practitioners should be cautious in deciding whether to follow a recommendation classified as Weak, and should exercise judgement and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.

Consensus: A Consensus recommendation beans that Expert opinion (Grade IV) supports the guideline recommendation even though the available scientific evidence did not present consistent results, or controlled trials were lacking. Practitioners should be flexible in deciding whether to follow a recommendation classified as Consensus, although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.

Insufficient Evidence: An Insufficient Evidence recommendation means that there is both a lack of pertinent evidence (Grade V) and/or unclear balance between benefits and harms. Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as Insufficient Evidence and should exercise judgement and be alert to emerging publications that report evidence that clarifies the balance of benefit versus harm. Patient preference should have a substantial influencing role.

Recommendation Label Definitions

Recommendations are categorized in terms of either conditional or imperative statements. While conditional statements clearly define a specific situation, imperative statements are broadly applicable to the target population and do not impose restraints on their application.

Conditional recommendations are presented in an if/then format, such that:

If CONDITION then ACTION(S) because REASON(S)

Fulfillment of the condition triggers one or more guideline-specified actions. In contrast, imperative recommendations include terms such as “require, ” “must, ” and “should, ” and do not contain conditional text that would limit their applicability to specified circumstances.

Academy of Nutrition and Dietetics Evidence Analysis Library disclaimers:

a. Academy of Nutrition and Dietetics Evidence-based Nutrition Practice Guidelines are intended to serve as a synthesis of the best evidence available to inform registered dietitians as they individualize nutrition care for their clients. Guidelines are provided with the express understanding that they do not establish or specify particular standards of care, whether legal, medical or other.

b. Evidence-based Nutrition Practice Guidelines are intended to summarize best available research as a decision tool for Academy members.

c. No endorsement by the Academy of Nutrition and Dietetics of any brand-name product or service is intended or should be inferred from a Guideline or from any of its components (including Questions, Evidence Summary, Conclusion Statement, Conclusion Statement Grade, Recommendation or Recommendation Rating).

Appendix B – Institutional Review Board Protocol Approvals

VirginiaTech

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24061
540/231-4991 Fax 540/231-0959
e-mail moored@vt.edu
www.irb.vt.edu
FWA00000572(expires 1/20/2010)
IRB # is IRB00000667

DATE: April 29, 2009

MEMORANDUM

TO: Brenda M. Davy
Richard A. Winett
Tina Savla

FROM: David M. Moore

Grant Compared 3/16/2009

Approval date: 4/13/2009
Continuing Review Due Date: 3/29/2010
Expiration Date: 4/12/2010

SUBJECT: **IRB Full IRB Approval:** "Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach" , IRB # 09-158

The above referenced protocol was submitted for full review and approval by the IRB at the April 13, 2009 meeting. The board had voted approval of this proposal contingent upon receipt of responses to questions raised during its deliberation. Following receipt and review of your responses, I, as Chair of the Virginia Tech Institutional Review Board, have, at the direction of the IRB, granted approval for this study for a period of 12 months, effective April 13, 2009.

Approval of your research by the IRB provides the appropriate review as required by federal and state laws regarding human subject research. As an investigator of human subjects, your responsibilities include the following:

1. Report promptly proposed changes in previously approved human subject research activities to the IRB, including changes to your study forms, procedures and investigators, regardless of how minor. The proposed changes must not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.
2. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.
3. Report promptly to the IRB of the study's closing (i.e., data collecting and data analysis complete at Virginia Tech). If the study is to continue past the expiration date (listed above), investigators must submit a request for continuing review prior to the continuing review due date (listed above). It is the researcher's responsibility to obtain re-approval from the IRB before the study's expiration date.
4. If re-approval is not obtained (unless the study has been reported to the IRB as closed) prior to the expiration date, all activities involving human subjects and data analysis must cease immediately, except where necessary to eliminate apparent immediate hazards to the subjects.

<u>Important:</u>
If you are conducting **federally funded non-exempt research**, please send the applicable OSP/grant proposal to the IRB office, once available. OSP funds may not be released until the IRB has compared and found consistent the proposal and related IRB appllication.

cc: File

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24061
540/231-4991 Fax 540/231-0959
e-mail moored@vt.edu
www.irb.vt.edu
FWA00000572(expires 1/20/2010)
IRB # is IRB00000667

DATE: December 8, 2009

MEMORANDUM

TO: Brenda M. Davy
Richard A. Winett
Tina Savla

FROM: David M. Moore

Approval date: 4/13/2009
Continuing Review Due Date:3/29/2010
Expiration Date: 4/12/2010

SUBJECT: **IRB Amendment 3 Approval:** "Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach" , IRB # 09-158

This memo is regarding the above referenced protocol which was previously granted approval by the IRB on April 13, 2009. You subsequently requested permission to amend your IRB application. The Board has granted approval for the requested protocol amendment, effective as of December 8, 2009. The anniversary date will remain the same as the original approval date.

As an investigator of human subjects, your responsibilities include the following:

1. Report promptly proposed changes in previously approved human subject research activities to the IRB, including changes to your study forms, procedures and investigators, regardless of how minor. The proposed changes must not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.
2. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.
3. Report promptly to the IRB of the study's closing (i.e., data collecting and data analysis complete at Virginia Tech). If the study is to continue past the expiration date (listed above), investigators must submit a request for continuing review prior to the continuing review due date (listed above). It is the researcher's responsibility to obtain re-approval from the IRB before the study's expiration date.
4. If re-approval is not obtained (unless the study has been reported to the IRB as closed) prior to the expiration date, all activities involving human subjects and data analysis must cease immediately, except where necessary to eliminate apparent immediate hazards to the subjects.

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Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: March 23, 2010

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires June 13, 2011)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

As of April 13, 2010, the Virginia Tech IRB Chair, Dr. David M. Moore, approved the amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/13/2010**
Protocol Expiration Date: **4/12/2011**
Continuing Review Due Date*: **3/29/2011**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

cc: File

VirginiaTech

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: July 19, 2010

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires June 13, 2011)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective July 16, 2010, the Virginia Tech IRB Chair, Dr. David M. Moore, approved the amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/13/2010 (protocol's initial approval date: 4/13/2009)**
Protocol Expiration Date: **4/12/2011**
Continuing Review Due Date*: **3/29/2011**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
3/16/2009	08138201	NIH, Center for Scientific Review	yes on 3/16/2009

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

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Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: March 1, 2011

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires October 26, 2013)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective March 1, 2011, the Virginia Tech IRB Chair, Dr. David M. Moore, approved the amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/13/2010 (protocol's initial approval date: 4/13/2009)**
Protocol Expiration Date: **4/12/2011**
Continuing Review Due Date*: **3/29/2011**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
3/16/2009	08138201	NIH, Center for Scientific Review	yes on 3/16/2009

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

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VirginiaTech

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: April 18, 2011

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires October 26, 2013)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective April 13, 2011, the Virginia Tech Institutional Review Board, at a convened meeting, approved the continuation request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/13/2011 (protocol's initial approval date: 4/13/2009)**
Protocol Expiration Date: **4/12/2012**
Continuing Review Due Date*: **2/27/2012**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
3/16/2009	08138201	NIH, Center for Scientific Review	yes on 3/16/2009

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

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VirginiaTech

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: May 4, 2011

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires October 26, 2013)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective May 4, 2011, the Virginia Tech IRB Chair, Dr. David M. Moore, approved the amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/13/2011 (protocol's initial approval date: 4/13/2009)**
Protocol Expiration Date: **4/12/2012**
Continuing Review Due Date*: **2/27/2012**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
3/16/2009	08138201	NIH, Center for Scientific Review	yes on 3/16/2009

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

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VirginiaTech

Office of Research Compliance
Institutional Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, Virginia 24060
540/231-4606 Fax 540/231-0959
e-mail irb@vt.edu
Website: www.irb.vt.edu

MEMORANDUM

DATE: April 5, 2012

TO: Brenda M. Davy, Richard A. Winett, Tina Savla, David Williams, Sheila Winett, Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires May 31, 2014)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective April 5, 2012, the Virginia Tech IRB Chair, Dr. David M. Moore, approved the amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report promptly to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at http://www.irb.vt.edu/pages/responsibilities.htm (please review before the commencement of your research).

PROTOCOL INFORMATION:
Approved as: **Full Board Review**
Protocol Approval Date: **4/5/2012 (protocol's initial approval date: 4/13/2009)**
Protocol Expiration Date: **4/4/2013**
Continuing Review Due Date*: **3/25/2013**
*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:
Per federally regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals / work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
3/16/2009	08138201	NIH, Center for Scientific Review	yes on 3/16/2009

*Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

cc: File

VirginiaTech

Office of Research Compliance
Institutational Review Board
2000 Kraft Drive, Suite 2000 (0497)
Blacksburg, VA 24060
540/231-4606 Fax 540/231-0959
email irb@vt.edu
website http://www.irb.vt.edu

MEMORANDUM

DATE: April 9, 2013

TO: Brenda Davy, Richard A Winett, Tina Savla, David Williams, Sheila Winett, Dr. Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires May 31, 2014)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective April 9, 2013, the Virginia Tech Institution Review Board (IRB) Chair, David M Moore, approved the Continuing Review request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

http://www.irb.vt.edu/pages/responsibilities.htm

(Please review responsibilities before the commencement of your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**April 13, 2013**
Protocol Expiration Date:	**April 12, 2014**
Continuing Review Due Date*:	**March 29, 2014**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:

Per federal regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals/work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
08/20/2012	08138201	National Institutes of Health	Compared on 03/16/2009

* Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

VirginiaTech

Office of Research Compliance
Institutational Review Board
North End Center, Suite 4120, Virginia Tech
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-4606 Fax 540/231-0959
email irb@vt.edu
website http://www.irb.vt.edu

MEMORANDUM

DATE: July 15, 2013

TO: Brenda Davy, Richard A Winett, Tina Savla, David Williams, Sheila Winett, Dr. Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires April 25, 2018)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective July 8, 2013, the Virginia Tech Institution Review Board (IRB), at a convened meeting, approved the Amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

http://www.irb.vt.edu/pages/responsibilities.htm

(Please review responsibilities before the commencement of your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**April 13, 2013**
Protocol Expiration Date:	**April 12, 2014**
Continuing Review Due Date*:	**March 29, 2014**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:

Per federal regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals/work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
08/20/2012	08138201	National Institutes of Health	Compared on 03/16/2009

* Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

VirginiaTech

Office of Research Compliance
Institutational Review Board
North End Center, Suite 4120, Virginia Tech
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-4606 Fax 540/231-0959
email irb@vt.edu
website http://www.irb.vt.edu

MEMORANDUM

DATE:	March 18, 2014
TO:	Brenda Davy, Richard A Winett, Tina Savla, David Williams, Sheila Winett, Dr. Soheir Boshra
FROM:	Virginia Tech Institutional Review Board (FWA00000572, expires April 25, 2018)
PROTOCOL TITLE:	Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach
IRB NUMBER:	**09-158**

Effective March 18, 2014, the Virginia Tech Institution Review Board (IRB) Chair, David M Moore, approved the Continuing Review request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

http://www.irb.vt.edu/pages/responsibilities.htm

(Please review responsibilities before the commencement of your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**April 13, 2014**
Protocol Expiration Date:	**April 12, 2015**
Continuing Review Due Date*:	**March 29, 2015**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:

Per federal regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals/work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
08/20/2012	08138201	National Institutes of Health	Compared on 03/16/2009

* Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

VirginiaTech

Office of Research Compliance
Institutional Review Board
North End Center, Suite 4120, Virginia Tech
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-4606 Fax 540/231-0959
email irb@vt.edu
website http://www.irb.vt.edu

MEMORANDUM

DATE:	March 2, 2015
TO:	Brenda Davy, Richard A Winett, Tina Savla, David Williams, Sheila Winett, Dr. Soheir Boshra
FROM:	Virginia Tech Institutional Review Board (FWA00000572, expires April 25, 2018)
PROTOCOL TITLE:	Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach
IRB NUMBER:	**09-158**

Effective February 9, 2015, the Virginia Tech Institution Review Board (IRB) Chair, David M Moore, approved the Continuing Review request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

http://www.irb.vt.edu/pages/responsibilities.htm

(Please review responsibilities before the commencement of your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**February 9, 2015**
Protocol Expiration Date:	**February 8, 2016**
Continuing Review Due Date*:	**January 25, 2016**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:

Per federal regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals/work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
08/20/2012	08138201	National Institutes of Health	Compared on 03/16/2009

* Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

VirginiaTech

Office of Research Compliance
Institutional Review Board
North End Center, Suite 4120, Virginia Tech
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-4606 Fax 540/231-0959
email irb@vt.edu
website http://www.irb.vt.edu

MEMORANDUM

DATE: January 11, 2016

TO: Brenda Davy, Richard A Winett, Tina Savla, David Williams, Sheila Winett, Dr. Soheir Boshra

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires July 29, 2020)

PROTOCOL TITLE: Maintaining Resistance Training in Older Prediabetic Adults: Theoretical Approach

IRB NUMBER: 09-158

Effective January 11, 2016, the Virginia Tech Institution Review Board (IRB) Chair, David M Moore, approved the Continuing Review request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

http://www.irb.vt.edu/pages/responsibilities.htm

(Please review responsibilities before the commencement of your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**February 9, 2016**
Protocol Expiration Date:	**February 8, 2017**
Continuing Review Due Date*:	**December 26, 2016**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

FEDERALLY FUNDED RESEARCH REQUIREMENTS:

Per federal regulations, 45 CFR 46.103(f), the IRB is required to compare all federally funded grant proposals/work statements to the IRB protocol(s) which cover the human research activities included in the proposal / work statement before funds are released. Note that this requirement does not apply to Exempt and Interim IRB protocols, or grants for which VT is not the primary awardee.

The table on the following page indicates whether grant proposals are related to this IRB protocol, and which of the listed proposals, if any, have been compared to this IRB protocol, if required.

Date*	OSP Number	Sponsor	Grant Comparison Conducted?
08/20/2012	08138201	National Institutes of Health	Compared on 03/16/2009

* Date this proposal number was compared, assessed as not requiring comparison, or comparison information was revised.

If this IRB protocol is to cover any other grant proposals, please contact the IRB office (irbadmin@vt.edu) immediately.

Appendix C – Eating Behavior Permission

Permission to Use doi: 10.1016/j.eatbeh.2014.04.004 in Dissertation

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--
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PhD Candidate
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Virginia Tech
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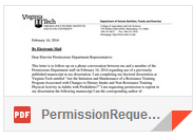
phone (cell): 978-618-2528
e-mail: tanyamh@vt.edu



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