PHYSICAL ACTIVITY, BODY COMPOSITION AND THEIR ASSOCIATIONS WITH HEALTH IN YUP'IK PEOPLE

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Abstract

Being active and preventing excess body fat are important for maintaining good health. The ability to measure activity and body composition accurately is important to understanding the role of activity and adiposity in health. This dissertation highlights key findings regarding assessment tools for physical activity and body composition and the associations between physical activity and body composition with health in Yup'ik people.

The main objectives of this dissertation were to: 1)assess the accuracy of bioimpedance and multiple regression models from anthropometry for estimating body composition (fat mass, fat-free mass, and percent body fat) as compared with doubly-labeled water (DLW) body composition estimates, 2) determined the associations between body size estimates, including simple anthropometry and body composition estimates, and obesity-related health risk factors and disease outcomes, 3) assess the accuracy of a combined heart rate/movement monitor (Actiheart) for determining physical activity energy expenditure (PAEE) as compared with DLW PAEE, and 4) determine the associations between physical activity subcomponents and obesity-related health risk factors in Yup'ik people in southwestern Alaska.

Body composition can accurately be estimated using only three variables – sex, waist circumference (WC), and hip circumference with a multiple R^2=0.9730 with DLW fat mass. WC and other anthropometrics were more highly correlated with a number of obesity-related risk factors than were direct estimates of body composition. When determining the accuracy of the Actiheart for determining PAEE as compared with DLW PAEE, none of the software PAEE models investigated were significantly correlated with DLW PAEE (ranging from r=0.02 (95% CI (-0.38, 0.41) to r=0.22 (-0.20, 0.56)). Limits of agreement (mean difference ± 1.96SD) for all software models were large, ranging from –-4540 to 1600 kcal/day. The best correlate of DLW PAEE from the Actiheart was the sum of accelerometer counts per day (r=0.50 (95% CI = 0.13, 0.74)). The associations between physical activity and obesity-related health risk factors showed that total movement throughout the day was positively associated with HDL cholesterol (r_s=0.13, r_s =0.15 men and women respectively) and negatively associated with body weight, body mass index, WC, percent body fat and triglycerides (r_s range from -0.17 to -0.25 in men and -0.19 to -0.21 in women). Sedentary time was positively associated with body weight, WC, and percent body fat (r_s range from 0.10 to 0.18 in women) and negatively associated with HDL cholesterol (r_s =-0.19 in women). Moderate-to-vigorous physical activity was only associated with fasting glucose.

We conclude that 1) body composition in Yup'ik people can be accurately estimated from simple anthropometrics and that simple anthropometrics like WC can be used to assess obesity-related health risk, 2) the Actiheart software does not accurately estimate free-living PAEE in Yup'ik people however, total movement per day correlates with DLW PAEE and can be used as a proxy for PAEE, and 3) the accumulation of regular movement of any intensity while decreasing sedentary time may be more important for health in Yup'ik people than moderate-to-vigorous physical activity.

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1 General Introduction

Obesity in humans is categorized as having a body mass index (BMI = weight in kg divided by height in m^2) ≥ 30 kg/m^2, and overweight as a BMI ≥ 25 kg/m^2 and <30 kg/m^2 (1). Since 1980, worldwide obesity rates have doubled (2) and are projected to continue to increase (3-6). In 2008, 1.4 billion adults were overweight; 200 million were obese. Obesity is not only an issue for adults, but has also become a concern for children (7-9). In 2010, over 40 million children under the age of 5 worldwide were overweight or obese (3). As these children become adults, it is projected that by the year 2030, the prevalence of overweight and obesity in adults will increase by as much as 69%. The prevalence of overweight and obesity among Yup'ik people who live on the western coast of Alaska is similar to the US Caucasian population (10-13).

Obesity is a major risk factor for chronic diseases including type 2 diabetes (T2D), cardiovascular disease (CVD), and cancer (14-23). In 2008, CVD was the leading cause of death worldwide (2). The prevalence of T2D and CVD is generally higher in indigenous groups than in the general US population (24-25). Although the prevalence of obesity in Yup'ik people is similar to the US Caucasian population, the prevalence of medically diagnosed T2D is lower among Yup'ik people at 3.2% (age-adjusted to the Std. U.S. 2000 Population) than in the general US population at 7.7% (aged ≥ 20 years in 2005-2006) (10,26-29). Chronic diseases reduce lifespan and add economic burden to families, communities, and countries worldwide (5-6,30-31). Chronic diseases linked to obesity are of particular concern as the prevalence of obesity continues to grow (32-33). Educating people about the health benefits of physical activity and weight management, as well as providing opportunities for physical activity, are important steps in alleviating the community and global obesity epidemic.

Body Composition Measurement

Understanding how body fat mass and distribution are related to health risk is central to addressing the obesity epidemic and delivering meaningful health advice. However, measuring obesity and fat distribution anywhere, but particularly in remote and rural settings, is challenging. The transportation of large equipment to remote areas for measuring adiposity is expensive and impractical and the measurement cost per person is significant. Methods that are practical for use yet accurate for quantifying adiposity and body fat distribution are needed to address the health care needs of rural communities where health care and resources may be minimal.

Several methods of estimating body fat mass and fat distribution are commonly used. Methods that quantify adiposity (fat mass and percent body fat) such as isotopically-labeled water, dual-energy x-ray absorptiometry (DXA), magnetic resonance imaging (MRI), and air displacement plethysmography are expensive and not necessarily feasible in remote locations. The most common measures of obesity and body fat distribution, body mass index (BMI), weight, waist circumference (WC), and waist-to-hip ratio (WHR) are inexpensive and very transportable, but do not quantify or show the distribution of adipose tissue. Adiposity can be measured indirectly using bioelectrical impedance (BIA) or estimated using multiple regression techniques from anthropometry (height, weight, circumferences, and skinfolds). BIA and multiple regression from anthropometry have a number of advantages: the equipment is small, easily transportable, and relatively inexpensive. However, the relationships between body size measurements and body composition or body fat distribution differ between ethnic groups (34). Measurement methods need to be tested in population specific groups to guarantee unbiased conclusions and accurately assess obesity related health risk. It is currently unknown if BIA or methods using multiple regression from anthropometry are accurate for assessing adiposity in Alaska Native people (12). It is also unknown how simple anthropometrics and indirect measures of obesity predict obesity-related health risk in Alaska Native and other peoples. The development and use of simple measures of adiposity are likely important for delivering health care or conducting research in remote locations where more complex methods are not available.

Physical activity energy expenditure (PAEE) is the most modifiable component of total energy expenditure and is thus a potential important factor in preventing obesity and associated chronic health complications. For sustained weight loss, energy output must be greater than energy input. To maintain weight, energy input must approximate energy output. The current physical activity recommendations for promoting health, but not necessarily weight loss, suggest 30 minutes of moderate-to-vigorous physical activity (MVPA) at least 5 days of the week (35-36). There is a large body of evidence, although based on self-report methods, supporting the association between regular physical activity and improved health. The evidence is highlighted in the 2008 Physical Activity Guidelines Advisory Committee Report (37). Physical activity helps control weight and reduces the risk for CVD, T2D, metabolic syndrome, and some cancers (38-41). Type 2 diabetes, CVD, and dyslipidemia can result from increased abdominal obesity and viscerally located fat (42-44). Increases in physical activity reduce total and visceral adiposity (surrounding the vital organs), leading to improved health outcomes (45-48). Physical activity strengthens bones and muscles, thereby helping to prevent falls and fractures (49-50). It also improves mental health, longevity, and overall quality of life (37,51-58).

Sustained patterns of physical activity in humans represent a complex behavior that includes subcomponents such as intensity, duration, and frequency. Although there is a large body of evidence showing the benefits of physical activity, these data are primarily collected using self-report methods which can be inaccurate. Therefore, which subcomponents of physical activity are most effective at decreasing the prevalence of obesity-related disease and improving health are not well understood. To understand the dose-response relationships among physical activity, inactivity, and chronic disease risk, physical activity must be accurately measured as people go about their daily lives.

Physical Activity/ Energy Expenditure Measurement

PAEE can be assessed by a variety of methods, including self-report and objective means. Self-report methods are relatively easy to use, can be used to inexpensively estimate broad categories of activity, and can be used to differentiate between subcomponents of physical activity. However, significant reporting bias (recall bias and socially acceptable response bias) is likely (59-61). Unfortunately, most of the physical activity data available have been collected using self-report methods (62).

Objective measures of physical activity reduce the potential for reporting bias. Common objective techniques include respired gas exchange indirect calorimetry, doubly labeled water (DLW), heart rate (HR), and accelerometry (ACC) or movement monitoring. Indirect calorimetry, including respired gas exchange and DLW, has been used extensively for validation of the HR, ACC, and combined HR/ACC methods. Indirect calorimetry is used to estimate energy expenditure by measuring oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). Chemical energy is liberated from food sources, releasing CO_2, water, and heat. The ratio of CO_2 production to O_2 consumption is defined as the respiratory exchange ratio (RER). The RER determines the completeness of burning and amount of heat (kcal) produced by comparing the amount of CO_2 produced to each liter of oxygen consumed. When the food source is strictly carbohydrates, the RER is 1.0; when the source is strictly fat, the RER is 0.70. Based on an individual's CO_2 production and O_2 consumption, energy expenditure is determined using Weir's formula: Energy expenditure (kcal/day) = [3.9 ($\dot{V}O_2$(mL/min)) + 1.1 ($\dot{V}CO_2$(mL/min))] 1.44 (63).

The DLW method indirectly estimates CO_2 production by measuring the difference in disappearance rates between labeled ^{18}O and ^{2}H from the body (64). ^{18}O and ^{2}H are safe, naturally occurring heavy isotopes of oxygen and hydrogen. ^{18}O is lost through CO_2 production during respiration and water loss. ^{2}H is only lost through water loss. Therefore the difference between the amount of ^{18}O and ^{2}H lost in the urine provides an indirect measure of the rate of CO_2 production, and O_2 consumption, making it possible to estimate energy expenditure. DLW can be used to measure energy expenditure as people go about their normal lives, but cannot differentiate between subcomponents of physical activity.

The equipment involved with respired gas exchange indirect calorimetry, such as a metabolic cart or metabolic chamber, is not suitable to measure free-living energy expenditure because it prohibits a person from true free-living conditions. The respired gas exchange and DLW methods are also rather expensive, and therefore not ideal for use in large studies. In an effort to gain cost effective, accurate methods to assess physical activity in free-living conditions, researchers have turned to the use of the HR and ACC methods for estimating PAEE.

The HR and ACC based methods have their own advantages and disadvantages. Both are more affordable than DLW or respired gas exchange indirect calorimetry methods, and both can differentiate between physical activity subcomponents including intensity, duration, and frequency of activity, and PAEE. Quantifying these subcomponents may elucidate which subcomponents of physical activity have the greatest effect on health-related variables. Recent advances in the technology of objective measurement sensors that measure HR and ACC make them lightweight and capable of storing large volumes of data over several days to weeks of wear and records time on a continuous basis which allows identification of time periods of physical activity or inactivity (65).

Heart rate monitoring records a physiological measure (HR) which can be used to estimate PAEE based on the linearity of the relationship of HR and PAEE. This relationship depends on factors such as age, sex, weight, fitness level, ambient temperature, stress, and dehydration (66-69). Adjustment methods include individual calibration of the HR to PAEE relationship in order to improve energy expenditure estimates (70). The HR to PAEE relationship is linear for physical activity intensities above resting energy expenditure (REE) that involve large muscle groups, but below a certain intensity threshold, changes in HR do not correlate with changes in PAEE. To account for the discrepancies at low intensity levels, the "flex heart rate" has been used as a cutoff point below which REE is assigned (56). The flex HR is the average of the lowest heart rate during light exercise and the highest heart rate during rest (67). Above this flex HR cutoff point, PAEE is determined using the linear HR to PAEE relationship, while below this flex point, energy expenditure is assigned as the REE. The accuracy of the flex HR method for estimating PAEE has been established against whole-body calorimetry with a correlation of r=0.943, a mean difference between flex HR and whole-body calorimetry PAEE of 1.2% (SD 6.2), and a range- 11.4 to + 10.6 %, however there can be large discrepancies (67,71).

The ACC method estimates PAEE using body movement or a change in gravitational acceleration. The raw acceleration data from a physical activity monitor are typically filtered to remove minor vibrations that are not associated with physiologically meaningful human movement. Then the filtered data are averaged over a defined epoch. The result is an arbitrary unit called a count. Similar to the relationship between HR and PAEE, the relationship between ACC counts and PAEE is assumed to be linear and can be established in laboratory environments or free-living environments. This linear relationship does not always hold, however, as most hip worn uniaxial accelerometers show a plateau in acceleration despite a rise in energy expenditure during some activities like high intensity running (72-73). Accelerometers used for assessing physical activity are typically worn on the hip or a limb, and measure movement in one direction, usually vertical acceleration. Triaxial accelerometers are becoming more common and measure movement in three directions. Depending on the type of accelerometer and its wear location, it may not fully capture physical activity movements such as bicycling, upper body movements, carrying heavy loads, or differentiate between walking /running on inclined slopes vs. flat ground. These are important considerations for measurement of PAEE, as the relationship between accelerometry and PAEE is dependent on accurate count measurement.

HR and ACC can be combined to potentially enhance the assessment of physical activity. The combined method takes advantage of the unique strengths of the HR and ACC methods, overcoming some of the weakness of each method when used alone. By combining the HR and ACC methods the accuracy of energy expenditure and PAEE estimates has been improved over either method alone in the laboratory setting (74-78). One combined HR/ACC monitor (Actiheart, Camntech) has been validated for use in free-living people by comparing PAEE values estimated using the Actiheart with PAEE values determined from DLW (79-80).

As the rates of obesity and chronic disease rise, it is vital to have tools that can be used by researchers and clinicians which are reliable, accurate, and affordable for use in free-living people (81). Validation of objective tools, including the Actiheart monitor, for monitoring physical activity behavior and energy expenditure in the population of interest, is critical to understanding the roles that subcomponents of physical activity play in health and developing valid physical activity recommendations.

The CANHR and CBPR

Health disparities exist in minority populations, including Alaska Native people (82). The Center for Alaska Native Health Research (CANHR) was established in 2001 to work with Alaska Native people and build trusting relationships and partnerships to reduce health disparities and improve health. CANHR uses a community-based participatory research (CBPR) framework to conduct research in rural Alaska. CBPR is a partnership approach to research that jointly involves community members and researchers in the research process. The goal is to address the research priorities and needs of the community members to gain an understanding of risk and protective factors and how to improve health. Researchers and community members work together to integrate the new knowledge into practical applications for improving community health. The CBPR framework is the approach used with the research for this dissertation.

A primary focus of CANHR is to investigate obesity and chronic disease related risk factors in Yup'ik people living in Southwestern Alaska who have traditionally lived a subsistence lifestyle and are increasingly exposed to influences of western society (activity and dietary habits). Increased exposure to sedentary lifestyles and market foods could negatively impact the health of Yup'ik people as has been seen in other indigenous cultures (24-25,83-84).

Understanding the relationships between body composition, physical activity subcomponents, and health in Yup'ik people may help health care workers provide health education and optimal health care to community residents. To understand the role of physical activity and its relationship to obesity and health in Yup'ik people, it is necessary to have accurate and reliable measurements of adiposity and objective measures of physical activity. This dissertation is subdivided into three chapters with three goals: 1) to evaluate tools to reliably assess body composition and how body composition is associated with health in

Yup'ik people; 2) to determine the accuracy of objectively measured PAEE in Yup'ik people; and 3) to objectively measure activity levels and determine how physical activity is associated with health in Yup'ik people.

Study Objectives

In Chapter 2, my collaborators and I evaluate the accuracy of different methods used to assess body composition and how the measurements are associated with health-related variables for chronic diseases such as T2D, heart disease, and stroke. In a sub-sample of Yup'ik participants, simple ways of estimating body composition, specifically fat free mass (FFM), fat mass (FM), and percent body fat (PBF), are investigated. Body composition is estimated using a tetra-polar bioelectric impedance analyzer and from linear regression models. In the regression models body composition values derived from DLW were determined using age, sex, and anthropometrics including height, weight, body circumferences, and skinfold measurements. These estimates of body composition are compared with criterion estimates of body composition estimated from the doubly labeled water (DLW) method. In a larger sample of Yup'ik people, associations between body size measurements and health-related variables are determined. This manuscript has been accepted for publication in the journal *Obesity* (85).

Chapter 3 describes the validation of a combined ACC/HR monitor, the Actiheart, for assessing physical activity energy expenditure (PAEE) in Yup'ik people. The DLW method is widely considered the most accurate method to estimate free-living energy expenditure in humans. Therefore the DLW method was used as criterion method for estimating PAEE to evaluate the accuracy of the Actiheart monitor. PAEE estimates using different analysis methods, including branched models (which use both the HR and ACC to determine PAEE), HR only, and ACC only, are compared with PAEE estimates from DLW. The most accurate model for estimating PAEE, compared with DLW, is established for use in future research involving Yup'ik people.

The focus of Chapter 4 is on physical activity and its association with health. We determined the associations between objectively measured physical activity subcomponents and obesity-related health variables and in order to determine which physical activity subcomponent is most important for health.

As lifestyles change and the prevalence of obesity and T2D increases in southwestern Alaska and around the world, it is increasingly important to have tools that can accurately assess body composition and physical activity in locations that are rural or have no access to large or expensive equipment. These tools will aid health care providers to identify individuals who may be at risk for obesity-related health complications as well as help in the development of culturally relevant physical activity recommendations and interventions that are effective at helping to maintain a healthy lifestyle. .

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Research Approval

The study protocol was approved by the University of Alaska Fairbanks IRB (protocol number 185087) and the Yukon-Kuskokwim Health Corporation Human Studies Committee and participants provided written informed consent.

2 Simple Anthropometrics are more Correlated with Health Variables than are Estimates of Body Composition in Yup'ik People[1]

Abstract

We aimed to: 1) evaluate the relationships between several indices of obesity with obesity-related risk factors; 2) compare the accuracy of body composition estimates derived from anthropometry and bioimpedance analysis (BIA) to estimates of body composition assessed by doubly-labeled water (DLW); and 3) establish equations for estimating fat mass (FM), fat-free mass (FFM), and percent body fat (PBF) in Yup'ik people. Participants included 1056 adult Yup'ik People from 11 communities in southwestern Alaska. In a substudy of 30 participants, we developed population-specific linear regression models for estimating FM, FFM, and PBF from anthropometrics, age, sex, and BIA against criterion measures derived from total body water assessed with DLW. These models were then used with the population cohort and we analyzed the relationships between obesity indices and several health-related and disease status variables: 1. fasting plasma lipids, 2. glucose, 3. HbA1c, 4. adiponectin, 5. blood pressure, 6) diabetes (DM), and 7) cerebrocoronary vascular disease

[1]Bray M, Pomeroy J, Knowler WC, Bersamin A, Hopkins S, Boyer BB, et al. Simple anthropometrics are more correlated with health variables than are estimates of body composition in Yup'ik people. Obesity. In Press.

(CCVD) which includes stroke and heart disease. The best model for estimating FM in the substudy used only three variables – sex, waist circumference (WC), and hip circumference and had multiple R^2=0.9730. FFM and PBF were calculated from FM and body weight. WC and other anthropometrics were more highly correlated with a number of obesity-related risk factors than were direct estimates of body composition. We conclude that body composition in Yup'ik people can be accurately estimated from simple anthropometrics.

Introduction

In an effort to help prevent further increases in the prevalence of obesity and associated comorbidities in minority and isolated populations with limited health care resources, identifying accurate, yet simple methods to quantify body adiposity and obesity-related health risk are desirable.

It is unknown whether simple, indirect measures of obesity predict obesity-related health risk as accurately as direct measures in Alaska Native people. We, therefore, determined if anthropometry and bioimpedance analysis (BIA) can accurately assess body composition in Yup'ik people. We assessed the relationships of direct and indirect measures of adiposity with obesity-related health variables, including diabetes (DM), cerebrocoronary vascular disease (CCVD) (stroke and heart disease), fasting plasma lipids, glucose, HbA1c, blood pressure, and adiponectin, an adipocyte derived hormone positively associated with insulin sensitivity and HDL cholesterol levels [1].

Methods

A cross-sectional health study was conducted from 2003-2007 among 1056 Yup'ik people aged 18-94 years living in 11 rural Yup'ik communities in southwestern Alaska. Participants included men and non-pregnant women (by self-report). In a substudy of 30 participants, anthropometry, age, and sex were used to estimate fat mass (FM) determined by the doubly labeled water (DLW) method, which was considered the true value. FM estimates using anthropometry were more strongly correlated with DLW FM (r=0.986) than were estimated FFM or percent body fat (PBF) estimates with DLW values. Therefore, we chose to estimate FM rather than FFM or PBF. Fat-free mass (FFM) and PBF were calculated from body weight and FM. We compared these estimates and PBF estimated by BIA with the "true" FM, FFM, and PBF by correlation analysis. We estimated body composition for each person in the population sample using BIA and the predictive equations derived in the substudy and correlated these estimates and simple anthropometrics with the health-related and disease variables: blood pressure, lipids, fasting plasma glucose, HbA1c, adiponectin, DM, and CCVD. The Tanita TBF-300A tetrapolar foot-to-foot BIA analyzer (Tanita Corporation, Tokyo, Japan) was used to measure impedance (ohms) and obesity-related risk factors were measured as previously described [2]. The same observers for laboratory methods were used to obtain all measurements. Total body water (kg) was determined using the DLW method [3]. FFM was calculated as (total body water)/0.73, assuming a hydration constant of 0.73, and FM was calculated as body weight -FFM. (DLW details in online appendix)

Disease diagnoses were abstracted from medical records. The following ICD-9 codes (2010) were included for disease diagnosis: DM – 250; CCVD – 410-414, 425, 426, 428, 429, 433, 434, 436-438, 786, and V45.82.

Statistical analyses

The best parsimonious regression model estimating FM in the substudy was determined by stepwise multiple linear regression and evaluated for multicollinearity by standard methods and for agreement with the DLW-determined FM with the Bland-Altman method. Variables considered for inclusion were age, sex, weight, height, waist circumference (WC), BMI, waist-to-height ratio, hip circumference (HC), arm circumference, thigh circumference, raw impedance, total body water, BIA estimates of FM, FFM, and PBF (FM_{BIA}, FFM_{BIA}, PBF_{BIA}). A second model also used skinfold thickness, but because this model performed only slightly better and skinfold thickness measurements add to protocol time and participant burden, we did not consider it further. This estimate of FM, the derived estimates of FFM and PBF, anthropometrics, and body composition estimates from BIA were correlated with the obesity-related risk factors using Spearman's correlation coefficients partialled for age and sex.

The association of the obesity indices with the disease variables was determined using logistic regression that included age and sex as covariates. All continuous variables were standardized to have mean=0 and SD=1, and odds ratios with 95% confidence intervals are reported.

All protocols were approved by the Alaska Area, Indian Health Service and the University of Alaska Fairbanks Institutional Review Boards (UAF IRB Approval # 185087), and the Yukon-Kuskokwim Health Corporation Human Studies Committee. Participants provided written informed consent.

Results

The model to estimate DLW-determined FM from demographic and anthropometric data in the substudy of 30 participants used only three variables: FM(kg) = -47.99639 -8.96151*male +0.58113*WC(cm) +0.254638*HC(cm). Multiple R^2 was 0.9730. Furthermore, DLW-derived FM was highly correlated with BMI, WC, HC, WC*HC, waist-to-height ratio, and BIA-estimated PBF (all r>0.9), but less strongly correlated with waist-to-hip ratio (r=0.58). Correlations of the aforementioned anthropometrics with DLW-derived FFM and PBF were lower (all r<0.80) than with DLW-derived FM.

Correlations and standardized odds ratios of the multiple obesity indices with obesity-related risk factors from the population study are shown in **Table 2-1**. None of the correlations were significant for total cholesterol (data not shown).

The simple anthropometric measurements were as strongly correlated with each of the obesity-related risk factors (other than LDL cholesterol) as were the more sophisticated measures of adiposity (FM, FFM, and PBF). In fact WC was consistently among the most highly correlated obesity indices with obesity-related risk factors. For the disease variables, the strongest odds ratios were seen from the modeled PBF (OR=2.51) and the modeled FFM (OR=1.54) with DM and CCVD respectively.

Overall, most of the correlations and odds ratios for each of the obesity-related risk factors and disease variables were of similar magnitude regardless of the body index used.

Discussion

In general, the simple measures of WC and other anthropometrics were as strongly associated with obesity-related risk factors as the more complex estimates, suggesting that for a particular application and study setting, the method used to estimate body composition or obesity can be chosen on the basis of feasibility or availability of equipment or trained observers. Moreover, body composition estimates (FM, FFM, and PBF) from the DLW substudy and from BIA were highly associated with several obesity-related risk factors and presence of diseases in this study population.

Our results agree with other reports that simple measurements that estimate body adiposity are strongly correlated with FM and PBF estimates from

DLW, and that these same measures are as strongly associated with obesity-related risk factors and disease variables as more direct measurements of adiposity [4,5]. Some investigators have assumed that direct measures of adiposity provide better predictive power than indirect measures when assessing associations between obesity and health risk [6]. However, in the present study, anthropometric estimates of body adiposity (WC, BMI, HC, WC*HC, and waist to height ratio) were at least as strongly associated with several obesity-related risk factors and disease variables as were the estimates of FM, FFM, and PBF derived from anthropometrics and DLW. The risk factors were more highly correlated with the simple anthropometrics in their original forms than when transformed to estimate body composition according to DLW. Similar findings that simple anthropometrics are highly associated with obesity-related risk factors have been reported with other methods including DXA and BIA [7-9]. The body size estimates mostly strongly related to disease were derived from the DLW model (PBF for diabetes, and FFM for CCVD). Several investigators have concluded that WC and other anthropometrics are among the best predictors of metabolic health outcomes [7,10-12]. Our results support the hypothesis that simple, indirect measures of adiposity such as WC, BMI and other anthropometrics are strongly associated with selected obesity-related risk factors and disease variables and are thus likely to predict clinical endpoints in Yup'ik people.

Waist circumference estimates abdominal distribution of fat that is not captured by estimates of total adiposity [13]. The variables that best estimate fat mass are not necessarily the same as those that are related to health measures. It is likely that the regional distribution of body fat, rather than total adiposity, is more important for health outcomes. However, body composition estimates including FM, FFM, and PBF, may also be important in physiologic, genetic, and longitudinal studies.

Strengths of the study include the large sample size and that several different obesity indices were evaluated simultaneously, many types of obesity-related biomarkers were analyzed, and the same standard protocols were used to measure the anthropometric variables in both the DLW and population studies.

The small sample size of the DLW subset did not allow us to evaluate sex specific models to estimate body composition. Also, while we used leave-one-out cross-validation methods to choose full and reduced models to predict body composition with the lowest generalization error (not shown), it is still possible that due to small sample size we still may have overfit the models.

In summary, obesity-related risk can be assessed accurately in Yup'ik people with simple anthropometric measures. Simple anthropometrics or BIA can also provide accurate estimates of adiposity. These findings may facilitate research and health counseling in remote areas where more sophisticated measures of body composition are impractical.

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Conflict of interest

None of the authors has any financial interest in this work.

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Table 2-1: Associations of Body Size Measures with Obesity-Related Risk Factors and Diseases

	Risk Factors								Diseases	
Body Size	HDL	LDL	triglyceride	glucose	HbA1c	adiponectin	syst bp	diast bp	DM	CCVD
BMI	-0.39	0.15	0.39	0.23	0.12	-0.4	***0.23***	0.39	1.74	1.38
	(-0.44, -0.34)	(0.09, 0.21)	(0.34, 0.44)	(0.17, 0.28)	(0.06, 0.18)	(-0.45, -0.34)	***(0.18, 0.29)***	(0.34, 0.44)	(1.18, 2.56)	(1.04, 1.84)
WC	***-0.43***	***0.17***	***0.41***	***0.24***	0.14	***-0.43***	***0.23***	0.39	1.98	1.37
	(-0.47, -0.38)	***(0.11, 0.22)***	***(0.36, 0.46)***	***(0.18, 0.30)***	(0.08, 0.19)	***(-0.48, -0.38)***	***(0.17, 0.28)***	(0.34, 0.44)	(1.32, 2.98)	(1.02, 1.84)
Hip Circumference	-0.36	0.15	0.34	0.19	0.08	-0.34	0.20	0.34	1.64	1.38
	(-0.42, -0.31)	(0.09, 0.21)	(0.28, 0.39)	(0.13, 0.25)	(0.02, 0.14)	(-0.40, -0.29)	(0.15, 0.26)	(0.29, 0.39)	(1.13, 2.38)	(1.03, 1.83)
Total Skinfold	-0.37	0.16	0.38	0.19	0.11	***-0.43***	0.22	0.38	1.83	1.35
	(-0.42, -0.32)	(0.10, 0.22)	(0.33, 0.43)	(0.13, 0.25)	(0.05, 0.17)	***(-0.48, -0.38)***	(0.16, 0.28)	(0.33, 0.43)	(1.17, 2.88)	(0.99, 1.84)
Waist to Hip Ratio	-0.34	0.16	0.38	0.22	***0.15***	-0.39	0.18	0.32	1.91	1.19
	(-0.39, -0.28)	(0.10, 0.21)	(0.32, 0.43)	(0.16, 0.28)	***(0.09, 0.21)***	(-0.44, -0.34)	(0.12, 0.24)	(0.26, 0.37)	(1.27, 2.88)	(0.86, 1.63)
Waist*Hip	-0.42	***0.17***	0.40	0.23	0.11	-0.41	0.22	0.38	1.71	1.43
	(-0.46, -0.36)	***(0.11, 0.22)***	(0.34, 0.44)	(0.17, 0.28)	(0.05, 0.17)	(-0.46, -0.36)	(0.17, 0.28)	(0.33, 0.43)	(1.21, 2.42)	(1.10, 1.88)
Waist to Height Ratio	-0.40	0.16	***0.41***	***0.24***	0.14	-0.42	***0.23***	***0.40***	2.00	1.34
	(-0.45, -0.35)	(0.10, 0.22)	***(0.36, 0.46)***	***(0.18, 0.29)***	(0.08, 0.20)	(-0.47, -0.37)	***(0.17, 0.29)***	***(0.35, 0.45)***	(1.31, 3.06)	(0.99, 1.82)
FM (model)	-0.42	0.16	***0.41***	0.23	0.12	-0.42	0.21	0.38	1.89	1.38
	(-0.47, -0.37)	(0.10, 0.22)	***(0.36, 0.46)***	(0.17, 0.28)	(0.06, 0.18)	(-0.47, -0.37)	(0.16, 0.27)	(0.33, 0.43)	(1.28, 2.80)	(1.03, 1.84)
FM (BIA)	-0.39	***0.17***	0.39	0.22	0.12	-0.41	0.20	0.39	1.77	1.40
	(-0.44, -0.34)	***(0.11, 0.22)***	(0.33, 0.44)	(0.16, 0.28)	(0.06, 0.17)	(-0.46, -0.36)	(0.15, 0.26)	(0.33, 0.44)	(1.23, 2.54)	(1.06, 1.84)
FFM (model)	-0.29	0.07	0.25	0.14	0.07	-0.27	0.13	0.24	1.36	***1.54***
	(-0.34, -0.23)	(0.01, 0.13)	(0.20, 0.31)	(0.08, 0.19)	(0.01, 0.13)	(-0.32, -0.21)	(0.07, 0.19)	(0.18, 0.29)	(0.85, 2.19)	***(1.12, 2.11)***
FFM (BIA)	-0.35	0.07	0.30	0.16	0.09	-0.31	0.16	0.25	1.46	1.47
	(-0.40, -0.29)	(0.01, 0.13)	(0.25, 0.36)	(0.10, 0.22)	(0.03, 0.15)	(-0.37, -0.26)	(0.10, 0.22)	(0.20, 0.31)	(0.95, 2.24)	(1.08, 2.00)
PBF (model)	-0.40	0.15	0.40	0.22	0.12	-0.41	***0.23***	0.36	***2.51***	1.12
	(-0.45, -0.35)	(0.10, 0.21)	(0.35, 0.45)	(0.17, 0.28)	(0.06, 0.18)	(-0.46, -0.36)	***(0.17, 0.29)***	(0.31, 0.41)	***(1.40, 4.50)***	(0.80, 1.56)
PBF (BIA)	-0.38	***0.17***	0.37	0.23	0.13	-0.41	0.21	0.38	2.26	1.21
	(-0.43, -0.32)	***(0.11, 0.22)***	(0.32, 0.43)	(0.17, 0.29)	(0.07, 0.19)	(-0.46, -0.36)	(0.15, 0.27)	(0.33, 0.43)	(1.37, 3.71)	(0.88, 1.66)

N=1056

DM = diabetes mellitus (22 cases); CCVD = cerebrocoronary vascular diseases, which includes stroke and heart disease (49 cases).

Values listed for the continuous variables are Spearman's Correlation coefficients and 95% CI, partialled for age and sex. Values listed for dichotomous variables (DM & CCVD) are odds ratios per standard deviation of the body size measurement with 95% confidence intervals, adjusted for age and sex. The obesity-indices most strongly correlated with each obesity-related risk factor and the obesity indices with the greatest odds ratio for each disease variable are indicated by ***bold and italic*** text.

FM (model) and FM (BIA) were estimated from the DLW substudy and from BIA, respectively. FFM and PBF were estimated from body weight and these estimates. All correlations were significant at p<0.001 except for FFM (model) and FFM (BIA) with LDL, and FFM (model) and hip circumference with HbA1c, all of which were significant at p<0.02.

Appendices

Supplementary Methods

A cross-sectional health study was conducted from 2003-2007 among 1056 Yup'ik people aged $\geq$ 18 years old living in 11 rural Yup'ik communities in southwestern Alaska. Two separate analyses were conducted in order to address the goals of this study. Participants in both analyses included men and non-pregnant women (by self-report). To determine if anthropometry and BIA could be used to accurately estimate body composition in Yup'ik people a sub-study of 30 participants living in one rural Yup'ik community was conducted (doubly labeled water sub-study, or DLW sub-study). In this study cohort, anthropometry and BIA were compared with DLW estimates of FM, FFM, and PBF (FM_{DLW}, FFM_{DLW}, PBF_{DLW}). Results from the DLW sub-study were used in the larger cohort of 1056 Yup'ik people to determine the relationship of direct and indirect measures of adiposity with obesity-related health risk (population study). Obesity-related risk factors that define the metabolic syndrome using the NCEP ATP III criteria [1], as well as diabetes risk factors (HbA1c and adiponectin) and other common lipids were investigated in the population study. Low levels of circulating adiponectin predict subsequent development of type 2 diabetes [2,3], and adiponectin has anti-inflammatory actions [4-6]. Diabetes mellitus, stroke and cardiovascular disease were also investigated in the population study.

All measurements for both the DLW sub-study and the population study were taken using the same methods and observers. Anthropometric, blood pressure, lipid, and hormone measurements were described previously [7]. Briefly, height was measured to the nearest 0.25 inch (6.4 mm) for each participant, and then they were weighed to the nearest 0.1 lb (45 grams) using a Tanita TBF300A bioimpedance analyzer. BMI in kg/m^2 was calculated from weight and height. Waist, hip, thigh, and triceps circumferences were measured to the nearest 1 mm using a Gulick II 150 cm anthropometric tape attached with a tension-meter (Country Technologies, Inc., GaysMills, WI). Abdominal, triceps, subscapular and thigh skinfolds were measured to the nearest 1 mm using a Lange caliper (Beta Technology Inc., Cambridge, USA). Systolic and diastolic blood pressures were taken after participants sat quietly for 5 minutes using an OMRON HEM907 automated blood pressure cuff (Omron Healthcare Inc, Bannockburn, IL). The mean of three blood pressure measurements was used in the analysis.

Lipids, Hormone, Glucose, and Disease Diagnoses

Fasting plasma glucose concentrations were estimated using the Cholestech LDX system (Cholestech Corporation, Hayward, USA). Hemoglobin A1c (HbA1c) levels were measured with a Bayer DCA 2000+ Analyzer (Bayer AG, Leverkusen, Germany). High-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), triglycerides and total cholesterol values were measured with a Poly-Chem System Chemistry Analyzer (Polymedco Inc., Courtlandt Manor, NY) as previously described [7]. Adiponectin was assayed with a radioimmunoassay kit using a I125-iodinated murine adiponectin tracer, a multi-species adiponectin rabbit antiserum, and human adiponectin standards from Linco Research (Millipore, Inc).

Disease diagnoses were abstracted from medical records. The following ICD-9 codes (2010) were included for disease diagnosis: DM – 250; CCVD – 410-414, 425, 426, 428, 429, 433, 434, 436-438, 786, and V45.82.

Doubly Labeled Water

Total body water in kg was determined from DLW. DLW was prepared by combining 300g of 97% Oxygen-18 water ($H_2{}^{18}O$) and 240.24g of 99.9% Deuterium water (^2H_2O) (Cambridge Isotope Lab). The total volume was transported in a sterile container to our study location. Prior to DLW administration, each participant provided two baseline urine samples (one the day before DLW administration and a second sample immediately before DLW administration). Weight and height were also measured just prior to DLW administration. DLW was administered to each participant at a quantity of 0.18g of pre-mix DLW per kg body weight (0.1 g ^{18}O and 0.08 g $^2H_2$ per kg body weight). The dose was diluted with tap water (~100ml) before drinking and the glass was then filled again with tap water which was also drunk. In addition to the baseline samples, urine samples were collected a mean of 19.2 hours after

DLW administration (range 8.2 - 25.7 hours), and again on day 3,5,7,9, & 10. This DLW protocol was used because this study also involved an assessment of free-living energy expenditure. Urine samples and samples of the dose and local water sources were frozen and transported to the University of Alabama Birmingham. Analysis of isotopic enrichments was carried out in duplicate. For $^{2}H/^{1}H$ ratios each sample was equilibrated with H_2 gas at 40 °C for 90 min in the presence of a Pt catalyst. The equilibrated gas samples were then measured by dual inlet isotope ratio mass spectrometry (OPTIMA – 3955, Micromass Inc., Beverly, MA, with Multiprep Interface and Gilson autosampler). For $^{18}O/^{16}O$ ratios, samples were equilibrated with CO_2 at room temperature for >3.5 hrs, and ratio measurements were performed using a continuous flow isotope ratio mass spectrometer (OPTIMA – 3955, Micromass Inc., with µGas Interface and Gilson autosampler). All pre- and post-dose samples were included in determining the ^{2}H and ^{18}O disappearance rates, the intercepts of which were used to calculate observed Oxygen and Hydrogen spaces as described elsewhere [8]. TBW was calculated as the average of the observed Oxygen and Hydrogen spaces, normalized by 1.01 and 1.04 respectively, to account for non-exchangeable ^{18}O and ^{2}H with water. FFM_{DLW} was determined assuming a hydration constant of 0.73 and using the formula FFM = TBW/0.73, and FM_{DLW} and PBF_{DLW} were calculated from FFM_{DLW} and total body weight.

Bioimpedance Analysis

Impedance (ohms) was measured with a Tanita TBF-300A tetrapolar foot-to-foot BIA analyzer (Tanita Corporation, Tokyo, Japan) on participants wearing only a light hospital gown. Participant height, age, and sex were entered into the instrument, and weight was measured by the instrument.

Statistical Analyses

SAS for Windows (version 9.2) was used for all statistical analyses. Variables were tested for normality; all continuous variables used in the regression analysis in the DLW study were normally distributed, but many of the continuous variables in the population study did not meet model assumptions. Therefore, Spearman's correlation coefficients were used throughout.

One participant's abdominal skinfold thickness was missing in the DLW sub-study data set from which the models for FM, FFM, and PBF were determined. This measurement was imputed by regressing all other anthropometric measures, age, and sex from the 29 participants for whom all data were available.

BIA was used to estimate body composition in this population, but we also sought to improve these BIA estimates if possible, and determine the best method for estimating FM, FFM and PBF that can feasibly be used for future studies in Yup'ik people. Two sets of models to estimate FM, FFM, and PBF were selected using stepwise multiple linear regressions (P-to-enter <0.15, P-to-exit

>0.05) with DLW values (FM_{DLW}, FFM_{DLW}, PBF_{DLW}) as the dependent variables in the DLW sub study of 30 persons. The first set of models, referred to as the "full" models, used age, sex, weight, height, BMI, WC, hip, arm, and thigh circumferences, impedance, TBW, BIA estimates of FM, FFM, and PBF (FM_{BIA}, FFM_{BIA}, PBF_{BIA}), and abdominal, subscapular, triceps, and thigh skinfolds. The second set, the "reduced" model, used the same variables, excluding skinfold measures. Skinfold measurements add to participant burden and are time consuming, so determining whether skinfold thickness significantly improved the models was important. The models were checked using leave-one-out cross-validation (PROC GLMSELECT). A variance inflation factor (VIF) of <12.5 was used to check for multicollinearity.

A "full" and a "reduced" estimate of FM, FFM, and PBF (FM_{Full}, FFM_{Full}, and PBF_{Full}, and $FM_{Reduced}$, $FFM_{Reduced}$, and $PBF_{Reduced}$) were determined from the multiple linear regression. Because each of the 6 models were different, FM, FFM and PBF were calculated using body weight and the modeled estimate, yielding 3 sets of full models and 3 sets of reduced models. Each set consisted of an estimate of one of the parameters derived from regression and the other two by simple arithmetic (e.g. FFM = body weight – FM). In total, 18 estimates were calculated; six each for FM, FFM and PBF. The set of full models whose estimates were most highly correlated with the DLW estimates was chosen for further analyses. Similarly, a "best" set of reduced models was chosen.

The Bland-Altman [9] method was used to assess agreement in estimates of FM, FFM, and PBF between BIA and DLW, as well as estimates from the full model and the reduced model.

When the linear models were used to estimate body composition in all members of the population study, negative values for FM and PBF were obtained in one person, a lean man in his 40's. These estimates were used only for the purpose of the correlation analyses and not for reporting back to the individuals, so we used these negative estimates without modification.

Correlation of Anthropometric Measures and Body Composition with Lipids, Hormones, and Blood Pressure in the Population Sample

The body composition estimates derived for use in the population analysis, along with BMI, WC, hip circumference, total skinfold, waist-to-hip ratio, waist-to-height ratio, waist X hip, FM_{BIA}, FFM_{BIA}, and PBF_{BIA}, were compared with one another with respect to their correlations with obesity-related and disease variables. Age and sex were controlled for in this analysis.

Spearman's correlation coefficient was used to determine the associations of the measures of anthropometry and body composition to the obesity-related risk factors (HDL & LDL cholesterol, total cholesterol, triglycerides, fasting glucose, HbA1c, adiponectin, systolic blood pressure, and diastolic blood pressure), controlled for age and sex. The association of the obesity indices with disease variables was determined using logistic regression that included age and sex as covariates. All continuous variables were standardized to have mean=0 and SD=1, and odds ratios with 95% confidence intervals are reported.

All protocols were approved by the Alaska Area and the University of Alaska Fairbanks Institutional Review Boards, and the Yukon-Kuskokwim Health Corporation Human Studies Committee. Participants provided written informed consent.

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3 Accuracy of the Combined Movement / Heart Rate Monitor Actiheart for Measuring Free-Living Energy Expenditure in Yup'ik People [2]

Abstract

Objective: To assess the accuracy of physical activity energy expenditure (PAEE) estimates derived from a combined heart rate (HR) and accelerometer monitor to PAEE estimates from doubly-labeled water (DLW) in free-living Yup'ik people.

Design: 30 Yup'ik participants from one community in southwestern Alaska were dosed with DLW. Participants wore the Actiheart monitor for 10 continuous days of free-living, and HR and movement data were collected. PAEE was estimated using the DLW method, calculated by the Actiheart CNT software, and estimated from movement data (accelerometer counts per day). Thirteen PAEE estimates (12 directly from the Actiheart software and one estimated from movement data) were compared with DLW PAEE values using Bland-Altman plots and Spearman correlation coefficients adjusted for age, sex, and fat free mass.

Results: The best correlate of DLW PAEE from the Actiheart was the sum of accelerometer counts per day (r=0.50 (95% CI = 0.13, 0.74)). None of the software PAEE models investigated were significantly correlated with DLW PAEE

[2] Bray M, Pomeroy J, Knowler WC, Brage S, Hopkins S, Boyer BB, et al. Accuracy of the Combined Movement / Heart Rate Monitor Actiheart for Measuring Free-Living Energy Expenditure in Yup'ik People. In preparation for Journal of Applied Physiology.

(ranging from r=0.02 (95% CI (-0.38, 0.41) to r=0.22 (-0.20, 0.56)). Limits of agreement (mean difference ± 1.96SD) for all software models were large, ranging from —4540 to 1600 kcal/day.

Conclusion: The Actiheart software does not accurately estimate free-living PAEE in Yup'ik people. However, total movement per day correlates with DLW PAEE and can be used as a proxy for PAEE.

Introduction

Obesity is a major risk factor for many chronic diseases (1). Adequate physical activity significantly contributes to maintenance of a healthy body composition and is positively associated with overall health. As the incidence of obesity and associated conditions rises, it is increasingly important to understand how energy expenditure, and especially physical activity energy expenditure (PAEE), is associated with obesity and other diseases. Moreover, valid, reliable, objective measures of free-living PAEE will facilitate the evaluation of lifestyle interventions on the relationship between PAEE and health.

The doubly labeled water (DLW) method has been extensively validated by comparing values with respiratory gas exchange for measuring total energy expenditure (TEE) (2-4) and serves as the criterion standard for estimating TEE in a free-living environment (5-6). Despite a handful of assumptions associated with the DLW method which may affect the accuracy of the estimates (2,7), in humans the correlation with TEE values from a metabolic chamber is r=0.97 (p<0.0001) and a mean difference (SD) of -65 (±183) kcal/day -accuracy of the method (2). When coupled with an estimate of resting energy expenditure (REE), DLW results can be used to estimate PAEE. However, the DLW method can be cost prohibitive for large-scale epidemiology studies. Attempts to measure PAEE using cost effective means in epidemiological studies have included the use of heart rate (HR) monitoring and accelerometry (ACC). The accuracy of both methods to estimate energy expenditure has been tested in laboratory and free-living settings (8-10). These methods are less expensive than others, yet each has limitations.

The HR method uses a physiological measure to determine PAEE assuming a linear relationship between HR and energy expenditure (EE). The slope and intercept of this linear relationship differ between individuals and depend on factors such as age, sex, fitness level, ambient temperature, stress, dehydration, and use of drugs that affect HR (11-13). Methods are available to adjust for some of these factors and involve determining the relationship between HR and EE for the individual (individual calibration) (14). Estimating EE from heart rate is limited by the fact that at low levels of activity, changes in PAEE are not reflected by changes in HR (Figure 3-1).

The ACC method uses the gravitational acceleration associated with body movement to estimate PAEE. Accelerometers used for assessing physical activity in humans typically measure the acceleration in one or more directions. Acceleration of the trunk in one direction, usually vertical, has typically been measured. Accelerations are measured by the device at sampling frequencies ranging from 10-100 Hz. In most devices, these raw accelerations are filtered to disregard vibration and other non-physiologically meaningful movement using proprietary algorithms stored in the device's firmware. The filtered data are then averaged over a period of time (usually 10-60 seconds) and then stored in the device's memory as a count. Because the filtering process is proprietary, a count from one model of accelerometer may not be equivalent to a count from another model. Usually an increase in counts corresponds with an increase in PAEE, but the slope and intercept will vary by device as well as activity. It is important to note that there are a number of activities that increase energy expenditure without a significant increase in vertical acceleration (and thus counts). Stationary bicycling is one example. Additionally, as running approaches maximum speeds, increases in speed are the result of increases in stride length instead of increases in vertical acceleration. As a result, as running approaches maximum speed accelerometry counts tend to plateau although energy expenditure increases (15-16). These are important considerations for measurement of PAEE, as the relationship between accelerometry and PAEE depends on count measurement. Combined ACC and HR monitoring takes advantage of the unique strengths of both the ACC and HR methods, thus negating some of the disadvantages of each method when used alone. Combining the ACC and HR methods increases the accuracy of energy expenditure and PAEE estimates compared to DLW, in the laboratory (17-21). Very few studies however (22-24), have investigated how the Actiheart monitor performs for estimating energy expenditure in free-living environments over several days. Most of the work regarding validation of this monitor and the models used for its analysis has been done for a short duration, less than one day (25-26), or in laboratory settings (20,25,27-28).

The main goal of this study was to determine the accuracy of the combined ACC and HR monitor (Actiheart) for measuring PAEE in free-living Yup'ik people by comparing PAEE estimates from the monitor with PAEE derived from DLW measurements in this study population.

Methods

Participants

To assess the accuracy of the Actiheart monitor (CamNtech Ltd, Cambridge UK), a combined accelerometer/heart rate (HR) monitor, for measuring free-living energy expenditure (EE) in Yup'ik people, we compared PAEE estimates derived from simultaneous wear of the monitor with PAEE estimates from doubly labeled water (DLW). Thirty-two participants, 18-40 years old, living in one rural community in southwestern Alaska wore the monitor for 10 continuous days. Participants in this analysis included men and non-pregnant women (by self-report). Two participants were excluded from the analysis because they did not complete the study. Anthropometric measurements were taken as described previously in Chapter 2.

The study protocol was approved by the University of Alaska Fairbanks institutional review boards, the Yukon-Kuskokwim Health Corporation Human Studies Committee, and participants provided written informed consent.

Energy Expenditure – Doubly Labeled Water

TEE was determined from the Coward method (29) as described previously in Chapter 2. Fat free mass (FFM) was determined assuming a hydration constant of 0.73 and using the formula FFM = total body water/0.73, and fat mass and percent body fat were calculated from FFM and total body water.

Resting and Physical Activity Energy Expenditure

Gas exchange was measured for 15 minutes with a breath-by-breath gas exchange measurement system (Cosmed $K4B^2$) while participants were lying quietly in light clothing at room temperature. These data were used to determine resting energy expenditure (REE). The first 4 minutes of data from each test were excluded; then the median of the remaining values for $\dot{V}O_2$ and $\dot{V}CO_2$ was calculated. $\dot{V}O_2$ and $\dot{V}CO_2$ were used to calculate REE using the Weir equation: REE (kcal/day)= [3.9 ($\dot{V}O_2$(mL/min)) + 1.1 ($\dot{V}CO_2$(mL/min))] 1.44 (30). Dietary induced thermogenesis (DIT) was assumed to be 10% of TEE. Physical activity energy expenditure was determined as PAEE = TEE – REE – DIT.

Energy Expenditure - The combined ACC and HR monitor

Participants were asked to wear the monitor at all times for 10 days of free-living activity, except during steam baths because the extreme heat melts the adhesive on the electrode. Heart rate and ACC data were recorded at 30 second epochs. The Actiheart assessment coincided with the period of DLW energy expenditure assessment.

Actiheart data were downloaded and processed using CamNtech software (version 4.0.87). This software includes a HR data cleaning algorithm and branched equation models which use both HR and ACC to estimate PAEE, as well as models which used ACC or HR alone for estimating PAEE. The EE estimates from the branched models have been validated against indirect calorimetry and DLW estimated EE in other study populations (11, 22). The branch models incorporate both HR and ACC to estimate energy expenditure. There are several options for analyzing the data, some which provide estimates directly using the software, while others involve downloading the data for analysis outside of the monitor software. The software also offers additional output options, including output style and options for imputing missing data. In the current analysis, estimates taken from the summary output obtained in the "Daily EE" tab in the monitor software were used. Specifically, comparisons were made when one summary row for each participant was calculated (summary output). The one summary row output ignores data from incomplete 24-hr days, typically the first and last day of wear. An additional output option exports one summary row for each day that the participant wore the monitor, providing daily estimates from which day-to-day variability could be detected; this option was not used in this analysis because after inspection of the wear time patterns, wear time and activity patterns were considerably uniform in this sample, and the criterion for comparison in this study was DLW TEE from which an overall estimate, not a daily estimate, is determined.

When there are recording gaps in the data where the device failed to pick up the electrical signal generated from the heart, the signal was very noisy (a HR value that is biologically implausible), or the participant did not wear the monitor, the software uses a cleaning algorithm to fill in missing HR data using inter beat intervals and HR data from the 4 minutes proceeding the missing values. Straight line interpolation is used if a reasonable HR cannot be determined and the missing time is less than 5 minutes. When the missing heart rates occur for greater than 5 minutes, the time is scored as "Not Worn" and HR is left as zero. Where there are gaps of missing data greater than 5 minutes, it is optional to fill this time with the average PAEE for the day ("autofill" option), or to leave these data as missing ("no autofill" option). If the data are left as missing, the missing points are set to REE which means that the points are set to zero if activity energy expenditure is output. In this analysis, both the "autofill" and "no autofill" options were evaluated for each model and compared with DLW values.

The branched equation models used included two individually calibrated models ("Step" in Table 3-1) and two group calibrated models ("Group" in Table 3-1) (11). In one individually calibrated model and one group calibrated model the "stress" option was employed. In the "stress" option the ACC and HR contributions are altered so that ACC is used at a ratio of 9:1 with HR in determining EE when HR is elevated in the absence of sufficient activity (<25 counts/min). In the models that do not include "stress", when HR is elevated and activity counts are <25 counts/min, the ACC and HR ratio is 1:1 (31). When using HR or ACC to estimate energy expenditure, the relationship between HR and $\dot{V}O_2$ (hence energy expenditure) and ACC and $\dot{V}O_2$ must be determined or estimated. For the individually calibrated models ("Step" in Table 3-1), the HR to PAEE relationship was established for each participant using an 8 minute graded step exercise (14). When the group calibrated models ("Group" in Table 3-1) models were used, the HR to $\dot{V}O_2$ relationship was estimated using previously determined regression parameter estimates (20). For the models which included ACC (all models other than the HR Only models), the ACC to $\dot{V}O_2$ relationship was derived from level walking and running in a separate population (14). The HR Only method used the flex HR method (20), in which PAEE is determined from the linear relationship between HR and energy expenditure above the flex HR. The flex HR is defined as the average of the lowest heart rate during light exercise and the highest heart rate during rest (32). Below the flex HR energy expenditure is assumed to be equal to REE.

Calibration

Prior to the calibration tests, each participant was fitted with two monitors. After light preparation of the skin with rubbing alcohol followed by light drying with a paper towel, 4 EKG electrode patches (Red Dot 2570, 3M) were applied to the chest and the monitors attached. A monitor was placed with the larger part positioned just below the apex of the sternum with the lateral lead placed horizontally (lower location). Another monitor was positioned with the larger part at the level of the third intercostal space with the lateral electrode placed horizontally on the major pectoral muscle without being under the armpit (upper location) (Figure 3-2). The outputs of each monitor were visually inspected after the step exercise, and the one with the subjectively cleaner HR tracings (i.e. less noise) was used for analysis. The monitor placement was then chosen based on the strength of the heart rate signal from the EKG for subsequent use by that individual.

For the step exercise, participants were instructed to step up and down on an 8 inch (200 mm) step paced by an audible signal, and the monitor was set up to record EKG (128Hz) and acceleration (32Hz) waveform data during the exercise. The rate of stepping increased linearly from 15 step cycles/min to 33 step cycles/min over the 8 minute period. During the step test participants wore a HR monitor which provided real time HR display. The exercise was ended early if the participant reached 90% of the estimated maximum heart rate (maximum heart rate was estimated at 220 beats/min - age in years) or if he or she was unable or unwilling to complete the exercise. If a participant stopped the exercise prior to 8 minutes, the HR to $\dot{V}O_2$ relationship was determined from the data that were successfully collected during the step exercise. After stepping was completed, the participant was asked to sit quietly without talking for 2 minutes.

The combined ACC and HR monitor for free-living conditions

Upon completion of the individual calibration from the step exercise, the monitor was programmed for long-term wear and set to record data in 30 second intervals. Participants were asked to wear it at all times for 10 full days, including during sleep. They were instructed to remove the unit only during steam baths. Participants developing rashes or skin irritation were treated with a hydrocortisone ointment and the monitor was repositioned in an alternate location (just above or below the original location). Monitors were downloaded every other day throughout the study period to ensure recording integrity and to encourage compliance, at which time urine samples were collected. An activity diary was provided, and participants were asked to record information about daily activities and the time and reason for any removal of the monitor.

Statistical analyses

SAS for Windows (version 9.3) was used for statistical analyses. Since age, sex and body size are associated with energy expenditure Spearman's correlation coefficient partialled for age and sex was used to determine which body size measurement was most strongly associated with PAEE. Spearman's correlation coefficient was then used to compare the correlation of PAEE estimates from the monitor with PAEE estimates from DLW. To compare individual PAEE estimates that are not explained by age, sex, or body size, these correlations were adjusted for age, sex, and the strongest body size correlate with PAEE. PAEE was not divided by body size (i.e. body weight) as this is an inappropriate method for adjusting for body size (33-35). The Bland-Altman (36) method was used to assess absolute agreement in DLW and the other estimates of PAEE. The limits of agreement from the Bland Altman method are calculated as 1.96 times the standard deviation for the difference between the PAEE from the other method for comparison and the DLW PAEE.

In addition to the 12 PAEE estimates determined by the models from the Actiheart software, we also determined the correlation of total counts per day with DLW PAEE. A strong association was seen between total counts per day and DLW PAEE, so multiple regression was used to model DLW PAEE from ACC counts per day (PAEE CPD model). Age, sex, and body weight were also included in the model to be consistent with the Actiheart software models which all included age, sex, and body weight. The PAEE CPD model was determined because in a given person higher CPD leads to higher PAEE, indicating that CPD can serve as a proxy for PAEE. In total, 13 models to estimate PAEE were compared with DLW PAEE estimates. These included the "autofill" and "no autofill" options for four branched equation models from the monitor software, ACC Only, HR Only, and the model we determined from multiple regression.

Results

Characteristics of the participants completing the study (n=30; 16 men and 14 women) are shown in Table 3-2. The ages ranged from 18-40 years with the median age for men being 25.7 and for women 36.3 years. Summary statistics for PAEE estimates from DLW and PAEE estimates from all the models analyzed for women and men respectively are presented in Table 3-3. PAEE for men and women significantly differed from one another.

Correlation of Energy Expenditure with Body Size

The correlations between energy expenditure estimates and body size variables are shown in Table 3-4. The strongest correlation was between TEE and FFM ($r=0.68$, $p<0.01$). REE was more strongly correlated with all other body size estimates than were TEE or PAEE. The strongest correlate with PAEE was DLW FFM ($r=0.35$, $p=0.06$). Since FFM was the strongest correlate with PAEE, it is the most appropriate measurement to adjust correlations to remove the effect of body size on PAEE. Researchers are usually able to determine only body weight however, whereas FFM may not always be measurable. Therefore, we also determined the correlations between PAEE estimates after adjustment for body weight.

PAEE Model Comparisons with DLW PAEE

The correlation (95% CI) of each model with DLW, as well as the mean difference and 95% limits of agreement between DLW and each model are listed in Table 3-5. The strongest correlation, and the only significant correlation, was found between total counts per day and DLW PAEE ($r=0.50$; 95% CI (0.13, 0.74)). Of all the PAEE models investigated, the PAEE CPD model had the smallest limits of agreement with DLW (-458, 953kcal/day) (Table 3-5), and did not have a significant correlation between the mean difference between estimates and the average PAEE in the Bland Altman plots.

After adjustment for FFM, all PAEE estimates from the software models evaluated were positively correlated with DLW PAEE values, ranging from the strongest correlation of r=0.22 (95% CI (-0.20, 0.56)) for the Step Stress model, to the weakest correlation of r=0.02 (95% CI (-0.38, 0.41) for Step AF model, however none of the Actiheart model PAEE estimate correlations with DLW PAEE were significant (Table 3-5). When adjusted for body weight instead of FFM, correlations of the software model PAEE estimates with DLW PAEE were slightly stronger, but none significant (Table 3-5).

The Actiheart models which performed the best overall in terms of correlation with DLW PAEE, limits of agreement with DLW, and which had no PAEE related bias were the models which included both the exercise calibration and the "stress" factor (Step Stress and Step Stress AF models) (Table 3-5). The non-exercise calibrated Actiheart model which performed best overall in terms of limits of agreement with DLW and which had no PAEE related bias was the Group Stress AF model (Table 3-5). The model with the smallest limits of agreement, as evidenced from the Bland Altman plots, was the Step Stress model which included the exercise calibration and the "stress" factor (limits of agreement, i.e., step stress model – DLW PAEE, =, -795, 1163kcal/day). This was followed closely by the ACC Only AF model (limits of agreement = -450, 1596 kcal/day). The largest limits of agreement came when the HR Only AF model was used (limits of agreement = -4540, 1309 kcal/day). If we compare only the branched equation models which included both HR and ACC to estimate PAEE, the Group AF model, which did not include an exercise calibration or the "stress" factor, had the largest limits of agreement (-2188, 1182kcal/day).

Autofill Option

When comparing the differences between using and not using the "autofill" option, the results were mixed in terms of correlations with DLW (Table 3-5). Specifically, the Group, Step, and Step Stress models performed better when the "autofill" option was not used, while the ACC Only, HR Only, and Group Stress models performed better when the "autofill" option was used.

Exercise vs. Non-Exercise Calibration

Exercise calibration improved PAEE estimates over non-exercise calibration when the "stress" factor was used (Table 3-5). Specifically, in the models which included the "stress" factor, the correlation with DLW PAEE was stronger and the 95% limits of agreement were narrower when exercise calibration was used (Step Stress) compared to when non-exercise calibration was used (Group Stress). In the models which did not include the "stress" factor (Step and Group), correlations with DLW PAEE were stronger with the non-exercise models

(Group) than with the exercise calibrated models (Step), but the limits of agreement were smaller for the exercise calibrated models (Step) than for the non-exercise calibrated models (Group). In addition, the Group models exhibited a significant correlation between the mean difference between estimates and the absolute magnitude of PAEE in the Bland Altman plots while the Step, Step Stress, and Group Stress models did not.

Combined HR and ACC vs. HR Only or ACC Only

One of the assumptions of using HR and ACC combined to estimate PAEE is that a more accurate estimate will be obtained than when PAEE estimates are made using ACC or HR alone. ACC alone performed poorly in terms of correlations with DLW (ACC Only r= 0.04; ACC Only AF r= 0.03), but the limits of agreements with DLW estimates for ACC alone were similar to the combined ACC and HR models (Table 3-5). When HR alone was used, correlations with DLW PAEE estimates were also low (HR Only r= 0.05; HR Only AF r= 0.04), and the limits of agreement were larger than all other models investigated (Table 3-5). In addition, both the ACC Only and HR Only models exhibited a significant correlation between the mean difference between estimates and the absolute magnitude of PAEE in the Bland Altman plots (Table 3-5 and Figures 3-3c & 3-3d respectively). ACC Only underestimates PAEE at low PAEE values and over estimates PAEE at high PAEE values while HR Only overestimated PAEE at low PAEE values and underestimated PAEE at high PAEE values.

In addition to the ACC Only and HR Only models, the Group (non-exercise calibrated) model also exhibited a significant correlation between the mean difference and absolute magnitude of PAEE in the Bland Altman plot (r=-0.44 p=0.008 and p=0.009 for the Group AF and Group models respectively). The remaining 7 models had no significant difference in the Bland Altman plots (Table 3-5).

Discussion

The Actiheart monitor combines heart rate and movement registration to measure PAEE, yet little is known regarding its validity for measuring PAEE over a several day period in free-living participants (20,23,27). We determined the accuracy of equations using data from the Actiheart monitor for measuring PAEE in a free-living environment in Yup'ik people. We also determined the most accurate model for estimating PAEE in this study population. Compared with DLW PAEE estimates, the software models do not accurately estimate free-living PAEE in Yup'ik people. Correlations with DLW PAEE were poor for all software models and limits of agreement were wide. In fact none of the PAEE estimates using the software models were significantly correlated with DLW PAEE. In contrast, the strongest and the only significant correlation with DLW PAEE was with total counts per day (r=0.50, 95%CI (0.13, 0.74)). On an individual level, higher CPD leads to higher PAEE, explaining why total CPD is strongly correlated with DLW PAEE. Therefore, total counts per day could be used as a proxy for PAEE.

When evaluating the agreement of the models compared with DLW for estimating PAEE, it is important to consider the correlation with DLW as well as the mean difference and the limits of agreement as seen in Bland Altman plots. A model with a small mean difference from DLW, but large limits of agreement may not be as useful as a model with a larger mean difference but small limits of agreement from the DLW estimates. A systematic mean difference can easily be adjusted for by simple arithmetic, but large limits of agreement cannot be adjusted. Mean differences from DLW PAEE were as low as 43 kcal/day. However, the limits of agreement were large, ranging from (-747, 1164 kcal/day) to (-4441, 1363 kcal/day) kcal/day. These large limits of agreement make it difficult to have confidence in the PAEE estimates.

When determining the accuracy of a model for estimating PAEE, it is also important to evaluate whether the model exhibits a PAEE related bias (a significant correlation between the mean difference and absolute magnitude of PAEE in the Bland Altman plot). In this study population the PAEE CPD Model, as well as the Step Stress, Group Stress, and Step software models were not biased, while the Group, ACC Only, and HR Only models were biased. Models that exhibit a PAEE related bias, such as the Group, ACC Only, and HR Only models, systematically over or under-estimate PAEE depending on the PAEE value. For example, the HR Only model over-estimated PAEE at low PAEE values and under-estimated at high PAEE values, whereas the ACC Only model under-estimated PAEE at low PAEE values and over-estimated at high PAEE values.

Individual calibration of the monitor should yield more accurate PAEE estimates than using a group calibration since the physical activity intensity (PAI) to HR relationship is determined for each person (14). This was true when the Step Stress and Group Stress models were used, however it was not entirely true for the Step and Group models. The Step model had narrower limits of agreement from DLW but the Group model was more strongly correlated with DLW. It is possible that individual calibration to estimate the PAI to HR slope using a submaximal test such as the step exercise is too far away from the maximum workload. Therefore, the PAI to HR slope estimated may not align with true maximum PAI to HR values and PAEE estimates would be biased. Moreover, when there is noisy HR data, the HR is most often biased high. Since the "stress" models make an adjustment to the weighting of the HR and ACC contribution in the calculation of PAEE when there is a high HR in the absence of sufficient ACC counts, the “stress” adjustment may act as an additional cleaning mechanism that the non-“stress” models do not employ, leading to improved PAEE estimates.

One of the proposed benefits of using the Actiheart is that both ACC and HR can be combined in an effort to improve PAEE estimates. The combined methods did perform better than the HR only and ACC only methods, but they were not significantly correlated with DLW PAEE, and are not reliable for estimating PAEE. The HR only method greatly overestimated PAEE, had wide limits of agreement (-4441, 1363 kcal/day) and had a significant negative PAEE related bias in the Bland Altman plots; at low mean PAEE values the HR only method over-estimated PAEE and at high mean PAEE values it under-estimated PAEE. The ACC only method was weakly correlated with DLW PAEE estimates and exhibited a positive PAEE related bias in the Bland Altman plots; at low mean PAEE values the ACC only method under-estimated PAEE and at high mean PAEE values it over-estimated PAEE. When using ACC or HR only methods, the PAEE related bias make PAEE estimates unreliable.

Adjusting PAEE for Body Weight Compared to Dividing PAEE by Body Weight

Body size significantly contributes to energy expenditure (Table 3-4). For example, heavier people perform more work (increased energy expenditure) to move their additional mass. Adjusting for body size should provide a more accuracy assessment of the association between PAEE from the models compared to DLW that is not due to body size. The adjustment approach taken by many investigators is to use the ratio of energy expenditure to body size, or specifically to divide energy expenditure by body weight. The ratio approach however is flawed, and is not an acceptable method to adjust for body size as others have shown (33-35,37-40). In order to accurately compare PAEE estimates independently of body size, the residuals from predicting PAEE from body size should be determined and the correlation between these residuals then calculated.

By adjusting PAEE for body size (specifically FFM) in the correlation analyses, we conclude that the Actiheart software does not accurately estimate PAEE as compared with DLW. Our results differed from those of Assah et al. who evaluated the accuracy of the Actiheart software for estimating PAEE as compared with DLW in a Cameroon cohort, but used the ratio method to adjust for body size (23). The difference in the results is likely due to the different analytic approaches used in each study.

Output option: Autofill

When the "autofill" option was used to fill gaps in the data with the average energy expenditure for that day, the results were similar to when these gaps were left as missing. In our study population, there was very little non-wear time (3%) and non-wear time primarily occurred during sleeping hours. The results would likely be different if there was more non-wear time, especially if the non-wear time was during activities that were considerably different from the activities during wear time. If the non-wear time occurred during periods of heavy activity such as exercise, filling the missing periods with the average energy expenditure for the day would underestimate PAEE. In contrast, if the non-wear time occurred during periods of sleep or low activity, filling these periods with the average energy expenditure for the day would over-estimate PAEE. For these reasons it is important to consider the monitor wear patterns of the population of interest to determine which output options are most appropriate.

Study Strengths and Limitations

Strengths of this study included the length of time which energy expenditure was monitored (10 days) simultaneously from DLW and the Actiheart, and excellent participant compliance. We acknowledge that this study was conducted in one community and in one cultural group, and that results may differ in other groups.

Conclusions

Valid methods for monitoring the subcomponents of physical activity are important to understand the role that physical activity (or inactivity) plays in health because it provides an opportunity to tease apart which aspects of physical activity are most influential to health. By combining the ACC and HR methods to estimate PAEE, more accurate measurement of PAEE should be possible. However, the combined ACC and HR method did not provide accurate PAEE estimates as compared with DLW. Total counts per day may provide the most reliable estimate of PAEE. Further investigation into different methods for processing and using the ACC and HR information are necessary to improve the accuracy of PAEE estimates.

The combined ACC and HR Actiheart monitor does make it possible to estimate the subcomponents of physical activity including frequency, intensity, and duration of activity. However, similar estimates of these subcomponents can also be estimated using any accelerometer capable of recording time-stamped data.

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Table 3-1: Model Attributes

Model Name from Actiheart	Short Model Name	ACC	HR	Stress	Autofill
ACC only – Autofill	ACC Only AF	X			
ACC only	ACC Only	X			X
HR Only – Autofill	HR Only AF		Step		X
HR Only	HR Only		Step		
Group Cal Jap2007 Autofill	Group AF	X	Group		X
Group Cal Jap2007	Group	X	Group		
Adult: GroupAct/GroupHR+stress - Autofill	Group Stress AF	X	Group	X	X
Adult: GroupAct/GroupHR+stress	Group Stress	X	Group	X	
Group Cal Jap2007/StepHR Autofill	Step AF	X	Step		X
Group Cal Jap2007/StepHR	Step	X	Step		
Adult: GroupAct/StepHR+stress Autofill	Step Stress AF	X	Step	X	X
Adult: GroupAct/StepHR+stress	Step Stress	X	Step	X	

ACC = Accelerometry; Group HR = the HR to $\dot{V}O_2$ relationship is estimated using the in-built algorithm; Step HR = the individual step calibration was used to establish the HR to $\dot{V}O_2$ relationship for each participant; Stress Adjustment = the model adjusted for stress (when HR was elevated without sufficient ACC counts); Autofill = Gaps of greater than 5 minutes of missing time were filled with the average PAEE for the day; No Autofill = Gaps of greater than 5 minutes of missing time were left as missing values. In all models, we used the summary output (one line summarizing all days of wear for each participant) rather than the 1 line/day option (one line per day for each participant). The PAEE CPD Model was determined by modeling DLW PAEE from age, sex, body weight (kg) and total counts per day. All PAEE estimates derived from the Actiheart software also include age, sex, and body weight (kg).

Table 3-2: Participant Characteristics

	Variable		Min	Lower Quartile	Median	Upper Quartile	Max
Women (n=14)							
	Age	years	19	30.8	36.3	40.1	40.7
	BMI	kg/m^2	17.1	22.0	29.8	34.1	41.1
	Height	m	1.46	1.54	1.62	1.64	1.72
	Weight	kg	44	61	72	91	110
	Waist/Hip Ratio		0.77	0.79	0.85	0.91	1.02
	WC	cm	64.4	74.8	96.0	105.5	117.3
	Pfat	%	12	31	37	44	46
Men (n=16)							
	Age	years	18.1	19.5	25.7	31.4	40.4
	BMI	kg/m^2	20.0	22.9	25.0	29.1	38.9
	Height	m	1.60	1.65	1.70	1.76	1.84
	Weight	kg	55	64	72	84	118
	Waist/Hip Ratio		0.82	0.85	0.87	0.91	1.13
	WC	cm	68.3	76.3	81.9	100.4	127.8
	Pfat	%	8	13	18	27	35

BMI = body mass index; WC = waist circumference; pfat = percent body fat

Table 3-3: PAEE Statistics

	Variable		Min	Lower Quartile	Median	Upper Quartile	Max
Wome	Resting EE	kcal/day	595	1142	1221	1430	1513
(n=14)	DLW PAEE	kcal/day	24	516	1007	1146	1359
	Summary Models						
	ACC Only AF	kcal/day	392	595	913	1067	1467
	ACC Only	kcal/day	338	595	865	1067	1381
	HR Only AF	kcal/day	1205	1738	2345	2946	5614
	HR Only	kcal/day	1205	1535	2345	2744	5614
	Group AF	kcal/day	836	1188	1498	1850	3473
	Group	kcal/day	836	1188	1422	1725	3362
	Group Stress AF	kcal/day	605	701	886	1169	1988
	Group Stress	kcal/day	593	633	858	1146	1838
	Step AF	kcal/day	742	1171	1275	1813	2245
	Step	kcal/day	742	1073	1237	1688	2211
	Step StressAF	kcal/day	523	744	898	1193	1595
	Step Stress	kcal/day	498	701	890	1193	1565
	PAEE CPD Model	kcal/day	476	620	855	1046	1251
Men	Resting EE	kcal/day	1115	1399	1523	1720	1950
(n=16)	DLW AEE	kcal/day	674	993	1416	1629	3204
	Summary Models						
	ACC Only AF	kcal/day	430	755	879	1081	1358
	ACC Only	kcal/day	430	755	879	1055	1319
	HR Only AF	kcal/day	893	2272	3407	4641	6241
	HR Only	kcal/day	893	2240	3391	4411	6241
	Group AF	kcal/day	667	1605	2069	2995	3526
	Group	kcal/day	667	1605	2059	2861	3526
	Group Stress AF	kcal/day	824	1478	1712	2139	2660
	Group Stress	kcal/day	824	1415	1712	2063	2660
	Step AF	kcal/day	759	1717	1948	2370	2611
	Step	kcal/day	759	1717	1938	2278	2611
	Step Stress AF	kcal/day	533	1428	1529	1749	2409
	Step Stress	kcal/day	533	1427	1529	1688	2336
	PAEE CPD Model	kcal/day	659	1129	1336	1546	2739

Resting EE = resting energy expenditure; DLW PAEE = doubly labeled water physical activity energy expenditure; CPD = counts per day

Table 3-4: Correlations of Energy Expenditure with Body Size

	REE	TEE	PAEE
Height (m)	0.36 (0.06)	0.23 (0.23)	0.10 (0.62)
Weight (kg)	0.62 (<.01)	0.49 (0.01)	0.15 (0.42)
BMI (kg/m^2)	0.56 (<.01)	0.41 (0.03)	0.09 (0.64)
WC (cm)	0.56 (<.01)	0.43 (0.02)	0.13 (0.51)
Fat mass $_{DLW}$ (kg)	0.57 (<.01)	0.35 (0.07)	0.03 (0.90)
Fat-free mass $_{DLW}$ (kg)	0.58 (<.01)	0.68 (<.01)	0.35 (0.06)
Fat mass $_{BIA}$ (kg)	0.60 (<.01)	0.43 (0.02)	0.10 (0.61)
Fat-free mass $_{BIA}$ (kg)	0.66 (<.01)	0.55 (<.01)	0.17 (0.37)

REE = resting energy expenditure (from expired gas indirect calorimetry);
TEE = total energy expenditure (from DLW);
PAEE = physical activity energy expenditure (PAEE=TEE-REE-(0.1XTEE);
DLW = doubly labeled water.
Spearman correlation coefficients and p-values, adjusted for sex, are reported.
Fat mass and fat-free mass were derived from DLW.

Table 3-5: Actiheart and DLW PAEE Comparison Statistics

Model	* Spearman Corr (95% CI) w/DLW Adjusted for FFM	† Spearman Corr (95% CI) w/DLW Adjusted for weight	Mean Diff from DLW (±1.96SD)	25th Centile	Median	75th Centile	Range of Diff from DLW	BA Corr	p-value (BA Corr)
ACC Only AF	-0.04 (-0.43, 0.36)	0.07 (-0.32, 0.44)	573(-450, 1596)	261	468	774	2046	0.63	<0.0001
ACC Only	-0.03 (-0.42, 0.37)	0.07 (-0.32, 0.44)	590(-421, 1600)	289	490	803	2021	0.64	0.0001
HR Only AF	0.05 (-0.36, 0.43)	0.20 (-0.20, 0.54)	-1616(-4540, 1309)	-2812	-1384	-536	5849	-0.79	<0.0001
HR Only	0.04 (-0.36, 0.43)	0.19 (-0.21, 0.53)	-1539(-4441, 1363)	-2665	-1283	-488	5804	-0.79	<0.0001
Group AF	0.12 (-0.29, 0.49)	0.25 (-0.15, 0.57)	-503(-2188, 1182)	-1103	-428	158	3370	-0.44	0.008
Group	0.13 (-0.28, 0.50)	0.24 (-0.16, 0.56)	-456(-2119,1206)	-1095	-419	158	3325	-0.44	0.009
Group Stress AF	0.10 (-0.31, 0.47)	0.20 (-0.20, 0.54)	43(-1100,1185)	-372	-5	366	2285	-0.06	0.77
Group Stress	0.06 (-0.35, 0.44)	0.16 (-0.24, 0.50)	73(-1062, 1207)	-359	-5	506	2269	-0.05	0.79
Step AF	0.02 (-0.38, 0.41)	0.08 (-0.31, 0.45)	-191(-1476, 1094,)	-630	-236	111	2570	0.03	0.88
Step	0.11 (-0.30, 0.48)	0.17 (-0.23, 0.52)	-181(-1246, 884)	-543	-215	164	2130	0.02	0.92
Step Stress AF	0.19 (-0.22, 0.54)	0.27 (-0.13, 0.58)	184(-795, 1163)	-121	115	467	1957	0.19	0.30
Step Stress	0.22 (-0.20, 0.56)	0.30 (-0.10, 0.61)	209(-747, 1164)	-72	163	564	1911	0.20	0.29
PAEE CPD Model			0 (-680, 680)	-145	49	249	1359	0.15	0.44
Counts per day	0.50 (0.12, 0.74)	0.51 (0.13, 0.75)							

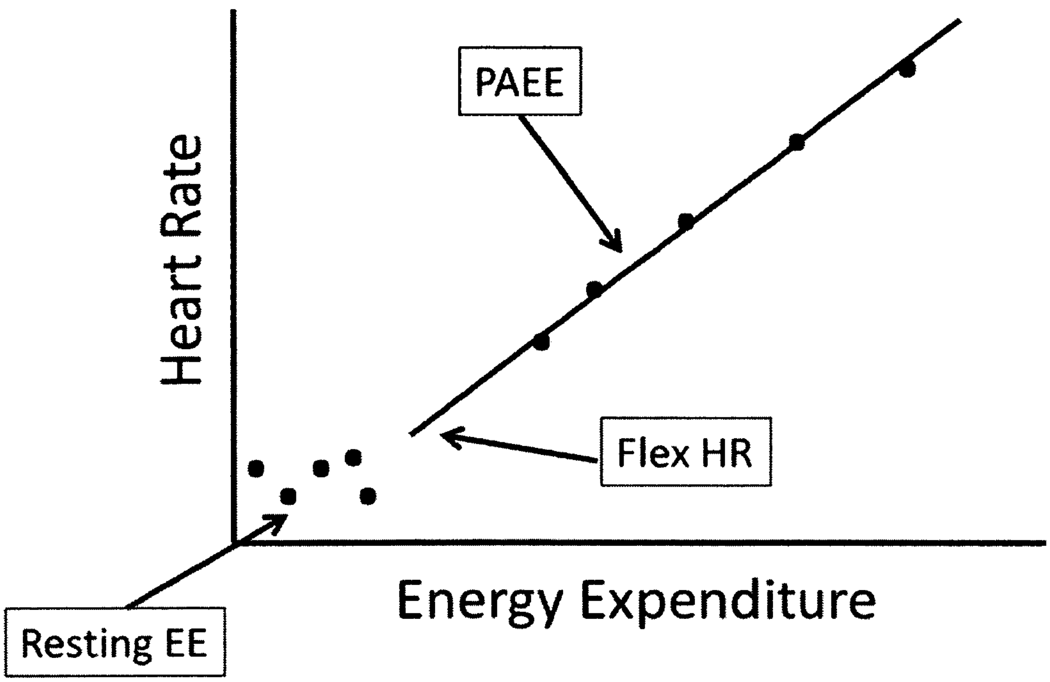
BA= Bland Altman; FFM = fat free mass

* Correlations are adjusted for age, sex, and FFM.

† Correlations are adjusted for age, sex, and body weight.

Units for Mean Diff from DLW (±1.96SD), 25th Centile, Median, 75th Centile, and Range of Diff from DLW are kcal/day. No correlation coefficient is given for PAEE CPD Model because this model was determined by regression CPD on DLW PAEE. Only the correlation coefficient is given for Counts per day (CPD) because CPD is not a direct estimate of PAEE.

Figure 3-1: The Flex Heart Rate - Physical Activity Intensity / Heart Rate Relationship



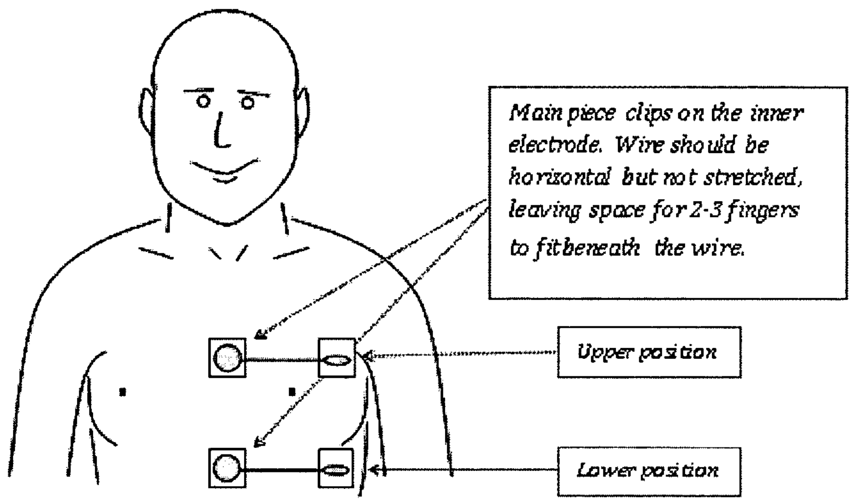


Figure 3-2: Actiheart Positions - Upper and Lower

Figure 3-3: Bland Altman Plots

Figure 3-3a

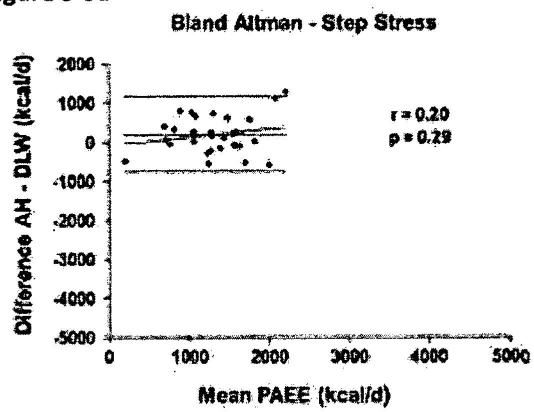


Figure 3-3b

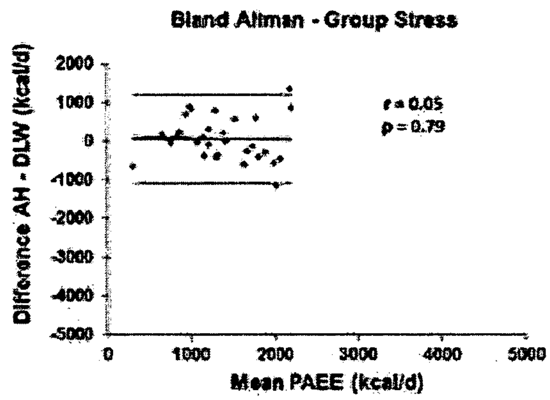


Figure 3-3c

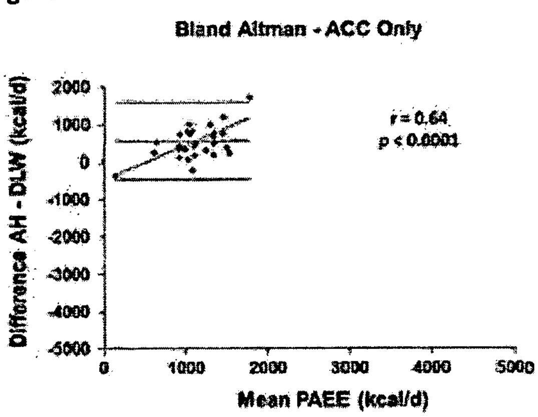
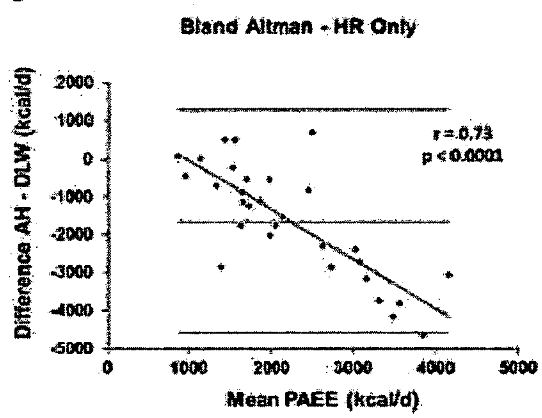


Figure 3-3d



DLW = doubly labeled water; PAEE = physical activity energy expenditure; AH = Actiheart derived PAEE; CPD = counts per day

Figures are Bland Altman plots showing the agreement between DLW PAEE and PAEE models. The center line is the mean difference and the upper and lower lines are 1.96XSD of the mean difference. Also shown is the regression line between the mean difference and absolute magnitude of PAEE and corresponding r and p-values.

4 The Associations of Objectively Measured Physical Activity with Cardiovascular and Metabolic Risk Factors in Yup'ik People [3]

Abstract

Objectives: The goals of this study were to: 1) measure the intensity, duration and frequency of physical activity; and 2) determine the relationships between these measures and health-related variables in a study population of Yup'ik adults living in a remote region of southwestern Alaska.

Methods: Physical activity was estimated with the Actiheart, a combined heart rate/movement monitor, in 580 Yup'ik adults from 11 communities in southwestern Alaska, of whom reliable activity data were obtained in 534. We determined Spearman correlations (r_s) between health-related variables and counts per day (CPD) from accelerometry movement registration, moderate-to-vigorous physical activity (MVPA), and sedentary time. Generalized linear models were used to predict weight, BMI, waist circumference (WC), percent body fat (PBF), total cholesterol, HDL cholesterol, LDL cholesterol, and non-HDL cholesterol, fasting glucose, and blood pressure from CPD, MVPA, and sedentary time. Age, sex, monitor wear time, and weight (when appropriate) were included as covariates.

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[3] Bray M, Pomeroy J, Knowler WC, Havel P, Hopkins S, Boyer BB, et al. The Associations of Objectively Measured Physical Activity with Cardiovascular and Metabolic Risk Factors in Yup'ik People. In preparation for Annals of Internal Medicine.

Results: After adjustment for covariates, accelerometry CPD was positively associated with HDL cholesterol (r_s=0.13, r_s =0.15 men and women respectively) and negatively associated with body weight, BMI, WC, PBF and triglycerides (r_s range from -0.17 to -0.25 in men and -0.19 to -0.21 in women). MVPA was only associated with fasting glucose. Sedentary time was positively associated with body weight, WC, and PBF (r_s range from 0.10 to 0.18 in women) and negatively associated with HDL cholesterol (r_s =-0.19 in women).

Conclusions: Accumulation of regular movement of any intensity while decreasing sedentary time may be more important for health in Yup'ik people than MVPA.

Introduction

Physical activity has a key role in health, but the importance of duration, frequency, and intensity of activity to health remains unclear. The World Health Organization (WHO) and the U.S. Department of Health and Human Services (DHHS) recommend 30 minutes of moderate-to-vigorous physical activity (MVPA) 5 days of the week (1-2). The optimal physical activity recommendations are inconsistent, however, with different recommendations emphasizing: 1) high intensity, short duration activity (3-5); 2) total movement accumulated, regardless of the intensity (6-7); or 3) decreasing sedentary time (8-12).

To understand which subcomponents of physical activity are most important for maintaining health, we must accurately quantify duration, frequency and intensity of habitual physical activity. Most research on the relationship between physical activity and health has relied on self-reported assessments (13). Self-report is convenient, but subject to recall bias and socially acceptable response bias (14). Accurate objective measurements are needed for understanding the dose-response relationship between physical activity and health (15). The Actiheart monitor, a combined heart rate (HR) monitor and accelerometer (ACC), provides an objective measure of physical activity from which intensity, duration, frequency, and physical activity energy expenditure (PAEE) can be estimated. Understanding associations of physical activity with obesity and obesity-related comorbidities will provide insight into developing effective prevention strategies.

The goals of this study were to: 1) measure the intensity, duration and frequency of physical activity; and 2) determine the relationships between these measures and health-related variables, including T2D in a study population of Yup'ik adults living in a remote region of southwestern Alaska.

Methods

A cross-sectional health study was conducted from 2007-2011 among Yup'ik people living in 11 rural communities located in the Yukon-Kuskokwim Delta region of southwestern Alaska. Physical activity was assessed using the Actiheart, a combined heart rate/accelerometer monitor (CamNtech Ltd, Cambridge UK). Study participants included 580 men and non-pregnant women (by self-report) aged ≥ 18 years. The study protocol was approved by the University of Alaska Fairbanks institutional review board and the Yukon-Kuskokwim Health Corporation Human Studies Committee. Participants provided written informed consent.

Anthropometric, blood pressure, fasting glucose, lipids, and hormone measurements were made as previously described (16). Low-density lipoprotein cholesterol (LDL) was calculated using the Freidwald formula (LDL = total cholesterol – HDL cholesterol – triglycerides/5) (17) and non-HDL cholesterol was calculated as total cholesterol – HDL cholesterol.

Previously diagnosed T2D was abstracted from medical records (ICD-9 code 250). Individuals having fasting glucose ≥126 mg/dL (7.0 mmol/L) or HbA1c ≥ 6.5% were considered to have T2D (18). Impaired fasting glucose (IFG) was defined as fasting glucose ≥ 100 mg/dL (5.6 mmol/L) and < 126 mg/dL (7.0 mmol/L).

The Actiheart

The Actiheart is a chest-worn monitor consisting of a heart rate monitor and accelerometer. It can record time-stamped HR and activity counts (from the ACC) at 15, 30 or 60 second intervals (epochs). It is light weight (8 grams) and can be worn during all activities, including swimming and bathing, except steam baths or sauna, only because the extreme heat melts the electrode adhesive.

Actiheart for Free-living Conditions

The monitor was programmed for long-term wear and set to record data at 30 second intervals. Participants were asked to wear it at all times for 4 days, including during sleep. They were instructed to remove the unit only during steam baths. Participants developing rashes or skin irritation were treated with hydrocortisone ointment, and the monitor was repositioned. Participants were asked to record information about daily activities in an activity diary and indicate the time and reason the monitor was removed. Participants who had less than 1000 minutes of wear time (43 people) or >150,000 activity counts per day (CPD) (3 participants) were excluded from the analysis if it was verified that they were not extremely active (based on their activity diary). Three other participants (all young men) with more than 150,000 CPD appeared to have good quality data and, according to self-report, were extremely active. Their data were used, although they were excluded from some analyses as influential outliers.

Physical Activity Subcomponents

The physical activity subcomponents analyzed included: 1) total movement in CPD taken from ACC counts only; 2) total ACC sedentary time (classified as minutes with less than 10 ACC counts and a valid heart rate); 3) time spent sedentary in periods of 30 minutes or greater; 4) total number of sedentary periods lasting at least 30 minutes; 5) total time spent in MVPA (min/day), defined by periods when the HR was at least 1.75 x sleeping HR; 6) time spent in MVPA in bouts of at least 10 consecutive minutes; and 7) total number of MVPA bouts lasting at least 10 minutes. The physical activity subcomponents were evaluated outside of the monitor software from the minute-by-minute data collected using SAS for Windows (version 9.3). Total CPD is correlated with PAEE r=0.500 95% CI(0.130 to 0.739), and thus was used as a proxy for PAEE (see Chapter 3). Time spent sedentary in bouts of 30 minutes or greater was chosen because increased sedentary time (≥ 30 minutes) is associated with decreased insulin sensitivity (11, 19). A threshold of 1.75X sleeping HR was used to identify MVPA rather than using the typical metabolic equivalent (MET) level of 3 METs. The MET level assumes a constant for resting metabolic rate (RMR) of 3.5 ml oxygen/kg/min based on a "standard" 70kg man, which often overestimates the true RMR (20-22). The time spent in MVPA in bouts of at least 10 minutes of duration was chosen because of the physical activity recommendations made by the WHO and DHHS to accumulate MVPA in bouts of at least 10 minutes in length (23-24).

Statistical analyses

SAS for Windows (version 9.3) was used for statistical analyses. Continuous variables were tested for normality; many were not normally distributed and could not be normalized with simple transformations. Therefore, Spearman's correlation coefficients and appropriate non-parametric tests were used.

Generalized linear modeling was used to investigate the relationship between non-wear time, CPD, MVPA, and sedentary time to ensure that a linear adjustment was appropriate. No quadratic relationship was seen; therefore a linear adjustment for non-wear time was used in subsequent analyses.

Correlation of Physical Activity with Lipids, Hormones, and Blood Pressure

Spearman's correlation coefficient was used to determine the associations of physical activity subcomponents to health-related variables (body weight, BMI, WC, percent body fat, total cholesterol, HDL cholesterol, LDL cholesterol, non-HDL cholesterol, triglycerides, fasting glucose, systolic and diastolic blood pressure) in men and women combined, as well as men and women separately. Correlations with body size variables (body weight, BMI, WC, and percent body fat) are controlled for age and monitor wear time. Correlations with lipids, glucose, and blood pressures are controlled for age, body weight, and monitor wear-time. When men and women are combined, correlations are controlled for sex as well. A test of equality of two correlations for a single sample (25) was used to determine whether correlations of each physical activity component and a given health-related variable were significantly different from the physical activity component with the highest correlation. Results are reported for combined men and women.

General linear models were used to predict each of the health-related variables from a subset of the physical activity subcomponents, including CPD, total MVPA time, and total sedentary time. Time spent sedentary in periods of at least 30 minutes, the total number of sedentary periods ≥ 30 minutes, total time spent in MVPA in bouts at least 10 minutes, and the total number of MVPA bouts lasting at least 10 minutes were not included in the models. The information gained from these variables was captured in total MVPA time and total sedentary time. All models included age, sex, and monitor wear time as covariates. In addition to age, sex, and monitor wear time, models for lipids, fasting glucose, and blood pressures also included body weight as a covariate. Variables were standardized to a mean=0 and a SD=1 and standardized beta coefficients are reported.

Analyses were conducted on the entire study population as well as stratified by sex and community location (inland or coastal). Stratification by community location was done to determine if there was a difference between activity patterns of different types of communities according to how far the participants lived from the hub city of Bethel, AK (population of 6200). Coastal communities (n=7, median population of 354) were on average 114 miles from Bethel, whereas inland communities (n=4, median population of 598) were less than 30 miles away.

Results

Demographic and health-related data are shown in Table 4-1. Men and women differed in age, height, weight, BMI, percent body fat, total cholesterol, HDL cholesterol, and systolic blood pressure, but not in fasting glucose, LDL cholesterol, non-HDL cholesterol, triglycerides or diastolic blood pressure. None of the demographic or health-related variables differed by community location (inland or coastal).

Activity data, stratified by sex are shown in Table 4-2. Men accumulated more CPD and time spent in MVPA than women (total MVPA, MVPA in bouts ≥ 10 min, and total MVPA bouts ≥ 10 min). Men and women did not differ in sedentary behavior (total sedentary time, total time spent in sedentary periods

≥30 min, and total sedentary periods ≥30 min) (Table 4-2). Men from inland and coastal communities did not differ in their activity behaviors (data not shown). Coastal and inland women however, differed from one another in total sedentary time, total MVPA time, and total MVPA time in bouts ≥10 min. Women on the coast had more MVPA, but also spent more time sedentary than did women from inland communities (data not shown). Stratifying by community location did not affect associations described below, so community location is not considered further.

In general, Yup'ik people in this study met or exceeded the recommendations for the minimum amount of MVPA set by the DHHS (≥ 150 min per week) to gain health benefits from physical activity (1-2). On average, Yup'ik men spent 156 min/day (1092 min/week) in MVPA (728% of the recommended 150 min per week) and Yup'ik women spent 100 min/day (700 min/week) in MVPA (467% of the recommended 150 min/week). Even Yup'ik women from inland communities (the least active group), far exceeded the physical activity recommendations by getting 553 min of MVPA/week (369% the recommendation for MVPA per week).

Physical Activity and Health-Related Variables – Correlations

Tables 4-3, 4-4, and 4-5 show the Spearman correlation coefficients of physical activity subcomponents with health-related variables for men and women combined, men only, and women only respectively. With men and women combined total CPD was negatively correlated with body weight, BMI, WC, percent body fat, and triglycerides and positively correlated with HDL cholesterol. Total sedentary time was positively correlated with body weight, BMI, WC, percent body fat, and triglycerides and negatively correlated with HDL cholesterol. Total MVPA, time spent in MVPA in bouts at least 10 min, and total bouts of MVPA in bouts at least 10 min were negatively correlated with fasting glucose. Total CPD was more strongly correlated with the greatest number of health-related variables than sedentary time or MVPA (Table 4-3).

In men, total CPD was correlated with the greatest number of health-related variables (Table 4-4). Total CPD was negatively associated with body weight, BMI, WC, percent body fat, and triglycerides, and positively associated with HDL cholesterol. In men, fasting glucose was negatively correlated with total MVPA, time spent in MVPA in bouts at least 10 min, and total bouts of MVPA in bouts at least 10 min. The only significant correlation found with sedentary behavior was a negative correlation with percent body fat. In men, no other physical activity subcomponents were significantly correlated with the health-related variables investigated.

In women, total CPD and total sedentary time were correlated with more health-related variables (Table 4-5) than were the other physical activity components. Total CPD was negatively correlated with body weight, BMI, WC, and percent body fat, and positively correlated with HDL cholesterol. Total sedentary time was positively correlated with body weight, BMI, WC, and percent body fat, and negatively correlated with HDL cholesterol. The number of sedentary periods lasting at least 30 min was positively correlated with SBP. No other significant relationships were found between PA subcomponents, including MPVA, and health-related variables in women.

Diabetes and Physical Activity Subcomponents

In this study population, only 7 participants had previously diagnosed T2D, while only 8 had diabetes discovered in the survey by fasting plasma glucose ≥126 mg/dl (3 participants) or a HbA1c ≥6.5% (5 participants). Therefore, the number of participants with diabetes was insufficient for meaningful analysis of associations with physical activity.

Modeling Health-Related Variables from Physical Activity Variables with Linear Regression – Expressing Standardized β Coefficients

Table 4-6 shows the standardized beta coefficients (SE) for modeling health-related variables from physical activity subcomponents. Total CPD was positively associated with HDL cholesterol and negatively associated with body weight, BMI, WC, percent body fat, and triglycerides. Sedentary time was negatively associated with HDL cholesterol and positively associated with BMI, WC, percent body fat, and triglycerides. MVPA was negatively associated with total cholesterol and fasting glucose.

Discussion

Physical activity is all activity performed throughout the day, including planned exercise and non-exercise activity. The subcomponents of physical activity that are most effective for staying healthy are unknown. Our research suggests that total activity (CPD), not MVPA or time spent sedentary, is the subcomponent most strongly associated with the health-related variables, including body weight, BMI, waist circumference, percent body fat, HDL cholesterol, and triglycerides. To our knowledge this study is novel in that we investigate the relationships of objectively measured MVPA, sedentary time, and total activity in CPD with a large number of health-related variables while others have only looked at the relationships of MVPA and time spent sedentary.

The physical activity recommendations from the WHO and DHHS focus on MVPA for improving health (1-2), however much of this evidence has been collected through self-report methods which can be biased. Our findings based on objectively measured physical activity do not support this recommendation. CPD was more strongly related to health variables than MVPA. In fact, MVPA was only associated with fasting glucose.

Many studies have shown a significant relationship between self-reported sedentary time (often TV watching, as a proxy for sedentary behavior) and an increased risk for all-cause mortality, CVD, and risk factors (12, 26-28). When sedentary time has been measured using objective measures, sedentary time was positively associated with fasting glucose, lipids, BMI, WC, percent body fat, blood pressure, and metabolic syndrome (8-11, 29-30). We found that total time spent sedentary (based on ACC counts) was positively associated with body weight, BMI, WC, percent body fat, and triglycerides and negatively associated with HDL cholesterol (Tables 4-3, 4-4, and 4-5). The lack of association that we observed between sedentary time and health-related variables like fasting glucose, blood pressure, and total and LDL cholesterol may in part be due to the way in which sedentary time is accumulated in this population. Healy et al. found that independent of total time spent sedentary, frequent breaks in sedentary behavior were beneficially associated with BMI, WC, triglycerides, and 2-hour plasma glucose (31). The remote subsistence lifestyle (hunting and gathering activities) of the people living in southwestern Alaska may promote frequent interruptions in sedentary activity, which may be why we do not see the negative associations of sedentary behavior on fasting glucose that is seen in other populations.

Total CPD (PAEE) accumulates through all forms of movement, including MVPA such as planned exercise as well as activities of self-care and non-planned physical activity of daily living. Non-exercise activity helps to maintain leanness (32-33) and is associated with changes in health-related variables that help to reduce the risk for metabolic related disease (34-37). It accounts for the daily activities that are not undertaken with the intent of "exercise". Non-exercise activities can be of any intensity. They accumulate and add to the energy expenditure above resting energy expenditure. Increases in activity would lead to increases in total CPD. Yup'ik people often report engaging in non-exercise activities like fishing, hunting, berry picking, or household work, and not "planned exercise." The activity of their subsistence lifestyle however, leads to increased CPD and increased PAEE.

Study Strengths and Limitations

Objectively measured heart rate and accelerometry for determining the subcomponents of physical activity, including MVPA, sedentary time, and CPD (PAEE) is a particular strength of this study. The finding that total activity in CPD is most strongly associated health-related variables is exciting; however it is acknowledged that this is a cross-sectional study in a single population which warrants future research of which investigates this relationship over time and in other populations.

Conclusions

Although current physical activity recommendations from the WHO and DHHS focus on recommendations that include the frequency, duration, and intensity of exercise, the positive health benefits found to be associated with non-exercise activities and our findings related to total CPD and MVPA time support the development of recommendations for increasing total movement, regardless of intensity.

Acknowledgements

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Table 4-1: Clinical Characteristics of Yup'ik People with Reliable Activity Measurements

	Units	Men	Women
N		248	286
Age *	years	37 (23, 51)	40 (25, 55)
Weight *	kg	70.1 (63.3, 81.0)	67.5 (58.6, 81.3)
Height *	m	1.69 (1.63, 1.73)	1.56 (1.52, 1.60)
BMI *	kg/m^2	24.3 (22.4, 29.2)	28.1 (24.0, 34.3)
Body fat *	%	18.7 (14.7, 26.4)	37.1(29.9, 42.6)
Fat free mass *	kg	56.8 (52.1, 61.2)	43.3 (40.6, 46.9)
Fat mass *	kg	12.5 (9.3, 20.5)	25.0 (17.1, 34.8)
Waist Circumference	cm	86.3 (78.4, 100.4)	90.0 (79.4, 102.0)
Total Cholesterol *	mg/dL	188 (159, 220)	195 (174, 226)
HDL Cholesterol *	mg/dL	55 (45.5, 68)	66 (55, 82)
LDL Cholesterol	mg/dL	110.2 (89.6, 143.1)	116.1 (93.2, 136.2)
Non-HDL Cholesterol	mg/dL	123.5 (103, 159)	130 (107, 154)
Triglycerides	mg/dL	60 (44, 92)	68 (46, 92)
Fasting glucose	mg/dL	92 (86, 99)	91 (87, 97)
Systolic BP *	mm/Hg	120 (112, 128)	113 (104, 124)
Diastolic BP	mm/Hg	69 (62, 75)	67(61, 75)

BMI = body mass index.

[1] Values listed are median (25^{th} centile, 75^{th} centile).

* Indicates that men and women differ significantly ($p<0.05$ by Wilcoxon's signed rank test).

Table 4-2: Physical Activity Characteristics of Yup'ik Participants

	Units	Men	Women
		248	286
Energy Expenditure	kcal		
PAEE CPD Model		1140 (961, 1370)	620 (493, 776)
REE		1692 (1591, 1827)	1412 (1310, 1545)
Activity			
Total activity *	1000 CPD	50.4 (34.9, 70.9)	32.6 (22.0, 43.4)
Total MVPA (based on HR) *	min/day	156 (68, 289)	100 (43, 227)
MVPA in bouts ≥ 10 min (based on HR) *	min/day	113 (48, 215)	66 (25, 166)
Total Sedentary time (based on ACC)	min/day	831 (741, 923)	848 (755, 922)
Sedentary time in bouts ≥ 30 min (based on ACC)	min/day	373 (277, 462)	399 (326, 466)
Total # of MVPA bouts ≥ 10 min	bouts/day	4.8 (2.0, 6.0)	2.9 (1.5, 5.0)
Total # of Sedentary periods ≥ 30 min	bouts/day	5.4 (4.5, 6.4)	5.3 (4.5, 6.2)

PAEE = physical activity energy expenditure, REE = resting energy expenditure, HR = heart rate, MVPA = moderate and vigorous physical activity, ACC = accelerometry , CPD = counts/day

[1] Values listed are median (25th centile, 75th centile).

* Indicates that men and women differ significantly at the alpha=0.05 level.

Table 4-3: Correlations of PA to Health-Related Variables in Yup'ik Men & Women Combined

Activity Measurements	body weight	BMI	WC	% body fat	total cholesterol	HDL	LDL	non-HDL cholesterol	triglyceride	glucose	syst bp	diast bp
Total Activity (counts/day)	***-0.23**** ***(-0.31, -0.14)***	***-0.20**** ***(-0.28, -0.12)***	***-0.21**** ***(-0.29, -0.13)***	***-0.22**** ***(-0.30, -0.14)***	0.003 (-0.09, 0.08)	***0.14**** ***(0.06, 0.23)***	-0.01 (-0.10, 0.07)	-0.06 (-0.15, 0.02)	***-0.14**** ***(-0.23, -0.06)***	-0.02 (-0.10, 0.07)	-0.07 (-0.16, 0.01)	-0.06 (-0.15, 0.02)
Total Sedentary time (min/day)	0.13* (0.04, 0.21)	0.09* (0, 0.17)	0.11* (0.03, 0.19)	0.12* (0.04, 0.2)	-0.02 (-0.11, 0.06)	-0.11* (-0.19, -0.02)	-0.01 (-0.10, 0.08)	0.02 (-0.06, 0.11)	0.09* (0.01, 0.18)	0.02 (-0.06, 0.11)	0.03 (-0.05, 0.12)	0.02 (-0.07, 0.10)
Sedentary time in periods ≥30 min (min/day)	0.02 (-0.07, 0.11)	-0.02 (-0.11, 0.06)	-0.01 (-0.01, 0.07)	-0.01 (-0.1, 0.07)	0.02 (-0.07, 0.10)	-0.02 (-0.10, 0.07)	0.03 (-0.06, 0.11)	0.02 (-0.06, 0.11)	-0.04 (-0.13, 0.04)	-0.07 (-0.15, 0.02)	0.003 (-0.09, 0.08)	-0.08 (-0.16, 0.01)
Total # of Sedentary periods ≥ 30 min (bouts/day)	0.03 (-0.06, 0.11)	0.01 (-0.08, 0.09)	0.02 (-0.07, 0.10)	0.05 (-0.04, 0.13)	-0.04 (-0.12, 0.05)	-0.04 (-0.13, 0.04)	-0.02 (-0.11, 0.07)	0.004 (-0.09, 0.08)	0.04 (-0.05, 0.12)	-0.02 (-0.11, 0.06)	0.04 (-0.05, 0.12)	0.06 (-0.03, 0.14)
Total MVPA (min/day)	-0.04 (-0.12, 0.05)	-0.02 (-0.11, 0.06)	-0.03 (-0.11, 0.06)	0.001 (-0.08, 0.09)	-0.03 (-0.11, 0.06)	-0.01 (-0.10, 0.08)	-0.01 (-0.09, 0.08)	-0.01 (-0.1, 0.07)	-0.06 (-0.14, 0.03)	-0.13* (-0.22, -0.05)	0.01 (-0.07, 0.10)	0.01 (-0.07, 0.10)
MVPA in bouts ≥10 min (min/day)	-0.0004 (-0.09, 0.09)	0.003 (-0.08, 0.09)	-0.002 (-0.09, 0.08)	0.03 (-0.06, 0.11)	-0.02 (-0.11, 0.06)	0.004 (-0.09, 0.08)	0.002 (-0.08, 0.09)	0.002 (-0.09, 0.08)	-0.05 (-0.14, 0.03)	-0.12* (-0.21, -0.04)	0.02 (-0.07, 0.11)	0.002 (-0.08, 0.09)
Total # of MVPA bouts ≥ 10 min (bouts/day)	-0.01 (-0.09, 0.08)	-0.01 (-0.1, 0.07)	-0.01 (-0.1, 0.07)	0.003 (-0.08, 0.09)	-0.01 (-0.10, 0.07)	0.01 (-0.08, 0.09)	0.01 (-0.08, 0.09)	0.002 (-0.08, 0.09)	-0.07 (-0.15, 0.02)	***-0.16**** ***(-0.24, -0.07)***	0.03 (-0.05, 0.12)	0.0006 (-0.08, 0.09)

N=531

* indicates significant correlation at alpha=0.05

PA = physical activity; BMI = body mass index; WC = waist circumference; MVPA = moderate-to-vigorous physical activity

Values listed for the continuous variables are Spearman's Correlation coefficients and 95% CI. Correlations between PA components and body size variables (body weight, BMI, WC, and percent body fat) are partialled for age, sex, and monitor wear time. Correlations between PA components and lipids, glucose, and blood pressures are partialled for age, sex, body weight, and monitor wear-time. The physical activity component that is significantly and most strongly correlated with a health-related variable is indicated by ***bold and italic*** text.

Table 4-4: Correlations of PA to Health-Related Variables in Yup'ik Men

Activity Measurements	body weight	BMI	WC	% body fat	total cholesterol	HDL	LDL	non-HDL cholesterol	triglyceride	glucose	syst bp	diast bp
Total Activity (counts/day)	-0.25* (-0.37 ,-0.13)	-0.19* (-0.31 ,-0.07)	-0.21* (-0.33 ,-0.09)	-0.18* (-0.30 ,-0.05)	-0.02 (-0.14 ,0.11)	0.13* (0.01 ,0.25)	0.003 (-0.13 ,0.12)	-0.06 (-0.19 ,0.07)	-0.17* (-0.29 ,-0.04)	0.02 (-0.11 ,0.14)	-0.06 (-0.18 ,0.07)	-0.09 (-0.21 ,0.04)
Total Sedentary time (min/day)	0.08 (-0.05 ,0.20)	0.02 (-0.11 ,0.14)	0.04 (-0.09 ,0.16)	-0.03 (-0.16 ,0.09)	-0.01 (-0.13 ,0.12)	-0.07 (-0.19 ,0.06)	-0.04 (-0.17 ,0.09)	-0.0009 (-0.13 ,0.13)	0.11 (-0.01 ,0.23)	0.01 (-0.12 ,0.13)	0.05 (-0.08 ,0.17)	0.04 (-0.09 ,0.16)
Sedentary time in periods ≥30 min (min/day)	-0.05 (-0.17 ,0.08)	-0.09 (-0.21 ,0.04)	-0.09 (-0.21 ,0.04)	-0.14* (-0.26 ,-0.02)	0.001 (-0.13 ,0.12)	0.03 (-0.09 ,0.16)	-0.03 (-0.16 ,0.10)	-0.03 (-0.15 ,0.10)	-0.06 (-0.18 ,0.07)	-0.05 (-0.17 ,0.08)	-0.02 (-0.15 ,0.11)	-0.07 (-0.19 ,0.06)
Total # of Sedentary periods ≥ 30 min (bouts/day)	-0.08 (-0.21 ,0.04)	-0.07 (-0.20 ,0.05)	-0.08 (-0.21 ,0.05)	-0.07 (-0.19 ,0.06)	0.005 (-0.12 ,0.13)	0.03 (-0.09 ,0.16)	-0.04 (-0.16 ,0.09)	-0.02 (-0.15 ,0.10)	0.03 (-0.09 ,0.16)	-0.02 (-0.15 ,0.10)	-0.03 (-0.16 ,0.09)	0.04 (-0.08 ,0.17)
Total MVPA (min/day)	0.004 (-0.13 ,0.12)	0.07 (-0.06 ,0.19)	0.05 (-0.07 ,0.18)	0.11 (-0.02 ,0.23)	-0.10 (-0.22 ,0.03)	0.04 (-0.09 ,0.17)	-0.09 (-0.22 ,0.03)	-0.10 (-0.22 ,0.03)	-0.09 (-0.21 ,0.04)	-0.18* (-0.29 ,-0.05)	-0.05 (-0.17 ,0.08)	-0.03 (-0.16 ,0.09)
MVPA in bouts ≥10 min (min/day)	0.04 (-0.08 ,0.17)	0.09 (-0.04 ,0.21)	0.08 (-0.05 ,0.20)	0.12 (-0.01 ,0.24)	-0.08 (-0.21 ,0.04)	0.05 (-0.08 ,0.17)	-0.07 (-0.20 ,0.05)	-0.08 (-0.21 ,0.04)	-0.10 (-0.23 ,0.02)	-0.18* (-0.30 ,-0.06)	-0.04 (-0.16 ,0.09)	-0.03 (-0.15 ,0.10)
Total # of MVPA bouts ≥ 10 min (bouts/day)	0.03 (-0.10 ,0.15)	0.05 (-0.07 ,0.18)	0.05 (-0.07 ,0.18)	0.08 (-0.05 ,0.20)	-0.05 (-0.17 ,0.08)	0.09 (-0.03 ,0.22)	-0.05 (-0.18 ,0.07)	-0.07 (-0.19 ,0.06)	-0.14 (-0.26 ,-0.01)	-0.24* (-0.36 ,-0.12)	-0.08 (-0.21 ,0.04)	-0.04 (-0.17 ,0.08)

N=245
* indicates significant correlation at alpha=0.05
PA = physical activity; BMI = body mass index; WC = waist circumference; MVPA = moderate-to-vigorous physical activity
Values listed for the continuous variables are Spearman's Correlation coefficients and 95% CI. Correlations between PA components and body size variables (body weight, BMI, WC, and %body fat) are partialled for age and monitor wear time. Correlations between PA components and lipids, glucose, and blood pressures are partialled for age, body weight, and monitor wear-time.

Table 4-5: Correlations of PA to Health-Related Variables in Yup'ik Women

Activity Measurements	body weight	BMI	WC	% body fat	total cholesterol	HDL	LDL	non-HDL cholesterol	triglyceride	glucose	syst bp	diast bp
Total Activity (counts/day)	-0.20* (-0.31 ,-0.09)	-0.19* (-0.30 ,-0.08)	-0.21* (-0.32 ,-0.10)	-0.20* (-0.31 ,-0.09)	0.02 (-0.10, 0.14)	0.15* (0.03, 0.26)	-0.03 (-0.15, 0.09)	-0.06 (-0.17, 0.06)	-0.10 (-0.22, 0.01)	-0.04 (-0.15, 0.08)	-0.07 (-0.18, 0.05)	-0.04 (-0.16, 0.07)
Total Sedentary time (min/day)	0.16* (0.05 ,0.27)	0.14* (0.03 ,0.25)	0.17* (0.06 ,0.28)	0.19* (0.07 ,0.30)	-0.02 (-0.14,0.10)	-0.13* (-0.24,-0.01)	0.03 (-0.09,0.15)	0.06 (-0.06,0.17)	0.08 (-0.04,0.20)	0.05 (-0.07,0.16)	0.01 (-0.10,0.13)	-0.01 (-0.13,0.10)
Sedentary time in periods ≥30 min (min/day)	0.07 (-0.05 ,0.18)	0.05 (-0.07 ,0.17)	0.07 (-0.05 ,0.18)	0.07 (-0.04 ,0.19)	0.04 (-0.08,0.15)	-0.07 (-0.18,0.05)	0.09 (-0.02,0.21)	0.09 (-0.03,0.2)	-0.01 (-0.12,0.11)	-0.08 (-0.19,0.04)	-0.01 (-0.13,0.11)	-0.08 (-0.2,0.03)
Total # of Sedentary periods ≥ 30 min (bouts/day)	0.10 (-0.02 ,0.21)	0.05 (-0.06 ,0.17)	0.08 (-0.04 ,0.19)	0.09 (-0.03 ,0.20)	-0.07 (-0.18,0.05)	-0.10 (-0.22,0.01)	0.0002 (-0.12,0.12)	0.02 (-0.10,0.14)	0.04 (-0.08,0.16)	-0.01 (-0.13,0.10)	0.13* (0.02,0.25)	0.06 (-0.05,0.18)
Total MVPA (min/day)	-0.06 (-0.18 ,0.05)	-0.11 (-0.22 ,0.01)	-0.10 (-0.22 ,0.01)	-0.06 (-0.18 ,0.05)	0.004 (-0.11,0.12)	-0.03 (-0.14,0.09)	0.04 (-0.08,0.16)	0.04 (-0.07,0.16)	-0.05 (-0.16,0.07)	-0.11 (-0.22,0.01)	0.02 (-0.10,0.14)	0.03 (-0.09,0.14)
MVPA in bouts ≥10 min (min/day)	-0.04 (-0.15 ,0.08)	-0.08 (-0.20 ,0.04)	-0.08 (-0.20 ,0.03)	-0.03 (-0.15 ,0.08)	0.002 (-0.11,0.12)	-0.03 (-0.15,0.08)	0.05 (-0.07,0.17)	0.05 (-0.07,0.17)	-0.03 (-0.15,0.09)	-0.08 (-0.19,0.04)	0.04 (-0.08,0.15)	0.004 (-0.11,0.12)
Total # of MVPA bouts ≥ 10 min (bouts/day)	-0.04 (-0.15 ,0.08)	-0.08 (-0.20,0.03)	-0.08 (-0.19 ,0.04)	-0.03 (-0.15 ,0.08)	0.004 (-0.12,0.11)	-0.04 (-0.16,0.07)	0.04 (-0.07,0.16)	0.05 (-0.07,0.16)	-0.03 (-0.14,0.09)	-0.10 (-0.21,0.02)	0.08 (-0.03,0.20)	0.02 (-0.10,0.14)

N=286

* indicates significant correlation at alpha=0.05

PA = physical activity; BMI = body mass index; WC = waist circumference; MVPA = moderate-to-vigorous physical activity

Values listed for the continuous variables are Spearman's Correlation coefficients and 95% CI. Correlations between PA components and body size variables (body weight, BMI, WC, and %body fat) are partialled for age and monitor wear time. Correlations between PA components and lipids, glucose, and blood pressures are partialled for age, body weight, and monitor wear-time.

Table 4-6: Associations of PA and Health-Related Risk in Yup'ik People

Dependent	Total Activity (counts/day)	MVPA (min/day)	Sedentary time (min/day)
	Standardized β coefficient (SE)		
Weight (kg)	-0.280 (0.049)*	-0.035 (0.048)	0.193 (0.054)*
BMI (kg/m^2)	-0.238 (0.047)*	-0.032 (0.045)	0.165 (0.052)*
Waist Circumference (cm)	-0.252 (0.048)*	-0.026 (0.046)	0.166 (0.053)*
Body fat (%)	-0.171 (0.036)*	0.006 (0.034)	0.105 (0.039)*
Total cholesterol (mg/dL)	-0.014 (0.046)	-0.085 (0.042)*	-0.051 (0.049)
HDL cholesterol (mg/dL)	0.095 (0.044)*	-0.062 (0.040)	-0.112 (0.046)*
LDL cholesterol (mg/dL)	-0.021 (0.048)	-0.062 (0.044)	-0.036 (0.051)
Non-HDL Cholesterol (mg/dL)	-0.058 (0.047)	-0.059 (0.043)	-0.002 (0.050)
Triglycerides (mg/dL)	-0.148 (0.047)*	-0.016 (0.044)	0.113 (0.051)*
Glucose (mg/dL)	0.002 (0.049)	-0.090 (0.045)*	0.008 (0.052)
SBP (mm Hg)	-0.042 (0.047)	0.024 (0.043)	0.017 (0.050)
DBP (mm Hg)	-0.063 (0.048)	0.004 (0.044)	0.023 (0.052)

N= 531
CPD = counts per day; MVPA= total time (min) of moderate and vigorous physical activity; PAEE = physical activity energy expenditure; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure.
* indicates significant at alpha=0.05
Age, sex, and monitor wear time were included as covariates in all models. Models for cholesterols, triglycerides, glucose, and blood pressure also included body weight in addition to age, sex, and monitor wear time as covariates. Each column (i.e., each activity measure) represents results of models with that variable alone as the dependent variable, without adjustment for the other activity measures.

5 General Conclusions

This dissertation had two primary goals: 1) To assess the validity of low cost, transportable and effective tools for estimating body composition and free-living physical activity in Yup'ik adults who live in remote regions of Southwest Alaska; and 2) to investigate the relationships between body composition and physical activity with health-related and disease variables in this study population.

Reliable, accurate, and cost effective methods to assess body composition and physical activity are essential to understand risk and protective factors for obesity-related metabolic disorders and to design culturally appropriate interventions. Obesity and inactivity often lead to the development of chronic disease. Identifying individuals at increased risk for developing chronic disease is important in order to improve their ultimate health outcomes.

Chapter 1 includes an introduction and background for the research in this dissertation. It outlines the problem of obesity, briefly describes current methods which are available for determining body composition and for measuring physical activity, and lays out the research goals.

Chapter 2 focuses on body composition estimation and the relationship between body composition and health-related variables. Simple measurements including body mass index (BMI), waist circumference (WC), hip circumference, and skin fold measurements are often used as a proxy for evaluating adiposity. In this chapter, we verify that these proxy measurements are accurate for evaluating adiposity by comparing them to body composition estimates from the doubly-labeled water method. We also investigate the associations of simple proxy measurements with health-related and disease variables and compare their associations with more complex measurements of body composition. Body composition can be reliably estimated using simple measurements, including WC, hip circumference, and sex (model R^2=0.973), making anthropometry a practical method for use in remote areas where access to heavy and expensive equipment is not feasible. The health-related variables investigated included: 1) fasting plasma lipids, 2) fasting glucose, 3) HbA1c, 4) adiponectin, and 5) blood pressure. Disease status variables included diabetes (DM) and cerebrocoronary vascular disease (CCVD) which includes stroke and heart disease. We find that the simple (proxy) body measurements of WC and BMI are more strongly correlated with the health-related and disease variables than are the estimates of body composition (fat free mass, fat mass, and percent body fat) from bioelectrical impedance or linear regression. This is an important finding for researchers and health care professionals, as it gives assurance that the simple measurement of WC can identify those who may be at risk for developing chronic disease.

Chapter 3 focuses on determining the accuracy of a combined movement and heart rate monitor (Actiheart), to objectively assess physical activity energy expenditure (PAEE) among Yup'ik adults. Actiheart PAEE estimates are compared with PAEE estimates derived from the doubly labeled water method (DLW). In this work we investigated the association of PAEE from the Actiheart and DLW that is not due to age, sex, or body size. PAEE estimates from the Actiheart monitor do not accurately estimate free-living PAEE in Yup'ik people when compared with DLW PAEE. Total accelerometry (ACC) counts per day (CPD) however, was more strongly, and significantly, correlated with DLW PAEE than were any of the Actiheart PAEE models. Use of the Actiheart may have important limitations, including incorrect PAEE estimates, which should be recognized by researchers who plan to use it for individual consultation and interventional studies. If PAEE estimates are desired, using total CPD as a proxy for PAEE is suggested. However, using the PAEE information from the Actiheart software to address energy balance issues for individuals may be inappropriate because of the potential for large discrepancies from the true PAEE value.

Although the Actiheart may not be ideal for estimating PAEE, it does provide important features for assessing physical activity behavior. The Actiheart can be used to assess duration, frequency, and intensity of physical activity as well as an estimate of fitness and sleep duration. The relationship between these subcomponents of physical activity and health-related variables is not well understood. The ability to differentiate between these subcomponents of physical activity will enable researchers to identify which physical activity subcomponents are most influential in staying healthy.

In Chapter 4, we evaluate how the subcomponents of physical activity are associated with health-related variables. The Actiheart is used to evaluate total CPD, moderate-to-vigorous physical activity (MVPA), and sedentary time. Total CPD is more strongly associated with body weight, BMI, WC, percent body fat, HDL cholesterol and triglycerides than are MVPA or time spent sedentary. Higher CPD can be accumulated through maintaining frequent low intensity activity, through less frequent but higher intensity bouts of activity, or both. The finding that total activity, measured in CPD, is the physical activity component most strongly associated with health-related variables is in contrast to the World Health Organization (WHO) and the Dept. of Health and Human Services (DHHS) recommendations, which focus on the accumulation of 150 minutes/week of MVPA (1,2). Our results suggest that increasing regular movement of any intensity greater than resting may be a more important public health target than focusing on 150 minutes/week of MVPA.

The scope of this dissertation provides the foundation for future longitudinal and interventional studies related to the role that body composition and physical activity play in health outcomes of Yup'ik people. Further, this research highlights an important finding that may be relevant for all people, that movement of any type, regardless of intensity, may be more important for metabolic and cardiovascular health than MVPA. Most research in this field looks at the impact of MVPA and sedentary behavior on metabolic and cardiovascular health, but our research argues for rigorously designed, longitudinal studies investigating the impact of total movement in CPD on metabolic and cardiovascular health.

Highlighting the active lifestyle of Yup'ik people, and how total CPD is associated with health, may be relevant to the health of other cultures. Based on our study sample, the Yup'ik people far exceeding the physical activity recommendations from the WHO and DHHS of 150 minutes per week of MVPA. Living a rural subsistence lifestyle provides numerous opportunities to increase total CPD while performing normal daily activities. Future research should be directed at physical activity education and interventions in an attempt to prevent chronic diseases such as type 2 diabetes, heart disease, and stroke in Yup'ik people.

References

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