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Postprandial exhaled nitric oxide responses in older and younger adults with and without acute exercise

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Postprandial Exhaled Nitric Oxide Responses in Older and Younger Adults With and Without Acute Exercise

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Abstract

A single high fat meal (HFM) increases airway inflammation in young, healthy individuals. Additionally, aging increases airway resistance and inflammation, though the airway inflammatory response to a HFM has not been investigated. Exercise is a natural anti-inflammatory, but has yet to be administered with a HFM as a method to study postprandial airway inflammation in older adults. Purpose: To investigate whether older individuals have greater postprandial airway inflammation compared to younger counterparts, and to explore whether exercise may modify the postprandial airway response in older adults. Methods: 12 younger adults (23.3±3.9 years; 5 M/7 F) and 12 older adults (67.7±6 years, 8 M/4 F) completed two HFM challenges (HFM=12 kcals/kg BW: 57% fat, 39% CHO, 4% PRO), in a randomized order. For both sessions, participants abstained from exercise 48 hours prior to the HFM session and adhered to a 12 hour overnight fast. In the HFM paired with exercise session, participants performed exercise on a cycle ergometer at a heart rate that corresponded to 65% VO2Peak until caloric expenditure matched 75% of the caloric content of the HFM, then adhered to a 12 hour overnight fast before consuming the HFM. Airway inflammation (measured via exhaled nitric oxide; eNO) and airway function (measured via pulmonary function tests) were assessed at baseline, 2h and 4h postprandially. Blood triglycerides (TG) and glucose was assessed at baseline and every hour postprandially. Results: eNO post-HFM did not increase across time-points from baseline to four hours, ($p=0.071$), between HFM alone and HFM with exercise, nor did responses differ between younger and older groups. Conclusion: There was no airway inflammation following a HFM in older or younger individuals. Additionally, exercise did not alter the airway inflammation response.

Chapter I

I. *Westernized Diet and Inflammation*

The western diet is categorized by being high in calories, refined sugars, salt, cholesterol, processed meats, purified animal fats, processed convenience foods and nutrient dense foods. Substances in a western diet that contribute to immune response include saturated and unsaturated fats, high cholesterol, and red meat/dairy products (Christ et al. 2019). Chronic high fat diets contribute to a higher prevalence of chronic inflammatory diseases such as cardiovascular disease, atherosclerosis, type II diabetes mellitus, and many more. These diseases are all characterized by elevated levels of systemic inflammation. High inflammation can occur both systemically and in the airways, and pulmonary inflammation is associated with the development and/or progression of respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) (Wood et al. 2009, Varraso et al. 2007).

With even a single high fat meal (HFM) that is typical in the western diet, the immune system may be activated due to elevations in postprandial lipids, including triglycerides and cholesterol (Teeman et al. 2016a). Consumption of dietary trans fats and sugars can lead to increased low-density lipoprotein cholesterol (LDL), or from glycated substances from hyperglycemia which can impair endothelial function (Christ et al. 2019, Hamilton et al. 2013). When endothelial damage occurs, monocytes are attracted to the area and once inside the intima they differentiate into macrophages. Circulating postprandial lipids begets the production of reactive oxygen species (ROS) that oxidize LDL. Macrophages and T-cells engulf the oxidized LDL (OxLDL), becoming foam cells in the process, and signal the production of proinflammatory cytokines (Christ et al. 2019,

Teeman et al. 2016b, Beutler 2004). Cytokines are low molecular weight glycoproteins that regulate inflammatory responses by binding to the surface of cells and through secondary signals, where they then stimulate or suppress other cytokines (Moldoveanu et al. 2009). They increase inflammation locally and systemically by recruiting intermediate messengers, altering vascular tone, increasing adhesion, and stimulating smooth muscle cell migration (Rea et al. 2018, Beutler 2004). Cytokines are necessary to regulate immunity but persistent accumulation can cause damage to tissues.

Elevated cytokines and subsequent endothelial dysfunction can be observed postprandially for hours after fat ingestion (Gill et al. 2003). While the elevated postprandial metabolic and immune responses would return to baseline after a single meal, a "typical" western diet consists of multiple meals consumed per day with the possibility of snacks throughout the day as well. This places the individual in a postprandial state throughout the day, which could potentially lead to chronic elevations of triglycerides, cholesterol, glucose, and systemic inflammation. Chronically elevated levels could then increase the risk of chronic disease development and progression. A chronic high-fat diet may lead to elevated systemic and airway inflammation, and even a high carbohydrate diet will see impairments like attenuated triglyceride clearance (Gill et al. 2003). A single HFM or a high fat, high carbohydrate (HFHC) meal can transiently increase systemic pro-inflammatory cytokines and airway inflammation. While a HFHC meal may stimulate a transient increase in both systemic and airway inflammation, the mechanisms that underpin the increase and time-course may differ (Johnson et al. 2016, Kurti et al. 2015, Kurti et al. 2017a).

II. Single HFM and Airway Inflammation

An acute HFM increases postprandial airway inflammation, even in young healthy individuals (Baylis et al. 2013, Kurti et al. 2017a). The transient increase in airway inflammation can be assessed by various techniques such as directly measuring immune cells in the airways through bronchoalveolar lavages or sputum induction, or non-invasively by using exhaled nitric oxide (eNO). During an immune response nitric oxide is produced in the upper and lower respiratory tract. Through gaseous diffusion nitric oxide can then move to the lumen where it is exhaled (ATS/ERS recommendations). eNO is a validated, non-invasive, measurement that can be used to assess airway inflammation (ATS/ERS recommendations). While research has illustrated an association between dietary fat consumption and inflammation, the direct mechanisms remain unclear. It has been hypothesized that increased eNO is due to systemic cytokines (Wood et al. 2011). There are also several mechanisms that may explain the increase in eNO from lipopolysaccharides (LPS), a component of saturated fatty acids found in HFM, which increases Toll-like receptor (TLR) activation. The TLR4-dependent pathway utilizes both inhibitor κB kinase β (IKKβ) and nuclear factor-kappa-B (NF-κB) transcription factors to increase interleukin 6 (IL-6). TLR4-independent pathway increases reactive oxygen species (ROS), and interleukin-1β (IL-1β) levels increase through the NLRP-ASC pathway (Teng et al. 2014, Johnson et al. 2016). Proinflammatory cytokine IL-1β upregulates inducible nitric oxide (iNO) increasing eNO, while also decreasing insulin sensitivity to beget more inflammation (Ricciardolo et al. 2004, Teng et al. 2014).

In the lung, macrophages and dendrites are adequate at addressing phagocytosis but in doing so they increase cytokines, chemokines, and other inflammatory mediators. Following a HFM increased inflammation response causes increased accumulation of

neutrophils (Moldoveanu et al. 2009, Rosenkranz 2010) and eNO (Wood et al. 2011, Kurti et al. 2015), increasing independently of each other.

If excessive inflammation is left untreated, or the transient rise occurs over and over to the point where inflammation is elevated chronically, there can be tissue damage and structural changes to the bronchial walls (Moldovenanu et al. 2009). These alterations are termed airway remodeling, which may lead to decreased pulmonary function and respiratory ailments. Postprandial neutrophils contribute to endothelial dysfunction and remodeling by impairing bronchodilatory recovery and leading to narrowing of the airways (Van Oostrom et al. 2002, Wood et al. 2011, Bartemes et al. 2012), however this is primarily found in individuals who have already been diagnosed with airway diseases. Through secondary messengers, eosinophils are hypothesized to increase basement membrane thickness and subepithelial fibrosis, which play a role in airway remodeling (Elias et al. 1999). Other structural changes can include airway wall thickening and increased smooth muscle (Elias et al. 1999, Bartemes et al. 2012) which are activated by cytokines produced during an inflammatory response (Bartemes 2012). Interestingly, increased airway inflammation and airway sensitivity may occur prior to any decrements in pulmonary function, and therefore could be used as an early measure of airway dysfunction.

In asthmatic individuals, a HFM has been shown to impact bronchodilatory recovery (Wood et al. 2011), however this has not been shown in healthy individuals (Rosenrkanz et al. 2010, Kurti et al. 2017b). Accumulation of airway inflammation can eventually lead to airway hypersensitivity and airway hyperresponsiveness, characteristics of asthma (Lapraise et al. 1999, Wood et al. 2009). Specifically Rosenkranz et al. found

that following a single HFM young adults saw a significant increase in eNO, with no changes to pulmonary function (Rosenkranz et al. 2010). In existing studies in healthy individuals, pulmonary function evaluated using the maximal flow volume loop (MFVL) was not impacted by acute changes in airway inflammation, however airway resistance may be elevated using impulse oscillometry (Johnson et al. 2016). Still, young healthy individuals likely do not have enough long-term damage systemically and in the airways from HFM's, and therefore it may be important to elucidate the impact of a HFM meal on the airways in populations more at risk for developing lifestyle related diseases, such as older adults.

III. Aging and Airway Inflammation

As we age, the immune system decreases responsiveness and communication with other cells (Baylis et al. 2013). This deleterious effect with age is termed immunosenescence, and affects the immune system, lungs, airway functioning, and metabolic clearing (Baylis et al. 2013, Bush 2016, Emerson et al. 2018). This decline leads to an increased risk of airway diseases, like COPD, which are attributable to structural decline of the lungs, environmental exposures, and genes (Sharma 2006, Bush 2016).

When responding to stimulants, younger individuals alter their airway environments at a lower inflammatory level than older individuals (Murtolahti 2017). With aging, work of breathing increases due to decreases in chest wall compliance, decreased respiratory muscle strength, increased dead space, and increased lung inflammation (Sharma 2006, Busse et al. 2010). The aging population also tends to be less physically active, leading to obesity where there will be an exaggerated immune response (Ye et al. 2010). Aging is associated with reduced lung and airway function, subsequently increasing

airway resistance and airway inflammation, however postprandial airway inflammation has not yet been investigated in this population. Considering even healthy, physically active older adults have elevated triglycerides and glucose after a HFM meal compared to their younger physically active counterparts, a greater magnitude of increase in airway inflammation post-HFM may be present. Considering this group is more likely to have an elevated response compared to younger individuals, determining whether the adverse response can then be modified is important to elucidate.

IV. Exercise and Acute Airway Inflammation

Acute exercise prior to HFM consumption has been shown to ameliorate postprandial lipemia and triglycerides (Freese et al. 2014, Gill et al. 2003), which are risk factors for cardiovascular disease (Nordestgaard et al. 2007). Exercise stimulates an anti-inflammatory cascade of cytokines which may reduce systemic inflammation postprandially (Johnson et al. 2016, Peterson and Pederson 2005) and thus the use of exercise to mitigate airway inflammation has been investigated, particularly in young adults. Exercising 12 hours prior to a HFM challenge did not attenuate airway inflammation (Johnson et al. 2016, Emerson et al. 2016), nor has exercise 1 hour post-HFM (Kurti et al. 2015, Teeman et al. 2015). When looking at chronic exercise (≥150 min moderate-vigorous PA/week) compared to sedentary individuals, airway inflammation still increased post-HFM even when paired with acute exercise (Kurit et al. 2017). While exercise has been shown to attenuate systemic inflammation (Petersen and Pedersen 2005, Starkie et al. 2003) it appears exercising the night prior, immediately after a HFM, or chronic physical activity (PA) does not attenuate airway inflammation in young healthy individuals. However since younger individuals have only a slight elevation in the airway

inflammatory response post-HFM, older adults who may experience a larger magnitude of postprandial response is an important demographic to better understand. Additionally, since attenuations with exercise are not present in younger individuals, exercise may be more advantageous for an older population, especially since older individuals are at higher risk of disease.

V. *Purpose and Hypothesis*

The primary purpose of this study will be to assess the airway inflammatory response to a HFM in older adults compared to younger adults. A secondary aim is to elucidate whether exercise had any impact on postprandial airway inflammation in older adults compared to younger adults. Exploratory aims are to assess changes in pulmonary function after a HFM in older and younger and elucidate whether it was modified by acute exercise. We hypothesize that (1) older individuals will exhibit a larger inflammatory response post-HFM meal compared to their younger counterparts and (2) that exercise will reduce airway inflammation in older but not younger adults.

Chapter II

Methodology

Subjects:

Twenty-four total subjects will be recruited for this study; 12 younger subjects between 18-35 years old and 12 older adults between 60-80 years old. Participants will be recruited by word-of mouth and fliers at James Madison University and the surrounding Harrisonburg-Rockingham area. Participants must be free from diagnosed diseases including; cardiovascular, metabolic, or renal disease and currently be free from antioxidants, anti-inflammatory agents, or medications that alter the primary outcomes of the study. Informed consent will be taken upon arrival to the laboratory and prior to experimental testing, along with a physical activity readiness questionnaire (PAR-Q) and an International Physical activity Questionnaire (I-PAQ) to determine physical activity in MET/min/week.

Study design:

This study will consist of three separate visits to the laboratory: an initial screening visit followed by two HFM sessions. Upon subjects arrival to the laboratory for their initial visit, anthropometric measures will be taken with familiarization and baseline testing of pulmonary function tests and exhaled gases as well as an incremental exercise test to exhaustion. Subjects will then be randomly assigned an order to perform the following two HFM sessions; HFM meal alone sessions first or acute exercise session prior to the HFM meal first. The two meal sessions will start at the same time in the morning for each, with a minimum of seven days between the two sessions.

Anthropometrics:

Participant's anthropometrics will be taken upon arrival. Height will be measured to the nearest 0.1 inch, without shoes, using a portable stadiometer (Charder Model HM 200P, Charder Electronic Co Ltd., Taichung, Taiwan). Weight will be taken to the nearest 0.1 kg using a standard physician's scale (Dymo Pelouze model 4040, Newell Brands, Hoboken, NJ). A three compartment DEXA (Lunar iDXA, General Electric Company, Fairfield, CT, USA) assessment will be performed to determine lean mass, fat mass, and percent body fat. Blood pressure will be taken twice and an average of the two will be recorded using an automatic sphygmomanometer (ProBP 3400 Welch Allyn, Skaneateles Falls, NY). Waist circumference will be measured at the narrowest part of the waist using a Gulick tape measure (Creative Health Products, Ann Arbor, MI).

High Fat Meals and Testing Protocols:

Subjects will be asked to arrive at the lab after a twelve hour fast and will be asked to remain seated in the lab for the duration of the study. Baseline measurements will be taken prior to the HFM; glucose and triglycerides will be measured using an indwelling safelet catheter inserted into a forearm vein via a 22-gauge needle (Fisher Scientific, Waltham, MA). The HFM challenge will consist of consuming a Marie Callender's Chocolate Satin Pie, with portions standardized to 12 kcal/kg body weight. Twenty min will be allocated to consume the HFM. Following the conclusion of the meal, eNO, pulmonary function tests (PFTs) and iOS measurements will be collected at 120 min and 240 min. Glucose will be assessed at baseline and then 30, 60, 90, 120, 240, 300, and 360 min post-HFM, while triglycerides will be measured at baseline and every 60 min until 360 min post-HFM.

Exercise:

On their initial visit, each participant will perform an incremental exercise test to exhaustion on a cycle ergometer (VIAsprint 150P) to determine VO_{2peak}. Metabolic and ventilatory data will be collected continuously and 30-sec averages will be used for analyses (Vmax Encore, Vyaire Medical, Lake Forest, IL). Subjects will be required to pedal at 50 rpm, until the patient cannot keep cadance or until they voluntarily stop. In the acute exercise prior to the HFM meal session, exercising testing will occur twelve hours pre prandially, performed at a HR corresponding to 60-70% of VO_{2peak} until a total of 75% of calories that will be consumed at HFM challenge are expended.

Exhaled gases:

Airway inflammation will be assessed using a Niox Vero (Circassia AB, Morrisville, NC) at baseline, and postprandially every 30 min until 120 min. This equipment measures eNO from exhaled gases and is a validated noninvasive way to assess airway inflammation. Subjects will perform a steady exhale at a constant flow rate for 6-10 s into a mouthpiece of the eNO analyzer. At each time point, eNO assessment will be completed twice and then averaged if results are within 10% of each other. If results are not within 10% of one another, a third measurement will be taken, with the closer two measurements being averaged. Tests will be performed according to ATS/ERS guidelines for eNO assessment (ATS/ERS rec 2005).

iOS - impulse oscillometry airway

Airway resistance will be measured with an impulse oscillometry system (iOS) at baseline, and postprandially every 30 min until 120 min. Participants will be asked to breathe normally while a Vmax Encore Metabolic cart sends repeated bursts of air into the subject's mouth, which is followed by recoil of the elastic components of lung tissues

creating backpressure, measuring airway resistance. Three airway resistance measurements within 20% of each other will be averaged.

Pulmonary function testing:

Pulmonary function will be assessed with maximal flow volume loops (MFVL) using Vmax Encore metabolic cart (Vyaire Medical, Lake Forest, IL) at baseline, 120 min and 240 min postprandially. This will determine participant's forced expiratory volume in 1-second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), and forced expiratory flow between 25% and 75% (FEF_{25-75}% of FVC) will then be calculated. Tests will be performed according to ATS/ERS guidelines for pulmonary function assessment (ATS/ERS rec 2005).

Statistical Analysis:

Statistical analysis for this study will be performed using SPSS v. 27 (IBM Corp, Armonk, NY, USA). Airway inflammation, PFTs, and iOS data will be checked for normality (using the Sharpiro-Wilk test), and analyzed with repeated measures ANOVAS. If data is not normally distributed, comparable non-parametric statistics will be used.

Chapter III

Manuscript

Postprandial Exhaled Nitric Oxide Responses in Older and Younger Adults With and Without Acute Exercise

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Abstract

A single high fat meal (HFM) increases airway inflammation in young, healthy individuals. Additionally, aging increases airway resistance and inflammation, though the airway inflammatory response to a HFM has not been investigated. Exercise is a natural anti-inflammatory, but has yet to be administered with a HFM as a method to study postprandial airway inflammation in older adults. **Purpose**: To investigate whether older individuals have greater postprandial airway inflammation compared to younger counterparts, and to explore whether exercise may modify the postprandial airway response in older adults. **Methods**: 12 younger adults (23.3±3.9 years; 5 M/7 F) and 12 older adults (67.7±6 years, 8 M/4 F) completed two HFM challenges (HFM=12 kcals/kg BW: 57% fat, 39% CHO, 4% PRO), in a randomized order. For both sessions, participants abstained from exercise 48 hours prior to the HFM session and adhered to a 12 hour overnight fast. In the HFM paired with exercise session, participants performed exercise on a cycle ergometer at a heart rate that corresponded to 65% VO_{2Peak} until caloric expenditure matched 75% of the caloric content of the HFM, then adhered to a 12 hour overnight fast before consuming the HFM. Airway inflammation (measured via exhaled nitric oxide; eNO) and airway function (measured via pulmonary function tests) were assessed at baseline, 2h and 4h postprandially. Blood triglycerides (TG) and glucose was assessed at baseline and every hour postprandially. **Results:** eNO post-HFM did not increase across time-points from baseline to four hours, ($p=0.071$), between HFM alone and HFM with exercise, nor did responses differ between younger and older groups. **Conclusion**: There was no airway inflammation following a HFM in older or younger individuals. Additionally, exercise did not alter the airway inflammation response.

Introduction

The diets of individuals in industrialized western nations, termed western diet, are typically categorized by being calorically dense, nutrient poor, and high in fats. These dietary characteristics contribute to systemic and airway inflammation (Christ et al. 2019, Hamilton et al. 2013, Teeman et al. 2016a, Beutler 2004). While postprandial metabolic and immune responses will return to baseline after a few hours following a single meal, a "typical" western diet consists of multiple meals consumed per day which places an individual in a postprandial state throughout the day (Kerver et al. 2006). Chronically elevated levels of airway and systemic inflammation from high fat diets increase the risk of development and progression of chronic lifestyle-related diseases (WHO/FAO 2002) such as cardiovascular disease, atherosclerosis, type II diabetes mellitus, asthma and chronic obstructive pulmonary disease (COPD) (Wood et al. 2009, Varraso et al. 2007).

Chronic airway inflammation can lead to structural changes in the airway and subsequent development of respiratory disease if left untreated (Moldovenanu et al. 2009). Interestingly, even a single high fat meal (HFM) has been shown to elevate postprandial airway inflammation in young healthy individuals, without changing pulmonary function (Baylis et al. 2013, Kurti et al. 2017a, Rosenkranz et al. 2010). Thus allowing the use of an acute HFM challenge as a method to better understand the airway inflammatory response and how to modify it. Specifically, exhaled nitric oxide (eNO), a validated, non-invasive method to assess airway inflammation has been shown to transiently increase following an HFM in young adults (ATS/ERS Guidelines rec 2005). Aging is associated with increased inflammation and decreased immune function, which can impact airway functioning and metabolic clearing to ultimately increase airway resistance and inflammation (Baylis et al.

2013, Bush 2016). Therefore, there may be elevated eNO post-HFM in older individuals compared to their younger counterparts, though postprandial airway inflammation has not yet been investigated in an older population.

If the transient rise of airway inflammation occurs over and over to the point where inflammation is elevated chronically and is left untreated it can be damaging, thus it is vital to identify methods that can attenuate adverse postprandial responses. Though there are mixed findings, acute exercise prior to HFM consumption has been shown to lower postprandial lipemia and systemic inflammation (Freese et al. 2014, Gill et al. 2003, Petersen and Pedersen 2005, Starkie et al. 2003), and thus the use of exercise to mitigate airway inflammation has been investigated. However, in young healthy adults exercising the night prior or immediately after a HFM, acute exercise does not appear to modify postprandial airway inflammation. However since older adults may experience greater airway inflammatory responses post-HFM, determining whether acute exercise can be employed within this demographic to attenuate inflammation is important to evaluate. Thus, the primary purpose of this study was to assess the postprandial eNO response in older adults compared to younger adults. A secondary aim was to elucidate whether exercise influenced postprandial airway inflammation in older adults compared to younger adults. Exploratory aims were to assess changes in pulmonary function after a HFM in older and younger and determine whether it was modified by acute exercise. We hypothesized that (1) older individuals would exhibit a larger inflammatory response post-HFM meal compared to their younger counterparts and (2) that exercise would reduce airway inflammation in older but not younger adults.

Methodology

Subjects:

Twenty-four total subjects were recruited for this study; 12 younger subjects between 18-35 years old and 12 older adults between 60-80 years old. Participants were recruited by word-of mouth and fliers at James Madison University and the surrounding Harrisonburg-Rockingham area. Participants were not consuming diagnosed diseases including; cardiovascular, metabolic, or renal disease and were free from antioxidant supplements, anti-inflammatory agents, or medications known to influence the primary outcomes of the study. Informed consent provided upon arrival to the laboratory and prior to experimental testing, along with a physical activity readiness questionnaire (PAR-Q) and an International Physical activity Questionnaire (I-PAQ) to determine physical activity in MET/min/week.

Study design:

This study consisted of four separate visits to the laboratory: an initial screening visit followed by two HFM sessions, one with exercise 12 hours prior. Upon subjects arrival to the laboratory for their initial visit, anthropometric measures were taken along with familiarization of pulmonary function tests (PFTs) and exhaled gases as well as an incremental exercise test to exhaustion. Subjects were then randomly assigned an order to perform the following two HFM sessions; HFM meal alone or acute exercise session prior to the HFM meal. The two meal sessions started at the same time each morning, with a minimum of seven days between the two sessions.

Anthropometrics:

Participant's anthropometrics were taken upon arrival to the lab. Height was measured to the nearest 0.1 inch, without shoes, using a portable stadiometer (Charder Model HM 200P, Charder Electronic Co Ltd., Taichung, Taiwan). Weight was taken to the nearest 0.1 kg using a standard physician's scale (Dymo Pelouze model 4040, Newell Brands, Hoboken, NJ). A DEXA (Lunar iDXA, General Electric Company, Fairfield, CT, USA) assessment was then performed to determine lean mass, fat mass, and percent body fat. Blood pressure was taken twice and the average of the two measurements was recorded using an automatic sphygmomanometer (ProBP 3400 Welch Allyn, Skaneateles Falls, NY). Waist circumference was measured at the narrowest part of the waist using a Gulick tape measure (Creative Health Products, Ann Arbor, MI).

High Fat Meals and Testing Protocols:

Subjects were asked to arrive at the lab after a twelve hour fast and to remain seated in the lab for the duration of the study. Baseline measurements were taken prior to the HFM; glucose and TG were measured using an indwelling safelet catheter inserted into a forearm vein via a 22-gauge needle (Fisher Scientific, Waltham, MA). The HFM challenge consisted of consuming a Marie Callender's Chocolate Satin Pie, with portions standardized to 12 kcal/kg body weight. Twenty min were allocated to consume the HFM. Following the conclusion of the meal, eNO, and PFTs were collected at 2 h and 4 h. Glucose and TG levels were assessed at baseline, 2 h, and 4 h post-HFM. Since these data were part of a larger study, glucose and TG data are included in a manuscript under revision elsewhere and are not presented here.

Exercise:

On their initial visit, each participant performed an incremental exercise test to exhaustion on a cycle ergometer (VIAsprint 150P) to determine VO_{2peak}. Metabolic and ventilatory data were collected continuously and 30-sec averages were used for analyses (Vmax Encore, Vyaire Medical, Lake Forest, IL). Subjects were required to pedal at 50 rpm, until the subject could not keep cadence or until they voluntarily stopped. In the acute exercise prior to the HFM meal session, exercising testing occurred twelve hours before the HFM, and it was performed at a HR corresponding to 65% of VO_{2peak} until a total of 75% of calories to be consumed at the HFM challenge were expended.

Exhaled gases:

Airway inflammation was assessed using a Niox Vero (Circassia AB, Morrisville, NC) at baseline, 2 h, and 4 h postprandially. To assess eNO, subjects performed a steady exhale at a constant flow rate for 6-10 s into a mouthpiece on the eNO analyzer. At each time point, eNO assessment was completed twice and then averaged if results were within 10% of each other. If results were not within 10% of one another, a third measurement was taken, with the closer of the two measurements averaged. Tests were performed according to ATS/ERS guidelines for eNO assessment (ATS/ERS rec 2005).

Pulmonary function testing:

Pulmonary function was assessed with maximal flow volume loops (MFVL) using a Vmax Encore metabolic cart (Vyaire Medical, Lake Forest, IL) at baseline, 2 h and 4 h postprandially. This test was used to assess pulmonary variables including: forced expiratory volume in 1-second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), and forced expiratory flow between 25% and 75% (FEF_{25-75}% of FVC). Tests were

performed according to ATS/ERS guidelines for pulmonary function assessment (ATS/ERS rec 2005).

Statistical Analysis:

Statistical analyses for this study were performed using SPSS v. 27 (IBM Corp, Armonk, NY, USA). Airway inflammation and PFT were checked for normality using the Sharpiro-Wilk test. All data were normally distributed. Hypothesis testing was completed using repeated measures ANOVAs with time as the within-subjects factor as a pre-planned contrast (baseline, 2 and 4 hours), and condition (exercise or no exercise) and age (younger or older) as the between-subjects factors. For all analyses, significance was set to $p<0.05$.

Results

Subject Characteristics

Subject characteristics are shown in Table 1. There were 24 total subjects recruited for this study, 12 younger adults (23.3±3.9 years, 5 M/7 F, weight 71.3±17.3 kg) and 12 older adults (67.7±6.0 years, 8 M/4 F, weight=80.7±15.1 kg). One of the older participants' data was excluded from data analysis due to diagnosed pulmonary disease, however their data was included in the larger study. Between younger and older adults, there were no differences in weight ($p=0.172$), body mass index (BMI) ($p=0.722$), body fat percentage ($p=0.158$), absolute VO_{2peak} ($p=0.995$), calories utilized while exercising ($p=0.172$), MET-minutes per week ($p=0.262$), or meal size ($p=0.172$). There were differences in age ($p<0.001$), height ($p=0.023$), and relative VO_{2peak} ($p=0.005$) between the younger and older adults.

Exhaled Nitric Oxide

The post-HFM eNO response post-HFM is shown in Figure 1. There was no between-subjects effect for eNO by age or condition ($p > 0.05$). eNO did not significantly change across time-points as a linear function from baseline to four hours, ($p=0.115$), or as a pre-planned quadratic contrast, where it increases from baseline to 2 hours and returns to baseline by 4 hours ($p=0.071$). There were no interaction effect of time*age ($p=0.715$), time*condition*age ($p=0.904$), or time*condition ($p=0.514$). From baseline to 2 h eNO increased by 10.86%, and decreased by 1.40% from 2 h to 4 h post-HFM.

Pulmonary Function

Lung function measurements are shown in Table 2. There were no between-subjects' effects for any pulmonary function outcomes ($p > 0.05$) except for $FEF_{25-75\%}$

(p=0.041) and FEV_1/FVC (p=0.026), which were lower in the older compared to younger adults. For FVC, FEV_1, and PEF there was no change across time-points from baseline to 4 hours post-HFM (FVC; p=0.298, FEV_1; p=0.179, PEF; p=0.190). FEV_1/FVC, and $FEF_{25-75\%}$ increased slightly from baseline to 4h (FEV_1/FVC; p=0.031, $FEF_{25-75\%}$; p=0.003). There were no interaction effects between time*condition*age (FVC; p=0.302, FEV_1; p=0.247, FEV_1/FVC; p=0.530, $FEF_{25-75\%}$; p=0.0.524, PEF; p=0.285) or time*age (FVC; p=0.580, FEV_1; p=0.373, FEV_1/FVC; p=0.295, $FEF_{25-75\%}$; p=0.0.616, PEF; p=0.533). There were also no interaction effects between time*condition (FVC; p=0.328, FEV_1; p=0.630, FEV_1/FVC; p=0.692, $FEF_{25-75\%}$; p=0.0.460, PEF; p=0.239).

Percent of predicted values for PFT's are shown in Table 3. There were no between-subjects' effects for any of the percent of predicted PFT outcomes ($p > 0.05$) except for FEV_1/FVC (p=0.017), which were lower in the older compared to younger adults. For FVC, FEV_1, FEV_1/FVC, and PEF there was no change across time-points from baseline to 4 hours post-HFM (FVC; p=0.602, FEV_1; p=0.654, PEF; p=0.56). FEV_1/FVC, and $FEF_{25-75\%}$ changed across time, where they slightly increased (FEV_1/FVC; p=0.030, $FEF_{25-75\%}$; p=0.049). There were no interaction effects between time*condition*age (FVC; p=0.398, FEV_1; p=0.374, FEV_1/FVC; p=0.598, $FEF_{25-75\%}$; p=0.385, PEF; p=0.560), or time*age (FVC; p=0.087, FEV_1; p=0.238, FEV_1/FVC; p=0.362, $FEF_{25-75\%}$; p=0.429, PEF; p=0.440), or time*condition (FVC; p=0.905, FEV_1; p=0.333, FEV_1/FVC; p=0.198, $FEF_{25-75\%}$; p=0.521, PEF; p=0.097).

Discussion

Major findings:

The primary purpose of this study was to assess the airway inflammatory response to a HFM using eNO in older adults compared to their younger counterparts. An exploratory aim was to assess whether exercise modified postprandial airway inflammation. We hypothesized that (1) older individuals will exhibit a larger airway inflammatory response post-HFM meal compared to their younger counterparts and (2) exercise would reduce airway inflammation in older but not younger adults. Our results did not support these hypotheses; eNO did not differ between older or younger adults, indicating age does not impact postprandial airway inflammation. Our results also illustrated that exercise did not impact postprandial airway inflammation.

Postprandial Exhaled Nitric Oxide in Older and Younger Adults

eNO did not increase after the HFM in older or younger individuals, which is conflicting with the existing literature. Typically, eNO increases following a HFM at approximately 2 hours and returns to baseline around 4 hours post-HFM (Ade et al. 2014, Johnson et al. 2016, Kurti et al. 2017b). Research has illustrated an association between dietary fat consumption and inflammation, however the direct mechanisms remain unclear. It has been hypothesized that increased eNO, a validated, non-invasive measurement to assess airway inflammation (ATS/ERS Guidelines), is due to systemic cytokines (Wood et al. 2011) or from lipopolysaccharides (LPS), a component of saturated fatty acids found in HFM. LPS increases Toll-like receptor (TLR) activation that has an independent and dependent pathway. TLR4-independent pathway increases ROS, and interleukin-1β (IL-1β) levels through the NLRP-ASC pathway (Teng et al. 2014, Johnson et al. 2016).

Proinflammatory cytokine IL-1β upregulates inducible nitric oxide (iNO) increasing eNO, while also decreasing insulin sensitivity to beget more inflammation (Ricciardolo et al. 2004, Teng et al. 2014). If excessive inflammation is left untreated, or the transient rise occurs over and over to the point where inflammation is elevated chronically, there can be tissue damage and structural changes to the bronchial walls that can eventually lead to airway hypersensitivity and airway hyperresponsiveness, which are characteristics of asthma (Moldovenanu et al. 2009, Lapraise et al. 1999, Wood et al. 2009). Previous work in healthy adults has reported that this acute increase in eNO may be clinically insignificant but is consistently statistically significant with absolute eNO increases between ~3.4 ppb and 6.5 ppb (Rosenkranz et al. 2010, Johnson 2016). This absolute increase in eNO in individuals with asthma, however, may be sufficient to impair bronchodilator recovery and impact pulmonary function (Wood et al. 2011). Therefore, understanding the eNO response post-HFM and possibly mitigating the airway inflammatory response may be important to deter structural changes in the airway that could lead to disease development and progression.

Our findings that eNO did not increase post-HFM is therefore surprising compared to existing studies. It is relevant to consider that previous work demonstrating increases in eNO following HFM noted responders and non-responders to the HFM challenge. Therefore, one potential explanation for the lack of an increase in eNO is that the participant sample represented in the current study may have been disproportionally comprised of ‘non-responders’. Specifically in the present study, 8 of the 28 subjects (3 younger, 5 older) responded to the HFM with an increase in eNO, with an absolute increase of only ~1.08 ppb, which is lower than the literature where the average was over 3 ppb. In

the older individuals who increased, there was a total change of 1 ppb for both HFM alone, and HFM paired with exercise. In the younger individuals who showed increases in the HFM alone condition, there was only an average increase of 1.83 ppb which decreased to 0.5 ppb when HFM was paired with exercise. Although the sample size for younger adults who showed increases is low, these findings suggest that exercise may modify postprandial eNO if we were to see larger increases in eNO post-HFM. Additionally, 22 of the 28 subjects (2 younger, 4 older) had a similar or attenuated eNO response with the HFM paired and exercise, compared to the HFM alone. In the current study, the changes in eNO were not associated with decreased pulmonary function, which is consistent with previous work with healthy subjects (Rosenkranz, 2010).

Considering there was a lack of an elevated postprandial eNO response, acute exercise before the HFM did not attenuate postprandial airway inflammation. One possible reason for the discrepancies and high amount of non-responders in this study was the population used in the current study was relatively fit. The older adults reported a lifetime of physical activity with no major periods of inactivity. A major strength of the study is that the younger and older adults were similar in their chronic physical activity and fitness levels, allow for a uniquely clear investigation of the impact of aging on postprandial airway inflammation. However, this could also be a reason that we did not see changes post-HFM in the older adults. Specifically, a HFM can increase ROS postprandially through the TLR4-independent pathway to increases eNO (Teng et al. 2014, Kim and Sears 2010, Mohanty et al. 2002, Gomez-Cabrera et al. 2008, Ricciardolo et al. 2004). Healthy or asthmatic individuals who are chronic exercisers, or those who engage in an acute moderate bout of exercise, upregulate antioxidant enzymes that can defend against ROS

seen post-HFM and have lower levels of eNO (Gomez-Cabrera et al. 2008, Scott et al. 2015). Thus our chronically active population could have a lower eNO response from moderate exercise's ability to combat ROS post-HFM. The present studies results are similar to recent data from Kurti et al, who reported that younger adults who exceeded PA guidelines did not have an attenuated eNO level response after a HFM when they engaged in preprandial exercise (Kurti et. al 2017a). However, subjects in their study were active and did have an elevated eNO response in the HFM alone condition. While the results are surprising and are conflicting with existing literature, further research should be done with older populations paired with preprandial exercise to elucidate whether acute and chronic exercise may play a role in postprandial airway inflammation.

Another possible explanation for the large number of non-responders to the HFM challenge in the present study is chronic diets of participants. Prior to the HFM challenge we asked participants to complete a food log, and to abstain from high nitrate-containing foods and medication. These steps help control for factors which may elevate baseline eNO levels, however baseline antioxidant status is still variable based on diet. Diets like the typical western diet have been said to be pro-inflammatory whereas in contrast a Mediterranean diet that is based on fruits, vegetables and whole grains promote an anti-inflammatory environment (Guilleminault et al. 2006). Therefore, it is conceivable that a greater number of participants in the present study may have consumed diets that contributed to anti-inflammatory effects.

Differences in the specific food type and fat percent of the HFM may have contributed to differences in outcomes between studies. In the present study the HFM consisted of 12 Kcal/kg/bw with 57% fat with 68% saturated fat. Others had HFM that

consisted of 9-10 kcal/kg/bw (450-2160 kcals) and 45%-63% fat, of which 49%-75% was saturated fat (Rosenkranz et al. 2010, Johnson et al. 2016, Ade et al. 2014, Emerson et al. 2016, Kurti et al. 2015, Kurti et al. 2017a, Li et al. 2016). Specifically, other studies completed in our research laboratory utilized a Jimmy Dean's Meat Lovers Breakfast Bowl or Eddy's Grand Vanilla ice cream with whipped topping. Dietary fat increases airway inflammation by increasing the innate immune response through LPS activation of TLR4 pathway (Shi et al. 2006). Fat will also increase ROS generation and lipid peroxidation which both contribute to inflammation (Mohanty et al 2002). Specifically in asthmatics, following a HFM challenge there was inflammatory gene expression that may contribute to increased airway neutrophilia (Li et al. 2016). Saturated fat is pro-inflammatory (Christ et al. 2019) and the slightly lower total saturated fat consumed in this study may explain the lack of an eNO response. Even a small decrease in fat could attenuate the inflammatory response by a small percentage (Teng et al. 2014). The current study did have a higher total kcal/kg/bw than other studies however the meal was still representative of a true to life serving size seen in the western diet. Since dietary fat increases inflammation through multiple mechanisms, and that the current study total fat and saturated fat fell within the ranges that previous studies used to see an increase in postprandial eNO at 2h, this may not be the primary reason for the attenuated eNO response, yet may still contribute to the lack of increase of eNO postprandially.

Finally, the difference in eNO results of the present study and existing literature could be explained by the different equipment used to assess eNO. The present study used a Niox Vero whereas prior research has used various methods such as the Sievers Nitric Oxide Analyzer 280 by Sievers Instruments Inc (Kurti et al. 2015, Kurti et al. 2017,

Rosenkranz et al. 2010, Ade et al. 2014, Johnson et al. 2016). Other measurements of airway inflammation include more direct assessments of airway inflammation such as induced sputum induction cell count and Toll-like receptor 4 mRNA expression by real-time PCR (Wood et al. 2011, Kurti et al. 2017), or sputum gene expression confirmed with PCR (Li et al. 2016). Niox Vero has been shown to be valid and reliable (Alving et al. 2017) and used previously in beetroot juice supplementation studies (Baranauskas et al 2021, Babateen et al. 2020). The Niox Vero and Sievers have significantly high correlations with one another, however some report that Niox Vero tends to report eNO values at about 30% lower than the Sievers (Tanabe et al. 2019), while others report the Niox Vero to report higher eNO levels (Endo et al. 2016). Still, considering our primary interest was in assessing the change postprandially, it was very surprising that there was no significant increase from baseline to 2 hours post-HFM.

Pulmonary Function

Finally, while not a primary aim of the study, there were no significant changes in pulmonary function tests (PFT) in older or younger individuals. Changes in PFT are unlikely to be seen in a healthy population, even with increased triglycerides or eNO (Rosenkranz et al. 2010, Johnson et al. 2016, Kurti et al 2015, 2017). However, pulmonary function has been shown to change post-HFM in clinical populations. Wood et al. found that in asthmatic individuals there were changes in pulmonary function, specifically in attenuating the increase of FEV_1 and FEV_1/FVC due to impaired bronchodilatory recovery (Wood et al. 2011). The current study population was healthy and free from diagnosed pulmonary disease which explains why PFT did not change over time post-HFM. Although this is the first study to explore whether changes occurred post-HFM in an older population.

Conclusion

Our findings showed no increase in airway inflammation following a HFM challenge, regardless of age. Additionally exercise did not seem to alter airway inflammation. Further research should be done to explore airway inflammation in older adults, specifically in individuals who may be chronically inactive or already have pulmonary disease. Further, the role of acute exercise in mitigating postprandial airway inflammation should be better understood within a clinical or less healthy demographic.

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Table 1: Subject characteristics. Mean ± SD

	Younger N=12 (7F/5M)	**Older N=11 (4F/7M)**	**P value**
Age (years)	25.22 ± 3.80	67.36 ± 5.03*	<0.001
Height (cm)	168.23 ± 8.10	176.01 ± 8.93*	0.023
Weight (kg)	71.29 ± 17.26	80.73 ± 15.07	0.172
Body mass index (BMI) (kg/m^2)	25.04 ± 5.02	25.88 ± 3.15	0.722
Body Fat (%)	29.11 ± 8.74	33.14 ± 6.45	0.158
Absolute VO_{2peak} (L/min)	2.25 ± 0.42	2.33 ± 0.84	0.995
Relative VO_{2peak} (mL/kg/min)	32.81 ± 5.31	28.31 ± 6.69*	0.005
Exercise Calories	641.62 ± 155.36	726.60 ± 135.65	0.172
Meal Size	856.79 ± 207.15	968.80 ± 180.86	0.172

*indicates significance between younger and older groups.

Figure 1: Postprandial exhaled nitric oxide (eNO) in CON and EX conditions from baseline to 4h in older and younger individuals.

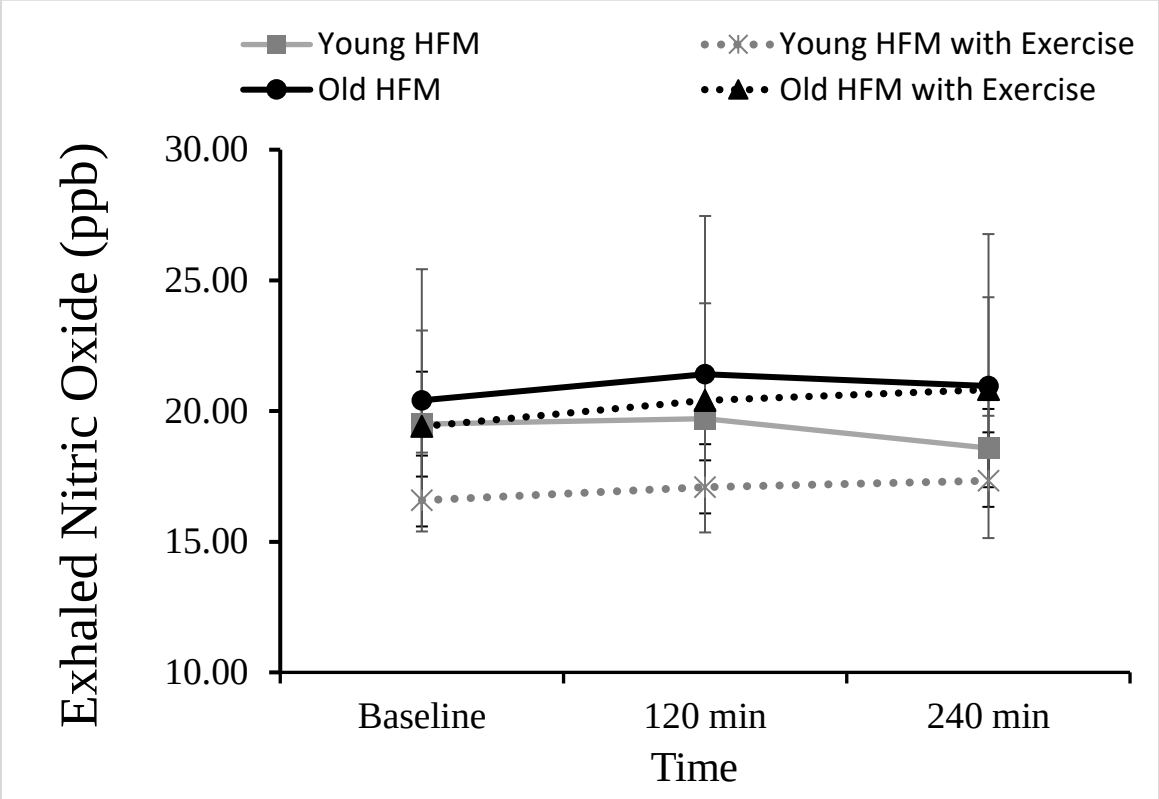

Table 2: Pulmonary function test (PFT) data from baseline to 4h postprandially following a HFM high in younger and older individuals.

		Young (n=12, 7F/5M)		Old (n=11, 4F/7M)		
		HFM	**HFM + Exercise**	**HFM**	**HFM + Exercise**	**P Value**
FVC	Baseline	4.14 ± 0.85	5.16 ± 3.10	4.05 ± 0.91	4.10 ± 0.97	0.302
	2h	4.21 ± 0.79	4.28 ± 0.94	3.98 ± 0.88	4.03 ± 1.00	
	4h	4.22 ± 0.82	4.21 ± 0.92	3.94 ± 1.00	4.02 ± 0.94	
FEV_1	Baseline	3.26 ± 0.50	3.31 ± 0.51	3.05 ± 0.78	3.03 ± 0.83	0.247
	2h	3.34 ± 0.45	3.36 ± 0.57	3.04 ± 0.82	3.06 ± 0.89	
	4h	3.32 ± 0.46	3.34 ± 0.54	2.99 ± 0.82	3.09 ± 0.88	
FEV_1/FVC	Baseline	79.51 ± 7.68	79.03 ± 7.30	75.03 ± 5.46	73.33 ± 4.60	0.530
	2h	80.24 ± 8.03	79.24 ± 7.43	75.82 ± 5.67	75.30 ± 5.93	
	4h	79.61 ± 7.37	79.49 ± 7.71	75.97 ± 3.92	75.21 ± 5.30	
$FEF_{25-75\%}$	Baseline	3.14 ± 0.88	3.14 ± 0.83	2.57 ± 1.21*	2.38 ± 1.09	0.524
	2h	3.36 ± 0.92	3.35 ± 1.04	2.63 ± 1.28*	2.64 ± 1.37	
	4h	3.20 ± 0.82	3.22 ± 0.91	2.58 ± 1.06	2.61 ± 1.18	
PEF	Baseline	6.87 ± 1.62	7.32 ± 1.48	7.54 ± 1.97	7.82 ± 2.54	0.285
	2h	7.50 ± 1.31	7.17 ± 1.47	7.77 ± 2.25	7.99 ± 2.28	
	4h	7.30 ± 1.18	7.28 ± 1.45	7.39 ± 2.15	7.84 ± 2.40	

FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; FEV_1/FVC (%): ratio of forced expiratory volume in 1 s to forced vital capacity; FEF25-75%: forced expiratory flow between 25 and 75%; PEF: peak expiratory flow.
(*) Denotes a statistical difference between old and young

Table 3: Percent of predicted values

		Young (n=12, 7F/5M)		Old (n=11, 4F/7M)		
		HFM	**HFM + Exercise**	**HFM**	**HFM + Exercise**	**P Value**
FVC	Baseline	95.71 ± 11.62	97.75 ± 12.16	96.08 ± 14.40	97.79 ± 14.03	0.398
	2h	97.08 ± 10.37	98.70 ± 12.32	94.38 ± 14.55	96.23 ± 15.10	
	4h	97.67 ± 10.60	97.24 ± 11.17	93.29 ± 16.31	96.23 ± 15.51	
FEV_1	Baseline	89.05 ± 13.68	90.48 ± 12.54	95.73 ± 17.76	95.63 ± 18.46	0.374
	2h	91.38 ± 12.30	91.81 ± 13.50	95.01 ± 18.19	88.15 ± 30.88	
	4h	90.71 ± 11.65	91.24 ± 13.41	93.75 ± 19.12	97.18 ± 20.02	
FEV_1/FVC	Baseline	93.59 ± 7.31	93.34 ± 7.69	99.31 ± 8.23	97.13 ± 6.67	0.598
	2h	94.51 ± 7.78	93.71 ± 7.70	100.23 ± 8.36	99.61 ± 8.25	
	4h	93.59 ± 6.99	94.47 ± 8.42	100.05 ± 7.04	100.47 ± 9.49	
$FEF_{25-75\%}$	Baseline	80.08 ± 27.02	81.32 ± 25.78	98.35 ± 42.35	91.43 ± 36.66	0.560
	2h	85.69 ± 28.40	85.32 ± 31.47	99.04 ± 40.05	98.23 ± 43.30	
	4h	81.34 ± 25.44	82.12 ± 27.91	98.48 ± 37.09	99.88 ± 40.38	
PEF	Baseline	86.87 ± 17.51	92.21 ± 18.55	95.38 ± 17.03	98.88 ± 21.89	0.385
	2h	95.70 ± 18.10	90.87 ± 16.04	102.32 ± 25.61	101.12 ± 17.71	
	4h	93.03 ± 14.58	92.38 ± 16.21	94.59 ±15.86	99.25 ± 21.03	

FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; FEV1/FVC (%): ratio of forced expiratory volume in 1 s to forced vital capacity; FEF25-75%: forced expiratory flow between 25 and 75%; PEF: peak expiratory flow.

Appendices

Postprandial Exhaled Nitric Oxide Responses in Older and Younger Adults With and Without Acute Exercise

Consent to Participate in Research

Identification of Investigators & Purpose of the Study

You are being asked to participate in a research study conducted by Drs. Stephanie Kurti and Elizabeth Edwards from James Madison University. To participate, you must be in good health and able to exercise (per the physical activity readiness-questionnaire and medical records). The purpose of this study is to determine whether being active impacts how your body responds to a high-fat meal. Previous research tells us that this response after a meal is actually a more accurate prediction of your disease risk than fasting levels. We also want to see if how active you are on a regular basis changes how your body responds to a high-fat meal. This study will contribute to the knowledge of both practitioners and clinicians, and may provide an important public health message in promoting exercise as a way to affect how your body responds to high-fat meals, without the need for prescription drugs. Should you decide to participate in this research study, you will be asked to sign this consent form once all your questions have been answered to your satisfaction.

Research Procedures

This study consists of a series of surveys, a body composition scan, and fitness test that will be administered to individual participants in the Human Performance Laboratory at James Madison University. There will be one acute exercise session and two meal sessions. The total time required for participation in the research study is outlined on the following page (time required section). The specific procedures during each visit are included here:

Initial visit: If you are older, you will have already have had to receive medical clearance from your physician to participate in this study prior to your initial visit. On the first visit to the laboratory, you will be briefed on the study and asked to complete a series of questionnaires, including the international physical activity questionnaire, the physical activity readiness-questionnaire plus, and a medical history form. If you'd like to see any of these questionnaires prior to consenting, please ask a researcher and we'll be happy to provide one for you.

On this first day, you'll also undergo a few tests. First, we'll assess your height and weight. Then we'll perform a DEXA scan to assess your body composition scan (how much of your body is fat vs. lean mass). Finally, you'll perform an exercise test on a cycle ergometer. The exercise test is a test to assess your peak aerobic capacity, which is the best measure of cardiorespiratory fitness. The exercise bout lasts approximately 12 to 15

minutes until you need to stop or cannot maintain the required cadence. Before and after the exercise testing, standard pulmonary function tests (PFTs) will be performed, which will be repeated at 2 minutes and 20 minutes after the bout of exercise. These tests are noninvasive and commonly used to assess the capacity of the pulmonary system. An example of these tests are a breathing maneuver simply requires you to maximally inhale, then forcefully exhale and hold for 6 seconds, and then to maximally inhale again.

Following the measurements and exercise testing, you will be given an accelerometer to wear for one week and will return to the laboratory for your second testing session after the one-week period. Your next visit will either be a meal testing session with exercise the night before or a meal testing session without exercise the night before.

Meal testing sessions: Your HFM testing sessions will be after a 12 hour fast. We'll place an indwelling intravenous catheter inserted into a forearm vein to allow for repeated blood draws. You will be asked to perform several experimental measurements prior to consumption of a single high-fat meal (Marie Callender's Chocolate Satin Pie, 63% fat, 12 kcal/kg body weight). The meals contain dairy and gluten. These same measurements will be performed every hour until 6 hours after the HFM. These include the following: Pulmonary function testing, exhaled nitric oxide, exhaled breath condensate, blood draws for glucose, triglycerides, and inflammatory and angiogenic markers.

Acute exercise session: On the day that you're completing the exercise, you'll come to the lab 12 hours prior to your meal testing session. At this session, you will exercise long enough to expend 75% of the calories that will be consumed in the HFM session. You will exercise on a cycle ergometer at a moderate intensity at 65% of your VO_{2peak} (which will be based on the cycle test from the first day). Throughout this exercise session, heart rate data will be monitored continuously.

Blood sample Storage: After collection, your blood will be stored in a deep freezer on JMU's campus until all samples have been collected. At that point, the blood will either be analyzed here at JMU or shipped off to partner labs (e.g. UVA or EVE Technologies) for analysis there. Any blood shipped to partner sites will be destroyed or returned after those analyses are complete.

Time Required

Participation in this study will require about 18 hours of your time over the course of 4 separate visits. Upon completion of the study, you will be compensated $75.00 upon completion of the study. The visits are outlined below:

Baseline Testing: On the first visit to the laboratory, completing the required forms and questionnaires, performing the acute exercise test, and undergoing the body composition scan will take approximately 2 hours.

HFM Visits: Two HFM sessions will each be ~7 hours in length. During this time, an intravenous catheter will be inserted into the median cubital vein of the forearm and blood samples will be obtained before the HFM and every hour post-meal for 6 hours. Approximately 10ml of blood will be obtained during each time-point post-HFM. The catheter will be kept patent by a slow, continuous flow (1 drop/second) of saline solution. The catheter will remain in the antecubital vein of the participant for the remainder of the measurement period in order to prevent clotting in the catheter (thus allowing a single venipuncture for multiple blood samples). The following variables will

be analyzed from these samples: triglycerides, glucose, insulin, angiogenic and inflammatory markers.

Acute exercise session: This session will involve an acute bout of exercise that should last between 30-45 minutes, however may vary from person to person. The exercise bout will not last longer than 90 minutes in any individual.

Risks

Participation in this study does have some risks, although they are small. The risk of any serious event during this study is very small. Possible risks include:

Catheter: You may experience discomfort with the placement of the catheter. The catheter is plastic tubing and allows the arm to be moved throughout the 6-hour testing session. If excessive discomfort exists, the catheter can be taken out at any time during the study.

Exercise bout: Both the baseline exercise test and the exercise bout may be associated with some discomfort and soreness on the following days. This is a normal physiological response and is not dangerous. During the exercise test, you will have a mouthpiece in for the duration of the test. This may be uncomfortable and you may withdraw from the study at any time. Supervision will be provided by research assistants trained in CPR and AED to minimize any potential risk from the exercise bout. Also, your heart rate, ventilatory and metabolic data will be continually monitored throughout the entire exercise bout. If any aberrant responses are recorded, investigators will ask you to discontinue the exercise.

High-fat meal: The high-fat meal protocol is of very short duration, and any changes in blood lipids, glucose, or inflammatory markers are unlikely to create any long-term health problems. Additionally, this meal is not out of line with meals consumed on a regular basis by a significant portion of the US population.

DEXA: The DEXA scan entails a low dose of radiation equivalent to approximately one transatlantic flight (0.015 mSv= millisievert). While there is no validated questionnaire to define extensive exposure, increased radiation correlates with increased risk of cancer and consequently, increased risk of death. However, for reference, the annual permissible dose for a radiation worker is 5,000 mrem or 5 rem, - which would be over 3,000 of these scans in one year. The limit for a pregnant worker, the most conservative level given, is 500mrem - over 300x the dose we are using.

Benefits

By participating in this study, you will learn about your current level of valuable blood, body composition, and pulmonary values. Your data will be provided to you upon completion of your participation in the study. If an emergency arises and you must drop out, you may still receive your data. Having these tests done in a lab would cost several hundreds of dollars. Additionally, you will be compensated $75 via a JMU Prepaid gift card for your time during the study.

Society may benefit from more knowledge about how lifestyle affects the inflammatory, lipemic and angiogenic response to a high-fat meal, which is associated with cancer and cardiopulmonary disease development. Additionally, society will learn whether

acute exercise is an effective method in older adults to attenuate these deleterious postprandial responses.

Confidentiality

The results of this research will be presented at the American College of Sports Medicine Annual meeting as well as the Experimental Biology annual conference. The results of this project will be coded in such a way that the respondent's identity will not be attached to the final form of this study. The researcher retains the right to use and publish non-identifiable data. While individual responses are confidential, aggregate data will be presented representing averages or generalizations about the responses as a whole. All data will be stored in a secure location accessible only to the JMU researchers. Upon completion of the study, all information that matches up individual respondents with their answers will be destroyed.

Participation & Withdrawal

Your participation is entirely voluntary. You are free to choose not to participate. Should you choose to participate, you can withdraw at any time without consequences of any kind.

Questions about the Study

If you have questions or concerns during the time of your participation in this study, or after its completion or you would like to receive a copy of the final aggregate results of this study, please contact:

Researcher's Name: Dr. Stephanie Kurti
Email Address: kurtisp@jmu.edu
Cell-Phone number: 630-205-6363
Department of Kinesiology
James Madison University
Office Telephone: 540-568-3947

Researcher's Name: Dr. Elizabeth Edwards
E-mail Address: edwardes@jmu.edu
Office Telephone: 540-568-5220
Department of Kinesiology
James Madison University

Questions about Your Rights as a Research Subject

Dr. Taimi Castle
(540) 568-5929
castletl@jmu.edu
Chair, Institutional Review Board
James Madison University

Giving of Consent

I have read this consent form and I understand what is being requested of me as a participant in this study. I freely consent to participate. I have been given satisfactory answers to my questions. The investigator provided me with a copy of this form. I certify that I am at least 18 years of age.

_____

Name of Participant (Printed)

_____ _____
Name of Participant (Signed) Date

_____ _____
Name of Researcher (Signed) Date

Attn. Dr. _____

Your patient needs the following physician approval to participate in our JMU research project.

Physician Approval Form

Patient Name: _____

Project Description:

The purpose of the study is to investigate to determine whether an acute bout of moderate-intensity exercise will attenuate the lipemic response to a high-fat meal in active and inactive older adults. We hypothesize that an acute bout of moderate-intensity exercise will

attenuate the lipemic response to a high-fat meal in active and inactive older adults, with a greater attenuation of the lipemic response in the inactive older adults.

When the participant arrives at the laboratory, we will take resting blood pressure and heart rate, and several pulmonary function tests. These will be performed before and after an exercise test. The exercise test is performed on a cycle ergometer, where the intensity will increase every minute by 10-25 watts until volitional exhaustion (it is too hard to turn the pedals). We monitor heart rate, oxygen saturation, and blood pressure throughout the exercise test.

Usually the test lasts ~10 minutes, with only 1 or 2 minutes of very hard work, until the participant wishes to stop the test. All researchers are trained in CPR and our laboratory has an AED present. We have tested ~50 participants thus far, and nobody has had any issues during or after the exercise test to fatigue.

We are using American College of Sports Medicine guidelines to determine whether participants are eligible for participation in the research project. If the individual does not have a previous heart condition, chest pain when they currently exercise, and is not on any heart medications, they are able to participate in the test without medical supervision.

However if they have not been exercising recently we ask for physician approval to participate in the research study. The participant can stop whenever they want during the test if they feel uncomfortable. Maximal oxygen consumption is the best measure of fitness level and overall health, and we will discuss the results with them after their session.

Contact: Hannah Frick (frickh1@jmu.edu: (c) 703-638-8892) or Scott Wisseman (wissemws@dukes.jmu.edu: (c) 703-268-9976) if you have any questions.

Our departmental fax number is: 540-568-3338

I have reviewed the project description and believe the individual is able to complete a maximal exercise test for the research project.

Printed Name: _____ Date: _____

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The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

Signed Name:

Additional notes:

GENERAL HEALTH QUESTIONS

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

☑ **If you answered NO to all of the questions above, you are cleared for physical activity.**
Go to Page 4 to sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow International Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at **www.eparmedx.com** before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.

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FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)

1. Do you have Arthritis, Osteoporosis, or Back Problems?

If the above condition(s) is/are present, answer questions 1a-1c — If **NO** ☐ go to question 2

1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES ☐ NO ☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	YES ☐ NO ☐

2. Do you currently have Cancer of any kind?

If the above condition(s) is/are present, answer questions 2a-2b — If **NO** ☐ go to question 3

2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?	YES ☐ NO ☐
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES ☐ NO ☐

3. Do you have a Heart or Cardiovascular Condition? *This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm*

If the above condition(s) is/are present, answer questions 3a-3d — If **NO** ☐ go to question 4

3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)	YES ☐ NO ☐
3c.	Do you have chronic heart failure?	YES ☐ NO ☐
3d.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	YES ☐ NO ☐

4. Do you have High Blood Pressure?

If the above condition(s) is/are present, answer questions 4a-4b — If **NO** ☐ go to question 5

4a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
4b.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure)	YES ☐ NO ☐

5. Do you have any Metabolic Conditions? *This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes*

If the above condition(s) is/are present, answer questions 5a-5e — If **NO** ☐ go to question 6

5a.	Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies?	YES ☐ NO ☐
5b.	Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.	YES ☐ NO ☐
5c.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, **OR** the sensation in your toes and feet?	YES ☐ NO ☐
5d.	Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?	YES ☐ NO ☐
5e.	Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?	YES ☐ NO ☐

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6. Do you have any Mental Health Problems or Learning Difficulties? *This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome*

If the above condition(s) is/are present, answer questions 6a-6b — If **NO** ☐ go to question 7

6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
6b.	Do you have Down Syndrome **AND** back problems affecting nerves or muscles?	YES ☐ NO ☐

7. Do you have a Respiratory Disease? *This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure*

If the above condition(s) is/are present, answer questions 7a-7d — If **NO** ☐ go to question 8

7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
7b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	YES ☐ NO ☐
7c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	YES ☐ NO ☐
7d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES ☐ NO ☐

8. Do you have a Spinal Cord Injury? *This includes Tetraplegia and Paraplegia*

If the above condition(s) is/are present, answer questions 8a-8c — If **NO** ☐ go to question 9

8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
8b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES ☐ NO ☐
8c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES ☐ NO ☐

9. Have you had a Stroke? *This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event*

If the above condition(s) is/are present, answer questions 9a-9c — If **NO** ☐ go to question 10

9a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
9b.	Do you have any impairment in walking or mobility?	YES ☐ NO ☐
9c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES ☐ NO ☐

10. Do you have any other medical condition not listed above or do you have two or more medical conditions?

If you have other medical conditions, answer questions 10a-10c — If **NO** ☐ read the Page 4 recommendations

10a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?	YES ☐ NO ☐
10b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES ☐ NO ☐
10c.	Do you currently live with two or more medical conditions?	YES ☐ NO ☐

PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE:

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

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

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

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

You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the **ePARmed-X+ at www.eparmedx.com** and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ **at www.eparmedx.com** before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION

- All persons who have completed the PAR-Q+ please read and sign the declaration below.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

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

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

For more information, please contact

www.eparmedx.com
Email: eparmedx@gmail.com

Citation for PAR-Q+
Warburton DER, Jamnik VK, Bredin SSD, and Gledhill N on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Health & Fitness Journal of Canada 4(2):3-23, 2011.

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

Key References

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3. Chisholm DM, Collis ML, Kulak LL, Davenport W, and Gruber N. Physical activity readiness. British Columbia Medical Journal. 1975;17:375-378.
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01-01-2017

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

(October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

☐ **Yes**

☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ **days per week**

☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐

No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Food Intake Record Directions and Tips

You will have to input all the food that you consume in a day into a nutrition database at your first and second testing sessions. *Also, your food consumption should be the same on both days before your high-fat meal session*.

We will give you a copy of the food that you have consumed so you can remember what to eat the next time before visiting the laboratory.

Instructions on Use:

- In the first two columns, note the time and location the food or beverage was consumed.
- In the third column, record the food or beverage consumed.
    - Be as detailed as possible in describing the food item. For example not just chicken, but how it was prepared (fried, grilled, baked, etc.) and include any sauces or dressings put on any food item. If you eat a salad, try and write own everything that was in the salad with appropriate portion sizes.
    - Include brand names or restaurant names with the item names whenever possible. Examples: Kraft, General Mills, Campbell's' McDonalds 6 piece McNuggets, etc.
    - Include toppings such as mustard, ketchup, mayo, cream sugar, steak sauce, salsa, dressing, gravy, etc.
    - If you are at a restaurant, it is more than OK to ask the staff or waiter/waitress how something was prepared or about the ingredients in a particular item. Additionally, if you want, you can include the description off the menu.
    - If you have a recipe or a label of a common food you consume, feel free to bring it in. The more detail you can provide, the better analysis we can provide.
- Determine serving size for food and beverage (columns 4-6):
    - *Portion Size: How many?:* How many of this item did you consume?
    - *Portion Size: Food Model:* Estimate the size of your food. Options:
        - Use the *Food Amounts Booklet* as a visual guide.
        - OR if you're cooking at home and you know the measured amount, include the measurements. You can use household measures such as measuring cups and spoons to further help you estimate how much you consumed.
        - OR if a weight from the package is available, include the weight.
        - Notes: Leave this blank unless there is something you would like us to know.
- Remember to include all beverages (even water) and snacks consumed.

- Be as honest as possible! This really helps with the accuracy of the data that is collected. We are simply trying to document what you consumed of the recording period.
- If you have any questions please contact a researcher.
- Thank you again for your participation. Your accuracy not only assists us with our research, but provides us a great tool for understanding the impact on your nutrition on several of the responses to the exercise and acute high-fat feeding sessions.

Food Intake Record

Name of the person you are interviewing _____

Day of the week:_____ Day (circle one) 1 2

Time	*Location*	**DETAILED Description** (Be as detailed as possible in describing the food item. For example not just chicken, but how it's cooked (fried, grilled, baked, etc), and include any sauces or dressings put on any food item. Remember beverages too.)	*Amount Eaten (be specific)*	*Comments*

Is this intake unusual in any way? If so, explain:

ID _____ AC _____ m0

Using Your Activity Monitor

Thank you for agreeing to wear this Activity Monitor. The Activity Monitor is attached to a black belt with a clasping buckle that you will put around your waist like a belt. These instructions are intended to help you get started wearing your Activity Monitor. A phone number is provided at the end of these instructions should you need to contact us.

Checklist

1. **Read all materials in this packet. These instructions contain important information regarding the proper use of your Activity Monitor.**
2. **Begin wearing the monitor when you wake up on the Requested Start Date. The monitor will start working automatically – you DO NOT need to activate it.**
3. **Wear the monitor during all waking hours for the seven requested days.**
4. **Stop wearing the monitor at the end of the day on the Requested End Date.**
5. **For each day you wear the unit, record the exact time of day you put it on, the exact time you took it off, and any time you did not wear the unit on your Accelerometer Log.**
6. **After you have worn the Monitor for seven days, place it back in the padded envelope and mail it back to us with the completed activity log.**

When to Wear the Activity Monitor

- **First, consult the Accelerometer Log form for the actual dates that you should be wearing your Activity Monitor.**
- **The total time you will be wearing the Activity Monitor will be <u>seven days</u>.**

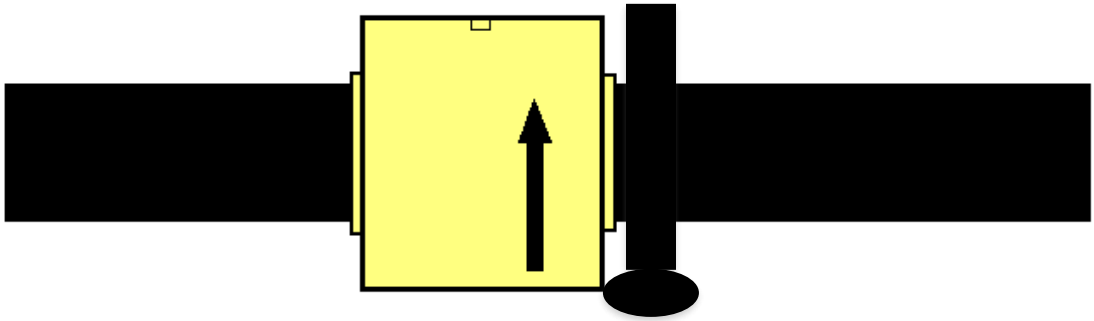
- **You should wear it throughout the <u>entire day</u>. We cannot use the data if the monitor has not been worn during all waking hours. The only times you should NOT wear the monitor are:**
    - **While you are sleeping**
    - **When you shower, bathe, or swim (water will damage it)**
- **We would like you to wear the monitor for the seven days indicated on the Accelerometer Log. (See example below.) However, if you are unable to start wearing the monitor on the requested start date, or you forget to wear it on one of the requested days, you should continue wearing the monitor until you have worn it for seven full days.**

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date	**11/28**	**11/29**	**11/30**	**12/1**	**12/3**	**12/4**	**12/5**
Time of day you put on the unit	6:35 am	7:20 am	7:45 am	7:25 am	5:50 am	6:15 am	6:50 a
Time of day you took off the unit	8:25 pm	9:40 pm	9:25 pm	9:00 pm	8:35 pm	8:15 pm	8:55 p
Any time you did not wear the unit? (e.g. naps, bathing)	-------	12:30 - 12:50 pm	6:00-6:50 pm	-------	--------	9:15-9:40 am	-------
Please provide comments about problems that occurred while you were wearing the unit.							
I forgot to wear the monitor on 12/2, so I wore it on 12/5 instead.							

How to Wear the Activity Monitor

The Activity Monitor is already attached to a belt that you will wear around your waist. Following these step-by-step instructions should help you begin wearing your Activity Monitor:

1. **Taking the belt, place it around your waist so that the arrow on the Activity Monitor is facing away from you and is pointed up towards your head, as in the picture below:**



2. **Take both ends of the buckle and connect them so that the belt is attached loosely around your waist.**

3. **You may adjust the tightness of the belt by pulling on the straps to make it tighter or by pulling on the back of the buckle to make it looser. Your belt should be snug, but not uncomfortably tight. (See "Caring for the Activity Monitor" if you need to make alterations to your belt.) You may wear the monitor over or under your clothing.**

4. **The activity monitor should be worn on your <u>left hip</u>. The Activity Monitor should slide into place along the belt with gentle pressure.**

Caring for the Activity Monitor

- **You will probably not need to clean the Activity Monitor. If it gets dirty, however, simply wiping it with a damp (not wet) rag should be sufficient.**
- **If after tightening your belt, there is a lot of excess belt hanging from the buckle, you may wish to trim it back. To do so, you should:**
    - **Make sure to leave about 3-4 inches excess for adjustment purposes.**
    - **Cut the belt evenly with a pair of scissors.**

  - **Seal the cut end of the belt with some clear nail polish to prevent fraying (if necessary).**

- **You may use a safety pin or rubber band to tie up extra belt rather than cutting it if you prefer.**

Other important notes about your activity monitor:

- **This piece of equipment is very expensive, so please take good care of it!**
- **The Activity Monitor is not waterproof, so please avoid getting it wet, as this could cause damage.**
- **The Activity Monitor may or may not flash. Either way, it is not a cause for any concern. Trust us – it's working!**

Returning the Activity Monitor

After you have worn the Activity Monitor for a full week, we ask that you return it to us so that we can collect the data and use it for other participants. When returning the Activity Monitor to us, you should:

- **Remove the Activity Monitor from your waist.**
- **Remember to record your actual end date on the Accelerometer Log and ensure the rest of the form is complete.**
- **Wrap the belt around the Activity Monitor and hold secure with a rubber band.**
- **Place the Activity Monitor back in the padded envelope and mail it back to us with the completed Accelerometer Log.**

Activity Monitor Troubleshooting

If you are experiencing problems with your Activity Monitor or have questions, please contact study coordinator Stephanie Kurti and kurtisp@jmu.edu or 630-205-6363.

Frequently Asked Questions

My activity monitor was blinking and then stopped. Is it still working? Yes, some of the monitors blink before they start recording activity but some of our newer versions don't blink at all. Either way, keep wearing your monitor.

I don't want the monitor to show when I wear it. Can I wear it underneath my clothes? Yes, you can wear it over or under your clothes – whatever is most comfortable for you.

My activity monitor seems to ride up and won't stay on my hip. Some people have said they have this issue. It will still record but it's better to have it closer to your hip if possible. You can try tightening it, pinning the band to your pants, or running the band through your belt loops.

I accidentally wore the monitor upside down one day. Do I need to wear it for an extra day? No, as long as you wore the monitor during all of your waking hours you do not need to wear it for an extra day. The data it collects are still accurate even if it's upside down.

I forgot to put on my monitor and then went out for the morning. Should I wear it for the afternoon/evening or just skip today? It is very important that you wear the monitor for the entire day. If you forget to wear it for part of the day, it is best to skip that day and add an extra full day to the end instead. Be sure to record this on your log.

My schedule for the week I'm supposed to wear the monitor is not a normal week for me. Should I still wear it? Yes. The important thing is that you wear it during the time we have specified. If needed you can make note of any special circumstances on your log.

I am going to be traveling when I'm supposed to wear my monitor. Will I be able to go through security at the airport? Yes. You will need to take it off just as you do your jewelry. The x-ray will not harm the device.

ID _____ AC _____ m0

Activity Monitor Log

As a participant in this program, we ask that you wear your Activity Monitor for one week. Begin wearing the monitor on the **Requested Start Date**. Please try to wear the monitor for seven consecutive days, but if you do need to skip a day for any reason, continue wearing it until you have worn it for a full seven days.

Requested Start Date: __/ / 18__ When you get up in the morning

Requested End Date: __/ / 18__ When you go to bed at night

Please record the actual dates/times you wore the accelerometer in the table below. Please be as precise as possible in reporting the times you put on and removed the monitor.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date							
Time of day you put on the unit							
Time of day you took off the unit							
Any time you did not wear the unit? (e.g. naps, bathing)							
Please provide comments about problems that occurred while you were wearing the unit.							

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