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The Relationship Between Pediatric Asthma and Obesity in Nevada

Jennifer Anne Lucas
University of Nevada, Las Vegas, lucasj23@unlv.nevada.edu

THE RELATIONSHIP BETWEEN PEDIATRIC ASTHMA AND OBESITY IN NEVADA

By

Jennifer Anne Lucas

Bachelor of Arts – Journalism
Metropolitan State College of Denver
2006

Master of Public Health
University of Nevada, Las Vegas
2012

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Jennifer Anne Lucas

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Department of Environmental and Occupational Health

Sheniz Moonie, Ph.D.
Examination Committee Chair

Kathryn Hausbeck Korgan, Ph.D.
Graduate College Interim Dean

Shawn Gerstenberger, Ph.D.
Examination Committee Member

Mary Beth Hogan, M.D.
Examination Committee Member

Alona Angosta, Ph.D.
Graduate College Faculty Representative

ABSTRACT

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Asthma and Obesity in Nevada

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Asthma and obesity are two of the most common comorbid health problems in the U.S. Currently nearly 8% of Nevada youth are affected by asthma and more than 30% are overweight or obese. Obesity is a risk factor for asthma, yet asthma-related factors such as decreased physical activity and use of oral corticosteroids for asthma control can lead to obesity. This study examined the relationship between asthma and obesity in two pediatric populations in Nevada. It was hypothesized that children with asthma and elevated BMI would have more severe asthma symptoms, decreased lung function, poorer quality-of-life measures, and different atopic profiles than those with a BMI in the healthy weight category. This was evaluated using pilot data collected from a University of Nevada, School of Medicine pediatric allergy/immunology clinic in Reno, NV. This study also evaluated whether or not a 12-week physical activity intervention is feasible to complete for pediatric overweight/obese who have asthma compared with overweight/obese without asthma. Weight loss in youth who have asthma has been shown to improve asthma control and lung function. Intervention data were obtained from medical records at the Children's Heart Center (CHC) Nevada Healthy Hearts Program (HHP) in Las Vegas. Statistical analyses included descriptive statistics, multivariable binary and multinomial logistic regression, Cox regression, and one-way and repeated measures analyses of variance. The Reno population (N=125) had a median age of 7 years old, was 61% male, 65% white, and nearly one-third were overweight or obese. Main findings showed that obese youth with asthma had higher odds of having severe asthma than those at healthy weight, though not significantly higher (p=0.162). Lung function was not different among BMI percentile groups, yet those who were obese did have nearly 8 times higher odds of needing oral steroids for asthma control than those who were healthy weight (p=0.003). Children who were overweight had 79% lower odds of allergen sensitization (aOR 0.21, p=0.010). The CHC population (N=232) had a mean

age of 11 years, 54% male, 64% Hispanic, and 37% had asthma. Crude analyses of the HHP population showed that BMI did decrease significantly among those with asthma (p=0.002) and without asthma (0.001) from pre- to post-intervention. Cardiorespiratory health increased significantly among girls (p=0.004) and boys (p=0.003) who have asthma, as well as among both girls (p=0.001) and boys (p=0.001) without asthma. Multivariable analysis demonstrated no difference in attrition between those with and without asthma (p=0.300), and no difference in weight loss (p=0.951) or cardiorespiratory health (males, p=0.263, females, p=0.655) between participants with and without asthma, indicating that this intervention was feasible for asthmatics to complete as a form of physical activity engagement and weight management. These results show that obese youth had poorer asthma control than healthy weight children as evidenced by oral steroid use at the initial visit to the clinic, and a high degree of allergen sensitization among the entire population, although lower among overweight children. It is important to make sure all children with asthma in Nevada are tested for allergen sensitization regardless of weight status. Mean BMI decreased and VO2 max increased indicating that this program was also beneficial in improving respiratory outcomes for youth who have asthma. Future studies may be conducted to expand this intervention in order to determine the efficacy of physical activity, weight reduction and lung function improvement among a larger clinical population of asthmatics.

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CHAPTER 1. INTRODUCTION

Purpose of the Study

Asthma is a chronic inflammatory respiratory disease in which airflow to and from the lungs is restricted or limited. Asthma currently affects 300-334 million people worldwide, and in the United States, the disease burdens more than 25 million people, including nearly 7 million youth (those under age 18) (Asher & Pearce, 2014; Moonie, Seggev, Shan, Pergola, & Teramoto, 2014; National Heart, Lung, and Blood Institute [NHLBI], 2007; & NHLBI, 2014). Overweight and obesity are associated with the development of pediatric asthma. Additionally, obese people with asthma are more likely to have more asthma symptoms, more severe symptoms, and require increased healthcare utilization (Black, Zhou, Takayanagi, Jacobsen, & Koebnick, 2013; Dixon et al., 2010; Porter et al., 2012; Sutherland, 2014). The current National Health and Nutrition Examination Survey (NHANES) data from 2011-2012 show 31.8% of U.S. 2-19 year olds have a body mass index (BMI) at or above the 85th percentile (considered overweight or obese), and 16.9% have a BMI at or above the 95th percentile (obese) based on Centers for Disease Control and Prevention (CDC) growth charts (Ogden, Carroll, Kit & Flegal, 2014). While the literature has shown obesity is a risk factor for asthma (Dixon et al., 2010; NHLBI, 2007), factors related to asthma, such as decreased physical activity and use of corticosteroids for asthma control have also been found to be potential risk factors for developing overweight or obesity (Abd El-Kader, Al-Jiffri, & Ashmawy, 2010; Lang, 2014; NHLBI, 2007).

Atopy is a genetic predisposition to develop allergies (American Academy of Allergy, Asthma, & Immunology [AAAAI], 2015b). Allergies are present in the majority of those who have asthma (approximately 80%) (Cohn, Elias, & Chupp, 2004). In Nevada, very little research has been done regarding aeroallergen sensitization, but Wong, Wilson, Peele, and Hogan (2012) found youth in Nevada become sensitized at very young ages, and to allergens not seen in the rest of the country. Early sensitization can be a predictor of wheezing, which is a risk factor for asthma (Wong et al., 2012).

Analysis of NHANES data found outdoor aeroallergen sensitization is highest in the Western U.S. (Salo et al., 2014).

Study Goals

This study has two goals. The first is to examine relationships between asthma/allergy and obesity in two pediatric Nevada populations to determine how these two common conditions are associated with each other. It is hypothesized that pediatric asthma patients with high Body Mass Index (BMI) will have more severe asthma symptoms, decreased lung function, and poorer quality-of-life and financial cost measures compared to those who are at a healthy weight. It is also hypothesized that allergen sensitization as measured by skin prick tests will differ between those who have an elevated BMI and those at healthy weight.

The second goal is to evaluate a 12-week physical activity intervention for pediatric patients to determine if it is feasible for overweight/obese youth with asthma compared to overweight/obese youth without asthma. It is hypothesized that the intervention may not be as feasible for those who have asthma due to respiratory stress, as measured by time in the program, as well as pre- and post- intervention clinical indicators.

Significance of the Study

The unique arid climate and wind patterns in the Great Basin region, which includes both Reno and Las Vegas, contribute to the growth and dispersion of aeroallergenic flora not found in other areas in the U.S. These allergens can increase wheezing and other allergic symptoms that contribute to the development and exacerbation of asthma (Jewell & Nicoll, 2011; Wong et al., 2012).

More than 20 states are included in the Centers for Disease Control and Prevention's (CDC) National Asthma Control Program (NACP). Nevada is not one of the included states although the rates are comparable to the nation. The goal of the NACP is to help the "millions of people with asthma in the United States gain control over the disease" (CDC, 2015b). The NACP helps to improve asthma

surveillance at local and state levels, and to help educate people with asthma, and the general public about the disease. State level data are provided regarding treatment, management, and control of asthma (CDC, 2015b). Until Federal funding becomes available for the addition of new states, Nevada does not have the opportunity to benefit from this federal-level surveillance and education. Consequently, asthma research is needed in Nevada until the occasion arises to work with the Nevada Division of Public and Behavioral Health (DPBH) to seek funding from the CDC's NACP.

Adult and adolescent overweight and obesity rates in Nevada are comparable to the national rates (Division of Nutrition, Physical Activity and Obesity [DNPAO], 2015). However, 4-6 year olds in Nevada have been found to have high rates of obesity: 19.0% of those entering kindergarten in 2013 were obese, up from 18.2% in 2012. In the past year, this number has increased: 21.7% of those entering kindergarten in 2014 were obese (Nevada Institute for Children's Research and Policy [NICRP], 2014; NICRP, 2015). Data from the National Survey of Children's Health shows that among Nevadans aged 10-17 years, 18.6% are obese, which is slightly above the national average of 15.7% (Data Resource Center for Child and Adolescent Health [DRC], 2012).

Asthma and obesity are comorbid disorders, but since they are both complex disorders with multiple causes it is complex to understand if one actually causes the other. Obesity is a known risk factor for the development and severity of asthma (Dixon et al. 2010). Additionally, treatments that have been used for decades to control asthma are not always effective in those with elevated BMI (Forno et al., 2011).

Weight loss has been shown to improve lung function, and asthma severity, yet asthmatic children who struggle with breathing during exercise are a complex population to implement successful exercise interventions. Young asthma patients tend to avoid physical activity and report that symptoms interfere with all types of physical activity. Additionally, parental restriction of exercise in children with shortness of breath is not uncommon (Ostrom et al. 2013; Wanrooij, Willeboordse, Dompeling & van de Kant, 2014; Westergren et al., 2015). However, when young asthmatics do lose weight symptoms

improve, including exercise-induced bronchoconstriction (EIB) (Abd El-Kader et al., 2010; van Leeuwen, Hoogstrate, Dulverman, & Thio, 2014).

One of the objectives of this research project is to evaluate a pre-existing weight loss intervention among young patients with elevated BMI, and to determine if asthmatic youth with elevated BMI in Nevada can benefit and successfully complete the intervention. Previous studies have found exercise interventions are effective for weight loss for obese asthmatic youth It is important to determine the feasibility and efficacy of this intervention among a pilot population of children with asthma and elevated BMI in order to increase outreach to this clinical population. Asthma and obesity are two of the most common health problems that youth currently face. To our knowledge this research has not yet been attempted in Nevada. Finding a feasible intervention to moderate the high obesity and asthma rates in Nevada's youth could bring awareness to Nevada, as well as assist in securing federal funding.

CHAPTER 2. LITERATURE REVIEW

Asthma

Pathophysiology

The word "asthma" originates from a Greek word meaning "to gasp for breath" or "to pant heavily" (McFadden, 2004). Asthma is a common chronic respiratory condition characterized by airway inflammation, obstruction, and hyperresponsiveness, with a number of symptoms including, but not limited to wheezing, breathlessness, and cough. The severity and recurrence of these signs and symptoms varies greatly among asthma patients (Asher & Pearce, 2014; Cohn, et al., 2004; NHLBI, 2007; NHLBI 2014; & WHO, 2013). Numerous genetic and environmental factors contribute to the development and progression of asthma. Asthma has two forms: allergic, which affects approximately 80% of those with asthma, and non-allergic which is primarily genetic in origin (Busse & Lemanske, 2001; Cohn et al. 2004).

Airway inflammation and airflow obstruction occur in all people with asthma. Limited airflow is caused by inflammation and changes in the airway, including bronchoconstriction, airway wall thickening, edema and excess mucus secretion, airway remodeling, and airway hyperresponsiveness. Bronchoconstriction is a narrowing of the airways in response to inflammation caused by inhaled irritants to smooth muscle (Novak & Bieber, 2003; NHLBI, 2007). The walls of the airway thicken when mucus mixes with inflammatory cells, which leads to smaller airways, and edema. Airway remodeling refers to structural changes to the airway, including the thickening of airways walls and increases in tissue mass which can become permanent and cause decline in lung function. These structural changes are likely due to damage to structural cells after inflammatory responses (Busse & Lemasnske, 2001; Cohn et al., 2004; NHLBI, 2007). Inflammation and airway remodeling lead to airway hyperresponsiveness, an increased response to stimuli in which bronchoconstriction occurs (Cohn et al., 2004; NHLBI, 2007).

Irritants that cause inflammation can include many allergens. Allergic (or atopic) asthma is generally characterized by sensitization to allergens, positive skin-prick tests to specific allergens and elevated Immunoglobulin E (IgE) antibody levels in response to the allergens. Approximately 80% of asthmatics are allergic (Busse & Lamanske, 2001; Novak & Bieber, 2003; Cohn et al., 2004; Raedler et al., 2015). IgE antibodies, which are responsible for allergic reactions, act together with inflammatory cells in the pathogenesis of allergic diseases and asthma (Galli & Tsai, 2012; NHLBI, 2007). Multiple inflammatory cells play roles in the development of airway inflammation, including mast cells, eosinophils, and lymphocytes. Inflammatory mediators, such as cytokines, (signaling proteins), also influence airway inflammation in asthma patients (NHLBI, 2007).

Mast cells, which originate in bone marrow and travel to the mucosal areas of airways, have IgE receptors, to which IgE antibodies bind. After exposure to IgE antigens, the mast cells are activated and release bronchoconstrictor facilitators such as histamine, which elicit allergic reactions. Activation of mast cells can also occur without IgE, which may lead to exercise-induced bronchospasm (Busse & Lemanske, 2001; NHLBI, 2007). Knock-in mouse studies have shown that IgE and mast cells are a factor in chronic airway inflammation, and in turn, may influence airway remodeling (Galli & Tsai, 2012). Mast cells also release cytokines, in this case to promote inflammation (NHLBI, 2007).

The connection between asthma and eosinophils has been recognized since 1908, when a physician found excess quantities of eosinophils in the airways of patient who died of an asthma attack (Ellis, 1908). Eosinophils, which are markers for inflammatory activity and regulated by cytokines, are often found in greater numbers in the airways of those who suffer from asthma than those who do not have asthma (Cianchetti et al., 2013; NHLBI, 2007). Eosinophils are believed to be the primary effector cells in asthma and persistent airway inflammation, meaning they are likely the main cells to mediate the removal of antigens or other causes of inflammation (Coico & Sunshine, 2015; Grotta et al., 2013; NHLBI, 2007).

More recently, lymphocytes known as T helper 1 cells (Th1) and T helper 2 cells (Th2) have been associated with asthma (McFadden, 2004; Robinson, 2010). Th1 and Th2 cells are believed to play a role in airway inflammation. Specifically, Th1 cells produce regulatory cytokines and mediate anaphylactic reactions. Th2 cells produce cytokines that promote inflammation by activating effector cells involved in allergen response (Busse & Lemanske, 2001; Coico & Sunshine, 2015). Th2 cytokine production may also lead to IgE antibody production, excess eosinophils, and development of airway hyperresponsiveness (Coico & Sunshine, 2015; NHLBI, 2007). Currently, research investigating T-cell subtypes and biomarkers with the goal of creating new asthma therapies targeting Th2 cytokines and inflammation is ongoing (Jia et al., 2012; Robinson, 2010).

Pathogenesis and Risk Factors

The pathogenesis of asthma is complicated and not definitive. The main factors in asthma pathogenesis are genetics (or host factors) and environmental exposures. Asthma is known to have genetic factors, but there is very little literature regarding pathogenesis (NHLBI, 2007; Olin & Wechsler, 2014). Candidate gene studies, in which researchers look for specific genes, and genome wide studies, in which entire genomes are examined, are approaches some researchers believe will help determine the pathogenesis of asthma. Additionally, twin studies have shown that asthma may be 60% heritable (Ober & Yao, 2011; Olin & Wechsler, 2014).

Other genetic factors include innate and adaptive immunity. Innate immunity refers to the mechanisms of the immune system people are born with, which provide quick response to foreign agents in the body. Adaptive immunity occurs when specific antigens activate B and T cells. The adaptive immune system forms memory responses to these antigens to create immunity (Coico & Sunshine, 2015; NHLBI 2007). Presently, immunological research on asthma pathogenesis includes Th1 and Th2 cytokine profiles, and the "hygiene hypothesis." With regard to asthma, the hygiene hypothesis may show how the imbalance of Th1 and Th2 cytokines may explain high asthma prevalence in developed

countries (Asher, 2014; NHLBI, 2007). This cytokine balance weighs protective factors, which favor Th1 phenotype against allergic diseases, which favor Th2 phenotype (Figure 1) (Busse & Lemanske, 2001; NHLBI, 2007). Robinson (2010) discusses the hygiene hypothesis using animal models, which have shown cytokines, rather than antigens activate certain memory T cells during some infections, which may explain why infections early in life can protect against allergic diseases. Epigenetic studies have shown changes in Th1 and Th2-associated genes after allergen exposure in mice (Olin & Wechsler, 2014).

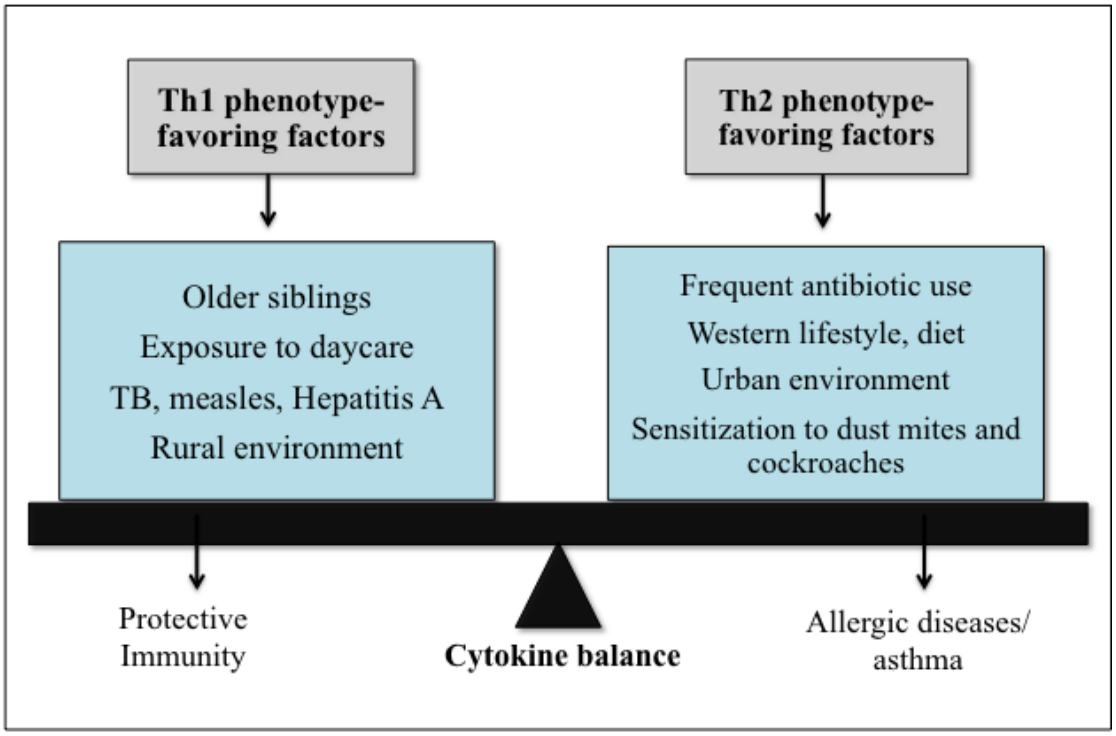

Figure 1. Cytokine Balance (Adapted from Busse & Lemanske, 2001)

Multiple environmental factors are associated with the development and severity of asthma. Allergens are associated with asthma – for example, some research has shown exposure to pets at early ages is protective, but other studies have shown the opposite. Other allergens have been shown to be risk factors for development of asthma, such as cockroaches, and dust mites (NHLBI, 2007). Approximately 20% of asthma diagnoses can be attributed to severe respiratory syncytial virus (RSV) in infancy, according to Olin & Wechsler (2014). Viral respiratory infections such as parainfluenza virus and some

rhinoviruses can also be risk factors for wheeze or asthma. Other possible risk factors for asthma include tobacco smoke and pollution (NHLBI, 2007; Ober & Yao, 2011).

Sociodemographic factors are also risk factors for developing asthma. Boys have higher risk for asthma than girls, however in adulthood, women are more likely to have asthma than men (NLHBI, 2014). Some research shows youth who live in urban areas ("inner-city") have higher risk for asthma due to more frequent exposure to respiratory infections from over-crowding, poor nutrition, and indoor air pollution, although socioeconomic status (SES) likely plays a larger role than urban or rural living in the development of asthma (Keet et al., 2015; Priftis, Mantzouranis, & Anthracopoulos, 2009).

Asthma risk also differs with regard to race and ethnicity in the U.S. Puerto Rican youth have the highest rates of asthma among any race or ethnicity in all U.S. states and territories (American Lung Association, 2011; Lara, Akinbami, Flores, & Morgenstern, 2006; Lara, Ramos-Valencia, Diaz, Reyes, & Gonzalez-Gavillán, 2014). Asthma prevalence rates are highest in Puerto Rican Island-born youth and Puerto Rican youth born in the contiguous states (Cohen et al. 2007; Keet et al., 2015; Lara et al. 2006). Black non-Hispanic youth also have higher risk of asthma compared to white non-Hispanics and Mexican-American youth (Akinbami, Moorman, & Liu, 2011; Keet et al., 2014; NHLBI, 2007).

Allergy and Atopy as Predictors for Asthma

Asthma is an allergic disease in approximately 80% of cases (Cohn et al., 2004; Novak & Bieber, 2003). The allergic triad is the association between asthma, allergic rhinitis (hay fever), and atopic dermatitis. These three conditions occur early in childhood, beginning with atopic dermatitis, and then allergic rhinitis and asthma – this orderly fashion of allergic manifestations is known as atopic march (Ober & Yao, 2011). Sensitization to two or more allergens is known as polysensitization (Migueres et al. 2014). Salo and colleagues found that allergen sensitization to outdoor aeroallergens, in particular grasses and Russian thistle weeds, is highest in the Western U.S. after analyzing NHANES data from 2005-2006 (Salo et al., 2014).

Wheezing is a risk factor for the development and exacerbation of asthma (Asher, 2014; Wong et al., 2012) Martinez et al., (1995) found in a prospective cohort study, the Tucson Children's Respiratory Study, that those with persistent wheezing within the first 9 months of life had significantly elevated IgE levels, however those levels were not associated with wheezing later in life. They also found some infants who wheeze might be predisposed to developing asthma (Martinez et al. 1995). Using data from the same longitudinal study, Castro-Rodriguez, Holberg, Wright, & Martinez (2000) created an Asthma Predictive Index to define risk of developing asthma in children who had persistent wheezing in the first three years of life. The index included wheezing, and one major risk factor or two-three minor risk factors. Major risk factors included parental history of asthma or eczema. Minor risk factors included eosinophilia, wheezing between colds, and allergic rhinitis (Castro-Rodriguez et al., 2000). They were able to predict asthma 59-76% of the time, and the specificity of the index was more than 95% (Castro-Rodriguez et al., 2000). The Asthma Predictive Index, as well as other predictive indices, which were later developed, are currently used to try to determine whether a child will develop asthma (Castro-Rodriguez, 2010).

Clinical Presentation of the Disease

Asthma symptoms are different for each person, and they vary in severity and occurrence. The most common symptoms are wheeze, shortness of breath, tightness in the chest, and cough. Common asthma symptoms are more likely to occur at night or early in the morning, or during physical activity, and are due to airway inflammation and changes to the airway, as mentioned above (NHLBI, 2007; NHLBI, 2014; WHO, 2013). These airway changes manifest by hyperplasia (increased tissue due to increased cell production) and hypertrophy (increased muscle size) of the airway wall smooth muscle, edema and excess mucus, permanent structural changes, bronchoconstriction (narrowing of the airways due to stimuli response), and airway hyperresponsiveness (Novak & Bieber, 2003; NHLBI, 2007).

When symptoms become more intense or more symptoms occur acutely, this is known as exacerbation (also called an asthma attack). This acute presentation of symptoms leads to swelling in

airways and bronchospasm, which require emergency bronchodilator medication. As symptoms increase they can also worsen, and exacerbations can be fatal (NHLBI, 2007; NHLBI, 2014; WHO, 2013). Common triggers for asthma symptoms and exacerbations include indoor and outdoor allergens (dust mites, pollens, mold, pet dander, cockroaches), exercise, environmental tobacco smoke, air pollution, and chemicals (NHLBI, 2007; WHO, 2013).

Diagnosis

Asthma is an under-diagnosed illness, especially in young people (Bitsko, Everhart & Rubin, 2014; NHLBI, 2007; WHO, 2013). However, it can also be misdiagnosed in youth who have exercise-induced shortness of breath or non-asthmatic wheeze or cough (Bitsko et al., 2014; NHLBI, 2007). Asthma diagnoses can also vary among populations and locations due to factors such as awareness of the disease, medical training, and cultural factors (Asher & Pearce, 2014). Asthma has no single cause; therefore, diagnosis is based on multiple factors including physical examination and clinical presentation of symptoms, medical history, and pulmonary function tests (Hargreave & Nair, 2009; NHLBI, 2007; Ober & Yao, 2012).

The Guidelines for the Diagnosis and Treatment of Asthma, Expert Panel Report 3 (EPR-3) is a guide for medical professionals in clinical practice of asthma care. The National Heart Lung and Blood Institute (NHLBI) and National Asthma Education and Prevention Program (NAEPP) coordinated the development of the report, and commissioned an expert panel (NHLBI, 2007). For the 3rd, most current revision of the report the expert panel conducted a current systematic review of the literature to reflect the greater understanding of asthma, and newer approaches to treatment since the previous version. The expert panel also updated recommendations for clinicians (NHLBI, 2007).

To diagnose asthma, clinicians will determine whether or not airway obstruction symptoms exist, determine whether or not the obstruction is at least partially reversible, meaning the airways respond to bronchodilator medication, and exclude other (differential) diagnoses. A number of indicators may be

considered for an asthma diagnosis: wheezing, increased or worsening symptoms in the presence of multiple triggers (allergens, air pollutants, physical activity, weather, emotional exposure) or at night, as well as history of recurring cough, tightness in the chest, and difficulty breathing (NHLBI, 2007). Atopic dermatitis is not considered to be a key indicator in asthma diagnosis, but may increase the probability of an asthma diagnosis. Medical history can also help in diagnosing asthma as noted above with recurring symptoms. Family history of allergy and asthma is important, since asthma is known to be somewhat genetic (NHLBI, 2007; Olin & Wechsler, 2014).

Pulmonary function tests (spirometry) are also used in diagnosis of asthma. These tests provide an objective, quantitative measure for airway obstruction by using a tool called a spirometer to test how much and how fast air can be inhaled and exhaled before and after use of a bronchodilator (NHLBI, 2014). Spirometry measurements used include forced expiratory volume in 1 second (FEV_1), the ratio of forced expiratory volume and forced vital capacity (FEV_1/FVC), and forced expiratory volume in 6 seconds (FEV_6) (Hargreave & Nair, 2009; NHLBI, 2007). FEV_1 is used to measure large airway volume (Spaulding, Devine, Duncan, Wilson & Hogan, 2012). FVC is the maximum volume of air that can be exhaled, however FEV_6 has been shown to be nearly equivalent to FVC in measuring airway obstruction, and is used in older adults who need a longer time to exhale. Bronchodilators (such as short acting beta-agonists [SABA]) are used to determine reversibility of obstruction to measure lung function growth and loss (NHLBI, 2007).

NHLBI guidelines recommend using spirometry to measure lung function in children age 5 and older. However, literature has shown established reference ranges do not always measure pulmonary function well in youth, and diagnosis and treatment for those aged 5-18 should be based on frequency and severity of symptoms and exacerbations first (NHLBI, 2007).

In the 1960s, the European Community for Coal and Steel (ECCS) developed spirometric reference value recommendations for occupational health measures. In 1970s, the first values for children and

adolescents were developed (Quanjer, Stanojevic, Stocks, & Cole, 2012b). There are currently a number of reference equations available to determine normal ranges. Normal or baseline values are based on predicted values, which take into account the variables age, height, race/ethnicity, and gender. Personal best values may also be used as reference for those with known pulmonary function problems (AAAAI, 2014; "Pulmonary function tests," 2013; Quanjer et al., 2012a; Simon et al., 2010). The most recently developed reference equation is the Global Lung Function Initiative (GLI) 2012 equation (Quanjer et al., 2012a). Two experts on pulmonary function were consulted by the AAAAI regarding reference equations. One expert recommended GLI 2012 equations if possible. The other expert stated that reference equations can be controversial and said that while there are advantages to the GLI equations, other equations are also good, and to choose based on the practice and population (AAAAI, 2014).

Although it is not the only reference equation available to clinicians, multiple associations and societies worldwide, including the American Thoracic Society (ATS), have endorsed the GLI equation from Quanjer et al. (2012). The final equation for predicted value, based on more than 160,000 datapoints from 33 countries is a regression equation which uses an LMS method to take into account the mean (mu), coefficient of variation (sigma), and skewness (lambda):

$$\log(Y) = a + b \bullet \log(H) + c \bullet \log(A) + \text{age-spline} + d \bullet \text{group}$$

in which Y=dependent variable, H=height standing in centimeters, A = age in years, a, b, c, and d are coefficients, spline is an age-adjustment to correct for age between 3 and 95 years and to correct skew if necessary. Group is a dummy variable (0 or 1) to adjust for race (Caucasian, African American, North or South East Asian) (Quanjer et al., 2012). Lower limits of normal are also calculated, as well as z-scores to determine deviation from the mean (Merkus, 2014). However, in everyday practice, percent predicted is often used to determine lung function (Table 1). NHLBI Guidelines do not have spirometry measures for those under age 5. For those age 5-11 with intermittent asthma severity, FEV_1 is normal between exacerbations, and >80% predicted, and FEV_1/FVC is >85%; for those aged 5-11 with mild persistent

asthma, FEV_1 is ≥80% predicted, and FEV1/FCV is >80%; for those age 5-11 with moderate persistent asthma, FEV_1 is 60-80% predicted, and FEV_1/FVC is 75-80%; and for those age 5-11 with severe persistent asthma FEV_1 is <60% predicted and FEV_1/FVC is <75% (Table 1). For those age 12 and older with intermittent asthma severity, FEV_1 is normal between exacerbations, FEV_1 is >80% predicted, and FEV_1/FVC is also normal; for those age ≥12 with mild, persistent asthma, FEV_1 is ≥80% predicted, and FEV_1/FVC is normal; for those age ≥12 with moderate, persistent asthma severity, FEV_1 is >60%, but <80% predicted and FEV_1/FVC is reduced 5%; and for those ≥12 with severe, persistent asthma, FEV_1 <60% predicted, and FEV_1/FVC is reduced >5% (Table 1). In addition to spirometry, peak expiratory flow, which is the speed of exhalation, may be tested with a peak flow meter. Ranges are based on standardized rates and the patient's own rate (ALA, 2016). The NHLBI does not recommend peak expiratory flow as a diagnostic tool over spirometry, rather it should be used for monitoring of asthma (NHLBI, 2007).

Diagnosis of other illnesses that have similar symptoms to asthma, such as pneumonia or chronic obstructive pulmonary disorder (COPD) must also be ruled out (Asher & Pearce, 2014, NHLBI, 2007). These diseases differ for children and adults. For infants and children, upper airway diseases, such as allergic rhinitis, obstructions involving the large (e.g. vocal cord dysfunction) or small airways (e.g. cystic fibrosis), and other causes, such as cough not due to asthma, must be considered. Other diagnostic possibilities for adults include conditions such as COPD, vocal cord dysfunction, or pulmonary embolism (NHLBI, 2007).

Classification of Severity

Treatment of asthma is dependent upon the severity of the disease, which is assessed in terms of impairment and risk. Asthma may be intermittent or persistent, and mild, moderate or severe. Before the most current (2007) NHLBI Guidelines for the Diagnosis and Treatment of Asthma, "intermittent" was

called “mild intermittent”, however this was changed since those who have intermittent asthma may still have moderate or severe exacerbations (NHLBI, 2007).

Impairment consists of 1) symptoms (which include quality-of life factors such as being woken up, need for SABAs, missed work or school, and ability to do everyday activities) and 2) lung function measured by spirometry (NHLBI, 2007). In 2007, prominence was put on using FEV_1/FVC instead of FEV_1 for assessment of severity in children because it may be a more sensitive measure of lung function (NHLBI, 2007). However, current research supports using forced expiratory flow at 25-75% ($FEF_{25-75\%}$), as it is a more sensitive measure of lung function, especially in children. Low $FEF_{25-75\%}$ in children is associated with poorly or uncontrolled asthma (Duncan et al., 2012; Simon et al, 2010). Simon et al. (2010) found that even when FEV_1 was normal, $FEF_{25-75\%}$ detected airway obstruction. An $FEF_{25-75\%}$ increase of 30% from baseline after bronchodilator medication is considered clinically significant. However if the baseline is below normal range, and the increase moves $FEF_{25-75\%}$ into the normal range after bronchodilator, the change is also considered successful, and clinically significant, even if it is below a 30% change (Spaulding et al., 2012). Ciprandi and colleagues also support using $FEF_{25-75\%}$ in children, as it is more sensitive and FEV_1 may appear normal in those with mild asthma. An $FEF_{25-75\%}$ value of less than 65% of the predicted value is considered to be abnormal (Ciprandi et al., 2012)

Assessment of risk refers to the prediction of risk of events such as exacerbations and death, which is based upon frequency of exacerbations needing oral steroid therapy, severe airflow obstruction, persistent severe airway obstruction, emergency department or hospitalizations, fear of asthma (as perceived by the patient), demographic, socioeconomic, and psychosocial factors (NHLBI, 2007). Table 1 (adapted from NHLBI, 2007 guidelines), shows classification of asthma severity in children and adults.

Table 1. Classification of Severity by Impairment & Risk in Patients Not Medicated for Long-Term Control (all ages) (adapted from NHLBI, 2007)

Severity Components		*Classification of Asthma Severity*				
		Age*	**Intermittent[a]**	**Persistent**		
				Mild	**Moderate**	**Severe**
Impairment	Symptoms	0-4y 5-11y ≥12y	≤2 days/week	>2 d/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0-4y	0	1-2x/month	3-4x/month	>1x/week
		5-11y ≥12y	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	SABA** use for symptom control ***	0-4y 5-11y	≤2 days/week	>2 d/week but not daily	Daily	Several times/day
		≥12y	≤2 days/week	>2 d/week but not >1x/d	Daily	Several times/day
	Interference with normal activity	0-4y 5-11y ≥12y	None	Minor limitation	Some limitation	Extremely limited
	Lung function†	0-4y	n/a‡	n/a	n/a	n/a
		5-11y	• Normal FEV_1 between exacerbations • FEV_1 >80% • FEV_1/FVC >85%	• FEV_1 ≥80% predicted • FEV_1/FVC >80%	• FEV_1 > 60-80% predicted • FEV_1/FVC 75-80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
		≥12y	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-4y	0-1/year	≥2 exacerbations in 6 months requiring oral steroids or ≥4 wheezing episodes/ 1y lasting >1d AND risk factors for persistent asthma		
		5-11y		≥2 in 1 year		
		≥12y		≥2/year		

Adapted from NHLBI, 2007,pp.72-74 (http://www.nhlbi.nih.gov/files/docs/guidelines/04_sec3_comp.pdf)

* Age ≥12y = 12 through adulthood

** Short-acting β_2-agonist

*** Not including SABA use for exercise-induced bronchospasm

† Normal FEV_1/FVC: 8-19 yr 85%; 20-39 yr 80%; 40-59 yr 75%; 60-80 yr 70%

‡ n/a = not applicable

[a] Intermittent was formerly classified as "Mild Intermittent." Now, "Intermittent" severity is classified as one category as intermittent asthma is not always mild, it can also be moderate or severe. However, the intermittent severity classification is not broken into the three severity levels (mild, moderate, severe)

Treatment and Management

After the diagnosis and classification of severity of asthma, the patient will begin treatment. Rather than using severity measures to assess whether or not treatment is working, asthma control, or day-to-day symptom management, is to be assessed and monitored. Asthma control is also defined in terms of reducing impairment and risk. Risk refers to having or not having exacerbations (NHLBI, 2007). Components of asthma control impairment include the same components as severity (Table 1), and in youth age 12 or older and adults, also include a validated questionnaire such as the Asthma Control Questionnaire, the Asthma Therapy Assessment Questionnaire, the Asthma Control Test, or the Asthma Control score (NHLBI, 2007).

Long-term management of asthma includes control of asthma (reduction of impairment risk), which is achieved by pharmacotherapy, as well as monitoring and follow-up (NHLBI, 2007; Reddy, Doshi, Covar, & Spahn, 2014). Doctors are encouraged to work with their patients or patients' parents to form Asthma Action Plans, which are written plans that address the daily management of asthma, such as medications and avoiding triggers, and how to identify and cope with the worsening of the disease. The identification and management of decreased asthma control includes items such as peak flow meter use and ranges, knowing which emergency medications to take, where to find emergency phone numbers, and which signs and symptoms indicate asthma is worsening (NHLBI, 2007).

Long-Term Pharmacotherapy

There are a number of types of medications used in the long-term management of asthma, including: corticosteroids (inhaled and oral, depending on severity of symptoms), cromolyn sodium and nedocromil, immunomodulators, leukotriene modifiers, long-acting beta$_2$-agonists (LABAs), methylxanthines, and the long-acting muscarinic antagonist (LAMA), tiotropium. Medication is prescribed by age (0-4, 5-11, ≥12 to adult), and in a stepwise approach, in that medication doses/types are

increased or decreased as asthma control worsens or improves (NHLBI, 2007; Olin & Wechsler, 2014; Reddy et al., 2014).

Corticosteroids reduce inflammation. Inhaled corticosteroids (ICS) are commonly used as long-term therapy for persistent asthma (Duncan et al., 2012; NHLBI, 2007). The use of long-term oral steroids for asthma began in the 1950s. This practice has been decreasing, due in part to newer, more potent ICS's, and more knowledge of adverse effects attributed to long-term use of older steroids, however, oral corticosteroids are still used in severe cases of persistent asthma (Reddy et al., 2014; NHLBI, 2007).

Cromolyn sodium and nedocromil work by stabilizing mast cells, which play a role in allergic response, and are used with mild persistent asthma when other medications are not available, or do not work (NHLBI, 2007). Some forms of cromolyn and nedocromil inhalers were discontinued in the U.S. in 2010 due to their contribution to ozone layer depletion (Food and Drug Administration [FDA], 2010).

For mild asthma, immunomodulators, which are antibodies that prevent binding of IgE to pro-inflammatory cells, and have been shown to decrease exacerbations (Olin & Wechsler, 2014). Leukotriene modifiers are antagonists to mediators (leukotrienes) released from inflammatory cells, and are often used as a back up to ICS therapy. Methylxanthines may have anti-inflammatory effects and may be used with ICS, but are not commonly prescribed due to safety issues such as seizures (NHLBI, 2007).

LABAs are bronchodilators given as the preferred treatment in combination with ICS for patients age 12 and older, and with ICS in children age 0-11 with moderate-severe asthma. LABA/ICS combination therapy has been shown to improve control and decrease exacerbations and hospitalizations (NHLBI, 2007; Reddy et al. 2014). Additionally LAMAs may be used in combination with ICS or ICS and LABAs in those over age 12 with moderate to severe asthma. LAMAs work in the smooth muscle tissue (Lipworth, 2014).

Short-Term (Relief) Medications

SABAs are the preferred treatment for acute bronchoconstriction. They have been shown to improve symptoms, hyperresponsiveness, quality of life, and lessen the frequency of exacerbations (NHLBI, 2007; Olin & Wechsler, 2014). Anticholinergics are relief medications that act by blocking acetylcholine neurotransmitters from binding to receptors, which are responsible for involuntary muscle constriction, and in turn relaxing smooth muscle airway constriction. They may be used with SABAs or as an alternative. Oral systemic corticosteroids may also be used for severe exacerbations (NHLBI, 2007).

Safety of Corticosteroids

As noted earlier, long-term, systemic first-generation corticosteroid use has been associated with negative effects such as suppression of growth and adrenal suppression, osteoporosis, hypertension, and myopathy, a disease of the skeletal muscles due to cell structure and metabolic dysfunction, which leads to muscle weakness. Additionally, long-term use of oral corticosteroids can increased risk of Cushing's syndrome (McFadden, 2004; Reddy et al., 2014; Cleveland Clinic, 2015). Cushing's syndrome is an endocrine disorder of the adrenal glands, which secrete cortisol as a metabolic function. In Cushing's syndrome there is too much cortisol – such as when corticosteroids are being used in high doses. The extra cortisol leads to increased insulin production and secretion, and glucose production (Nussey & Whitehead, 2001). Insulin and glucose lead to extra fat production, which is distributed around the abdomen, while the muscles in the limbs, shoulders and hips experience myopathy, and weakness. Those with Cushing's syndrome often develop "moon face" meaning the face becomes very full and round due to fat distribution on the sides of the face. Diabetes and impaired glucose tolerance may also occur (Nussey & Whitehead, 2001). First-generation corticosteroids required higher doses that led to the adverse effects noted earlier. Newer second-generation corticosteroids are more potent, so they require smaller doses. Additionally the addition of LABAs can decrease steroid doses even further, and still provide asthma control and decreased exacerbations (Reddy et al. 2014). However, there is a possibility

that even inhaled corticosteroids may be associated with growth suppression, and it is recommended that linear growth be observed in all youth (Castro-Rodriguez, Custovic, & Ducharme, 2016).

Asthma Prevalence

Worldwide Morbidity

Globally, 300-334 million people currently have asthma (Asher & Pearce, 2014; NHLBI, 2014). The International Study of Asthma and Allergies in Children (ISAAC), a standardized data collection project from 105 countries, contributed data for the Global Burden of Disease Study (GBD) 2010. The GBD 2010 showed infectious diseases are decreasing worldwide, and chronic respiratory conditions currently contribute to increasing disability rates (Asher & Pearce, 2014). Disability-adjusted life years (DALYs) are used by the GBD to measure the burden of disease by looking at the absolute health lost from disease, including mortality and years lived with the disease to determine healthy years of life lost. In 2010, asthma was the 8th highest cause of DALYs in youth age 5-9, 3rd highest in those 10-14, and 12th for those aged 15-19, globally.

United States Morbidity

In the U.S., asthma burdens more than 25 million people, including nearly 7 million children (Asher & Pearce, 2014; Moonie et al., 2014; NHLBI, 2014). Consistent with risk factors for asthma, Behavioral Risk Factor Surveillance System (BRFSS) asthma prevalence data, show that among youth in the U.S., males have significantly higher rates of lifetime and current asthma (lifetime: 16.3%, current: 9.2%) than females (lifetime: 11.8%, current: 8.0%). Adult males have significantly lower asthma rates (lifetime: 11.7%, current: 6.3%) than adult females (lifetime: 16.2%, current: 11.5%) (Table 2) (CDC, 2015a). The BRFSS is a random-digit-dialed telephone survey conducted in all U.S. states, Washington D.C. and three territories. Two questions are asked about asthma to obtain current and lifetime rates. The data are self-reported by adults, and by proxies for participants under the age of 18 using the Childhood Asthma Module (CDC, 2015a).

Table 2. 2013 Lifetime & Current Weighted Asthma Prevalence for Youth and Adults in the United States by Sex

	All		Male		Female	
	N	% (95%CI)*	N	% (95% CI)	N	% (95% CI)
Youth (0-17)		**All**		**Male**		**Female**
Lifetime	65,835	14.0 (13.5-14.6)	33,751	16.3 (15.5-17.1)	31,383	11.8 (11.1-12.6)
Current	65,559	9.2 (8.8-9.6)	33,607	10.4 (9.8-11.1)	31,295	8.0 (7.4-8.6)
Adults		**All**		**Male**		**Female**
Lifetime	482,317	14.0 (13.8-14.2)	197,569	11.7 (11.4-12.0)	284,748	16.2 (15.9-16.5)
Current	480,460	9.0 (8.8-9.1)	196,859	6.3 (6.1-6.5)	283,601	11.5 (11.2-11.7)

Adapted using 2013 BRFSS data (http://www.cdc.gov/asthma/brfss/2013/default.htm)
*CI = confidence interval

Race and ethnicity also affect asthma prevalence in the U.S. The National Health Interview Survey (NHIS) is an annual, in-person survey conducted by the National Center for Health Statistics at the CDC using a representative sample of the U.S. population. Data are weighted and standard error is reported with prevalence estimates to account for sampling error (CDC, 2016b). NHIS lifetime asthma prevalence rates for 2013 show that among all those under 18 years of age, black non-Hispanic youth have the highest rates of asthma (18.9%), until the Hispanic categories are stratified by Mexican/Mexican American (11.8%) and Puerto Rican (31.3%) (Figure 2) (CDC, 2016b).

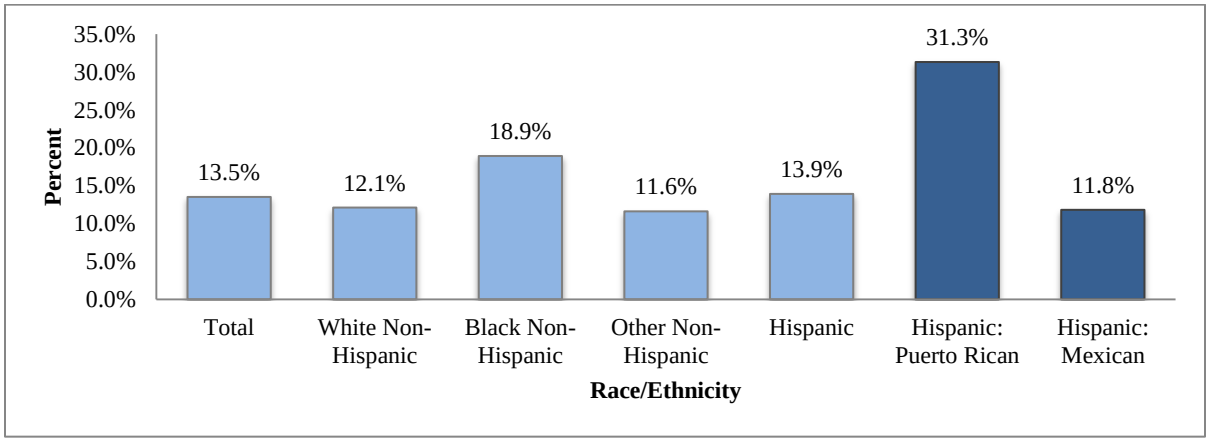

Figure 2. Rates of Lifetime Asthma by Race/Ethnicity, Ages <18, 2014, U.S.
Adapted from 2014 National Health Interview (NHIS) data (http://www.cdc.gov/asthma/nhis/2014/table2-1.htm)

Numerous studies found high prevalence of asthma among Puerto Rican youth in the U.S. with lifetime rates as high as 41.3% and 44% in those living in Puerto Rico (Cohen et al., 2007; Lara et al., 2014), and 35.3% for those living in the 50 states (Cohen et al., 2007). In recently published research, Keet et al. (2015) sought to examine how asthma predictors such as inner-city living, poverty levels, and race/ethnicity affected the prevalence of childhood asthma by linking 2009-2011 NHIS data to U.S. Census tract data from the NCHS. The authors found significantly higher rates of asthma in Puerto Rican children (adjusted Odds Ratio [aOR] = 2.38, 95% Confidence interval [CI] [1.82-3.11]) and black children (aOR = 1.87, 95% CI [1.59-2.19], compared to white children, after adjusting for age, sex, geographic region, urban or rural area, neighborhood-level poverty, and birth outside the U.S (Keet et al. 2015). These finding are consistent with the literature (Dorevitch et al., 2013; Lara, et al., 2006; Olin & Wechsler, 2013).

Nevada Morbidity

In Nevada, the childhood asthma rates are comparable among males and females for both current and lifetime asthma in pooled 2011-2014 data. Rates are highest in Washoe County (lifetime: 11.5%, current: 7.2%). Those aged 10-14 years had the highest lifetime and current rates from 2011-2014 (lifetime: 14.8%, current: 8.1%) (Table 3) (Moonie & Lucas, 2016). Black children have the highest rates of all race/ethnicities; the lifetime rate was 15.8% and the current rate was 7.0% (Table 3) (Moonie & Lucas, 2016).

Table 3. Nevada Lifetime/Current Weighted Asthma Prevalence: Ages 0-17 (Pooled 2011-2014 data)

		Lifetime Asthma		Current Asthma	
Demographic	**Grouping**	**N**	**% (95%CI)**	**N**	**% (95% CI)**
Statewide	Nevada	4,195	10.1 (8.7-11.4)	4,036	6.2 (5.1-7.2)
Region	Clark County	1,502	10.4 (8.6-12.2)	1,498	6.0 (4.6-7.3)
	Washoe County	1,363	11.5 (9.3-13.8)	1,357	7.2 (5.4-9.1)
	Balance of State	1,172	10.8 (8.5-13.1)	1,165	6.1 (4.5-7.8)
Age	0 – 4	416	5.7 (2.2-9.3)	414	3.7 (0.4-6.9)
	5 – 9	918	9.8 (7.1-12.6)	914	5.9 (3.7-8.1)
	10 – 14	1,167	14.8 (11.8-17.8)	1,162	8.1 (6.0-10.2)
	15 – 17	844	12.3 (8.7-15.8)	839	6.1 (3.8-8.5)
Sex	Boy	2,044	12.0 (10.0-14.0)	2,033	6.5 (5.0-8.0)
	Girl	1,938	9.6 (7.6-11.6)	1,932	6.1 (4.5-7.6)
Race/Ethnicity	Asian	106	6.9 (1.2-12.6)	106	4.2 (0.1-8.4)
	Black	187	15.8 (9.5-22.0)	185	7.0 (3.0-10.9)
	Hispanic	1,036	10.1 (7.6-12.5)	1,033	6.2 (4.2-8.2)
	White	2,402	10.3 (8.5-12.1)	2,391	6.5 (5.1-7.9)
	Other	276	11.6 (6.3-17.0)	275	4.3 (1.7-6.9)

Adapted from Moonie & Lucas, 2016

Mortality

Each year there are approximately 250,000 deaths from asthma worldwide. In the U.S., the mortality rate for asthma is 1.1 per 100,000, and 3,600 people in the U.S. died from asthma in 2013 (AAAAI, 2015a; CDC, 2015c). The use of inhaled corticosteroids has decreased asthma mortality, though in the U.S., women are still 30% more likely to die from asthma than men, and the risk of death is 75% higher for black people than for white people (Olin & Wechsler, 2014).

Asthma Costs

Financial Costs

In 2007, asthma costs in the U.S. were approximately $56 billion (Barnett & Nurmagambetov, 2011; Moonie et al. 2014). Barnett & Nurmagambetov (2011) estimated direct costs and loss-of-productivity costs, for the years 2002-2007 in 2009 U.S. dollars, and found the pooled estimates of direct

costs per year for a person with asthma was $3,259, which factored in outpatient hospital visits ($151/year), inpatient hospitalizations ($446/year), and ED visits ($110/year). Doctor's office visits were estimated to be $581 per year, and medications for asthma control were predicted to be $1,680/year. Additionally, loss of workdays was estimated to cost $301 and loss of school days $93 per year (Barnett & Nurmagambetov, 2011). The estimated deaths due to asthma cost $2.37 billion/year, or $14.25 billion for 2002-2007 (Barnett & Nurmagambetov, 2011). From 2009-2011, more than 439,000 to 500,000 asthma patients required hospital admission annually, and more than 2 million required ED visits. Hospital stays averaged 3.6 days (CDC, 2015c; Olin & Wechsler, 2014). Regionally, Moonie, et al., 2014 found asthma patients age 0-17 in Southern Nevada required significantly more ED use than adults, and the youth population also required more hospitalizations and primary care visits than adults with asthma. Furthermore, black people were 2.5 times more likely to need ED treatment and hospitalizations in Southern Nevada (Moonie et al. 2014).

Quality-of-Life

In addition to increased healthcare use and cost, asthmatic patients also have lowered quality-of-life than non-asthmatic patients as symptoms can worsen, and make it impossible to participate in usual activities and go to work and school. Children with asthma are more likely to be absent from school than those who do not have asthma (Asher & Pearce, 2014; Moonie, Sterling, Figgs, & Castro, 2008; Olin & Wechsler, 2014). In 2008, Moonie et al. found that although children with persistent asthma missed more school and had lower standardized test scores, those with asthma could still succeed academically as well as those without asthma (Moonie et al. 2008).

Obesity

Pathophysiology and Pathogenesis

Overweight or obesity is defined as an amount of adipose tissue greater than the ideal amount for healthy weight. Body mass index (BMI), calculated from weight and height measurements, is currently

considered to be an accepted and reliable way to categorize weight status in adults and children (CDC, 2014; Waters et al., 2011).

Adipose tissue is composed of adipocytes and other cells, such as pre-adipocytes, immune cells (such as macrophages), stem cells, muscle cells, and blood cells. The human body can efficiently store extra fat, which is needed if starvation occurs, but when more calories are consumed than expended (positive caloric balance), adipocytes can become dysfunctional (Capurso & Capurso, 2012; Redinger, 2007). During normal positive caloric balance, new adipocytes are created due to signaling of pre-adipocytes for proliferation and differentiation into adipocytes. When there is too much caloric imbalance, adipocyte dysfunction occurs, visceral fat accumulates and releases inflammatory cytokines called adipocytokines, or adipokines. Additionally, fatty acids are released from adipocytes, and taken up by adipose and non-adipose tissue, leading to obesity (Capurso & Capurso, 2012; Redinger, 2007). Adipose tissue also has endocrine functions such as secretion of hormones that work with insulin to regulate body fat, and the release of inflammatory adipokines. Due to the increased levels of adipokines in adipose tissue, those who are obese are believed to have chronic inflammation, which is associated with numerous health problems including metabolic syndrome, diabetes mellitus, hypertension, atherosclerosis, some cancers, chronic renal disease and nonalcoholic fatty liver disease (Capurso & Capurso, 2012; Kelsey, Zaepfel, Bjornstad, & Nadeau, 2014; Redinger, 2007).

Metabolic syndrome is a risk factor for type II diabetes mellitus and cardiovascular disease (CVD) with multiple signs and symptoms including insulin resistance, increased abdominal fat, high triglycerides, high blood pressure, and low levels of high-density lipoprotein cholesterol (HDL-C) ("good" cholesterol [American Heart Association, 2015]) (Kelsey at al., 2014). Along with free fatty acids, excess abdominal fat leads to increased inflammatory adipokines that contribute to insulin resistance by interfering with pancreatic cell function. Dysregulation of lipid and glucose metabolism accounts for insulin resistance in type II diabetes mellitus (Redinger, 2007). Adipokines lead to elevated macrophage response and infiltration in adipose and other tissue resulting in more inflammation, as well

as immune system dysfunction, contributing to metabolic syndrome and other comorbid conditions (Redinger, 2007).

Screening and Detection

Body Mass Index

BMI is a common way to measure weight status, as it is convenient and inexpensive, however the CDC considers it to be a screening tool for potential health problems, not a diagnostic tool. It is calculated the same way for children and adults, but interpreted differently (CDC, 2014). The formula for BMI, provided by CDC (2014) is:

Weight in kilograms / (height in meters)^2

Or

[Weight in pounds / (height in inches)^2] x 703

Table 4 shows BMI weight status categories for adults.

Table 4. Body Mass Index (BMI) Ranges for Adults

BMI	Weight Status
<18.5	Underweight
18.5-24.9	Normal weight
25.0-29.9	Overweight
≥30	Obese

Adapted from the CDC (http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html#Interpreted)

BMI for children and adolescents (defined as those age 20 and younger) is adjusted for age and sex because the amount of fat changes with age, and is different for boys and girls. Infants (age 0-36 months) can be measured using length-for-age percentile, weight-for age percentile, or head circumference-for age percentile and weight-for-length percentile. Children and teenagers aged 2-20 are measured using stature (height)-for age percentile and weight-for age percentile (CDC, 2014). The

calculated number is plotted using a growth chart or data tables (Appendix 1). Youth BMI is reported in percentiles (Table 5).

Table 5. Body Mass Index (BMI) Ranges for Children and Teenagers (Ages 0-20)

BMI Percentile Range	Weight Status
$<5^{th}$ percentile	Underweight
5^{th} to $<85^{th}$ percentile	Healthy weight
85^{th} to $<95^{th}$ percentile	Overweight
$\geq 95^{th}$ percentile	Obese

Adapted from the CDC (http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html)

Use of BMI to screen weight status is common in the U.S., however some research shows that it is not a good indicator of adult adiposity because it measures all body mass, and lean mass, such as muscle is not accounted for (Shah & Braverman, 2012; Romero-Corral et al. 2008). Romero-Corral et al. (2008) found that in a sample of more than 13,000 adults, the BMI was correlated with both body fat percent and lean mass, although lean mass is not body fat. They found that in predicting obesity (BMI ≥30) had high specificity (96%), but low sensitivity (43%). This shows a low number of obese individuals were false positives. However, when based on body-fat percent the BMI missed more than half of the people in the study who should have been classified as obese (Romero-Corral et al., 2008). Shah and Braverman (2012) also found the same misclassification of obesity when comparing BMI to direct body fat measurements in adults. Tools other than BMI to detect obesity include skinfold thickness and waist circumference measurement, waist-to-hip-ratio, underwater weighing, bioelectrical impedance analysis (using electrical currents to detect body tissue and calculating out water in the body), and dual-energy x-ray absorptiometry (DXA), which uses x-rays to detect adipose tissue, muscle, and bone mass (CDC, 2014; Romero-Corral et al. 2008; Shah & Braverman, 2012). BMI is considered to be an accurate and acceptable tool for detection of overweight or obesity in children (Waters et al., 2011).

Risk Factors for Obesity

Childhood overweight and obesity are risk factors for being overweight or obese as an adult. Furthermore, adults who had been obese as children have a higher risk of developing cardiovascular disease and some cancers, even if the weight is lost (Kelsey et al., 2014; Trasande, 2010; Waters et al., 2011). Risk factors for childhood obesity exist at population, community, and family/individual levels, and are often linked to health disparities. Contributing factors to obesity can also fall into environmental, genetic, and epigenetic categories (Institute of Medicine [IOM], 2012; Waters et al., 2011; Kelsey et al., 2014).

Minority children with lower SES have a higher prevalence of obesity in developed countries, however, in developing countries, children in families with high SES have higher rates of obesity. In the U.S., this could be explained, in part, by environment: low-income families live in areas that do not have safe areas for physical activity such as well-lit parks, walkable sidewalks or trails, or stores that offer fresh, healthy food (IOM, 2012; Waters et al., 2011). Increased sedentary behavior is becoming more common in younger generations due to increased technology and "screen time", which includes watching television, playing video games, and increased time on computers, as well as schools eliminating or decreasing time for recess or physical education classes. American families also do not eat at home as often as they used to, which leads to young people drinking more sugar-sweetened beverages and eating more fast food (Barnes, 2010).

Family and twin studies have shown obesity may be up to 50% genetic. However the environment and lifestyle impact genetic factors. The interactions between environmental and genetic (epigenetic) factors also play a role in obesity: fetal exposure to tobacco is a risk factor for overweight or obesity in childhood (Kelsey et al., 2014, Barnes, 2010). Additionally, women who are obese or have type II diabetes are also more likely to have children who become overweight, as the developing fetus is subject to the same mechanisms as the mother, specifically, insulin resistance, free fatty acids, and

increased inflammation (Kelsey et al., 2014). Gender also influences risk for obesity when puberty occurs. It is established in literature that girls develop more adipose tissue and have more distinctive patterns of fat distribution than boys. Girls are also less likely to participate in physical activity than boys, and that activity is not as beneficial during adolescence to girls as it is to boys (Kelsey et al., 2014; Wisniewski & Chernausek, 2009). It is not entirely clear why boys benefit more from physical activity, but the hormones insulin and leptin may be associated with lack of energy balance in girls. Girls are more likely than boys to have insensitivity to insulin during puberty, which can disrupt regulation of the metabolism, however it is unknown whether development of more adipose tissue leads to insulin insensitivity or whether insulin insensitivity leads to development of more adipose tissue during puberty (Wisniewski & Chernausek, 2009). Leptin is a hormone related to regulation of energy balance and obese individuals are insensitive to the hormone. Some studies propose that females may also become insensitive to leptin at puberty, which could lead to lack of regulation of energy (Wisniewski & Chernausek, 2009).

Prevalence of Overweight and Obesity

Worldwide Prevalence

Overweight and obesity have become prevalent around the world. As of 2014, 39% of adults (age ≥ 18) were overweight, and 13% were obese. In 2013, 42 million children worldwide under the age of 5 had a BMI of 85th percentile or higher (overweight or obese) (WHO, 2015).

United States Prevalence

Obesity rates in the U.S. are high: 34.9% of adults are obese (BMI ≥30), and 16.9% of youth are obese (BMI ≥95th percentile for age/sex). When stratified by race/ethnicity, Ogden and colleagues (2014) found that Hispanic youth had highest prevalence of overweight and obesity; 38.9% had a BMI greater than or equal to the 85th percentile for age/sex and of those, 22.4% had a BMI greater than or equal to the 95th percentile.

When further stratified for age group and sex, non-Hispanic Asian youth, age 2-5, had the lowest prevalence of overweight: 8.3% of males and 9.7% of females had BMIs greater than or equal to the 85th percentile for age/sex. Non-Hispanic, white females, age 2-5, had the lowest prevalence of obesity (BMI ≥95th percentile) for all females at 0.6%, and non-Hispanic Asian males, age 2-5, had the lowest prevalence of obesity for all males (1.9%) (Ogden et al., 2014). Hispanic youth ages 6-11 had the highest prevalence of both overweight and obesity: 48.7% of males and 43.6% of females had BMIs ≥ 85th percentile, and of those, 28.6% males and 23.4% females had BMIs ≥ 95th percentile. BMI percentile category increased with age in the youth population (Ogden et al., 2014).

Nevada Prevalence

The Nevada Institute for Children's Research and Policy [NICRP] 2013-2014 Annual Kindergarten Health Survey found that children entering kindergarten in Nevada in 2013, aged 4-6, have high rates of obesity (BMI ≥95th percentile for age/sex) at 19%. By the 2014 school year this number had increased to 21.7% (NICRP, 2015). In 2013, Clark County had the highest rate of obese kindergarteners at 20.4% and the rural areas outside Clark and Washoe Counties had the lowest obesity rate (18.4%). Among the children sampled, 16.9% were underweight (BMI <5th percentile for age/sex), 49.4% were healthy weight (BMI 5th to <85th percentile for age/sex), and 14.7% were overweight (BMI 85th to <95th percentile for age/sex) (NICRP, 2014). As of 2014, the rural counties had a kindergarten obesity rate of 23.7%, Clark County was at 21.6% and Washoe County had 20.3% obesity among children aged 4-6. Underweight decreased to 16.1%, healthy weight was 52.4%, and 9.8% of children were overweight (NICRP, 2015).

The Data Resource Center for Child and Adolescent Health (DRC), in a partnership with the National Center for Health Statistics at the CDC provides the 2011-2012 National Survey of Children's Health (NSCH) results from the random-digit dial survey. The NSCH survey shows that Nevada children aged 10-17 have an obesity rate of 18.6%, higher than the national rate of 15.7% for this age group.

Nevada children have lower rates of overweight (14.5%) than the national rate (15.6%) for youth age 10-17 (DRC, 2012).

Costs of Obesity

Financial Costs

Economic analyses of obesity costs have found annual healthcare is more expensive for overweight and obese people for those at healthy weight. Studies have found annual healthcare costs for overweight and obese youth increase by $172-$220 per child in the U.S. (IOM, 2012; Trasande & Elbel, 2012). Wang, McPherson, Marsh, Gortmaker, & Brown (2011) state that the increased prevalence of obesity combined with the spending on obesity-related costs may account for a 27% increase in U.S. health care expenditures from 1987-2001. Additionally, they believe that by 2030, medical costs associated with obesity will grow by $48-66 billion/year in the U.S. and by £1.9-2 billion/year in the U.K. (Wang et al., 2011).

Economic models estimate U.S. cost savings as much as $9 billion per year if the prevalence of diabetes and hypertension were reduced by 5%, and if other obesity-related comorbid health problems were also reduced, savings could be nearly $25 billion. Another model estimated that it would be cost-effective to spend $2 billion annually in the U.S. on prevention as long as obesity was reduced by 1% in 12-year-olds because the savings in both childhood and adulthood medical expenditures and quality-adjusted life-years (QALYs) would be greater (IOM, 2012; Trasande, 2010).

Quality-of-Life

The IOM (2012) has found that those who are obese have higher rates of absenteeism from work and school than those who are not, and obese people also complete fewer grades in school. Additionally, the IOM examined mortality and QALYs, and found a loss of 1-13 years of life per obese person and a

loss of 2.93 million QALYs in one year among those who are obese compared with those who are not (IOM, 2012).

Asthma and Obesity

Combined Pathogenesis

Members of the American Thoracic Society ad hoc Subcommittee on Obesity and Lung Disease have determined that obesity is a risk factor for asthma, and believe that "obese asthma" may be a new asthma phenotype. This may be due at least in part to the inflammatory mechanisms, which affect the functioning of the immune system in individuals with both obesity and asthma (Dixon et al., 2010). This phenotype is believed to be more severe and harder to control than atopic asthma due to physiologic differences and altered responses to current medications among obese asthma patients (Black et al., 2013; Sutherland, 2014).

Some research has shown eosinophils are not associated with the obese asthma phenotype, and these researchers believe inflammation due to obesity alone can lead to non-allergic asthma through the development of T-cells and other mechanisms (Ali & Ulrik, 2013; Jensen, Collins, Gibson, & Wood, 2011; Jensen, Wood, & Gibson, 2012). Fractional exhaled nitric oxide (FE_{NO}) is an indicator of eosinophil airway inflammation. In a study examining asthma and BMI, waist circumference and body fat percent in children, researchers determined that those who were overweight/obese had low FE_{NO} levels, showing an association between obesity and non-atopic asthma development (Han, Forno, & Celedón, 2014). Baumann & Lorentz (2013) found associations between atopic asthma and obesity, but very little evidence of allergic mechanisms, such as elevated mast cell numbers, or associations with other allergic diseases except atopic dermatitis in children under age 5. Elevated IgE levels were not found in adults, and results were inconclusive for children (Baumann & Lorentz, 2013). Studies have also found increased Th1 response and decreased Th2 response in obese individuals with asthma. It is hypothesized that there

is a Th1/Th2 imbalance due to the chronic, low-grade inflammation from excess adipokines, which triggers an innate immune response associated with the Th1 phenotype. Th2 response is associated with allergic disease, but not commonly with obese asthma (Ignacio, Kim, & Kim, 2014; Raj, Kabra, & Lodha, 2014; Rastogi et al., 2014)

Inflammation signaling cytokines such as tumor necrosis factor-alpha (TNF-α), and markers such as high-sensitivity C-reactive protein (hsCRP), and interleukin 6 (IL)-6 are found in higher concentrations in obese people than non-obese individuals, and positive associations exist between BMI and hsCRP levels, abdominal obesity and IL-6 levels, and adipocyte size and TNF-α levels (Ali & Ulrik, 2013). Magrone, Simone, Altamura, & Munno (2014) found inflammatory markers correlated positively with elevated BMI in pediatric patients with asthma.

Obesity is a risk factor for breathing problems in people with and without asthma, however, the problems are worse in those with asthma. Along with the pro-inflammatory cytokines and factors secreted by adipose tissue, obese individuals have excess pressure on the chest, not from inflammation but from extra weight (Dixon et al., 2010). Functional residual capacity (FRC), the amount of air left in the lungs after breathing out, is reduced in obese individuals, which is associated with pressure on the lungs, and reduction of airway diameter. Airway diameter reduction can also disrupt smooth muscle function and lead to airway obstruction (Dixon et al. 2010; Sutherland, 2014). Tidal volume (V_T), the volume of air in a normal breath, is also decreased in obese asthmatics. While lower V_T leads to less strain on the smooth muscle in the airway, it can lead to more muscle stiffness, which can lead to stronger contractions and increased narrowing of the airways during exacerbations (Ali & Ulrik, 2013; Dixon et al., 2010).

Asthma Severity and Obesity

Asthma is more severe in obese individuals. Mechanical factors such as extra weight on the chest and reduced airway diameter contribute to the severity of asthma. It has also been suggested that obesity

may lead to more frequent inflammatory responses, which trigger exacerbations (Stigone, Ramirez, Svensson, & Claudio, 2011; Sutherland, 2014). Those who are overweight or obese also have poorer control over asthma, and require more hospitalizations and emergency department visits. Research has shown that corticosteroid medication is not as effective for obese adults and children, so they require more emergency medication (Black et al., 2013; Forno et al., 2011; Sutherland, 2014).

Holguin et al., (2011) found the manifestations of comorbid obesity were different between those who developed asthma early (<12y) and those who had late onset (≥12y). The obese patients in both groups had more severe symptoms, but the patients with early onset asthma had more typical asthma symptoms (cough, wheezing, chest tightness), while the late-onset group did not have chest tightness or sputum production (Holguin et al., 2011). Holguin and colleagues also found a linear change in BMI among early-onset asthma patients, but not in the late onset group. They believe their results suggest when one develops asthma earlier in life, the burden of asthma may lead to the development of obesity, but when the onset of asthma comes later in life, the obesity leads to a more severe presentation of the disease (Holguin et al., 2011).

The association between childhood obesity and asthma control and therapy has not been well established in the literature. There has been evidence showing inhaled corticosteroids are not effective in controlling asthma in obese patients (Baffi, Winnica, & Holguin, 2015; Sutherland, 2014). One study found healthy weight asthmatic children had a 44% reduced risk of requiring ED visits and hospitalizations after a Childhood Asthma Management Program (CAMP) clinical trial, yet overweight and obese children with asthma who were taking the same ICS medication had no reduced risk after the trial. Those who were in the healthy weight group also had significantly better lung function with the ICS medication, while the overweight and obese children had no significant differences in response to medication (Forno et al., 2011). The authors believe since obese patients have more inflammation, which they hypothesize has a systemic component, a higher dose of steroids may be required to treat the airway inflammation. The higher dose of steroids may also contribute to production of more adipose tissue. Due

to this cycle, other medications may be needed for obese asthma patients to gain control of symptoms (Forno et al., 2011).

Weight Loss Interventions for Obese Youth with Asthma

Weight loss in pediatric asthma patients has been shown to improve asthma control and lung function. Interventions in which children with obesity and asthma lost weight also showed symptom improvement, including reduced exercise-induced bronchospasms (EIB) (Abd El-Kader, et al., 2013; van Leeuwen, et al., 2014). EIB occurs when airways are obstructed due to exercise, may be indicative of poorly controlled asthma, and is likely present in nearly 90% of those who have asthma. Associations between obesity and EIB severity have been seen in the literature (Ostrom et al., 2013; van Leeuwen et al., 2013).

Children and adolescents with asthma have shown lower levels of physical activity (PA) than those without asthma. Additionally, asthmatics avoid PA due to asthma symptoms, including EIB, interfering with the ability to participate in PA and sports (Abd El-Kader et al., 2013; Ostrom et al. 2013; Wanrooij et al., 2014). Research has also shown when parents restrict activity due to symptoms, youth with asthma may develop fear of breathlessness (Wanrooij et al, 2014). Results from a questionnaire regarding barriers to PA showed that parents saw asthma as a barrier to activity. However, there was no statistical difference between activity levels of children with and without asthma, though the asthma was self-reported as "well controlled" in this population (Santos-Silva, Melo, Conçalves, Coelho, & Carvalho, 2014). Social factors may also influence levels of PA. A Norwegian study of adolescents with asthma found support from peers and "competence-enjoyment" (wanting to participate in PA) were associated with time spent being active (Westergren et al., 2015).

Wanrooij and colleagues (2014) conducted a systematic review of 29 studies regarding asthma and PA. The authors recommended measures for effective interventions, which included individualized training intensity levels, and exercise twice at week for 60 minutes each time for at least three months.

These recommendations were provided for those with asthma, but not necessarily overweight/obese youth to improve overall cardiorespiratory health and EIB (Wanrooij, 2014).

Fedele, Janicke, Lim & Abu-Hasan (2014) found that obese asthma patients had lower levels of PA than obese non-asthmatics age 7-12 years, though this difference was not statistically significant. Abd El-Kader and colleagues (2013) enrolled obese asthmatic 12-18-year-olds in an intervention. The treatment group received diet and PA training in addition to medication and the control group only received medication to examine inflammatory biomarkers. They found significantly lower levels of TNF-α, IL-6, IL-8, leptin, and adiponectin in those who received the diet and PA training compared to those who did not receive diet and PA training (Abd El-Kader et al., 2013). Cardiovascular fitness has also been associated with asthma control and activity. Youth with poorly controlled asthma also had higher levels of inactivity and poorer cardiovascular fitness, while those with well-controlled asthma had similar outcomes to non-asthmatic children (Vahlkvist, Inman, & Pedersen, 2010).

It is known that PA decreases obesity and diseases that are linked to obesity, such as cardiovascular disease and type II diabetes, and can be beneficial for mental health as well (Barnes, 2010; Kelsey et al., 2014; Wisniewski & Chernausek, 2009). In those with asthma, weight loss can lead to increased cardiovascular health and lung function (Dixon et al., 2010; Sutherland, 2014). Gruenfeld, Zagarins, Walker, & Skinner (2013) conducted an evaluation of a pediatric exercise intervention called the "Fun and Fit Program." This program targeted children and adolescents who were at risk for obesity later in life, similar to the HHP in Southern Nevada. The Fun and Fit Program included PA, nutrition, and behavioral health support. The majority of participants were obese at the start of the program (Gruenfeld et al. 2013). The authors of this evaluation stated that the program was translated to be a "real world" program, and that this approach appeared to be successful.

This program evaluation did not address asthma specifically, however cardiorespiratory health was measured using the Rockport Fitness Walking Test, which estimates maximal oxygen uptake (VO2

max) (Gruenfeld et al. 2013). Gruenfeld and colleagues (2013) also examined metabolic equivalents (METs) among their population. METs examine the intensity of activity as a ratio of active metabolic rate to resting metabolic rate. A MET of 1 is equivalent to the energy expended sitting calmly, while moderate activity is equivalent to 3.0 to 6.0 METs , and vigorous activity is >6.0 METs (Heywood & Gibson, 2014). Gruenfeld et al. (2013) found that the exercise intervention increased the ability for more intense activity in their population with a mean change of +1.2 METs (Gruenfed et al., 2013).

There are multiple types of tests to estimate VO2 max, which is considered to be the best measure of cardiorespiratory fitness. VO2 max can be measured as absolute (liters per minute) and is used in non-weight-bearing tests such as cycling. Relative VO2 max is measured in milliliters x kilograms per minute ($mL \bullet kg^{-1} \bullet min^{-1}$), and is more commonly used than absolute VO2 max (Heyward & Gibson, 2014). Laboratory tests to estimate VO2 max include treadmill, cycle ergometer, recumbent stepper, bench stepping, stair climbing, and rowing ergometer tests. Field tests to estimate VO2 max include distance running, jogging, or walking tests, and step tests, as well as swimming or cycling tests in some cases (Heyward & Gibson, 2014). The Rockport test is a 1-mile walk test, which is optimal for those who may not exercise regularly. Klein and colleagues (1987) developed linear regression equations to estimate absolute and relative VO2 max. The absolute VO2 max is calculated:

$$\text{VO2max} = 6.9652 + 0.0091(\text{weight, pounds}) - 0.0257(\text{age, years})$$
$$+ 0.5955(\text{sex [male=1, female=0]}) - 0.2240(\text{time, min.})$$
$$- 0.0115(\text{heart rate, beats/min.})$$

The relative VO2 max ($mL \bullet kg^{-1} \bullet min^{-1}$), is calculated (Klein et al. 1987):

$$\text{VO2max} = 132.853 - 0.0769(\text{weight, pounds}) - 0.3877(\text{age, years})$$
$$+ 6.1350(\text{sex [male=1, female=0]}) - 3.2649(\text{time, min.})$$
$$- 0.1565(\text{heart rate, beats/min.})$$

Heywood and Gibson (2014) provide standard VO2 max values for adults (aged 20 and older) in their textbook, and refer readers to the Cooper Institute for Aerobics Research for reference values for children. The Cooper Institute has developed a reference guide and testing manual for a physical fitness program called FITNESSGRAM®, which is used in the United States for the Presidential Youth Fitness Program (Plowman & Meredith, 2013). The Presidential Youth Fitness Program helps train physical educators to teach and assess physical activity at schools, improve fitness, empower children to be active, and it provides grant funding to assist with these objectives. Partners of the Program include the President's Council on Fitness, Sports and Nutrition, the CDC, the Cooper Institute, the Society of Health and Physical Educators: SHAPE America, and the National Foundation on Fitness, Sports & Nutrition (Presidential Youth Fitness Program, n.d.). The Cooper Institute provides reference values for VO2 max ($mL \bullet kg^{-1} \bullet min^{-1}$) for a 1 mile walk test for children aged 5 to >17 using the equation developed by Klein et al. (1987). The values are categorized into three fitness levels: Healthy Fitness Zone, Needs Improvement, and Needs Improvement – Health Risk (Meredith & Welk, 2013). Table 6, adapted from the FITNESSGRAM®/ACTIVITYGRAM® Test administration manual, 4th ed., Meredith & Welk, 2013, provides these values.

Table 6. VO2 Max Reference Values for Youth Aged 5 to >17 (adapted from Meredith & Welk, 2013)

Age	Boys			Girls		
	Needs Improvement – Health Risk	Needs Improvement	Healthy Fitness Zone	Needs Improvement – Health Risk	Needs Improvement	Healthy Fitness Zone
5 **6** **7** **8** **9**	Completion of test. Timing not recommended.			Completion of test. Timing not recommended		
10	≤37.3	37.4-40.1	≥40.2	≤37.3	37.4-40.1	≥40.2
11	≤37.3	37.4-40.1	≥40.2	≤37.3	37.4-40.1	≥40.2
12	≤37.6	37.7-40.2	≥40.3	≤37.0	37.1-40.0	≥40.1
13	≤38.6	38.7-41.0	≥41.1	≤36.6	36.7-39.6	≥39.7
14	≤39.6	39.7-42.4	≥42.5	≤36.3	36.4-39.3	≥39.4
15	≤40.6	40.7-43.5	≥43.6	≤36.0	36.1-39.0	≥39.1
16	≤41.0	41.1-44.0	≥44.1	≤35.8	35.9-38.8	≥38.9
17	≤41.2	41.3-44.1	≥44.2	≤35.7	35.8-38.7	≥38.8
>17	≤41.2	41.3-44.2	≥44.3	≤35.3	35.4-38.5	≥38.6

Adapted from: FITNESSGRAM®/ACTIVITYGRAM® Test administration manual, 4th ed., Meredith & Welk, 2013, pgs 65-66

VO2 max values for overweight and obese children have been found to be lower than for healthy-weight children (Farpour-Lambert et al., 2009; Melo et al., 2015; Silva et al., 2014), and inversely correlate with BMI, BMI z-score, body fat percentage, and waist circumference (Starkoff, Eneli, Bonny, Hoffman & Devor, 2013). In two studies, mean VO2 max values for obese children and adolescents were as low as 19.7 SD±6.0 (Starkoff et al., 2013) and 27.7±4.17 Silva et al. (2014), considerably lower than the lowest standard FITNESSGRAM® values reported in Table 6. Melo and colleagues (2015) found that children with a "high" waist circumference, defined as ≥85th percentile had a mean VO2 max of 31.82±5.18, which was significantly lower than both those with "middle" waist circumference (>50th to <85th percentile) who had a value of 39.14±6.49, and those with low waist circumference (≤50th percentile) who had a VO2 max value of 46.68±7.03 (Melo et al., 2015).

Ernesti and colleagues (2013) found that among children with asthma, those who are overweight or obese also have significantly lower VO2 max than those who are healthy weight. Those with obesity

and asthma had a VO2 max of 38.3±5 and those who were overweight had a VO2 max of 40.6±8.7, while children with asthma who were classified as healthy weight had a VO2 max of 43±8.6 (Ernesti et al., 2013). Shim and colleagues (2013) found obese asthmatic adolescents (21.7±4.5) and obese non-asthmatic adolescents (21.4±5.4) both had significantly lower values than healthy weight, non-asthmatic controls (35.3±5.8) (Shim et al., 2013).

Many controlled exercise and/or nutrition interventions have been created for youth with obesity and asthma. While Gruenfed and colleagues (2013) have provided a promising evaluation of an exercise program for youth at risk for obesity in adulthood, there is still a gap in the literature as to whether such an intervention program could be beneficial to children who are obese and have asthma. This paper will evaluate an existing exercise program targeted at children who are at risk for adult obesity (the Healthy Hearts Program), and assess the feasibility of such a program for children with asthma, and if feasible, the benefit compared to youth without asthma.

CHAPTER 3. METHODOLOGY

Study Design

This research is a retrospective analysis of two Nevada populations, one from Reno, NV, and the other mainly from the Las Vegas area. The first dataset, from Reno, yielded a cross-sectional analysis examining the association between asthma and weight status. The Reno pilot data were collected from pediatric medical records at the UNSOM Pediatric Allergy/Immunology Clinic.

The second dataset was obtained from the main office of the Children's Heart Center Nevada (CHC) in Las Vegas. The data from CHC were obtained retrospectively from medical records of overweight and obese youth with and without asthma who were enrolled in the HHP. The CHC data were collected for routine CHC medical records and for HHP intervention purposes.

Data Collection and Study Populations

UNSOM Reno Pilot Study Data

The data for this study were obtained from medical records and new patient intake forms from patients at the UNSOM Pediatric Allergy/Immunology Clinic. Patients with asthma who had been seen by a pediatric allergy physician, and who had skin prick tests for IgE sensitization to Northern Nevada allergens performed between June 1, 2009 and June 1, 2012 were recruited for a final sample size of 101. Of these 101 children, 98 had complete BMI data, and were included in this study. The data for this portion of the study were de-identified before being uploaded to a password protected electronic database.

Twenty-seven additional subjects were able to be added to the dataset, from a concurrent allergy study (Great Basin Mold project), as both studies fell under the same Institutional Review Board (IRB) protocols. Only asthmatic patients in the Great Basin Mold study were eligible to be combined with the original asthmatic population. One of the conditions of the IRB required the de-identification of patients, which had already been performed prior to receiving the data. Another requirement from the funding

agency, the Nell J. Redfield Foundation, for combining populations was that the patients had skin prick test results performed for the Northern Nevada allergens mentioned above, with clinical results reported. Both populations met these criteria, and asthmatic patients from the Great Basin Mold study were combined with the original asthmatic population. The population is comprised of patients under age 18.

Additionally, appropriate statistical tests, including Pearson chi-square, Fisher exact tests, Wilcoxon W, and independent sample t-tests (depending on distribution and sample sizes within groups) were performed to determine whether or not the groups were demographically and clinically similar enough to be combined. Analyses between the two populations indicated that they were similar enough to be combined for analyses purposes (Table 7).

Table 7. Population Differences between Eligible Reno Study Participants (N=125)

Variable	Asthma Study (N=98)	Mold Study (N=27)	Test-statistic & value	p-value
Sex				
Male	n=61	n=15	Pearson chi-square=0.379	0.582
Female	n=37	n=12		
Insurance Status				
Private Insurance	n=73	n=20	Pearson chi-square=0.016	0.900
Other Insurance	n=24	n=7		
Race/Ethnicity				
White	n=58	n=23	Fisher's exact test=0.003	0.046
Hispanic/Latino	n=27	n=3		
Other	n=13	n=1		
Asthma Severity				
Mild	n=7	n=1	Fisher's exact test=0.008	0.512
Moderate	n=66	n=16		
Severe	n=17	n=6		
(Mild) Intermittent	n=7	n=4		
Atopy (Y/N)				
Positive	n=77	n=25	Fisher's exact test=0.080	0.158
Negative	n=19	n=2		
BMI Category (CDC)	n=61	n=21	Fisher's exact test=0.038	0.656
Under/healthy wt	n=18	n=4		
Overweight	n=12	n=2		
Obese				
BMI Percentiles				
0-25%	n=14	n=5	Fisher's exact test=0.0053	0.611
26-50%	n=13	n=6		
51-75%	n=22	n=6		
≥76%	n=41	n=9		
Atopy (# +allergens)	n=96, median=15.50, range (0,56)	n=27, median=9.00, range(0, 23)	Wilcoxon W=1398.5	0.091
Age (years)	n=98, median=6.00, range (1,15)	n=27, median=10.00, range (3,16)	Wilcoxon W=2196.0	0.003
FEV1%	n=70, μ=97.37, SD(14.17)	n=22, μ =95.41, SD(10.90)	t= -0.92	0.359
FEV1/FVC	n=70, μ =95.11, SD(8.68)	n=22, μ =96.32, SD(8.62)	t= -0.57	0.571
FEF25-75	n=70, μ =78.99, SD(20.90)	n=22, μ =82.68, SD(18.23)	t= -0.74	0.459

Abbreviations: SD standard deviation, μ mean

Reno Pilot Study Variables

The pilot study database included 66 original variables such as demographics: age, insurance status, sex, race/ethnicity; Obesity status: BMI percentile (calculated for age/sex per CDC standards using height and weight data collected at the initial clinic visit). BMI percentile had been collapsed into categories before de-identification occurred, and therefore, could only be used as a categorical variable. Individual height and weight data were not included in the de-identified dataset per the IRB.

Also included were clinical variables: signs and symptoms during physical examination, pulmonary function tests (spirometry measures), asthma severity as diagnosed by physician (one doctor at the Reno clinic assessed asthma severity for all patients); Medical history: history of respiratory syncytial virus, exacerbating factors, food and drug allergies, surgical history, and environmental triggers (animal exposure, smoking near child, bedding, heating and cooling in the home, type of home); and control measures, all measured from the previous year before visit/referral to an allergist: number of courses of oral steroids used in the past year before seeing the doctor at the Reno clinic, number of visits to the emergency department (ED) in the past year due to asthma, number of overnight hospitalizations in the past year due to asthma, number of missed school days in the past year due to asthma, and asthma medications/dose at first visit and after adjustment by a pediatric allergy physician.

Some variables had missing data and could not be used in this study. Additionally, skin prick tests results for IgE sensitization to numerous types of molds, weeds, inhalants, grass, trees, and animals were included in the dataset (Hogan et al. 2016) (Appendix 2). The cleaned, recoded data was transferred to IBM® SPSS® Statistics, versions 22 and 23 for the majority of analyses. All patients were assessed at the first visit in order to obtain baseline measures of asthma severity and control.

Reno Pilot Study Ethical Considerations

This protocol received an exemption from the IRB for the Office of Human Research Protection at University of Nevada, Reno (UNR) (Protocol #E12-074), approved 6/26/2012. Also approved were a

waiver of informed consent, and a HIPAA waiver for the use of medical records. An agreement for University of Nevada, Las Vegas (UNLV) intent to rely on the UNR IRB was finalized on 5/17/2013. All data were de-identified by clinic staff before any analyses occurred.

Healthy Hearts Program Background and Data

Data from two electronic health record (EHR) databases at CHC were collected to create a dataset of asthma patients, and control patients without asthma who participated in the 12-week HHP nutrition and exercise intervention for overweight and obese children. Much of the data came from the HHP intake form located in each patient's record. A copy of the intake form is located in Appendix 3.

The family-based HHP was created in 2002 with the goal of promoting healthy lifestyles by using behavior modification such as improving diet, physical activity levels, and self-esteem for overweight and obese children, and those otherwise at risk for heart disease. This behavior modification helps to reduce the risk of chronic diseases such as type II diabetes, hypertension, heart disease, and other comorbid disorders (CHC, 2015). CHC patients are referred to the HHP for the following reasons:

- Overweight (>85th percentile for age)
- High cholesterol (>170 mg/dL)
- Family history of premature heart disease ("first degree male relative before the age of 55 or a female relative before the age of 65")
- Have a parent with high cholesterol (>240 mg/dL)
- Have risk factors for heart disease, which include: obesity, hypertension, diabetes, hyperinsulinemia (high insulin levels), or hyperlipidemia (high lipid levels) (CHC, 2015).

The first step of the program is an evaluation with a cardiologist and an electrocardiogram (EKG) test to examine cardiac function. The next step is consultation with a dietician, after which the 12-week fitness and nutrition activities begin. At weeks 1, 6, and 12, height, weight, percent body fat, waist

circumference, and blood pressure are measured (Figure 3). Patients may continue to follow up with dieticians every three months, and they may repeat the program multiple times, and into adulthood if they choose. The goal for those entering the program with with a BMI between the 85th-96th percentiles is weight maintenance as long as there are no other risk factors for heart disease. The protocol is follow-up counseling every three months and laboratory tests every six months. The goal for those entering with with a BMI percentile ≥97th is weight loss, and the protocol for these patients is follow-up counseling and laboratory tests every three months (CHC, 2015). Cardiac rehabilitation is also offered to patients with cardiac diagnoses. The rehabilitation includes exercise tolerance improvement and education about heart disease (CHC, 2015). The program is conducted in both English and Spanish.

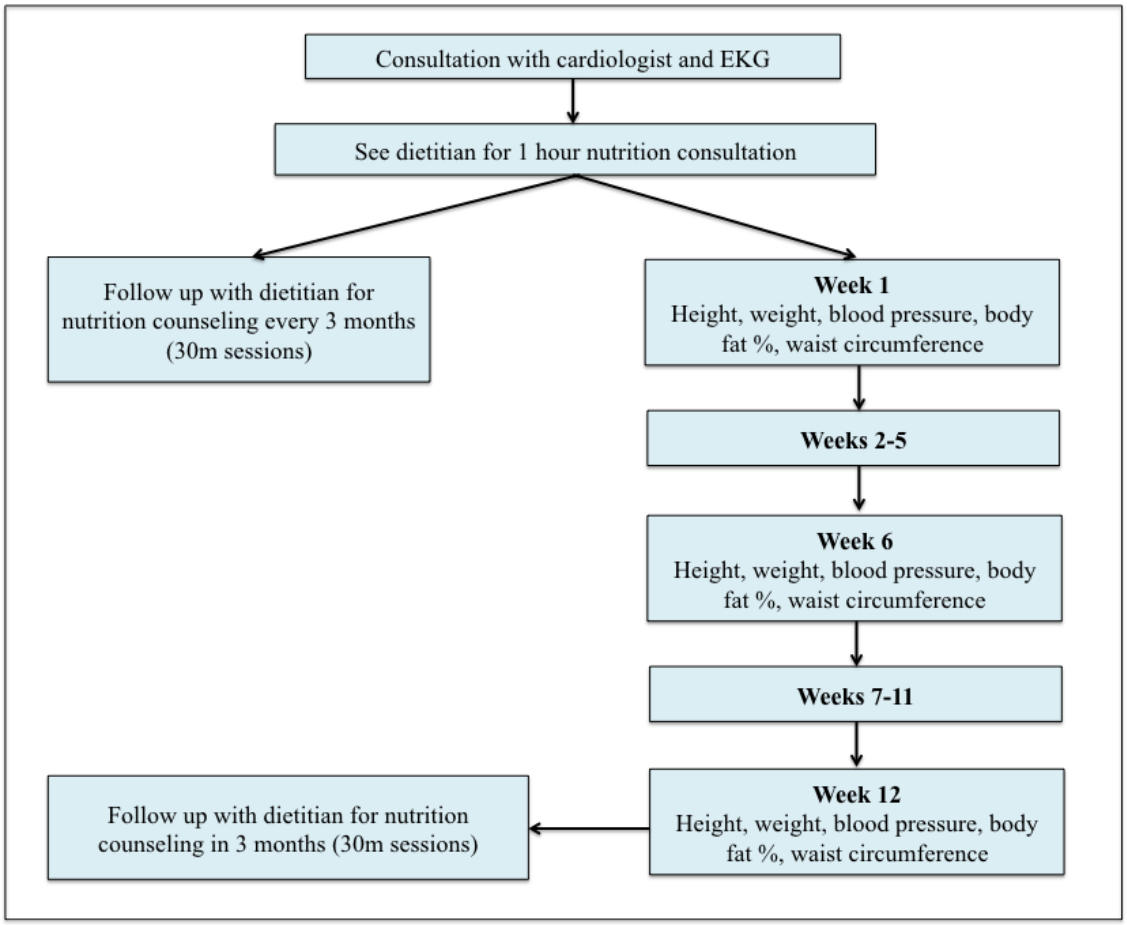

Figure 3. Healthy Hearts Program Procedure (adapted from HHP literature)

In this study, two groups of patients were compared:

1) Pediatric overweight or obese patients who were in the program and had asthma
2) A control group of pediatric overweight or obese patients who were in the program and who did not have asthma.

For this study, overweight/obese children had a BMI of 90th percentile or higher at the beginning of the intervention, as instructed by the CHC Director of Research. Asthma was defined as having a diagnosis of asthma, a diagnosis of reactive airway disease (RAD) and/or prescribed one or more medications for asthma control. Medical record searches included brand name and generic medications (Table 8).

Table 8. Asthma Medications taken by the Healthy Hearts Program Population

Type	Generic Name	Brand name(s)
Inhaled Corticosteroids (ICS)	Beclomethasone	QVAR®
	Budesonide	Pulmicort®
	Fluticasone propionate	Flovent® HFA, Flovent® Diskus®
	Mometasone	Asmanex®
ICS in combination with long-acting β-agonists (LABAs)	Budesonide/formoterol	Symbicort®
	Fluticasone/salmeterol	Advair®
	mometasone/formoterol	Dulera®
Emergency Medications		
Short acting β-agonists	Albuterol, Albuterol Sulfate	ProAir®, Ventolin®
	Levalbuterol HCl	Xopenex®
Anticholinergics (AC)	Ipratropium bromide	Atrovent®
	Titropium bromide	Spiriva HandiHaler®
Combined SABA/AC	Ipratropium bromide/ albuterol sulfate	DuoNeb®
Leukotriene Modifiers	Montelukast	Singulair®*

* Singulair included if in combination with another medication on the list, as this drug is also taken for allergies alone

In total, 86 children with asthma and 146 youth without asthma met inclusion criteria. Inclusion criteria were: male and female patients, age 5-18 years who participated in the HHP from 2004 to

December 2014. Exclusion criteria include records from patients with congenital heart disease, developmental delay, or other medical inability to do the exercise program (for reasons other than asthma). Data were de-identified before analyses were conducted. The majority of children who did the intervention program did so in Las Vegas, however a small number of participants lived in Reno, where the intervention program also took place prior to 2010.

CHC Study Variables

Pre and post intervention variables included in the dataset were:

- BMI percentile and z-score
- Metabolic equivalents (METs) for intensity of activity
- Maximal oxygen consumption (VO2max)
- Laboratory test results (total cholesterol, HDL/LDL, triglycerides, insulin, C-reactive protein [CRP])
- Vital signs: blood pressure (mmHg) and heart rate (beats/minute)

HHP protocol specifies to only repeat laboratory tests if the pre-tests are abnormal, therefore many patients did not have post-test laboratory results. Additionally, if a child quit the program before completion (attrition), other post-test variables were not available.

Other variables included sociodemographic variables: age in years, race/ethnicity (collapsed to Hispanic and non-Hispanic due to a high proportion of Hispanic children in the program [>60%]), sex (m/f), and insurance status (insured, uninsured, or Medicaid recipient – uninsured and Medicaid categories were combined for analysis due to the small sample of uninsured patients [n=10]); Asthma status (y/n) and medications for asthma/RAD (listed above in Table 7); Other medications, comorbid diagnoses, and allergies.

Also included were program completion variables: Start/end date of program, whether or not the child finished the program in 12 weeks, how many weeks the child showed up for the program, if the

program was done one time or more (first time in program was used for consistency and reduction of bias), how the visit was coded in the EHR (completed or not completed), and whether the staff coded the program as completed.

If a child missed a week during the program, but showed up the next week, the visits could be combined, for example if the child missed week 3 but showed up week 4 and completed all requirements, the visit could be coded as "week 3/4" and was regarded as two visits. For this reason, not all children who "completed" the program used the full 12 visits. Many patients completed the program by week 10, and some finished as early as weeks 6-9. The HHP staff determined whether the child met the requirements to be considered "completed", which is the time variable used in this study as "time in program," as a dichotomous variable for event in Cox proportional hazards regression, while "weeks in the program" is used continuously in other analyses. This measure was selected because I believe the staff working with the children and families on a regular basis are more likely than an EHR system to know whether or not the child has completed the requirements of the program.

Healthy Hearts Program Ethical Considerations

The IRB for the Sunrise Health Office of Research Compliance conducted a full review and approved the protocol for this study (Protocol # 14-025), approved 11/5/2014. A waiver of informed consent was also approved. An exemption was received from the IRB at the Office of Research Integrity – Human Subjects at UNLV, due to the use of de-identified data, and because the protocol had already been reviewed and approved by the Sunrise Health IRB (UNLV protocol #1412-5020M), approved 12/5/2014. All data were de-identified by the office of the Director of Research at the Children's Heart Center prior to analyses.

Research Questions and Hypotheses

The overall objective of this study was to examine the associations between pediatric asthma/allergy and obesity status in Nevada, and to determine whether or not a feasible intervention exists to help asthmatic youth with elevated BMI lose weight.

Question 1: Is elevated BMI associated with asthma severity within a select group of children with asthma from a Reno UNSOM pediatric allergy/immunology clinic?

H_o: There will be no difference among asthma severity by BMI percentile category

H_{a1}: Those with an elevated BMI (overweight or obese percentile groups) will have more severe asthma than those with a healthy BMI by doctor diagnosed severity

H_{a2}: Those with an elevated BMI (overweight or obese percentile groups) will have more severe asthma than those with a healthy BMI by pulmonary function tests

H_{a3}: Those with an elevated BMI (overweight or obese percentile groups) will have more severe asthma than those with a healthy BMI by proxies of severity, such as financial cost and quality-of-life measures

Question 2: Within the Reno pediatric pilot population is elevated BMI associated with allergen sensitization or asthma/allergy triggers?

H_o: There will be no difference among the number/type of allergies or the number of asthma/allergy triggers by BMI percentile

H_{a1}: There will be a difference in allergen sensitization as evidenced by positive skin prick tests, among those with elevated BMI and those in the healthy BMI category

Question 3: Will the 12-week physical activity intervention be feasible for overweight/obese children with asthma compared to overweight/obese children without asthma among the CHC population (due to those with asthma being prone to respiratory distress when exercising)?

H_o: There will be no difference between asthmatic and non-asthmatic children with elevated BMI in completion of the program

H_{a1}: There will be a difference in completion rate between asthmatics compared to non-asthmatics with elevated BMI

Analysis of data

Data were analyzed using SAS® version 9.4, IBM® SPSS® Statistics, version 22 and 23, and Microsoft® Excel® for Mac 2011 and Microsoft® Excel® 2010 for PC. Komolgorov-Smirnov and Shapiro-Wilk tests, as well as visual examination of histograms with normal curves were used to determine whether the use of parametric or non-parametric tests were appropriate (Pallant 2013). Descriptive statistics were performed separately for each population on both quantitative and re-coded qualitative (nominal and non-numeric categorical) variables to obtain frequencies and measures of central tendency to summarize each population's characteristics. Additionally, paired t-tests (or Wilcoxon Signed Ranks tests) were performed to examine crude pre-post differences in BMI percentile, BMI z-score, VO2max, METs, heart rate, and blood pressure among CHC populations with and without asthma pre-and post-intervention (Field, 2013). Independent sample t-tests or Mann-Whitney U tests were performed to test differences between those with and without asthma at baseline and after intervention (Field, 2013).

<u>Reno Pilot Study</u>

Research Question 1, Hypothesis 1

The first research question examines association between elevated BMI and asthma severity. To test the first alternative hypothesis, that asthma will be more severe in those with an elevated BMI

(overweight or obese percentile group) compared to those with healthy BMI, crude and adjusted multinomial logistic regressions were conducted (Field, 2013).

Asthma severity was the dependent variable. Mild and intermittent asthma were combined for adequate sample size giving the dependent variable three categories: mild/intermittent, moderate, and severe asthma. The independent variable was BMI percentile category (underweight/healthy weight, overweight, and obese). The underweight patients were combined with healthy weight patients due to the small sample size of the underweight group (n=4). The adjusted regression model also included age in years, race, and sex (m/f). The race/ethnicity variable was dichotomized (white and "other race"). "Other race" includes Hispanic/Latino youth (24%), and less than 5% each of Asian, black, Hawaiian Islander, Native American, multiracial, and "other race" patients. Pearson and Deviance goodness-of-fit tests were conducted (Field, 2013).

Research Question 1, Hypothesis 2

The second alternative hypothesis from Question 1, that those with elevated BMI will have more severe asthma based on pulmonary function was tested using one-way analyses of variance (ANOVAs). Measures of lung function are the continuous dependent variables. Spirometry measures (FEV_1%, FEV_1/FVC%, and FEF_{25-75}%) are continuous variables. BMI percentile is the independent variable (1=underweight, 2=healthy weight, 3=overweight/obese). The Levene test for homogeneity of variance was conducted for each measure (Field, 2013).

Research Question 1, Hypothesis 3

The third alternative hypothesis for Question 1 examines elevated BMI in relation to proxies for asthma severity. These proxies for asthma severity include:

- Number of courses of oral steroids used in the past year for asthma
- Number of hospitalizations in the past year due to asthma

- Number of ED visits in the past year due to asthma
- Number of missed school days in the past year due to asthma

All proxy measures for asthma severity were dichotomized due to positive skew and a large proportion of zero values. Chi-square tests were conducted to examine the associations between BMI percentile and the proxy measures. Two of the proxy variables (hospitalizations and missed school days) had more than 20% of cells with expected counts lower than 5, therefore chi-square tests were not appropriate (Pallant, 2013). Fisher exact tests were subsequently conducted on the hospitalization and missed school day variables to examine the associations between the variable and BMI percentile category. The only significantly associated variable, oral steroid use, was then used in crude and adjusted binary logistic regression as the dependent variable. BMI percentile category was the independent variable and the regression was adjusted for age in years, sex (m/f) and race (dichotomized, as stated above in Question 1, hypothesis 1). The Hosmer and Lemeshow goodness of fit test was used to examine model fit (Pallant, 2013).

Research Question 2

The hypothesis for the second research question regarding allergic sensitization associations to elevated BMI percentile, was tested using two separate multiple logistic regressions. The dependent variable for the first regression was atopy (allergen sensitization) (positive/not positive) and for the second regression polysensitization (y/n). For both regressions BMI percentile was the independent variable. The models were also adjusted for age in years, sex (m/f), and race (white and other race as defined above).

Skin prick test results for IgE sensitization to eight types of molds, 10 types of weeds, 10 types of indoor inhalants, six types of grass, 20 types of trees, and nine types of both household and non-household animals specific to Northern Nevada are included in the in the dataset (Hogan et al. 2016) (Appendix 2). Positive skin prick test results to the allergens were summed to create a continuous

variable. A number between 0 and 63 was assigned to each patient, in which 0=no allergic reactions and 63=allergic to every aeroallergen tested. Atopic patients are sensitized to at least one allergen. Polysensitized patients are sensitized to two or more allergens (Migueres et al. 2014). Kolmogorov-Smirnov tests and histogram examinations demonstrated non-normal distribution of atopy score. Polysentitization was a dichotomous variable (y/n).

Transformations were attempted to normalize the variable and included square root transformation, log(1+y) transformation (y=random variable), inverse transformation (1/[y + 1]), Box-Cox transformation (van Belle, Fisher, Heagerty, & Lumley, 2004) , and a two-step procedure to normalize data as described by Templeton (2011) which includes ranking cases and applying inverse normal distribution function to the ranked values to produce z-scores of the values (Templeton, 2011). No method produced a normally distributed atopy variable; atopy was dichotomized to use in logistic regression. Hosmer and Lemeshow goodness of fit tests were used to assess model fit for each regression model (Pallant, 2013).

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Research Question 3

The hypothesis to test the third research question, that there will be a difference in outcomes between overweight/obese children with and without asthma in the HHP intervention, Cox Proportional Hazards regression was utilized to examine attrition rates and repeated measures ANOVAs to examine outcome measures in the patients who finished the intervention. Adjusted models included age in years, race/ethnicity (Hispanic/non/Hispanic), sex (m/f), and insurance status (Insured/Medicaid recipient). As noted above Medicaid recipients and uninsured patients were combined due to the small number of uninsured patients (n=10, 4.3% of the population). The race variable was dichotomized because the proportion of patients who reported "Hispanic" as their race was 64.2% (n=149). The non-Hispanic group is comprised of 12.1% black children (n=28), 16.8% white children (n=39), 2.6% Asian children (n=6),

1.3% American Indian/Alaska Native (n=3), 1.3% who reported "other race" (n=3) and 1.7% with no reported race (n=4). Number of comorbid diagnoses was also added as a covariate to all multivariable analyses, but it did not end up in any final models as it was not significant.

Proportional hazards assumptions were tested on independent variables (asthma [y/n], race/ethnicity (Hispanic/not Hispanic), sex (m/f), insurance status (insured/Medicaid). Age is continuous, but the ages only range from 6-18. To determine whether the covariates violated the proportional hazards assumption, each variable was examined by computing a time dependent covariate in SPSS (T_*variable). Log minus log plots were examined as well (Hosmer, Lemeshow, & May, 2008).

In the Cox regression, the time variable was time in weeks in the program, the event was defined as "finished the program" ("1"), based upon the coding provided by the CHC staff as discussed previously in the CHC Variables section. Asthma status (y/n) was the independent variable, with age, race/ethnicity, and sex as covariates in the adjusted model.

Two main outcome measures from the program will be examined in this study to assess the difference between asthmatic and non-asthmatic patients. These measures are BMI z-score, which was selected because the objective of the program is to maintain or lose weight for heart health, and VO2 max. Oxygen consumption was examined because youth with asthma, especially those who are overweight or obese, have difficulty during physical activity due to exercise-induced bronchospasm (Ostrom et al., 2013; van Leeuwen et al., 2013). Asthma status (y/n) is the dichotomous predictor variable, and time in weeks is included in each model. Time for BMI z-score has three measures (weeks 1, 6, and 12), and VO2 max has two measures (weeks 1 and 12). The CHC staff uses the Rockport 1-mile walk test to calculate relative VO2 max (mL/Kg/min) using Klein et al.'s (1987) equation (Klein et al., 1987).

Repeated-measures ANOVAs were conducted on the two outcome measures from the program: BMI z-score and VO2max to determine whether the outcomes were different between children with and without asthma. Covariates were added to create repeated-measures analysis of covariance (ANCOVA)

models. The covariates included: race/ethnicity (Hispanic/not Hispanic), sex (m/f, for the BMI z-score model), insurance status (insured/Medicaid), and age (continuous). Two separate analyses were conducted to examine pre-post difference in VO2max, one for boys and one for girls. As seen in Table 6 in the literature review, VO2max reference values increase overall as health increases, yet the values also increase as age increases for boys, but decrease as age increases for girls (Meredith & Welk, 2013). A combined sex model was not appropriate hence stratification was performed.

Power analyses, using G*Power version 3.1.9.2, were conducted to determine adequate sample size. Effect size to calculate sample size was estimated (Lakens, 2013; Sullivan & Feinn, 2012) by using effect sizes from three meta-analyses in which interventions to reduce obesity in pediatric populations were examined (Janike et al., 2014; Kitzmann et al., 2010; Yavuz, van Ijzendoorn, Mesman, & van der Vook, 2015). The average effect size from a combined 136 studies was 0.321. Using this estimate to determine sample size for repeated measures ANOVA models using the F-statistic, for BMI z-score, a sample size of 24 patients overall was required for a power of 80%, and a sample of 38 children overall was required for a power of 95%. For VO2max, a sample of 22 children was required for a power of 80%, and a sample of 34 children was required for a power of 95%.

While BMI percentiles for children are adjusted for age and sex, they are not comparable among children of different ages or between males and females. Z-scores are comparable measures, which are defined by the number of standard deviations from a mean value (Wang & Chen, 2012). For example, if one were to look at the last BMI growth chart in Appendix I (Page 93) BMI for Age for girls, they could see that a BMI of 18 would put a 4-year-old girl at the 95th percentile, yet a 15-year-old girl would have a BMI slightly below the 25th percentile. While it is not necessary for clinicians to compare these two girls, by assigning a standardized value these girls can be compared using statistical software that can adjust for age as a number, but not for puberty or hormonal differences which alter body mass with age, as noted in the literature review.

BMI percentile is a rank, while the z-score is a continuous value between -3 and +3. In a normal distribution, -3 corresponds with a BMI percentile of 0.2nd, -1.96 is the 2.5th percentile, 0 is the 50th percentile, +1 is the 84th percentile, +1.96 is the 97.5th percentile, and +3 is 99.8th percentile, as would be expected in a normal curve (Wang and Chen, 2012). The equation for a z-score is:

$$Z = (x - \mu)/\sigma$$

Where x=individual value, μ=population mean (such as the national mean, which is an external measure needed to standardize the value [Must & Anderson, 2006]), and σ=standard deviation of the population (Wang and Chen, 2012).

The CDC provides a SAS program to calculate BMI z-scores (CDC, 2016a). Calculation using the SAS program includes the use of potentially identifiable variables (such as date of birth) meaning the calculation needed to be conducted at the CHC. The available CHC computers do not have SAS installed, therefore, an online calculator from the Children's Hospital of Philadelphia (CHOP) Research Institute was used to calculate z-scores for patients who did not have a calculated z-score and to double check those who did have a z-score in the medical records to avoid bias from rounding numbers at two decimal places. The CHOP Research Institute's program uses calculations based on CDC growth charts adjusted for age and sex (CHOP Research Institute, 2016); the CHC uses the same calculation.

CHAPTER 4. RESULTS

Reno Population – Demographics & Descriptive Characteristics

Table 9 shows demographic characteristics and BMI percentile categories for the Reno population (N=125). The population was comprised of youth aged 1-16 (median age: 7 years), of whom 60.8% (n=76) were male, 39.2% (n=49) were female, 64.8% (n=81) were white, and 24.8% (n=31) were of another race and/or ethnicity. Seventy-four percent (n=93) of these children had private medical insurance, while 24.8% (n=31) had another form of health insurance (other includes Medicaid, no insurance, tribal insurance, self-pay, or multiple forms of insurance); one case was missing insurance data. Eighty-two children (65.6%) were in the under/healthy weight BMI category (<85th percentile), 22 (17.6%) were classified as overweight, and 14 children (11.2%) were in the obese category (Table 9).

Table 9. Population Characteristics of Reno Patients (N=125)

Variable	N(%)
Sex	
Male	76 (60.8)
Female	49 (39.2)
Insurance Status	
Private Insurance	93 (74.4)
Other Insurance	31 (24.8)*
Race/Ethnicity	
White	81 (64.8)
Other	44 (35.2)
BMI Percentile Category	
Under/healthy weight (<85th percentile)	82 (65.6)
Overweight (85th to <95th percentile)	22 (17.6)
Obese (≥95th percentile)	14 (11.2)*
	Median (range)
Age (years)	7.00 (1-16)

*Insurance status, 1 missing case; BMI percentile category, 7 missing cases

Asthma and allergy related characteristics of the Reno population (N=125) are shown in Table 10. Asthma symptom severity was moderate in 82 cases (66%) and severe in 23 cases (18%), and severity was missing for one case. Atopy occurred in 82% of children (n=102), pollen atopy (sensitization to grass, weeds, and trees specifically) occurred in 74% (n=93) of the population, and 79% were

polysensitized (n=99). The children in this population were sensitized to a median of 11 allergens, and a median of 7.5 pollen allergens (Table 10). The number of courses of oral steroids required for asthma control in the past year ranged from 0-6; 38.4% (n=48) of patients required one or more courses of oral steroids in the past year due to asthma. Four percent (n=5) of the population missed 1 or more days of school in the past year due to asthma, 24.8% (n=31) required 1 or more ED visits, and 7.2% (n=9) required 1 or more overnight hospitalizations in the past year due to asthma. Cases missing data are also reported in Table 10.

Table 10. Asthma/allergy Characteristics of Reno Patients (N=125)

Variable	N(%)
Asthma Severity	
Mild/Intermittent	19 (15.2)
Moderate	82 (65.6)
Severe	23 (18.4)
Total*	124 (99.2)*
Atopy (Y/N)	
Positive	102 (81.6)
Negative	21 (16.8)
Total*	123 (98.4)*
Pollen Atopy (Y/N)	
Positive	93 (74.4)
Negative	21 (16.8)
Total*	114 (91.2)
Polysensitized (Y/N)	
Yes (≥2 allergens+)	99 (79.2)
No (0-1 allergens+)	24 (19.2)
Total*	123 (98.4)*
Number of courses of oral steroids in past year (range=0-6)	
0	77 (61.6)
1 or more	48 (38.4)
Total	125 (100)
Number of school days missed in past year (range=0-23)	
0	120 (96)
1 or more	5 (4)
Total	125 (100)
Number of emergency department visits in past year (range=0-9)	
0	94 (75.2)
1 or more	31 (24.8)
Total	125 (100)
Number of overnight hospitalizations in past year (range=0-2)	
0	116 (92.8)
1 or more	9 (7.2)
Total	125 (100)
	Median (Range)
Atopy score (# +allergens)*	11 (0-56)
Pollen atopy (# + allergens)*	7.5 (0-36)
	Mean (SD)
FEV_1% predicted*	93.10 (13.49)
FEV1%/FVC*	95.40 (8.64)
$FEF_{25\%-75\%}$*	79.87 (2.12)

*Asthma severity, 1 missing case (0.8% of population); Atopy (Y/N), 2 missing cases (1.6%); Pollen atopy (Y/N), 11 missing cases (8.8%); Polysensitized Y/N, 2 missing cases (1.6%), Atopy(#), 2 missing cases (1.6%); Pollen atopy (#), 11 missing cases (8.8%), all PFTs, 33 missing cases

A breakdown of asthma severity by BMI status is shown in Table 11. Of those who are overweight, 1.7% had mild or intermittent asthma, and of those who are obese, 1.7% had mild or

intermittent asthma. Seven obese children (5.9%) had moderate asthma, and 17 overweight youth (14.4%) had moderate asthma. Three overweight children (2.5%) had severe asthma, and five obese children (4.2%) had severe asthma (Table 11).

Table 11. Reno Pilot Population Asthma Severity by BMI Status (N=118)

	Under/Healthy Weight n (%)	**Overweight n (%)**	**Obese n (%)**	**Total n (%)**
Asthma Severity				
Mild/Intermittent	13 (11.0)	2 (1.7)	2 (1.7)	17 (14.4)
Moderate	56 (47.5)	17 (14.4)	7 (5.9)	80 (67.8)
Severe	13 (11.0)	3 (2.5)	5 (4.2)	21 (17.8)
Total	82 (69.5)	22 (18.6)	14 (11.9)	118 (100)

Reno Population Results

Associations between Asthma Severity and BMI

Research Question 1, Hypothesis 1

Research question 1, hypothesis 1 examined the association between asthma symptom severity and elevated BMI. Multinomial logistic regression analysis for asthma severity determined that after adjustment, age was the only statistically significant predictor for moderate asthma (AOR 0.78, p=0.003, 95% CI=0.66-0.92), and severity increased with age for those with severe asthma, though not significantly (p=0.420). Increased age (by year) was predictive of a 22% decrease in moderate asthma compared to mild or intermittent asthma; therefore as this population gets older, asthma severity lessens, at least from the moderate to mild categories.

Though not statistically significant, compared to healthy weight patients, overweight patients had 44% higher odds of having moderate asthma (p=0.666) and 40% more likely to have severe asthma

(p=0.740). Obese patients were 26% more likely to have moderate asthma (p=0.802) and more than 4 times more likely to have severe asthma (p=0.162) (Table 12). Race and sex were not significant predictors of asthma severity. Adequate model fit was assessed and determined (Pearson goodness-of-fit test, p=0.302, Deviance goodness-of-fit test, p=0.952) (Field, 2013). This result, while not significant does show a trend: as BMI is elevated, asthma becomes more severe. If this had been significant, it would mean that as public health professionals, it is up to us to see help obese children with asthma to lose weight so the severity of their asthma symptoms can decrease.

Table 12. Multinomial Logistic Regression Analysis of BMI Status and Asthma Severity (N=118)

	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Moderate Asthma*				
BMI Status				
Healthy weight (<85th percentile)	‡		‡	
Overweight (85th to <95th percentile)	1.97 (0.42-9.62)	0.401	1.44 (0.27-7.66)	0.666
Obese (≥95th percentile)	0.81 (0.51-4.37)	0.809	1.26 (0.20-7.88)	0.802
Age			0.78 (0.66-0.92)	0.003*
Race				
Other race			‡	
White			1.45 (0.45-4.69)	0.534
Sex				
Male			‡	
Female			3.16 (0.87-11.46)	0.080
Severe Asthma*				
BMI Status				
Healthy weight (85th to <95th percentile)	‡		‡	
Overweight (≥85th percentile)	1.50 (0.21-10.52)	0.683	1.40 (0.19-10.24)	0.740
Obese (≥95th percentile)	2.50 (0.41-15.29)	0.321	4.01 (0.57-28.15)	0.162
Age			1.08 (0.89-1.32)	0.420
Race				
Other race			‡	
White			2.07 (0.49-8.80)	0.327
Sex				
Male			‡	
Female			1.19 (0.40-8.53)	0.426

*Mild/intermittent asthma is the reference category for asthma status, ‡ reference category
**Statistically significant at p<0.05

Research Question 1, Hypothesis 2

Question 1, hypothesis 2 examines the relationship between lung function, as measured by spirometry, and elevated body mass. There were no significant differences between BMI categories and lung function, although the forced expiratory flow at 25-75% from the ANOVA approached significance (p=0.074) (Table 13). The variance was equal in all three models (Levene homogeneity test FEV_1% p=0.776, FEV_1/FCV p=0.321, and $FEF_{25-75\%}$ p=0.221) (Field, 2013).

Table 13. Associations between Weight Category and Pulmonary Function Test Measures

ANOVA	F	p-value
FEV_1 %	1.21	0.302
FEV_1/FCV	2.23	0.113
$FEF_{25-75\%}$	2.69	0.074

Research Question 1, Hypothesis 3

Question 1, hypothesis 3 examines proxy measures of asthma severity in relation to elevated body mass. These proxy measures included number of courses of oral steroids required in the past year due to asthma, number of emergency department visits in the past year due to asthma, number of school days missed in the past year due to asthma, and number of overnight hospitalizations in the past year due to asthma. The only proxy measure significantly associated with BMI percentile was oral steroid use (χ^2=9.86, p=0.007) (Table 14).

Table 14. Relationships between BMI Status and Asthma Severity Proxies (N=118)

	BMI Status	
	χ^2	p-value
Number of courses of oral steroids in past year	9.86	0.007*
Number of emergency department visits in past year	1.78	0.411
	Fisher exact	p-value
Number of school days missed in past year		0.624
Number of overnight hospitalizations in past year		0.108

*Statistically significant at p<0.05

To further examine the significant association between BMI and oral steroid use from the initial chi-square test, binary logistic regression was conducted. Table 15 shows that those in the obese category have nearly 8 times greater odds of having required at least one course of oral steroids in the past year due to asthma (AOR 7.76, p=0.003, 95% CI=2.0-30.11) after adjustment for age, sex, and race/ethnicity. Additionally, for each year increase in age, odds of requiring steroids decreased by 22% (Table 15). Race and sex were not significant predictors of oral steroid use. Model fit was assessed and determined to be adequate (Hosmer and Lemeshow test p=0.630) (Pallant, 2013). This result shows that before visiting a pediatric allergist, the obese children in the population likely had poorer asthma control than healthy weight or overweight youth, as evidenced by the need for more oral steroids.

Table 15. Binary Logistic Regression Analysis of BMI Status and Oral Steroid Use (N=118)

	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
BMI Status				
Healthy weight (<85th percentile)	‡		‡	
Overweight (85th to <95th percentile)	2.01 (0.77-5.28)	0.155	1.80 (0.66-4.85)	0.249
Obese (≥95th percentile)	6.04 (1.73-21.16)	0.005**	7.76 (2.0-30.11)	0.003*
Age			0.88 (0.78-0.99)	0.027*
Race				
White			‡	
Other race			0.90 (0.39-2.10)	0.812
Sex				
Female			‡	
Male			0.79 (0.34-1.88)	0.249

*Significant at p<0.05, ‡ reference category

Associations between Allergic Sensitization and BMI

Research Question 2

Research question 2, hypothesis 1 examines elevated BMI and allergic sensitization and polysensitization. The binary logistic regression model for allergen sensitization demonstrated BMI and age were significant predictors of allergen sensitization. Overweight patients were 79% less likely to be sensitized to allergens than those who were of healthy weight (AOR 0.21, p=0.010, 95% CI=0.06-0.69). Additionally, for each year increase in age, all patients had 28% greater odds of being sensitized to allergens (AOR 1.28, p=0.010, 95% CI=1.06-1.54) (Table 16).

Binary logistic regression for polysensitization demonstrated that BMI and age were significant predictors for polysensitization. Overweight patients were 73% less likely to be polysensitized than those who were of healthy weight (AOR 0.27, p=0.028, 95% CI=0.09-0.87) (Table 17). For each year increase in age, this population had 27% greater odds of being polysensitized to aeroallergens (AOR 1.27, p=0.006, 95% CI 1.07-1.50). Obese BMI percentile status, race, and sex were not associated significantly with atopy or polysensitization (Tables 16 & 17). Both models were assessed and yielded adequate model fit (Hosmer and Lemeshow test for allergen sensitization model, p=0.719; Hosmer and Lemeshow test for polysensitization model, p=0.887) (Pallant, 2013).

These results show that increases in age are associated with increased in allergen sensitization – this is logical; as a child gets older he or she will be exposed to more allergens. These results also show that overweight (but not obesity) is associated with lower allergen sensitization, although all children were sensitized, therefore all children should be tested for allergies if they have asthma because sensitization does occur in all weight status categories.

Table 16. Binary Logistic Regression Analysis of BMI Status and Allergen Sensitization (N=118)

	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95%CI)	p-value
BMI Status				
Healthy weight (<85th percentile)	‡		‡	
Overweight (85th to <95th percentile)	0.19 (0.06-0.61)	0.005*	0.21 (0.06-0.69)	0.010*
Obese (≥95th percentile)	0.67 (0.13-3.53)	0.633	0.46 (0.08-2.84)	0.407
Age			1.28 (1.06-1.54)	0.010*
Race				
White			‡	
Other race			1.70 (0.50-5.78)	0.369
Sex				
Female			‡	
Male			1.44 (.46-4.52)	0.537

*Statistically significant p<0.05, ‡ reference category

Table 17. Binary Logistic Regression Analysis of BMI Status and Allergen Polysensitization (N=118)

	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95%CI)	p-value
BMI Status				
Healthy weight (<85th percentile)	‡		‡	
Overweight (85th to <95th percentile)	0.25 (0.08-0.75)	0.013*	0.27 (0.09-0.87)	0.028*
Obese (≥95th percentile)	0.52 (0.12-2.21)	0.378	0.37 (0.08-1.81)	0.221
Age			1.27 (1.07-1.50)	0.006*
Race				
White			‡	
Other race			1.18 (0.40-3.43)	0.771
Sex				
Female			‡	
Male			1.33 (0.45-3.90)	0.603

*Statistically significant p<0.05, ‡ reference category

Children's Heart Center Population – Demographics & Descriptive Characteristics

The Children's Heart Center Healthy Hearts Program population was comprised of 232 patients, of whom, 54.3% were male (n=126), 64.2% were Hispanic (n=149), and 55.2% received Medicaid

(n=128). Most children participated the program in Las Vegas (91.4%, n=212), however between 2006 and 2009, 20 children (8.6%) participated in the program in Reno. The Reno location is no longer participating in the HHP. The mean age of the population was nearly 11 years old with a range from approximately 6.5 years to 18 years old (Table 18). Eighty-six children (37.1%) had asthma, and 146 (62.9%) did not have asthma, while 18.1% of this population had allergies to aeroallergens, food allergens, medications, or a mixture of allergens (Table 18). The median time in the program was 9 weeks, with a range of 1-12 weeks (Table 18).

Nearly 98% of the HHP population had at least one diagnosis (not including asthma, which was not counted as a "comorbid" diagnosis as asthma status was it's own variable). Only four patients did not have an existing diagnosis; one only had an asthma diagnosis (Table 18). Forty-seven percent of the population (n=109) had two coexisting diagnoses, 22% (n=51) had three coexisting diagnoses and 23 children (10%) had four or more coexisting diagnoses in their records. Metabolic diagnoses include those with International Classification of Disease, 9th revision (ICD-9) codes from 240-279: Endocrine, nutritional and metabolic diseases, and immunity disorders, or ICD 10 codes E00-E89: Endocrine, nutritional or metabolic diseases. These include diagnoses of metabolic syndrome, diabetes mellitus, elevated lipid, cholesterol or insulin levels, and obesity (CDC, 2015d; WHO, 2016). Metabolic syndrome was the most common metabolic disease in this population (n=140, 60.3%). Non-metabolic diseases in this population were mainly, hypertensive or heart diseases or functional murmur (n=56, 24.1%), and/or congenital heart conditions that did not prevent the child from participating in the intervention (n=20, 8.6%). The number of comorbid diagnoses differed significantly between the asthmatic (median 2 diagnoses) and non-asthmatic groups (median 1 diagnosis) (Mann-Whitney U=5235.0, p=0.022). The variable was added as a covariate to all further multivariable analyses, but it did not end up in any final models, as it was not significant in any adjusted models.

Table 18. Population Characteristics of Children's Heart Center Patients (N=232)

Variable	Non-Asthmatic n(%)	Asthmatic n(%)	Total n (%)
Sex			
Male	75 (32.2)	51 (22.0)	126 (54.3)
Female	71 (30.6)	35 (15.1)	106 (45.7)
Race/Ethnicity			
Black/African-American	16 (6.9)	12 (5.2)	28 (12.1)
Hispanic	96 (41.4)	53 (22.8)	149 (64.2)
White	24 (10.3)	15 (6.5)	39 (16.8)
Other	10 (4.3)	6 (2.6)	16 (6.9)
Insurance Status			
Private Insurance	66 (28.4)	28 (12.1)	94 (40.5)
Medicaid	73 (31.5)	55 (23.7)	128 (55.2)
No Insurance	7 (3.0)	3 (1.3)	10 (4.3)
Location			
Las Vegas	129 (55.6)	83 (35.8)	212 (91.4)
Reno	17 (7.3)	3 (1.3)	20 (8.6)
Allergies			
Yes	16 (6.9)	26 (11.3)	42 (18.2)
Food or Aeroallergens	4 (1.7)	9 (3.9)	13 (5.6)
Medication	9 (3.9)	12 (5.2)	21 (9.1)
Multiple categories	3 (1.3)	5 (2.2)	8 (3.4)
No	120 (51.7)	60 (25.9)	180 (77.6)
Unknown	10 (4.3)	0 (0)	10 (4.3)
Comorbid diagnoses			
Yes	142 (61.1)	85 (36.6)	227 (97.8)
Metabolic diagnosis (≥1 dx*)	78 (33.6)	46 (19.8)	124 (53.4)
Metabolic + other diagnosis (≥1dx*)	40 (17.2)	31 (13.4)	71 (30.6)
Other diagnosis (≥1dx*)	24 (10.3)	8 (3.4)	32 (13.8)
No	4 (1.7)	1 (0.4)	5 (2.2)
	Non-asthmatic (mean, SD)	**Asthmatic (mean, SD)**	**Total (mean, SD)**
Age (years) range: 6.44-18.02	10.57 (2.418)	11.26 (2.621)	10.83 (2.512)
	Non-asthmatic (med, range)	**Asthmatic (med, range)**	**Total (med, range)**
Weeks in program	9.00 (1-12)	8.00 (1-12)	9.00 (1-12)

*Abbreviation: dx= diagnosis

Crude baseline outcome measures from the intervention program are shown with follow-up measures, and stratified by asthma status in Table 19. Differences between pre (week 1) and post (week 12) measures were examined with paired t-tests or Wilcoxon signed ranks tests depending on whether the variable was normally distributed or not (Pallant, 2013). Means with standard deviation and mean changes are reported for all variables in Table 19.

Among the population with asthma, BMI percentile decreased significantly (mean change =-0.26, $p<0.042$) from 98.14 pre-intervention to 97.88 post-intervention. BMI z-score also decreased significantly mean change=-0.05 $p<0.002$) from 2.25 at week 1 to 2.20 at week 12. Non-asthmatic children also had a significant decrease in BMI percentile (mean change=-0.28 ($p=0.002$) from 98.44 pre-intervention to 98.16 post-intervention, and a significant decrease in BMI z-score (mean change=-0.05, $p=0.001$) from 2.36 pre-intervention to 2.31 post intervention (Table 18). VO2 max levels increased significantly for both males with asthma from 34.48 mL/Kg/min to 38.65 mL/Kg/min (mean change=4.17, $p=0.003$) and females with asthma, from 26.00 mL/Kg/min to 29.79 mL/Kg/min (mean change=3.79, $p<0.001$). Among patients without asthma, VO2 max levels for males also increased significantly (mean change=6.17,$p<0.001$) from 32.29 mL/Kg/min to 38.46 mL/Kg/min. VO2 max levels for females without asthma also increased significantly (mean change =5.0, $p<0.001$) from 25.75 mL/Kg/min at week 1 to 28.84 mL/Kg/min at week 12 (Table 19).

Exercise intensity, or metabolic equivalents (METs) increased significantly for patients with asthma from 3.49 pre-intervention to 3.79 post-intervention (mean change = 0.30, $p=0.033$), and for those without asthma from 3.29 at week 1 to 3.58 at week 12 (mean change=0.29, $p<0.001$). Heart rate also increased significantly for asthma patients (mean change=8.37, $p=0.002$), but not for youth without asthma. Blood pressure did not change significantly from pre- to post-intervention in either asthma group (Table 19).

Table 19. Comparison of Pre- and Post-test Scores of Select Outcomes from Healthy Hearts Program Participants with and without Asthma (N=232)

	Participants with Asthma			Participants without Asthma		
	N	**Mean (SD)**	**Mean change week 1-12 (1-tailed p)**	**N**	**Mean (SD)**	**Mean change week 1-12 (1-tailed p)**
BMI Percentile						
Week 1	86	98.14 (1.125)	-0.26 (0.042)*[a]	146	98.44 (1.213)	-0.28 (0.002)*[a]
Week 12	43	97.88 (1.665)		91	98.16 (1.797)	
BMI z-score						
Week 1	86	2.25 (0.372)	-0.05 (0.002)*[b]	146	2.36 (0.338)	-0.05 (0.001)*[a]
Week 12	43	2.20 (0.394)		91	2.31 (0.375)	
Vo2Max (mL/Kg/min)						
Week 1 – Male	39	34.48 (5.916)	4.17 (0.003)*[b]	63	32.29 (8.150)	6.17 (<0.001)*[b]
Week 12 – Male	21	38.65 (6.803)		38	38.46 (4.766)	
Week 1 – Female	25	26.00 (6.773)	3.79 (0.004)*[b]	65	23.75 (8.133)	5.09 (<0.001)*[b]
Week 12 – Female	19	29.79 (7.004)		42	28.84 (6.640)	
Metabolic Equivalents (METs)						
Week 1	10	3.49 (0.273)	3.00 (0.033)*[b]	82	3.29 (0.427)	0.29 (<0.001)*[b]
Week 12	7	3.79 (0.422)		55	3.58 (0.480)	
Pre-activity heart rate (BPM)						
Week 1	77	95.04 (13.633)	8.37 (0.002)*[b]	131	99.98 (15.042)	0.40 (0.388)[b]
Week 12	42	103.41 (13.111)		80	100.38 (13.478)	
Pre-activity systolic blood pressure (mmHg)						
Week 1	80	115.35 (12.424)	0.44 (0.347)[a]	143	114.71 (11.643)	-0.86 (0.388)[a]
Week 12	43	115.79 (13.041)		87	113.85 (11.218)	
Pre-activity diastolic blood pressure (mmHg)						
Week 1	79	65.57 (9.469)	0.69 (0.277)[a]	142	65.63 (8.443)	0.72 (0.204)[a]
Week 12	43	66.26 (10.248)		87	66.35 (10.285)	

* Statistically significant at $p<0.05$ (1-tailed); [a] significance measured by Wilcoxon signed rank test; [b] significance measured by paired t-test

Additionally, crude changes between those with and without first at baseline and separately at post-intervention were examined on the same measures using independent t-tests or Mann-Whitney U tests (depending on the variable's distribution) (Pallant, 2013). The only statistically significant finding between the groups was the post-intervention BMI percentile. Those with asthma had a mean post-intervention BMI percentile of 97.88 (SD 1.665) while those without asthma had a post-intervention BMI

percentile of 98.16 (SD 1.797) (p=0.041). The median BMI percentile was 99th percentile for both groups post intervention. All other pre- or post-intervention measures did not yield statistically significant differences between children with and without asthma (Table 20).

Pre-intervention laboratory test results for cholesterol, triglycerides, C-reactive protein, and insulin were available for 19-53% of the population (depending on the test). Post-test values were available/and or required for only 10-15% of the total CHC population. As stated in the methods section, post-intervention laboratory tests are conducted only when the pre-tests are abnormal. Therefore, the post-test values are from the least healthy 10-15% of the population. Along with the low number of test results obtained from medical records, this may have contributed to bias and therefore are not included in the analyses.

Table 20. Differences between Healthy Hearts Program Participants with and without Asthma at Baseline (Week 1) and Post-intervention (Week 12) (N=232)

	Baseline			Post-intervention		
	N	**Mean (SD)**	**Mean difference (p)**	**N**	**Mean (SD)**	**Mean difference (p)**
BMI Percentile						
Asthma	86	98.24 (1.127)	0.12 (0.132)[a]	43	97.88 (1.665)	0.28 (0.041)*[a]
No Asthma	146	98.36 (1.423)		91	98.16 (1.797)	
BMI z-score						
Asthma	86	2.29 (0.360)	0.05 (0.141)[a]	43	2.20 (0.394)	0.11 (0.050)[a]
No Asthma	146	2.34 (0.339)		91	2.31 (0.374)	
Vo2Max (mL/Kg/min)						
Asthma – Male	39	34.30 (7.234)	-2.83 (0.419)[b]	21	38.69 (6.634)	-2.02 (0.990)[b]
No Asthma –Male	63	31.47 (8.279)		38	36.67 (4.850)	
Asthma – Female	25	26.74 (7.358)	-2.91 (0.152)[a]	19	29.79 (7.004)	-1.08 (0.565)[b]
No Asthma – F	65	23.83 (6.854)		42	28.71 (6.608)	
Metabolic Equivalents (METs)						
Asthma	10	3.51 (0.233)	-0.26 (0.073)[b]	7	3.79 (0.422)	-0.23 (0.241)[b]
No Asthma	82	3.25 (0.436)		55	3.56 (0.476)	
Pre-activity heart rate (BPM)						
Asthma	77	95.75 (12.785)	5.84 (0.149)[b]	42	103.40 (13.478)	-3.02 (0.236)[b]
No Asthma	131	101.59 (15.99)		80	100.38 (13.111)	
Pre-activity systolic blood pressure (mmHg)						
Asthma	80	115.24 (40.915)	-1.11 (0.514)[a]	43	115.97 (13.041)	-2.12 (0.628)[b]
No Asthma	143	114.13 (11.98)		87	113.85 (11.218)	
Pre-activity diastolic blood pressure (mmHg)						
Asthma	79	64.20 (8.379)	2.43 (0.069)[a]	43	66.12 (10.170)	0.23 (0.631)
No Asthma	142	66.63 (8.717)		87	66.35 (10.285)	

* Statistically significant at $p<0.05$ (2-tailed); [a] significance measured by Mann-Whitney U test; [b] significance measured by independent samples t-test

Children's Heart Center Results

Outcomes from the Healthy Hearts Program Intervention

Research Question 3

Cox regression analysis was performed to examine attrition between the participants with and without asthma in the CHC Healthy Hearts Program. There was no significant difference between the two

groups (p=0.300), nor were any other variables statistically significant (Table 21). This indicates that asthmatic children were able to successfully complete the intervention compared with the non-asthmatic group. This suggests that the intervention could be a feasible approach for weight loss and lung function improvement, even among youth experiencing respiratory distress. A final adjusted model was also performed with age (1% contribution) and ethnicity (5% contribution) removed as they did not contribute much to the model. The model was not significantly improved; these data are not shown. No covariates violated the proportional hazards assumption, and each variable was checked by time dependent covariate in SPSS (T_*variable) as well by visual examination of log minus log plots (Hosmer, Lemeshow, & May, 2008).

Table 21. Attrition among the Children's Heart Center Healthy Hearts Program Participants (N=165)

	Crude Hazard Rate (95% CI)	p-value	Adjusted Hazard Rate (95%CI)	p-value
Asthma				
Yes	‡		‡	
No	0.79 (0.52-1.14)	0.207	0.82 (0.56-1.19)	0.300
Age			1.01 (0.94-1.07)	0.860
Race/Ethnicity				
Non-Hispanic			‡	
Hispanic			0.80 (0.55-1.17)	0.251
Sex				
Female			‡	
Male			1.05 (0.74-1.49)	0.792
Insurance Status				
Insured			‡	
Medicaid			1.24 (0.87-1.77)	0.236

‡ reference category

Power analyses were conducted; the sample size was adequate to run all ANOVA models with 95% power. Program outcomes for weight loss (BMI z-score) and cardiorespiratory health, specifically maximal oxygen uptake (VO2 max) were examined using repeated measures ANOVA models; covariates were then added to the models.

In the BMI model, the assumption of sphericity was violated as demonstrated by Mauchly's test of sphericity, $\chi^2(2)=94.20$, $p<0.001$. Accordingly, the Greenhouse-Geisser estimate of sphericity (=0.655) was used to correct the degrees of freedom. Time in the program is the only variable which significantly affected change in BMI z-score, $F(1.3, 166.4)=5.33$, $p=0.014$ (Table 22). There was an inverse association between BMI z-score and time in the program. The mean z-score at week 1= 2.314, and the mean z-score at week 12= 2.265. This result shows that after adjustment for all covariates, the mean BMI significantly decreased among the HHP population.

Table 22. Weight loss in the Healthy Hearts Program Population Represented by BMI z-score (N=133)

	Crude model		Adjusted model	
	F (p)	Effect size	F (p)	Effect size
Time in Program (weeks)	27.20 (<0.001)*	0.172	5.33 (0.014)*	0.040
Asthma (y/n)	0.047 (0.888)	<0.001	0.01 (0.951)	<0.001
Age in years			0.64 (0.463)	0.005
Race/Ethnicity (Hispanic/Non-Hispanic)			0.50 (0.529)	0.004
Sex (m/f)			2.13 (0.141)	0.016
Insurance status			0.27 (0.665)	0.002

*Statistically significant p<0.05

For VO2 max, the population was stratified by sex, as the values for VO2 increase differently for boys and girls when they reach puberty. As stated earlier, while the values increase with greater oxygen uptake and better cardiorespiratory health, the values continue to increase as age in males increases, however, the values begin to decrease as female age increases with regard to each specific health category as described in the FITNESSGRAM® standards outlined in detail in Chapter 2, page 39 (Meredith & Welk, 2013).

The assumption of sphericity was not violated in any VO2 max models; therefore degrees of freedom did not need to be corrected. In both the male and female unadjusted models, time in the program significantly affects VO2 max: males $F(1, 54)=30.49$, $p<0.001$; females $F(1, 58)=20.41$, $p<0.001$. However, in the adjusted models for both males and females, none of the variables were associated with VO2 max (Tables 23 and 24).

Table 23. Cardiorespiratory Health Changes in the Healthy Hearts Program Population as Represented by VO2 max for the Male Population (N=133)

	Crude model		Adjusted model	
	F (p)	Effect size	F (p)	Effect size
Time in Program (weeks)	30.49 (<0.001)*	0.361	2.36 (0.130)	0.044
Asthma (y/n)	1.16 (0.287)	0.021	1.28 (0.263)	0.024
Age in years			2.89 (0.095)	0.054
Race/Ethnicity (Hispanic/Non-Hispanic)			1.49 (0.121)	0.046
Insurance status			0.82 (0.368)	0.016

*Statistically significant p<0.05

Table 24. Cardiorespiratory Health Changes in the Healthy Hearts Program Population as Represented by VO2 max for the Female Population (N=133)

	Crude model		Adjusted model	
	F (p)	Effect size	F (p)	Effect size
Time in Program (weeks)	20.41 (<0.001)*	0.260	0.03 (0.855)	0.001
Asthma (y/n)	0.44 (0.510)	0.008	0.20 (0.655)	0.004
Age in years			0.03 (0.854)	0.001
Race/Ethnicity (Hispanic/Non-Hispanic)			2.58 (0.114)	0.045
Insurance status			0.01 (0.919)	0.000

*Statistically significant p<0.05

CHAPTER 5. DISCUSSION

The objectives of this study were 1) to examine the relationship between asthma/allergy and obesity and how these conditions affect each other in two pediatric Nevada populations, and 2) to evaluate a 12-week physical activity and nutrition intervention for children at risk for heart disease to determine if the intervention was also feasible for children who have asthma. It was predicted that youth with elevated BMI would have more severe asthma symptoms, decreased lung function, and poorer quality-of-life proxy measures for asthma severity than those at a healthy weight. It was predicted that there would be a difference in atopy among those with elevated BMI and those with healthy BMI. It was also hypothesized that children with asthma would have higher attrition and poorer outcomes in the intervention program.

Discussion & Interpretation of Research Questions

Research questions 1 and 2 regarding asthma and allergies and the effect of BMI utilized data provided by the Reno clinic population (N=125). These children had a median age of 7 years, were approximately 60% male and nearly 65% white. Nearly one-third of the Reno population was in the overweight (85^{th} to $<9^{th}$ BMI percentile category) or obese ($\geq 95^{th}$ BMI percentile category). This population had many children in the severe or moderate asthma symptom categories at diagnosis, and was highly atopic with a median of 11 allergens to which the population was sensitized. Nearly 40% had required at least one course of oral steroids in the past year, and 25% had required a visit to the emergency department in the past year due to asthma.

This study did find more severe asthma in those with elevated BMI, though this measure was not statistically significantly higher. The spirometric measures of lung function did not differ between groups. The quality-of-life proxy measures for asthma severity were oral steroid courses required, hospitalizations, ED visits, and school days missed all in the past year due to asthma. Oral steroid use was

significantly associated with BMI category; further analysis demonstrated that obesity was a predictor of the need for oral steroids.

Research question 1, hypothesis 1 tested the association between asthma symptom severity and elevated BMI in the Reno pilot study population. While none of the BMI percentile groups were statistically significant in this population, those with BMI values in the obese category were more than four times more likely to have severe asthma compared to mild asthma The p-value was not statistically significant (p=0.162), however the confidence interval was relatively large with the lower bound close to one (95% CI 0.57 to 28.15). This large interval could be indicative of a true effect that is not evident due to the small sample of obese youth (n=14) even though the model was appropriate as evidenced by goodness-of-fit tests (Hennekens & Buring, 1987; Pallant, 2013).

The literature demonstrates a clear link between increased weight and more severe asthma due to many factors including excess weight upon the chest, increased inflammation in the airways, and decreased effectiveness of common corticosteroid medications (Black et al., 2013; Dixon et al., 2010; Kim, Sutherland & Gelfand, 2014; Sutherland 2014). While the first alternative for question 1 must be rejected, due to the lack of a significant association between asthma severity and obesity, the possibility of a true association should not be ruled out (Hennekens & Buring, 1987), rather tested with a larger sample of obese, asthmatic, and atopic youth in Nevada.

Question 1, hypothesis 2 examined the relationship between lung function as measured by spirometry, and BMI percentile in the Reno population. FEV_1%, FEV_1/FCV, and $FEF_{25-75\%}$ were all tested in separate one-way ANOVAs. The hypothesis must be rejected; none of the measures were statistically significant, although $FEF_{25-75\%}$ did approach significance (p=0.074). $FEF_{25-75\%}$ is the pulmonary function test believed to be the most sensitive for children, (Ciprandi et al., 2012; Spaulding et al., 2012).

This finding is inconsistent with the academic literature demonstrating significantly poorer lung function in children who are obese (Jensen, Gibson, Collins, & Wood, 2013; Krishnan, Hettiaracchi,

Scharbach, & Dozor, 2016; Vinding, Stockholm, Chawes & Bisgaard, 2016). Although the samples among groups were adequate according to Levene's test of homogeneity (Field, 2013), it is still possible that the number of obese youth was too small to detect a true effect. Additionally, this population may simply not have had poorer lung function among the overweight or obese children.

Question 1, hypothesis 3 tests the associations between proxy measures of asthma severity in relation to elevated body mass. These measures included number of courses of oral steroids required in the past year due to asthma, number of emergency department visits in the past year due to asthma, number of school days missed in the past year due to asthma, and number of overnight hospitalizations in the past year due to asthma. The only measure significantly associated with BMI percentile was oral steroid use, therefore multiple logistic regression analysis was conducted to further examine this association. After adjustment for age, race, and sex, the odds of requiring at least one course of oral steroids among the obese patients was nearly 8 times greater than for the patients at healthy weight ($p=0.003$). The children in this population were assessed at the initial visit, as previously noted. This may indicate a potential view of the natural progression of symptoms in children with poorly managed asthma (Lucas, Moonie, Olsen-Wilson, & Hogan, 2016).

Prescription of long-term oral steroids is no longer common practice, as newer ICS medications are more potent, thus requiring smaller doses, and safer than oral steroids which can lead to numerous metabolic and other issues including weight gain. Generally oral steroids are now only used for control in severe, persistent cases of asthma (NHLBI, 2007; Reddy et al., 2014). However, inhaled corticosteroids have decreased effectiveness in obese patients, leading to poorer control of asthma and the need for oral steroids (Baffi et al., 2015; Forno et al., 2011; Sutherland, 2014). While the other proxy measures were not significantly associated with elevated BMI in this population, oral steroid use was, which is consistent with current literature.

Research question 2 tested the associations between elevated BMI and allergen sensitization and polysensitization. The analysis of the Reno population showed that overweight youth with asthma had nearly 80% lower odds of being sensitized to allergens than healthy weight patients (p=0.010), and 73% lower odds of being polysensitized than those in the healthy weight BMI percentile category. Obese youth also had lower odds of both sensitization and polysensitization compared to healthy weight children, although not significantly lower (p=0.407 and p=0.221, respectively).

While asthma severity and obesity have an established link in literature (Black et al., 2013; Dixon et al., 2010; Sutherland 2014), research regarding allergen sensitization and overweight/obesity is conflicted. Some research has found positive associations between atopy and elevated weight status (Loid et al., 2015). Other studies have determined that there is no association between atopy and obesity (Ali & Ulrick, 2013; Jensen et al., 2011; Jensen et al, 2012). Research consistent with this study found negative associations between allergic sensitization and elevated weight status in children (Han, Forno, Gogna, & Celedon 2016; Lucas et al., 2016). The lower odds of allergen sensitization may also be due to the Th1/Th2 imbalance found in some obese asthmatics due to excess adipokines that trigger an innate (Th1-favoring) immune response rather than the allergic (Th2) response associated with allergic asthma (Ignacio et al. 2014; Raj et al, 2014; Rastogi et al., 2014).

Worldwide, approximately 10-30% of people are atopic, and in the U.S approximately 10% of white children and 7% of black children have atopy (AAAAI, 2016). However, the presence of atopy in nearly the entire Reno population suggests that the Great Basin climate may play a role in the allergic risk factors for asthma. Sensitization to specific allergens such as pine and willow trees, and sagebrush and pigweed is common to this region, but not the rest of the country (Wong, 2012).

The third research question utilized data from the second population comprised of children who participated in the HHP (N=232). The children in this population were all overweight or obese, and 37% also had asthma. The mean age of the participants was nearly 11 years old. Slightly more than half of this

population was male (54%), 64% were of Hispanic ethnicity, and more than half of the population received Medicaid. Almost every child in this population (97.8%) had at least one diagnosis (other than asthma), the majority of which were metabolic disorders (metabolic syndrome, diabetes mellitus type 2, etc.) or heart or hypertensive conditions; more than half of the population suffered from more than one coexisting condition.

Unadjusted analyses of program outcomes showed significant decreases in BMI percentile and z-score for children with and without asthma, as well as increases in cardiorespiratory health (VO2 max) and exercise intensity (METs) in both groups. Crude analyses looking at baseline and post-intervention differences between children with and without asthma found that the only measure significantly different was BMI percentile post-intervention; it was 0.28 percentile lower in the asthmatic population ($p=0.041$). These results, measured by t-tests and non-parametric equivalents could potentially be indicative of a program that is not only possible for children with asthma to participate in with their non-asthmatic peers, but is significantly beneficial as evidenced by decreased BMI, increased cardiorespiratory health, and the ability to increase exercise intensity.

In multivariable evaluation of the CHC HHP, attrition was not significantly different between youth with and without asthma, indicating further that the program could be practical for those with asthma, as they do not quit at higher rates than the non-asthmatic participants. The patients with asthma also have a likely probability of EIB and they had significantly more comorbid disorders than the non-asthmatic patients.

The outcome measure weight loss (measured using BMI z-score), when adjusted for age, ethnicity, sex, and insurance status was not significantly different between children with and without asthma. The only significant measure was time in the program – the mean BMI decreased if participants stayed in the program longer. The outcome measure VO2 max, stratified by sex and analyzed in two separate models, had no significant associations after adjustment for age, ethnicity, and insurance status.

Numerous studies have found that weight loss is essential to the improvement of symptoms in obese asthmatics, as are other benefits from physical activity such as improved cardiorespiratory and cardiovascular health and improved mental health (Abd El-Kader et al., 2013; Dixon et al., 2010; Sutherland, 2014). Programs tailored for asthmatics are recommended to help increase physical activity for youth who have asthma (Wanrooij, 2014). A program, such as the Healthy Hearts Program, which appears to benefit children with asthma, could be a way to increase physical activity in more Nevadans who have asthma, thus decreasing the severity of asthma symptoms.

Public Health Impact and Policy Recommendations

The availability of clinical data provided an opportunity to use epidemiological study designs to examine problems faced by patients with asthma and obesity and the physicians who treat them, in a way that can be translated to clinicians. For instance, the high atopic prevalence in obese youth, which is not common in obese children with asthma, demonstrates a possible need for recommendations for clinicians to test obese youth for allergen sensitization. In addition, this study also contributed to gaps in research regarding pediatric asthma, allergies, and obesity in a climate conducive to aeroallergen sensitization (Lucas et al., 2016). This research may be beneficial to public health professionals in need of knowledge and intervention strategies to help with both weight loss and asthma control on a larger scale than the individual clinical level.

While the high degree of atopy in the Reno population may result in a lack of generalizability, the findings could be useful for other areas of the country with high allergen sensitization, for example, the Southeast U.S., which has the highest prevalence of both indoor aeroallergen and food allergen sensitization, as well as high rates of childhood obesity (Salo et al., 2014; DNPAO, 2015). While generalizability is certainly an important epidemiological concept (Gordis, 2014; Hennekens & Buring, 1987), chronic conditions such as asthma and obesity will not necessarily be generalizable. Conditions

that affect people in different ways based on different factors, from genetics to environmental conditions to socioeconomic factors, may not be generalizable to the entire U.S or world population. Yet research into these conditions still adds to academic literature. Causality of disease is also part of the backbone of epidemiology (Gordis, 2014; Hennekens & Buring, 1987; Hulley, Cummings, Browner, Grady, & Newman, 2007). However, trying to find definitive cause for conditions with as many risk factors as asthma and obesity is extremely difficult, maybe impossible. In some cases, perhaps the most beneficial public health research is not to try and find cause, rather to focus on how these conditions impact the health of communities, and to focus on disparities that can be lessened or even eliminated. This study does examine who is impacted by asthma and obesity in Nevada, and assesses methods to lessen the burden.

The Children's Heart Center's Healthy Hearts Program appears to be feasible and beneficial for obese asthmatic youth. This program has existed since 2002. It is a private program run by the Children's Heart Center and requires referrals from other doctors, but it is a program that already exists. There are already protocols and there is already equipment and a place for activity as well as offices with nutritionists who meet with families to provide education and advice. This program has already been helpful to many Nevada children at risk for heart disease, with and without asthma. This program design could also serve as a helpful model or template for similar programs in other Nevada areas besides Las Vegas, or even in other states. Follow up studies should be expanded to larger populations, particularly those at greater risk of morbidity and mortality. For example, this intervention could be feasibly expanded to those of minority status and the uninsured with appropriate funding, such as through the CDC's National Asthma Control Program (NACP), Medicaid, or private insurance companies.

Furthermore, many children do not have safe neighborhoods in which to do physical activity (IOM, 2012;waters et al., 2011). While it is possible to do activities indoors, children tend to enjoy activity more and choose to participate when encouraged by peers (Herbert, Lohrmann, Seo, Stright, & Kolbe, 2013; Lorusso, Pavlovich, & Lu, 2013). Partnering with schools, school-based after-school

programs, or after-school programs though community-based non-profit organizations could provide a place to expand intervention programs.

Healthy People 2020 is a health promotion initiative from the Office of Disease Prevention and Health Promotion (ODPHP) through the U.S. Department of Health and Human Services that provides 10-year goals for health promotion and disease prevention (ODPHP, 2016a). One of the objectives regarding respiratory health is to reduce limitations to activity in people with asthma. Another one is to increase the number of states with comprehensive asthma surveillance programs (ODPHP, 2016b). These Healthy People 2020 initiatives demonstrate that there are currently already goals to increase physical activity in people with asthma, and this study has a good intervention program for asthmatic children.

Nevada does not currently receive federal funding from the CDC's NACP, a program that helps with state and local level asthma surveillance and education (CDC, 2015b). With a sustainable program such as the HHP, which is available to Nevada children with obesity and asthma, Nevada should apply for funding from the CDC's NACP. This could help Nevada asthmatics have better health, and it would contribute to the Healthy People 2020 nationwide goal of more comprehensive asthma surveillance.

Study Limitations

This study had a number of limitations. Among the Reno pilot population, the high amount of allergen sensitization meant that the population may have been be too similar and not be truly representative of obese asthma patients elsewhere. The population was also nearly 65% white, which is also not necessarily generalizable. Additionally, BMI percentile categories were used as a measure of weight status. BMI is not always the most accurate measure of weight as there is no way to distinguish fat mass from healthy lean mass, such as muscle (Shah & Braverman, 2012; Romero-Corral et al., 2008). This could lead to non-differential misclassification of cases. The pilot dataset also did not include birthdate, height, and weight data due to IRB requirements so BMI z-scores could not be calculated and

the BMI percentiles had to be categorized, which can result in a lack of statistical power as well as the inability to conduct specific statistical analyses (Field, 2013).

While the pilot population had BMI category groups large enough for appropriate statistical tests (Field, 2013; Pallant, 2013), the practical breakdown of the groups (nearly 70% of the population were healthy weight) could have led to smaller than ideal sample sizes among the groups, and potential missed findings as evidenced by large confidence intervals with small group sizes (Hennekens & Buring, 1987). The potential non-differential misclassification may also dilute results (Gordis, 2014), leading to an even stronger possibility that severe asthma is truly associated with obesity, although the p-value was not significant.

The CHC data also had limitations. The data were collected using electronic medical records systems. They were secondary data originally collected as part of regular procedure for the hospital or the Healthy Hearts Program. While some data were electronic, other data were handwritten on scanned forms. Data errors were evaluated by myself as well as by the Research Director of Children's Heart Center, and numerous staff members were available for questions, yet information bias, specifically differential misclassification, could still exist (Gordis, 2014). Multiple people originally collected the data and there is no way to know if they were all trained to do so in exactly the same way. Additionally, it is not known how many separate doctors provided asthma diagnoses; that information was not available.

BMI was also the measurement used to measure weight in this population so some misclassification of weight status could have occurred; yet the use of a z-score provides a standardized, continuous variable. Also, all patients were either overweight or obese, and nearly all were at the 90^{th} percentile at baseline and post-intervention, therefore, misclassification of BMI category is unlikely. Additionally, the participants were seen many times by the same staff in a clinical setting in which both asthma and weight could be observed by professionals, and at the time of data collection, this study had not been designed yet, therefore, asthma cases and controls without asthma did not exist as defined for

this study. Although there are many issues with the use of retrospective secondary data, the probability of differential misclassification being problematic in this particular study is likely quite low (Gordis, 2014).

There were substantial missing data for certain variables in the CHC dataset, often due to the fact that the collection was not necessary (as with children who had normal laboratory test values at baseline), sometimes due to attrition, and other times it was unknown why data were missing. Variables with a great deal of missing data were not used in any analysis. Yet, one of the key strengths of this study is that data in both datasets were comprised of clinically measured variables collected by clinicians or their staff, thus, recall bias was likely not an issue (Gordis, 2014).

Conclusion & Recommendations for Future Research

This study has found that in Nevada, pediatric obese asthmatics have more severe asthma, and though it is not statistically significantly more severe, it may be clinically important. Overweight and obese youth with asthma also had higher odds of requiring oral steroids for asthma control than healthy weight peers. In addition, overweight and obese asthma patients were sensitized and polysensitized to aeroallergens, though the odds of atopy were lower in those who were overweight.

Finally, in evaluating a 12-week intervention program for those at risk for heart disease, overweight and obese children with asthma did not have higher rates of attrition than their overweight and obese peers without asthma. Additionally, there were no significant differences between BMI decrease or cardiorespiratory health increase between the two groups, although completion of the program produced both decreased BMI and increased cardiorespiratory health in both groups.

Future research is needed to determine how atopy affects pediatric obese asthmatics in climates where allergens are so common, such as in Nevada. Research on a larger scale, such as with a bigger sample size of obese children with asthma should be conducted. Studies on steroid medication in

overweight asthmatic children are also needed. Very little research exists regarding the use of ICS in obese asthmatic youth, and the consequences of decreased ICS effectiveness, such as the requirement of more emergency medication or oral steroids. Longitudinal research on weight loss in overweight children with asthma would be valuable to examine how symptoms improve over time, and with age. Obesity and asthma, in youth and adults, is a topic that produces new literature daily; any future recommendations for research may already be in progress, and all literature that contributes to this body of work could potentially be beneficial to children who suffer from asthma and obesity.

APPENDIX 1

Body Mass Index Growth Charts
by Sex and Age (0-20 years)

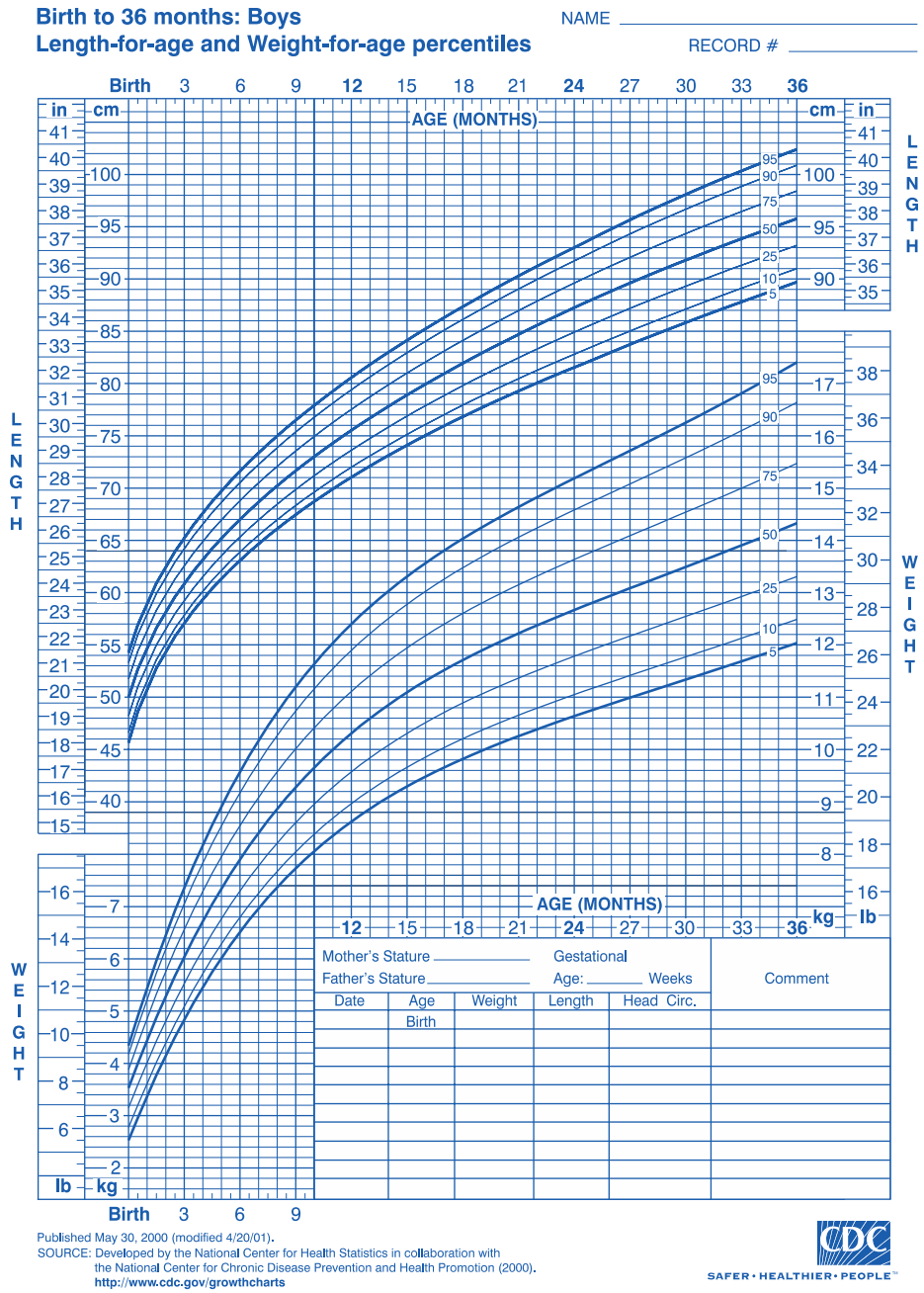

Figure 4. Length for Age and Weight for Age Percentiles for Boys, Aged Birth to 36 Months (from: http://www.cdc.gov/growthcharts/data/set1clinical/cj41c017.pdf)

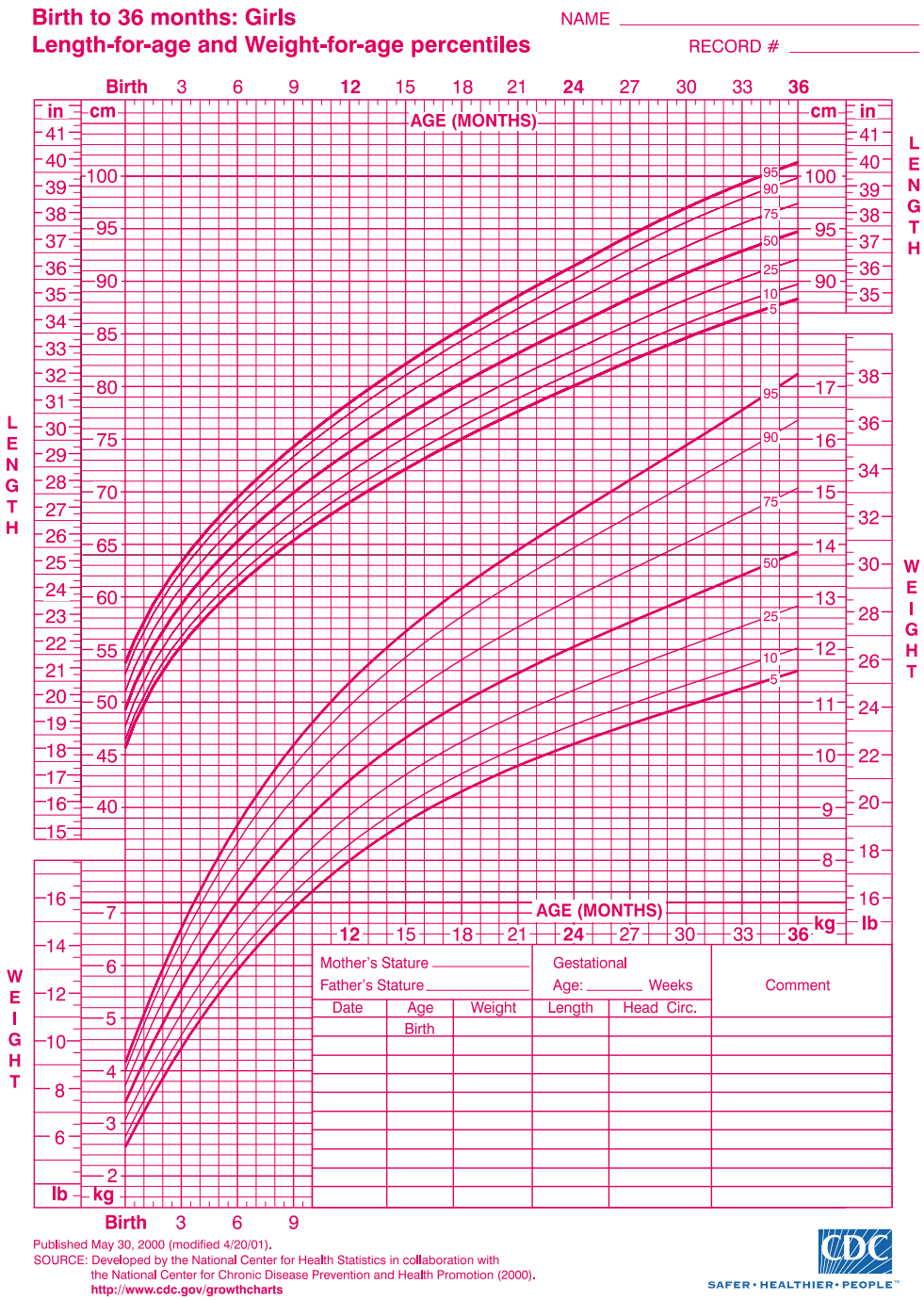

Figure 5. Length for Age and Weight for Age Percentiles for Girls, Aged Birth to 36 Months (from: http://www.cdc.gov/growthcharts/data/set1clinical/cj41c018.pdf)

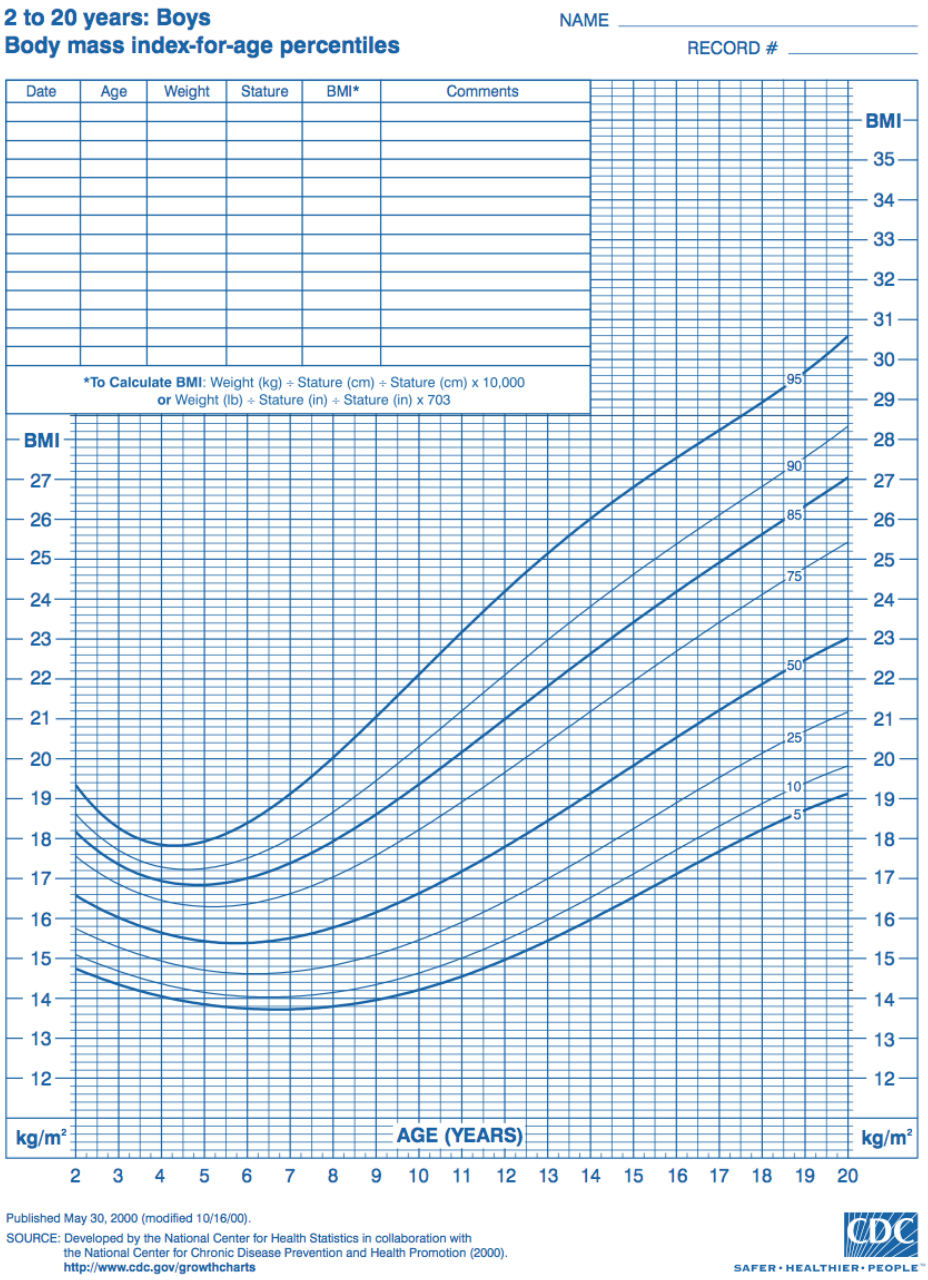

Figure 6. Body Mass Index for Age Percentiles for Boys Aged 2 to 20 (from: http://www.cdc.gov/growthcharts/data/set1clinical/cj41c023.pdf)

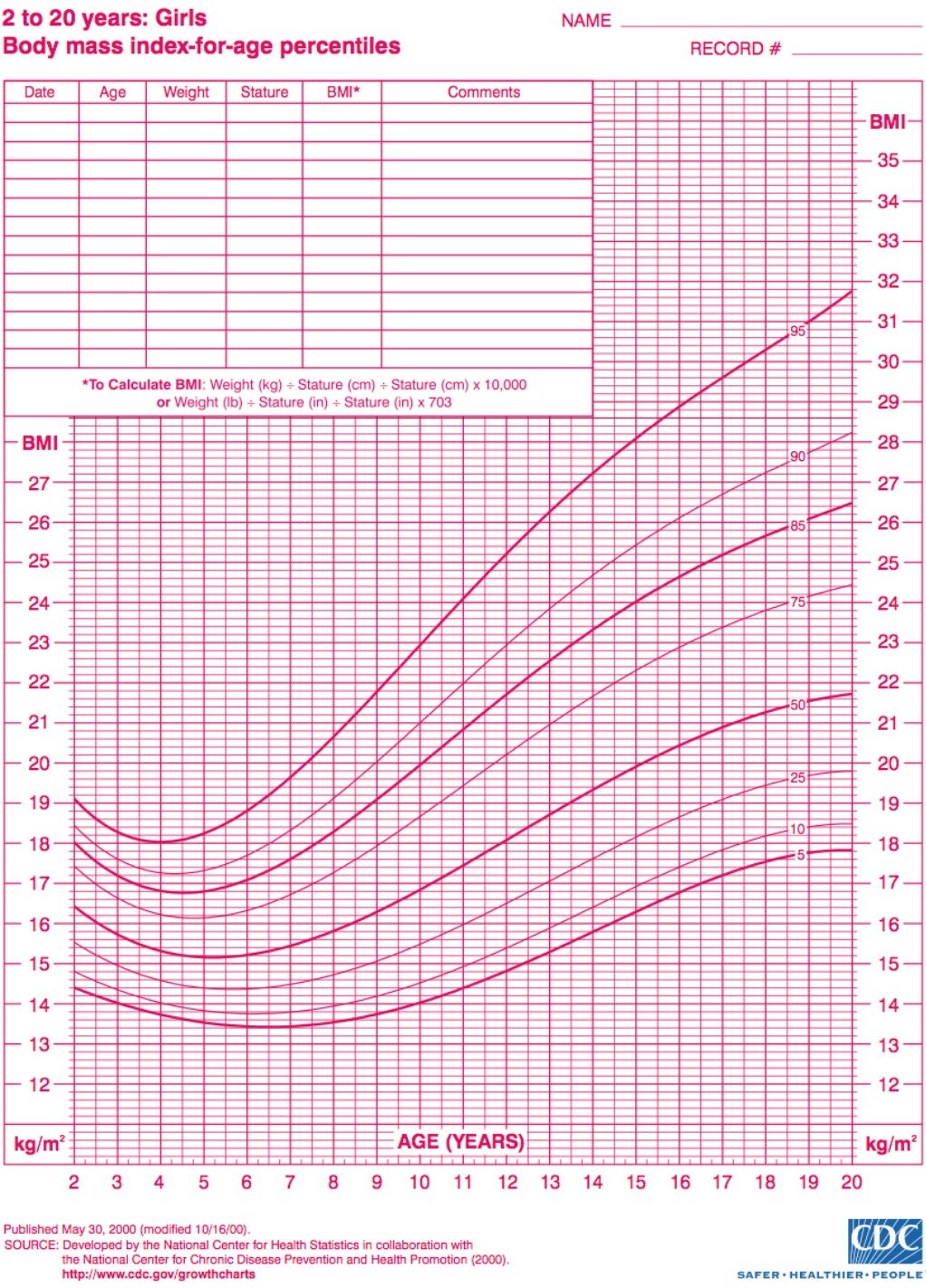

Figure 7. Body Mass Index for Age Percentiles for Girls Aged 2 to 20 (from: http://www.cdc.gov/growthcharts/data/set1clinical/cj41c024.pdf)

APPENDIX 2

Table 25. Northern Nevada Allergens Used in Skin Prick Tests by the Reno Clinic

Type of Allergen	Specific Allergen
Molds	*Alternaria*
	Aspergillus
	Penicillium
	Cladosporium
	Dreschlera
	Curvularia
	Mold Mix II
	Smuts
Weeds (pollen producing)	Pigweed
	Sagebrush
	Plantain
	Dock
	Ragweed
	RG Mix
	Marsh elder
	Russian thistle
	Rabbitbrush
	Saltbush
Inhalants	*Dermatophagoides farina* (dust mite)
	Dermatophagoides pteronyssinus (dust mite)
	Cat
	Dog
	Mouse
	Cockroach
	Ant
	Housefly
	Moth
	Rhodotorula
Grass (pollen producing)	Timothy
	Brome
	Bermuda
	Saltgrass
	Johnson
	Alfalfa
Trees (pollen producing)	Pecan
	Juniper
	Alder
	Oak
	Elm
	Ailanthus
	Willow
	Locust
	Cottonwood
	Birch
	Maple
	Privet
	Aspen
	Olive
	Sycamore

	Pine Walnut Sweet Gum Mulberry Ash
Animals	Horse Hamster Gerbil Guinea Pig Feather Rabbit Cattle Goat Hog

APPENDIX 3

Children's Heart Center
Healthy Hearts Program Data Intake Form

HHProgram Patient Info

Start Date: _____

Physician: _____

☐ **Spanish Speaking**

Place patient name label here

	Date	Walk test	HR	BP
WEEK 1				
WEEK 6				
WEEK 12				

Diagnosis/Risk Factors:

☐ High BMI ☐ Hypercholesterol
☐ Hypertension ☐ Hypertriglycerides
☐ Hyperinsulinemia ☐ Diabetes
☐ Elevated LFT's ☐ Hypothyroid
☐ Elevated HgA1C ☐ Asthma
☐ Low Vitamin D ☐ _____

Medications:

_____
_____
_____
_____
_____

☐ Schedule with Dr. Creel

_____
_____

Anthropometrics: **Age:** _____

	Date	Height	Weight	WC	BMI	BMI%ile	Wt change
Consult							
Week 1							
Week 6							
Week 12							

Lab Results:

Date	Glu	AST	ALT	Chol	HDL	LDL	TG	Ins	HbA1c	TSH	Vit D

☐ **Labs WNL** ☐ **Need to Order Week 12 Labs** ☐ **Labs Ordered:** _____

Figure 8. Healthy Hearts Program Patient Information Form (page 1)

CONSULT NOTES:

WEEK 1: accompanied by: _____

Changes made: Concerns/Barriers: Goals:

WEEK 6: accompanied by: _____

Changes made: Concerns/Barriers: Goals:

WEEK 12: accompanied by: _____

Changes made: Concerns/Barriers: Goals:

☐ Week 1 Labs	☐ Week 12 Labs ordered
☐ Pre-walk Test	☐ Post-walk Test
☐ Consents	

Figure 9. Healthy Hearts Program Patient Information Form (page 2)

REFERENCES

Abd El-Kader, M.S., Al-Jiffri, O., & Ashmawy, E.M. (2013). Impact of weight loss on markers of systemic inflammation in obese Saudi children with asthma. *African Health Sciences, 13*(3), 682-688. http://dx.doi.org/10.4314/ahs.v13i3.23

Akinbami, L.J., Moorman, J.E. & Liu, X. (2011). *National health statistics reports: Asthma prevalence, health care use, and mortality: United States 2005-2009*. (Report No. 32). Retrieved from: http://www.cdc.gov/nchs/data/nhsr/nhsr032.pdf

Ali, Z. & Ulrik, C.S. (2013). Obesity and asthma: A coincidence or a causal relationship? A systematic review. *Respiratory Medicine, 107*(9), 1287-1300. doi:10.1016/j.rmed.2013.03.019

American Academy of Allergy, Asthma, and Immunology. (2016). Allergy statistics. Retrieved from: http://www.aaaai.org/about-aaaai/newsroom/allergy-statistics

American Academy of Allergy, Asthma, and Immunology. (2014). Ask the expert: Spirometry normal values. Retrieved from: http://www.aaaai.org/ask-the-expert/spirometry-values.aspx

American Academy of Allergy, Asthma, and Immunology. (2015a). Asthma Statistics. Retrieved from: http://www.aaaai.org/about-the-aaaai/newsroom/asthma-statistics.aspx

American Academy of Allergy, Asthma, and Immunology. (2015b). Atopy defined. Retrieved from: http://www.aaaai.org/conditions-and-treatments/conditions-dictionary/atopy.aspx

American Heart Association. (2015). Good vs. bad cholesterol. Retrieved from: http://www.heart.org/HEARTORG/Conditions/Cholesterol/AboutCholesterol/Good-vs-Bad-Cholesterol_UCM_305561_Article.jsp

American Lung Association. (2014). Luchando por el aire: The burden of asthma on Hispanics. Retrieved from: http://www.lung.org/assets/documents/publications/lung-disease-data/asthma-in-hispanics-english.pdf

American Lung Association. (2016). Lung health & diseases: Measuring your peak flow rate. Retrieved from: http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/asthma/living-with-asthma/managing-asthma/measuring-your-peak-flow-rate.html

Asher, I. & Pearce, N. (2014). Global burden of asthma among children. *International Journal of Tuberculosis and Lung Disease, 18*(11), 1269-1278. doi: 10.5588/ijtld.14.0170

Baffi, C.W., Winnica, D.E., & Holguin, F. (2015). Asthma and obesity: Mechanisms and clinical implications. *Asthma Research and Practice, 1*(1). doi:10.1186/s40733-015-0001-7

Barnes, M. (Chair of the Task Force on Childhood Obesity). (2010). Solving the problem of childhood obesity within a generation: White House Task Force on Childhood Obesity report to the President. Retrieved from: http://www.letsmove.gov/sites/letsmove.gov/files/TaskForce_on_Childhood_Obesity_May2010_FullReport.pdf

Barnett, S.B.L. & & Nurmagambetov, T.A. (2011). Costs of asthma in the United States: 2002-2007. *Journal of Allergy and Clinical Immunology, 127*, 145-152.

Baumann, S. & Lorentz, A. (2013). Obesity – A promoter of allergy? *International Archives of Allergy and Immunology, 162*, 205-213. doi:10.1159/000353972

Bitsko, M., Everhart, R.S., & Rubin, B.K. (2014). The adolescent with asthma. *Paediatric Respiratory Reviews, 15*(2), 146-153. doi: 10.1016/j.prrv.2013.07.003

Black, M.H., Zhou, H., Takayanagi, M., Jacobsen, S.J., & Koebnick, C. (2013). Increased asthma risk and asthma-related health care complications associated with childhood obesity. *American Journal of Epidemiology, 178*(7), 1120-1128. DOI: 10.1093/aje/kwt093

Busse, W.W., & Lemanske, R.F. (2001). Advances in immunology: Asthma. *New England Journal of Medicine, 344(*5), 350-362.

Capurso, C. & Capurso, A. (2012). From excess adiposity to insulin resistance: The role of free fatty acids. *Vascular Pharmacology, 57*(2-4), 91-97. doi:10.1016/j.vph.2012.05.003

Castro-Rodriguez, J.A. (2010). The Asthma Predictive Index: A useful tool for predicting asthma in young children. *Journal of Allergy and Clinical Immunology, 26*(2), 212-216. doi: 10.1016/j.jaci.2010.06.032

Castro-Rodriguez, J.A., Custovic, A, & Ducharme, F.M. (2016). Treatment of asthma in young children: evidence-based recommendations. *Asthma Research and Practice, 2*(5). doi:10.1186/s40733-016-0020-z

Castro-Rodriguez, J.A., Holberg, C.J., Wright, A.L., & Martinez, F.D. (2000). A clinical index to define risk of asthma in young children with recurrent wheezing. *American Journal of Respiratory and Critical Care Medicine, 162*, 1403-1406. doi: 10.1164/ajrccm.162.4.9912111

Centers for Disease Centers for Disease Control and Prevention. (2016a). Division of Nutrition, Physical activity and Obesity – Nutrition: Growth chart training: A SAS program for the 2000 CDC growth charts (ages 0 to <20 years). Retrieved from: http://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm

Centers for Disease Control and Prevention. (2014). Healthy Weight: Assessing your weight: Body mass index. Retrieved from: http://www.cdc.gov/healthyweight/assessing/bmi/

Centers for Disease Control and Prevention. (2015a). Asthma: Behavioral Risk Factor Surveillance System (BRFSS) prevalence data. Retrieved from: http://www.cdc.gov/asthma/brfss/default.htm

Centers for Disease Control and Prevention. (2015b). Asthma: CDC's National Asthma Control Program. Retrieved from: http://www.cdc.gov/asthma/nacp.htm

Centers for Disease Control and Prevention. (2015c). FastStats: Asthma. Retrieved from: http://www.cdc.gov/nchs/fastats/asthma.htm

Centers for Disease Control and Prevention. (2015d). International Classification of Diseases, Ninth Revision (ICD-9). Retrieved from: http://www.cdc.gov/nchs/icd/icd9.htm

Centers for Disease Control and Prevention. (2016b). National Health Interview Survey (NHIS) data. Retrieved from: http://www.cdc.gov/asthma/nhis/default.htm

Children's Heart Center Nevada. (2015). Healthy Hearts Program: About HHP. Retrieved from: http://www.childrensheartcenter.com/healthyhearts/about/

Children's Hospital of Philadelphia Research Institute. (2016). Pediatric z-score calculator. Retrieved from: http://stokes.chop.edu/web/zscore/index.php

Cianchetti, S., Bacci, E., Ruocco, L., Pavia, T., Bartoli, M.L., Cardini, C….Paggiaro, P. (2013). Are sputum eosinophil cationic protein and eosinophils differently associated with clinical and functional findings of asthma? *Clinical & Experimental Allergy, 44*, 673-680. doi:10.1111/cea.12236

Ciprandi, G., Capasso, M., Tosca, M., Salpietro, C., Salpietro, A., Marseglia, G., & La Rosa, M. (2012). A forced expiratory flow ay 25-75% value <65% of predicted should be considered abnormal: A real-world, cross-sectional study. *Allergy and Asthma Proceedings, 33*, e5-e8. doi:10.2500/aap.2012.33.3524

Cleveland Clinic. (2015). Medical publications: Myopathy. Retrieved from: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/neurology/myopathy/

Cohen, R.T., Canino, G.J., Bird, H.R., Shen, S., Rosner, .B.A., & Celedón, J.C. (2007). Area of residence, birthplace, and asthma in Puerto Rican children. *Chest, 131*(5), 1331-1338. doi:10.1378/chest.06-1917

Cohn, L., Elias, J.A., & Chupp, G.L. (2004). Asthma: Mechanisms of disease persistence and progression. *Annual Review of Immunology, 22,* 789-815. doi:10.1146/annurev.immunol.22.012703.104716

Coico, R. & Sunshine, G. (2015). *Immunology: A short course* (7th ed.). Hoboken, NJ: Wiley Blackwell.

Data Resource Center for Child and Adolescent Health. (2012). 2011-12 National Survey of Children's Health. Retrieved from: http://childhealthdata.org/browse/survey/results?q=2462&r=1

Desai, D., Newby, C., Symon, F., Haldar, P., Shah, S., Gupta, S….Brightling, C.E. (2013). Elevated sputum interleukin-5 and submucosal eosinophilia in obese individuals with severe asthma. *American Journal Respiratory Critical Care Medicine, 188*(6), 657-663. doi:10.1164/rccm.201208-1470OC

Division of Nutrition, Physical Activity and Obesity. (2015). Trends and Maps web site. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), National Center for Chronic Disease Prevention and Health Promotion. Retrieved from: http://www.cdc.gov/nccdphp/DNPAO/index.html

Dixon, A.E., Holguin, F., Sood, A., Salome, C.M., Pratley, R.E., Beuther, D.A….Shore, S.A. on behalf of the American Thoracic Society ad hoc Subcommittee on Obesity and Lung Disease. (2010). An official American Thoracic Society Workshop Report: Obesity and asthma. *Proceedings of the American Thoracic Society, 7,* 325-335. DOI: 10.1513/pats.200903-013ST

Dorevitch, S., Conroy, L., Karadkhele, A., Rosul, L., Stacewicz-Sapuntzakis, M., & Fantuzzi, G. (2013). Associations between obesity and asthma in a low-income, urban, minority population. *Annals of Allergy, Asthma, and Immunology, 110*(5), 340-346. doi: 10.1016/j.anai.2013.02.001

Duncan, C.L., Hogan, M.B., Tien, K.J., Graves, M.M., Chorney, J.M., Zettler, M.D.…Portnoy, J. (2012). Efficacy of a parent-youth teamwork intervention to promote adherence in pediatric asthma. *Journal of Pediatric Psychology, 38*(6), 617-628. doi:10.1093/jpepsy/jss123

Ellis, A.G. (1908). The pathological anatomy of bronchial asthma. *American Journal of Medical Sciences, 186*(3), 407-428.

Ernesti, I., Tancredi, G., Bardanzellu, F., Castanga, G., De Vittori, V., Palma Carbone, M. & Duse, M. (2013). Cardiopulmonary assessment in overweight/obesity children with asthma. *European Respiratory Journal, 42*(Suppl 57), P1101. Retrieved from: http://erj.ersjournals.com/content/erj/42/Suppl_57/P1101.full.pdf

Farpour-Lambert, N.J., Aggoun, Y., Marchand, L.M., Martin, X.E., Herrmann, F.R., & Beghetti, M. (2009). Physical activity reduces systemic blood pressure and improves early markers of atherosclerosis in pre-pubertal obese children. *Journal of the American College of Cardiology, 54*(25), 2396-2406. doi:10.1016/j.jacc.2009.08.030

Fedele, D.A., Janicke, D.M., Lim, C.S., & Abu-Hasan, M. (2014). An examination of comorbid asthma and obesity: Assessing differences in physical activity, sleep duration, health-related quality of life and parental distress. *Journal of Asthma, 51*(3), 275-281. doi:10.3109/02770903.2013.873807

Field, A. (2013). *Discovering statistics using SPSS*. 4th ed. London UK: Sage Publications, Ltd.

Food and Drug Adminsitration (FDA). (2010). Questions and answers: Phase-out of CFC metered-dose inhalers containing flunisolide, triamcinolone, metaproterenol, pirbuterol, albuterol and

ipratropium in combination, cromolyn, and nedocromil (Archived drug safety communication). Retrieved from: http://www.fda.gov/drugs/drugsafety/drugsafetypodcasts/ucm209072.htm

Forno, E., Lescher, R., Strunk, R., Weiss, S., Fuhlbrigge, A., & Celedon, J.C. for the CAMP Research Group. (2011). Decreased response to inhaled steroids in overweight and obese asthmatic children. *Journal of Allergy and Clinical Immunology*, *127*(3), 741-749. doi:10.1016/j.jaci.2010.12.010

Galli, S.J. & Tsai, M. (2012). IgE and mast cells in allergic disease. *Nature Medicine, 18*(5), 693-704. doi:10.1038/nm.2755

Gordis, L. (2014). *Epidemiology* (5th ed.). Philadelphia, PA: Elsevier Saunders.

Grotta, M.B., Squebola-Cola, D.M., Toro, A.A.D.C., Ribeiro, M.A.G.O., Mazon, S.B., Ribeiro, J.D., & Antues, E. (2013). Obesity increases eosinophil activity in asthmatic children and adolescents. *BMC Pulmonary Medicine, 13*(39). Retrieved from: http://www.biomedcentral.com/1471-2466/13/39

Gruenfeld, E.A., Zagarins, S.E., Walker, A.P., & Skinner, S.S. (2013). Fun and Fit: Evaluation of a pediatric exercise program. *Journal of Pediatric Nursing, 28,* 557-562. doi:10.1016/j.pedn.2013.02.033

Han, Y.Y., Forno, E. & Celedón, J.C. (2014). Adiposity, fractional exhaled nitric oxide, and asthma in U.S. children. *American Journal of Respiratory and Critical Care Medicine, 190*(1), 32-39. doi:10.1164/rccm.201403-0565OC

Han, Y.Y., Forno, E., Gogna, M., & Celedón, J.C. (2014). Obesity and rhinitis in a nationwide study of children and adults in the United States. *Journal of Allergy and Clinical Immunology,137*(5),1460-1465. doi:10.1016/j.jaci.2015.12.1307

Hargreave, F.E. & Nair, P. (2009). The definition and diagnosis of asthma. *Clinical & Experimental Allergy, 39*, 1652-1658. doi: 10.1111/j.1365-2222.2009.03321x

Hennekens, C. & Buring, J. (1987). *Epidemiology in Medicine*, Boston/Toronto: Little, Brown and Company.

Herbert, P.C., Lohrmann, D.K., Seo, D.C., Stright, A.D., & Kolbe, L.J. (2013). Effectiveness of the Energize elementary school program to improve diet and exercise. *Journal of School Health, 83*(11), 780-786. doi: 10.1111/josh.12094

Heyward, V.H. & Gibson, A.L. (2014). *Advanced fitness assessment and exercise prescription* (7th ed.). Champaign, IL: Human Kinetics.

Hogan, M.B., Allenback, G.L., Chawla, V., Mehta, N., Plunkett, G., & Wilson, N.W. (2016). Sensitization to a non-native plant without exposure is a marker of panallergen sensitization. *Journal of Allergy and Clinical Immunology: In Practice, 4*(5), 982-983.e1. doi:10.1016/j.jaip.2016.02.017

Holguin, F., Bleeker, E.R., Busse, W.W., Calhoun, W.J., Castro, M., Erzurum, S.C….& Wenzel, S.E. (2011). Obesity and asthma: An association modification by age of asthma onset. *Journal of Allergy and Clinical Immunology, 127*(6), 1486-1493. doi:10.1016/j.jaci.2011.03.036

Hosmer, D. W., Lemeshow, S. & May, S. (2008). *Applied survival analysis: Regression modeling of time-to-event data*, 2nd ed. New York, NY: Wiley.

Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D.G. & Newman, T.B. (2007). *Designing clinical research* (3rd ed.). Philadelphia, PA: Lippincott, Williams & Wilkins.

Ignacio, R.M.C., Kim, C.S., & Kim, S.K. (2014). Immunological profiling of obesity. *Journal of Lifestyle Medicine, 4*(1), 1-7. doi: 10.15280/jlm.2014.4.1.1

Institute of Medicine. (2012). Accelerating progress in obesity prevention: Solving the weight of the nation. Washington D.C.: National Academies Press. Retrieved from: http://www.iom.edu/Reports/2012/Accelerating-Progress-in-Obesity-Prevention.aspx

Janike, D.M., Steele, R.G., Gayes, LA., Lim, C.S., Clifford, L.M., Schneider, E.M…& Westen, S. (2014). Systematic review and meta-analysis of comprehensive behavioral family lifestyle interventions addressing pediatric obesity. *Journal of Pediatric Psychology 39*(8), 809-825. doi:10.1093/jpepsy/jsu023

Jensen, M.E., Collins, C.E., Gibson, P.G., & Wood, L.G. (2011). The obesity phenotype in children with asthma. *Paediatric Respiratory Reviews, 12*(3), 152-159. doi:10.1016/j.prrv.2011.01.009

Jensen, M.E., Gibson, P.G., Collins, C.E., & Wood, L.G. (2013). Airway and systemic inflammation in obese children with asthma. *European Respiratory Journal, 42*, 1012-1019. doi:10.1183/09031936.00124912

Jensen, M.E., Wood, L.G., & Gibson, P.G. (2012). Obesity and childhood asthma-mechanisms and manifestations. *Current Opinion in Allergy and Clinical Immunology, 12*(2), 186-192. doi: 10.1097/ACI.0b013e3283508df5

Jewell, P.W. & Nicoll, K. (2011). Wind regimes and Aeolian transport in the Great Basin U.S.A. *Geomorphology, 129*(1-2), 1-13. doi:10.1016/j.geomorph.2011.01.005

Jia, G., Rikson, R.W., Choy, D.F., Mosesova, S., Wu, L.C., Solberg, O.D….Arron, J.R. (2012). Periostin is a systemic biomarker of eosinophilic airway inflammation in asthmatic patients. *Journal of Allergy & Clinical Immunology, 130*(3), 647-654. http://dx.doi.org/10.1016/j.jaci.2012.06.025

Keet, C.A., McCormack, M.C., Pollack, C.E., Peng, R.D., McGowan, E., & Matsui, E.C. (2015). Neighborhood poverty, urban residence, race/ethnicity, and asthma: Rethinking the inner-city

asthma epidemic. *Journal of Allergy and Clinical Immunology, 135*(3), 655-662. doi: 10.1016/j.jaci.2014.11.022

Kelsey, M.M., Zaepfel, A., Bjornstad, P., & Nadeau, K.J. (2014). Age related consequences of childhood obesity. *Gerontology, 60*(3), 222-228. doi: 10.1159/000356023

Kim, S.H., Sutherland, E.R., & Gelfand, E.W. (2014). Is there a link between obesity and asthma? *Allergy Asthma & Immunology Research, 6*(3), 189-195. doi:10.4168/aair.2014.6.3.189

Kitzmann, K.M., Dalton, W.T., Stanley, C.M., Beech, B.M., Reeves, T.P., Buscemi, J….&Midgett, E.L. (2010). Lifestyle interventions for youth who are overweight: a meta-analytic review. *Health Psychology, 29*(1), 91-101. doi:10.1037/a0017437

Klein, G.M., Porcari, J.P., Hintermeister, R., Freedson, P.S., Ward, A., Mccarron, R.F….& Rippe, J.M. (1987). Estimation of VO2 max from a one-mile track walk, gender, age, and body weight. *Medicine and Science in Sports and Exercise, 19*(3), 253-259. http://www.uni.edu/dolgener/Advanced_exercise_physiologyy/Electronic%20Articles/Rockport%20Walking%20Test.pdf)

Krishnan, S., Hettiaracchi, D., Scharbach, M., & Dozor, A.J. (2016). Obesity and pulmonary function in school-age children with asthma. *American Journal of Respiratory and Critical Care Medicine, 193*, A3797. doi:10.1164/ajrccm-conference.2016.193.1

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for *t*-tests and ANOVAs. *Frontiers in Psychology, 4*(article 863). doi:10.3389/fpsyg.2013.00863.

Lang, J.E. (2014). Exercise, obesity, and asthma in children and adolescents. *Jornal de Pediatria, 90*(3), 215-217.

Lara, M., Akinbami, L., Flores, G., & Morgenstern, H. (2006). Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. *Pediatrics, 117*(1), 43-53. DOI: 10.1542/peds.2004-1714

Lara, M., Ramos-Valencia, G., Diaz, C., Reyes, B.M., & Gonzalez-Gavillán, J. (2014, November). *Alarmingly high prevalence of asthma in Puerto Rican island children.* Poster presented at the 143rd annual meeting and exposition of the American Public Health Association, New Orleans, LA.

Lipworth, B.J. (2014). Emerging role of long acting muscarinic antagonists for asthma. *Journal of Clinical Pharmacology, 77*(1),55-62. doi:10.1111/bcp.12123

Loid, P., Goksör, E., Alm, B., Pettersson, R., Mollborg, P., Erdes, L….Wennergren, G. (2015). A persistently high body mass index increases the risk of atopic asthma. *Acta Paediatrica, 104*, 707-712. doi:10.1111/apa.13015

Lorusso, J.R., Pavlovich, S.M., & Lu, C. (2013). Developing student enjoyment in physical education. *Physical & Health Education Journal, 79*(2), 14-18.

Lucas, J.A., Moonie, S., Olsen-Wilson, K., & Hogan, M.B. (2016). Asthma, allergy, and obesity: Examining the relationship among Nevada children. *Journal of Asthma.* (Accepted Oct. 2016).

Lucas, J., Moonie, S., & Towle, B. (2014, September). *Assessment of childhood asthma disparities in Nevada*. Poster presented at the annual conference of the Nevada Public Health Association, Las Vegas, NV.

Magrone, T., Simone, M., Altamura, M. & Munno, I. (2014). Characterization of the immune inflammatory profile in obese asthmatic children. *Endocrine, Metabolic, & Immune Disorders - Drug Targets, 14*(3), 187-195. http://dx.doi.org/10.2174/1871530314666140526095211

Martinez, F.D., Wright, A.L., Taussig, L.M., Holberj, C.J., Halonen, M., Morgan, W.J., & the Group Health Medical Associates. (1995). Asthma and wheezing in the first six years of life. *New England Journal of Medicine, 332*(3), 133-138. DOI: 10.1056/NEJM199501193320301

McFadden, E.R. (2004). A century of asthma. *American Journal of Respiratory and Critical Care Medicine, 170*, 215-221. DOI: 10.1164/rccm.200402-185OE

Melo, X., Santa-Clara, H., Pimenta, N.M., Silva Martins, S., Minderico, C.S., Fernhall, B. & Sardinha, L.B. (2015). Intra-media thickness in 11- to 13-year –old children: Variation attributed to sedentary behavior, physical activity, cardiorespiratory fitness, and waist circumference. *Journal of Physical Activity and Health, 12*, 610-617. doi:10.1123/jpah.2013-0501

Meredith, M.D. & Welk, G. J. (Eds.). (2013). *FITNESSGRAM®/ACTIVITYGRAM® Test administration manual* (4th ed.). Dallas TX: The Cooper Institute.

Merkus, P. (2014). A tribute to Philip Quanjer. *Pediatric Pulmonology, 49*, 103-105. doi:10.1002/ppul.22913

Migueres, M., Dávila, I., Frati, F., Azpeitia, A., Jeanpetit, Y., Lhéritier-Barrand, M… & the PluRAL Study Group. (2014) Types of sensitization to aeroallergens: definitions, prevalences and impact on the diagnosis and treatment of allergic respiratory disease. *Clinical and Translational Allergy, 4*(16), 8p. http://ctajournal.biomedcentral.com/articles/10.1186/2045-7022-4-16

Moonie, S., & Lucas, J.A. (2016). Nevada 2011-2014 Childhood Asthma Prevalence Statewide Report. University of Nevada, Las Vegas and Nevada Division of Public and Behavioral Health, Nevada State Department of Health and Human Services.

Moonie, S., Seggev, J.S., Shan, G., Pergola, B., Teramoto, M. (2014). Longitudinal trends in asthma health care use in Southern Nevada. *Annals of Allergy, Asthma & Immunology, 114*(1), 70-72.e2. doi: 10.1016/j.anai.2014.10.010

Moonie, S., Sterling, D.A., Figgs, L.W. & Castro, M. (2008). The relationship between school absence, academic performance, and asthma status. *Journal of School Health, 78*(3), 140-148.

Must, A. & Anderson, S.E. (2006). Body mass index in children and adolescents: considerations for population-based applications. *International Journal of Obesity, 30*, 590-594. doi:10.1038/sj.ijo.0803300

National Heart, Lung, and Blood Institute. (2007). National asthma education and prevention: Expert panel report 3: Guidelines for the Diagnosis and Management of Asthma. Retrieved from: http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines

National Heart, Lung, and Blood Institute. (2014). What is Asthma? Retrieved from: http://www.nhlbi.nih.gov/health/health-topics/topics/asthma

Nevada Institute for Children's Research and Policy. (2015). Health status of children entering kindergarten in Nevada: Results of the 2014-2015 Kindergarten Health Survey. Retrieved from: http://nic.unlv.edu/files/KHS%20Year%207%20Report_Final_.pdf

Nevada Institute for Children's Research and Policy. (2014). Health status of children entering kindergarten in Nevada: Results of the 2013-2014 Kindergarten Health Survey. Retrieved from: http://nic.unlv.edu/files/KHS%20Year%206%20Report_Final.pdf

Novak, N & Bieber, T. (2003). Allergic and nonallergic forms of atopic diseases. *Journal of Allergy and Clinical Immunology, 112*(2), 252-262. Retrieved from: http://www.jacionline.org/article/S0091-6749(03)01461-1/pdf

Nussey, S. & Whitehead, S. (2001). *Endocrinology: An integrated approach*. Oxford, UK: BIOS Scientific Publishers.

Ober, C. & Yao, T.C. (2011). The genetics of asthma and allergic disease: A 21st century perspective. *Immunology Reviews, 242*(1), 10-30. doi:10.1111/j.1600-065X.2011.01029.x.

Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services (2016a). Healthy People 2020: About Healthy People. Retrieved from: https://www.healthypeople.gov/2020/About-Healthy-People

Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services (2016b). Healthy People 2020: Respiratory Diseases: Objectives. Retrieved from: https://www.healthypeople.gov/2020/topics-objectives/topic/respiratory-diseases/objectives

Ogden, G.L., Carroll, M.D., Kit, B.K., & Flegal, K.M. (2014). Prevalence of childhood and adult obesity in the United States, 2011-2012. *Journal of the American Medical Association (JAMA), 311*(8), 806-814. doi:10.1001/jama.2014.732

Olin, J.T. & Wechsler, M.E. (2014). Asthma: Pathogenesis and novel drugs for treatment. *BMJ, 349*:g5517. doi: 10.1136/bmj.g5517

Ostrom, N.K., Parsons, J.P., Eid, N.S., Craig, T.J., Stoloff, S., Hayden, M.L., & Colice, G.L. (2013). Exercise-induced bronchospasm, asthma control and obesity. *Allergy and Asthma Proceedings, 34*(4), 342-348. doi: 10.2500/aap.2013.34.3674

Pallant, J. (2013). *SPSS survival manual: A step by step guide to data analysis using IBM SPSS* (5th ed.). New York, NY: Open University Press.

Plowman, S.A. & Meredith, M.D. (Eds.). (2013). *Fitnessgram®/Activitygram® Reference Guide* (4th ed.). Dallas, TX: The Cooper Institute.

Porter, M., Wegienka, G., Havstad, S., Nageotte, C.G., Johnson, C.C., Ownby, D.R. & Zoratti, E.M. (2012). Relationship between childhood BMI and young adult asthma. *Annals of Allergy, Asthma & Immunology, 109*(6): 408–411.e1. doi:10.1016/j.anai.2012.09.009

Presidential Youth Fitness Program (n.d.). How it works. Retrieved from: http://www.presidentialyouthfitnessprogram.org/how-it-works

Priftis, K.N., Mantzouranis, E.C. & Anthracopoulous, M.B. (2009). Asthma symptoms and airway narrowing in children growing up in urban versus rural environment. *Journal of Asthma, 46,* 244-251. DOI: 10.1080/02770900802647516

Pulmonary function tests. (2013). In *NIH U.S. National Library of Medicine MedlinePlus Medical encyclopedia* online. Retrieved from: http://www.nlm.nih.gov/medlineplus/ency/article/003853.htm

Quanjer, P.H., Stanojevic, S., Cole, T.J., Baur, X., Hall, G.L., Culver, B.H.…Stocks, J. on behalf of the European Respiratory Society Global Lung function initiative. (2012a). Multi-ethnic reference values for spirometry for the 3-95 year age range: The Global Lung Function 2012 equations: report of the Global Lung Function Initiative (GLI), ERS Task Force to establish improved lung function reference values. *European Respiratory Journal, 40*(6), 1324-1343. doi:10.1183/09031936.00080312

Quanjer, P.H., Stanojevic, S., Stocks, J., Cole, T.J. (2012b). GLI-2012 All-age multi-ethnic reference values for spirometry: Summary and overview. Retrieved from: http://lungfunction.org/files/GLI-2012_Reference_values.pdf

Raedler, D., Ballenberger, N., Klucker, E., Bock, A., Ragna, O., da costa, O.P.…Schaub, B. (2015). Identification of novel immune phenotypes for allergic and nonallergic childhood asthma. *Journal of Allergy and Clinical Immunology, 135*(1), 81-91. doi: 10.1016/j.jaci.2014.07.046

Raj, D., Kabra, S.K., Lodha, R. (2014). Childhood obesity and risk of allergy or asthma. *Immunology and Allergy Clinics of North America, 34*(4), 753-765. doi:10.1016/j.iac.2014.07.001

Rastogi, D., Fraserm S., Oh, J., Huber, A.M., Schulman, Y., Bhagtani, R.H.…Macian, F. (2014). Inflammation, metabolic dysregulation, and pulmonary function among obese urban adolescents with asthma. *American Journal of Respiratory and Critical Care Medicine, 191*(2), 149-160. doi:10.1164/rccm.201409-1587OC

Reddy, M.B., Doshi, J., Covar, R., Spahn, J.D. (2014). The changing face of severe childhood asthma: A comparison of two cohorts of children evaluated at National Jewish Health over the past 20 years. *Allergy and Asthma Proceedings, 35,* 119-125. doi: 10.2500/aap.2014.35.3727

Redinger, R.N. (2007). The pathophysiology of obesity and its clinical manifestations. *Gastroenterology & Hepatology, 3*(11), 856-863.

Robinson, D.S. (2010). The role of the T cell in asthma. *Journal of Allergy and Clinical Immunology, 126,* 1081-1091. doi:10.1016/j.jaci.2010.06.025

Romero-Corral, A., Somers, V.K., Sierra-Johnson, J., Thomas, R.J., Bailey, K.R., Collazo-Clavell, M.L.…Lopez-Jimenez, F. (2008). Accuracy of body mass index to diagnose obesity in the US adult population. *International Journal of Obesity, 32*(6), 959-966. doi:10.1038/ijo.2008.11

Salo, P.M., Arbes, S.J., Jaramillo, R., Calatroni, A., Weir, C.H., Sever, M.L.… Zeldin, D.C. (2014). Prevalence of allergic sensitization in the United States: Results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. *Journal of Allergy and Clinical Immunology,134*(2), 350-359. doi:10.1016/j.jaci.2013.12.1071.

Santos-Silva, R., Melo, C., Gonçalves, D., Coelho, J., & Carvalho, F. (2014). Comparison between exercise performance in asthmatic children and healthy controls – Physical Activity

Questionnaire application. *Revista Portuguesa de Pneumologia, 20*(3), 138-145. doi: 10.1016/j.rppneu.2013.11.005

Shah, N.R. & Braverman, E.R. (2012). Measuring adiposity in patients: The utility of body mass index (BMI), percent body fat, and leptin. *PLoS One, 7*(4), e33308. doi:10.137/journal.pone.0033308

Shim, Y.M., Burnette, A., Lucas, S., Herring, R.C., Weltman, J., Patrie, J… Platts-Mills, T.A. (2013). Physical deconditioning as a cause of breathlessness among obese adolescents with a diagnosis of asthma. *PLoS ONE 8*(4): e61022. doi:10.1371/journal.pone.0061022

Silva, L.R., Cavaglieri, C., Lopes, W.A., Pizzi, J., Coelho-e-Silva, M.J.C., & Leite, N. (2014). Endothelial wall thickness, cardiorespiratory fitness and inflammatory markers in obese and non-obese adolescents. *Brazilian Journal of Physical Therapy, 18*(1), 47-55. doi:10.1590/S1413-35552012005000133

Simon, M.R. Chinchilli, V.M., Phillips, B.R., Sorkness, C.A., Lemanske, R.F., Szefler, S.J…Morgan, W. (2010). FEF_{25-75} and FEV_1/FVC in relation to clinical and physiologic parameters in asthmatic children with normal FEV_1 values. *Journal of Allergy and Clinical Immunology, 126*(3), 527-534.e8. doi:10.1016/j.jaci.2010.05.016

Spaulding, S.A., Devine, K.A., Duncan, C.L., Wilson, N.W., & Hogan, M.B. (2012). Electronic monitoring and feedback to improve adherence in pediatric asthma. *Journal of Pediatric Psychology, 37*(1), 64-74. doi:10.1093/jpepsy/jsr059

Starkoff, B.E., Eneli, I.U., Bonny, A.E., Hoffman, R.P., & Devor, S.T. (2014). Estimated aerobic capacity changes in adolescents with obesity following high intensity interval exercise. *International Journal of Kinesiology & Sports Science, 2*(3), 1-8. doi:10.7575/aiac.ijkss.v.2n.3p.1

Stingone, J.A., Ramirez, O.F., Svensson, K., & Claudio, L. (2011). Prevalence, demographics, and health outcomes of comorbid asthma and overweight in urban children. *Journal of Asthma, 48*, 876-885. doi:10.3109/02770903.2011.616615

Sullivan, G.M. & Feinn, R. (2012). Using effect sizes – or why the *p* value is not enough. *Journal of Graduate Medical Education, 4*(3), 279–282. doi:0.4300/JGME-D-12-00156.1

Sutherland, E.R. (2014). Linking obesity and asthma. *Annals of the New York Academy of Sciences, 1311*, 31-41. doi: 10.1111/nyas.12357

Templeton, G.F. (2011). A two-step approach for transforming continuous variables to normal: Implications and recommendations for IS research. *Communications of the Association for Information Science, 28*(1), 41-58. Available at: http://aisel.aisnet.org/cais/vol28/iss1/4

Trasande, L. (2010). How much should we invest in childhood obesity? *Health Affairs, 29*(3), 372-278. doi: 10.1377/hlthaff.2009.0691

Trasande, L. & Elbel, B. (2012). The economic burden placed on healthcare systems by childhood obesity. Expert Review of Pharmacoeconomics & Outcomes Research, 12(1), 39-45. doi:10.1586/erp.11.93

Vahlkvist, S., Inman, M.D., & Pedersen, S. (2010). Effect of asthma treatment on fitness, daily activity and body composition in children with asthma. *Allergy, 65*(11), 1464-1471. doi:10.1111/j.1398-9995.2010.02406.x.

van Belle, G., Fisher, L.D., Heagerty, P.J., & Lumley, T. (2004). *Biostatistics: A methodology for the health sciences* (2nd ed.). Hoboken, NJ: John Wiley and Sons.

van Leeuwen, J.C., Hoogstrate, M., Duiverman, E.J., & Thio, B.J. (2014). Effects of dietary induced weight loss on exercise induced bronchoconstriction in overweight and obese children. *Pediatric Pulmonology, 49*(12), 1155-1161. DOI:10.1002/ppul.22932

Vinding, R.K., Stockholm,J., Chawes, B.L.K., Bisgaard, H. (2016). Blood lipid levels associate with childhood asthma, airway obstruction, bronchial hyperresponsiveness, and aeroallergen sensitization. *Journal of Allergy and Clinical Immunology, 137*(1), 68-74.e4. doi:10.1016/j.jaci.2015.05.033

Wang, Y. & Chen, H.J. (2012). Use of percentiles and z-scores in anthropometry. In Preedy, V.R. (Ed.), *Handbook of anthropometry: Physical measures of human form in health and disease* (29-48). New York, NY: Springer Science+Business Media LLC

Wang, Y.C., McPherson, K., Marsh, T., Gortmaker, S.L., & Brown, M (2011). Health and the economic burden of the projected obesity trends in the USA and the UK. *The Lancet, 378*, 815-825.

Wanrooij, V.H.M., Willeboordse, M., Dompeling, E., & van de Kant, K.D.G. (2014). Exercise training in children with asthma: A systematic review. *British Journal of Sports Medicine, 48*, 1024-1031. doi:10.1136/bjsports-2012-091347

Waters, E., deSilva-Sanigorski, A., Hall, BJ., Brown, T., Campbel, K.J., Gao, Y….Summerbell, C.D. (2011). Interventions for preventing obesity in children. *Cochrane Collection, Issue 12.* Art. No.: CD001871. DOI: 10.1002/14651858.CD001871.pub3

Westergren, T., Ommundsen, Y., Lødrup Carlsen, K.C., Carlsen, K.H., Mowinckel, P., Fegran, L., & Berntsen, S. (2015). A nested case-control study: Personal, social and environmental correlates of vigorous physical activity in adolescents with asthma. *Journal of Asthma, 52*(2), 55-161. doi:10.3109/02770903.2014.955190

Wisniewski, A.B. & Chernausek, S.D. (2009). Gender in childhood obesity: family environment, hormones, and genes. *Gender Medicine*, *6*(Suppl 1), 76-85.

Wong, V., Wilson, N.W., Peele, K., & Hogan, M.B. (2012). Early pollen sensitization in children is dependent upon regional aeroallergen exposure. *Journal of Allergy, Vol. 2012,* Art. ID: 583765. doi: 10.1155/2012/583765.

World Health Organization (WHO). (2013). Asthma: Fact sheet No. 307. Retrieved from: http://www.who.int/mediacentre/factsheets/fs307/en/

World Health Organization (WHO). (2015). Obesity and overweight: Fact sheet No. 311. Retrieved from: http://www.who.int/mediacentre/factsheets/fs311/en/

World Health Organization (WHO). (2016). Classification of Diseases (ICD). Retrieved from: http://www.who.int/classifications/icd/en/

Yavuz, H.M., van Ijzendoorn, M.H., Mesman, J, & van der Veek, S. (2015). Interventions aimed at reducing obesity in early childhood: A meta-analysis of programs that involve parents. *Journal of Child Psychology and Psychiatry*, *56*(6), 667-692. doi:10.1111/jcpp.12330

CURRICULUM VITAE

Graduate College

University of Nevada, Las Vegas

Jennifer Anne Lucas, MPH

lucasj23@unlv.nevada.edu

Education:
University of Nevada, Las Vegas
PhD in Public Health, expected December 2016 in Epidemiology and Biostatistics
MPH in Epidemiology and Biostatistics, 2012

Metropolitan State College of Denver
BA in Journalism

Publications:

Lucas JA, Moonie S, Olsen-Wilson K, Hogan MB. Asthma, allergy, and obesity: Examining the relationship among Nevada children. J Asthma. Accepted 2 Oct. 2016. http://dx.doi.org/10.1080/02770903.2016.1244829

Thomason D, Moonie S, **Lucas J.** Adolescent perceptions of facilitators, barriers, and self-efficacy to participating in PE: Differences by gender, grade, ethnicity, and socioeconomic status. Journal of School Nursing (March 2016)

Moonie S, **Lucas JA.** Nevada 2011-2014 Adult Asthma Prevalence Statewide Report. University of Nevada, Las Vegas and Nevada Division of Public and Behavioral Health, Nevada State Department of Health and Human Services. April 2016

Moonie S, **Lucas JA.** Nevada 2011-2014 Childhood Asthma Prevalence Statewide Report. University of Nevada, Las Vegas and Nevada Division of Public and Behavioral Health, Nevada State Department of Health and Human Services. April 2016

Selected Presentations:

Lucas JA, Moonie S, Hogan MB. *Overweight as a Protective Factor for Aeroallergen Sensitization Among Pediatric Asthmatics in Nevada.* Poster session: Council of State and Territorial Epidemiologists 2016 Annual Conference, Anchorage, AK, June 19-23, 2016.

Lucas JA, Moonie S, Hogan MB. *Characteristics of a Pilot Population of Pediatric Asthma Patients*

in Nevada. Poster Session: University of Nevada, Las Vegas, Division of Health Sciences 9th Annual Interdisciplinary Research & Scholarship Day, Las Vegas, NV, April 1, 2016

Lucas J. *The Emerging Relationship Between Asthma And Obesity.* Invited presentation: Nevada Statewide Asthma Control Conference, Nevada Statewide Asthma Coalition and Positively Kids Foundation, Inc. Roseman University, Summerlin Campus, Las Vegas, NV, March 11, 2016.

Lucas JA, Moonie S, Hogan MB. *Association Between Asthma and Body Mass Index in a Pediatric Nevada Population.* Poster session: Council of State and Territorial Epidemiologists 2015 Annual Conference, Boston MA, June 14-18, 2015.

Coughenour C, Clark S, **Lucas J**, Haboush A, Phebus T. *Association between home and community environment on body mass index of kindergarten age children in Clark County, NV*. Poster session: American Public Health Association 142nd Annual Meeting & Exposition, New Orleans, LA, Nov. 15-19, 2014.

Lucas J, Moonie S, Towle B. *Assessment of Childhood Asthma Disparities in Nevada*. Poster session: Nevada Public Health Association Conference, Las Vegas, NV, Sep. 25, 2014.

Lucas JA, Labus B, Cochran C. *Timeliness of Disease Reporting between Electronic and Traditional Laboratory Methods: An Evaluation of Four Gastrointestinal Illnesses in Southern Nevada*. Oral presentation: Council of State and Territorial Epidemiologists 2013 Annual Conference, Pasadena, CA, June 9-13, 2013.

Dissertation Title:
The relationship between pediatric asthma and obesity in Nevada

Dissertation Examination Committee:
Chairperson, Sheniz Moonie, Ph.D.
Committee Member, Shawn Gerstenberger, Ph.D.
Committee Member, Mary Beth Hogan, Ph.D.
Graduate Faculty Representative, Alona Angosta, Ph.D.