8-3-2016 12:00 AM

Body and Organ Measurements in Infants and Neonates: An Autopsy Study

Audrey-Ann M. Evetts, *The University of Western Ontario*

Supervisor: Dr. E. Tugaleva, *The University of Western Ontario*
Joint Supervisor: Dr. M. Shkrum, *The University of Western Ontario*
A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Pathology

Abstract

Introduction: A pathologist doing a pediatric autopsy will commonly assess child's development by comparing the postmortem data to standardized population parameters using body and organ measurement charts. Although a number of resources are available, many are outdated and have significant limitations.

Objectives: To create Ontario population-specific organ and body measurement mean charts for infants and to explore relationships between body measurements/organ weights and cause of death, age, and gender of the deceased.

Methods: A database of 900 cases of infant and neonatal deaths that were investigated by Ontario coroners from 2000 to 2010 was retrospectively analyzed.

Results and Conclusions: No differences were found between the cause of death groups in relation to the body weight, heart, and pancreas weights. Lungs, brains, livers and spleens tended to be heavier in SIDS and SUDS cases compared to Control group while adrenal glands and kidneys had a tendency of being smaller.

Keywords

Forensic medicine and pathology, pediatric autopsy, organ weights, body measurements.

Acknowledgments

I have many wonderful people to thank for their support, guidance and assistance throughout this endeavor. First and foremost, I would like to thank my thesis supervisors Dr. Elena Tugaleva and Dr. Michael Shkrum who took me on as a student and mentored me. I appreciate all of your support, ongoing assistance and teaching throughout this process. I would like to thank my committee members, Dr. Zia Khan, Dr. Charmaine Dean, and Dr. John Koval for their support and input throughout this project. I gratefully acknowledge the respondents to the survey, the resource staff at Allyn and Betty Taylor Library at Western University, and the Department of Pathology & Laboratory Medicine, at London Health Sciences Center, especially Lynn James and Paula Miller, for their guidance and support. I would like to thank the Information Management Leads, June Lindsell and Andrew Stephen from the Ontario Chief Coroner's Office, for their help with retrieving and reviewing the files, and Dr. Richard Mann, the Regional Supervising Coroner, for the use of his office space. I also appreciate all the assistance in analyzing the statistics provided by Jingjia (Victoria) Chu, a Ph.D. candidate, Statistical Consultant at Western University. Most of all I would like to thank my husband Chris and my family for their support, guidance and patience.

Table of Contents

Tables

Figures

Appendices

Chapter 1

1 Introduction

1.1 Current Tendencies in Infant Mortality

Infant mortality rate is defined as the rate at which the children of less than 1 year of age die. It is a significant indicator of the well-being of a society because it strongly correlates with the socioeconomic development of a country.

According to the World Health Organization, in 2015 there were 5.9 million pediatric deaths under the age of 5 years worldwide[1]. Of these, 75% occurred in the first year of life. A child's risk of dying is highest during the neonatal period, i.e. within the first 28 days of a child's life (45% of deaths under the age of 5)[2]. The highest incidence of these deaths occurs in low- and middle-income countries because of a lack of access to affordable health care. In low-income countries, the mortality under the age of 5 is about 14 times higher than in developed regions[2].

The government of Canada monitors and documents the data on infant deaths. The infant and neonatal death rate for Canada in 2015 was 4.9 per 1000 live births and for Ontario – 5.0 per 1000 live births. This translates to approximately 300 infant deaths per year in Canada, 200 of which are reported in Ontario[3]. Although Canada has significantly reduced its infant mortality rate over the last few decades, the rate continues to be relatively high for its level of socioeconomic development, ranking second-to-last among 17 peer countries[4]. This could be attributed to the advances in management of high-risk deliveries, increased rate of successful deliveries of preterm/low birth weight infants, and improved fertility therapies, which increase the number of multiple births. All of these factors could be contributing to relatively high infant mortality in Canada. In addition, the registration of live births and stillbirths is not standard amongst the peer countries, allowing for the exclusion of low birth weight infants which are at higher risk of mortality, therefore leading to underreporting of infant deaths[4].

According to Statistics Canada, in 2009, ten leading causes of infant mortality included: congenital malformations and chromosomal abnormalities (22.4%); preterm gestation

and low birth weight (13.4%); sequelae of maternal complications of pregnancy (9.8 %); deaths related to placental complications (6.5%); Sudden Infant Death Syndrome (SIDS) (6.1%); intrauterine hypoxia and birth asphyxia (3.2%); neonatal hemorrhages (2.7%); bacterial sepsis of newborn (2.2%); complications of labour and delivery (1.8%); and accidental and unintentional injuries (1.6%)[5].

A great number of early childhood deaths are preventable through low-cost practical interventions addressing maternal health and effective antenatal and early childhood care[2]. Thorough investigation of pediatric deaths is a major component in the prevention of future fatalities. This has been documented by an increased awareness that Sudden Unexplained Death in Infancy (SUDI) associated with unsafe sleeping environments led to a 50% decrease in infant deaths since 2000[6,7]. Data pertaining to the causes of pediatric mortality are important to prioritize future disease specific interventions and to assess trends in burden of various diseases[8,9].

Pediatric death investigation is a complex process with multiple parties involved. Although many components of the investigation are crucial, postmortem examination of the deceased child is frequently a key component in identifying why the child died. In the course of a postmortem examination, a pathologist assesses the overall physical development of the child by comparing the body and organ measurements against published reference values. Currently used reference sources on pediatric body and organ parameters have been shown to be outdated and difficult to understand[10–13].

1.2 Sudden Death in Infancy

Several studies have identified a number of risk factors associated with sudden infant death, including infant's sleeping position, nature of bedding, maternal smoking during pregnancy, and environmental temperature[7,14]. Only roughly 15 percent of sudden infant death cases can be explained after a complete autopsy is performed[15]. Among common known causes are infections, cardiovascular anomalies, child abuse, and metabolic or genetic disorders[16,17]. Of the remaining 85%, the most common is Sudden Infant Death Syndrome (SIDS).

SIDS or “crib death” refers to death of a child younger than 1 year of age who dies suddenly and unexpectedly during sleep, and the death remains unexplained after a thorough death investigation and complete postmortem examination[18]. In essence, SIDS is a diagnosis of exclusion and should not be applied to situations of accidental asphyxia, inflicted injuries, or significant disease[15].

SIDS was first defined in 1969 by the National Institute of Child Health and Human Development[15]. The original definition described the syndrome as “sudden death of an infant or young child which is unexpected by history, and in which a thorough postmortem examination fails to demonstrate an adequate cause of death”[19]. However, with the evolving knowledge on SIDS, in 1989 the definition was amended to “sudden death of an infant under 1 year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history”[15,19]. SIDS deaths are unlikely in the 1st month of life, when other causes of death are more prevalent (e.g. infections, congenital, genetic and metabolic disorders). SIDS has the highest prevalence in the 2nd and 3rd months of life partly attributed to the fact that infants use their nasal passages to breath[20]. There is a decrease in incidence after 6 months of age once an infant has greater functional mobility in being able to roll[14,15].

1.3 SIDS Terminology

Scientific and medical literature is inconsistent in using definitions and terminology on sudden and unexpected death in infants. The term “Sudden Unexpected/Unexplained Death in Infancy” (SUDI) is based on the 2005 publication of the National Association of Medical Examiners referring to SUDI as an umbrella diagnosis for deaths that are initially unexplained. It should not be confused with SIDS diagnosis. The variable use of terminology in different death investigation systems hampers clear understanding and effective classification of sudden infant death.

.

There are ongoing efforts to standardize the certification and classification of infant deaths across Canada. The Ontario death investigation system uses the term SIDS as a classification of a unique category of natural infant deaths, for which a specific

underlying natural cause (i.e. cardiac, neurologic or metabolic) may be found in the future[21]. The SIDS definition is strictly applied to exclude cases with sleep associated circumstances and social risk factors.

To standardize cause and manner of death reporting in Ontario, all infant deaths are classified into four distinct categories[22]. The first category (category 1) includes any case with a definitive cause of death revealed at autopsy. The second category (category 2) is for cases fitting the SIDS definition, excluding cases where sleep-associated circumstances (adult bed, waterbed, sofa, child carrier, car seat, non-approved playpen or bassinet) and/or social risk factors (involvement with child welfare agencies, history of domestic violence, alcohol or other substance abuse in the caregivers) are present. The third category (category 3) includes cases with no anatomical or toxicological cause of death when there are sleep-associated circumstances, social risk factors or cases that do not meet the SIDS definition. The fourth category (category 4) represents deaths where anatomical/toxicological findings do not establish a cause of death (e.g. healed fractures) and non-accidental injury cannot be excluded.

1.4 Sleep Environment

One of the most important risk factors for sudden unexpected death in infants relates to prone (facedown) sleeping position of the infant[7]. Launching of the "Back to Sleep" campaign in 1994 as a way to increase public awareness of risks of sudden death in infants, initially aimed at reducing "crib deaths" by 10%[6,7]. The campaign exceeded expectations with an approximately 50% decline in sudden infant deaths observed over the next 5 years[7,16], further emphasizing the important role of the sleep environment. In addition to the sleeping position of the child, other unfavorable factors include: unsuitable/soft sleeping surfaces, loose bedding, bed sharing, overheating during sleep, unaccustomed sleeping position (putting an infant in a position other than the one he/she usually sleeps), and exposure to smoking (either in the environment or in the womb)[14]. The Government of Canada Public Health Agency continues to raise awareness about safe sleep environment for infants providing evidence-based information to health care practitioners and caregivers[7]. Among five main recommended principles of safe sleep

addressing modifiable risk factors are: placement of the infant in a supine sleep position, use of certified cribs/cradles/bassinets, avoidance of bed sharing and smoking, and promotion of breastfeeding.

1.5 Ontario Pediatric Death Investigation

The Ontario death investigation system is the largest in North America and is a partnership of the Office of the Chief Coroner for Ontario (OCCO) and the Ontario Forensic Pathology Service (OFPS) operating under the authority of the Ministry of Community Safety and Correctional Services. The OCCO investigates about 15,000 deaths annually including approximately 5,800 cases requiring autopsies. In Ontario, approximately 250 pediatric deaths are investigated by coroners yearly[23].

The main objective of any death investigation system is to ensure that every death under its mandate is investigated and explained. Recommendations on preventing deaths in certain circumstances may be made. Five questions must be answered during a coroner's investigation (the five "W"s): who was the deceased; when did he/she die; where did the death occur; what was the cause of death, and what were the means or manner of death (natural, accident, suicide, homicide, undetermined)[24].

Death investigation in cases of pediatric fatalities follows general investigative guidelines, but in contrast to adult deaths can be more challenging because of their potential complexity. Coordination among many participants (coroner, pathologist, police, toxicologist, Children's Aid Society workers, pediatricians, radiologist etc.) is essential. In the majority of the cases, the cause and manner of death are not apparent on initial presentation. In a significant proportion of the cases, the cause and manner of death remain unknown even following a comprehensive death scene investigation and a complete autopsy.

The coroner plays the central role in a pediatric death investigation and has a statutory responsibility for the overall investigation[23]. He/she examines the body at the death

scene, communicates with the family, police, Children's Aid Society and others, obtains and reviews the medical records of the deceased child and maternal records when applicable[25]. The Investigative Questionnaire for Sudden and Unexpected Deaths of Infants is completed by the coroner. It includes detailed information such as: the circumstances of death, the child's sleep environment, his/her past or recent health and development patterns, and findings observed during the external examination of the body at the scene. The coroner issues a warrant to the pathologist to conduct a postmortem examination. The coroner and police are the major sources of information for the pathologist who conducts the postmortem examination[25]. Based on the results of postmortem examination in conjunction with ancillary tests and the police investigation, the coroner completes the Coroner's Investigation Statement and Medical Certificate of Death.

Within the OFPS Service, pediatric autopsies are done by Category A and C pathologists. The category A pathologists have additional training and/or certification in forensic pathology and can perform medicolegal autopsies on all pediatric cases including criminally suspicious deaths and homicides. The category C pathologists do autopsies on non-suspicious pediatric deaths.

An autopsy serves to determine the cause and mechanism of death (the latter refers to a physiological derangement that results in death) and to assist the coroner in certifying the manner of death. The OFPS has guidelines for a standardized approach to infant autopsies[26]. These cases require an extensive history about the child's birth and development, as well as, the medical history of the child and his/her family. This allows the pathologist to tailor the autopsy to address specific questions raised by the history. The external examination, in addition to routine observations includes measurements, allowing evaluation of the child's physical development. In the course of this evaluation, the pathologist commonly records various body measurements [body weight, length (crown-heel, crown-rump), circumferences of the head, chest and abdomen, and foot length][27]. These are compared to the normal reference values to establish if the infant meets normal growth parameters. Many of the reference sources that are used for comparison are based on autopsied rather than living populations. The comparison helps

to identify infants who are failing to thrive or whose parameters are above the normal ranges. Failure to thrive could be from poor feeding, a variety of diseases (such as chronic medical conditions, infections, malignancies), or physical neglect[28]. Above normal observations could be related to unhealthy nutrition, underlying metabolic syndromes or other diseases. A skeletal radiological survey can detect not only recent and old fractures but also bony abnormalities due to nutritional deficiencies.

Recording various organ weights in the course of the internal examination guides the pathologist in differentiating healthy organs from those diseased[26]. Major organs and tissues are sampled for microscopy to diagnose specific pathological abnormalities. Additional ancillary tests that are frequently conducted in infant autopsies include: toxicological, biochemical (vitreous humour sampling) and microbiological analyses, metabolic screening, cytogenetic studies, and any other tests deemed necessary[26]. All findings are reviewed by the pathologist to reach a conclusion about a cause and mechanism of death.

Police play a significant role in the pediatric death investigation. They are among the first responders to the scene. Police have primary role in the documentation and preservation of the death scene and question the family, caregivers and other witnesses to help reconstruct the events leading to a death. A police identification officer commonly attends the scene and autopsy to further document findings by photography and to collect evidence if necessary[25].

Cause of death is defined as "all those diseases, morbid conditions or injuries which either resulted in or contributed to death and the circumstances of the accident or violence which produced any such injuries"[29]. The pathologist will identify immediate and antecedent causes of death, as well, as other significant conditions contributing to the death. To correlate this with previously discussed Ontario classification of infant deaths (see Section 1.3 SIDS Terminology above), the first category cases have a definitive cause of death which directly impacts the manner of death (natural, accident or homicide). In "true" SIDS cases (category 2), the manner of death is natural. In cases in categories 3 and 4, the cause of death and therefore manner remain undetermined. By

definition, the manner of death is undetermined "when the information pointing to one manner of death is no more compelling than one or more other competing manners of death when all available information is considered"[30].

To ensure the high quality of pediatric death investigation in Ontario, selected pediatric deaths are reviewed by specialized committees at the OCCO. The multidisciplinary Death Under Five Committee reviews the deaths of children under5 years of age investigated by coroners in Ontario[31]. The committee consists of coroners, police, forensic pathologists, crown attorneys, child maltreatment and welfare experts, Health Canada product safety specialists, and Coroner's Office support staff[32]. The committee reviews individual case findings and assesses the quality and comprehensiveness of the investigation and postmortem examination. The committee identifies recurrent or emerging issues which will guide in creating interventions to decrease pediatric mortality.

1.6 Infant and Neonatal Development

1.6.1 Physical Development of a Young Child

Fetal development is a gradual process with major structures formed during the second half of the pregnancy. There is a steady increase in fetal weight with 85% of the birth weight gained during the final half of gestation[20]. The most critical structural change is the maturation of the lungs from the canalicular to saccular and further alveolar stage, and development of surfactant. This transformation occurs between the 24th to 35th weeks of gestation, making the fetus viable. Although viable, the newborn is immature at this stage. Prematurity describes neonates born prior to 37 weeks of gestational age, and could be divided into the following subgroups: extremely preterm (less than 28 weeks), very preterm (28 to 32 weeks) and late preterm (32 to 37 weeks)[33]. Term birth occurs between 37 to 41 weeks gestational age and is further subdivided into early term (37-38 weeks), full term (39-40 weeks), and late term (41 weeks)[34]. Post-term births occur at 42 weeks and greater[35]. The perinatal period is defined as the days or weeks surrounding the child's birth[36]. Depending on definition, it commences at 20-28 completed weeks of gestation and ends 1-4 weeks after the birth. An infant is any live birth up to 1 year of life.

The average newborn weighs from 2500 to 4900 grams at term[13]. Newborns weighing below this range are considered small for gestation age (SGA) and newborns heavier than 4900 grams – large for gestational age (LGA)[13]. Newborns that are SGA are at increased risk of perinatal asphyxia, respiratory distress and sepsis during the neonatal period (birth to 28 days of life)[8]. LGA neonates show increased incidence of birth defects and respiratory distress[13].

Body growth follows specific growth trends, such as rapid growth separated by periods of steady or slow growth[37]. Weight, for instance, drops immediately after birth (5% drop in birth weight in formula-fed and 10% in breastfed infants). This drop could be explained by the slow production of maternal milk and low enteral intake[38]. The lost weight is regained within the next 10-14 days. The infant weight increases by 900 grams a month for the next 3 months, doubling the birth weight by 5 months. After this time, there is a further increase by 450 grams per month, tripling the birth weight by the end of the first year of life[39].

Length tends to be between 48 and 53 cm at term and increases by approximately 2.5 cm per month for the first 6 months of infancy. By the first year of life, the infant's length increases by 25 cm[20,37].

An increased or decreased rate of growth can indicate improper nutrition, chronic illness, hormonal imbalances or other underlying pathological conditions, including congenital syndromes or chromosomal abnormalities commonly seen in neonatal period and infancy.

Monitoring young child growth and development is an essential component of primary health care for children and adolescents. Recommended growth monitoring includes obtaining serial measurements of weight and height/length of all children and head circumference, in addition, for infants and toddlers. These parameters are further interpreted relative to the reference growth charts to confirm the healthy growth and development or to identify a potential health or nutritional problem requiring early intervention.

Routine infant well-being checkups are recommended at 1 to 2 weeks following birth, and 1, 2, 4, 6, 9 and 12 months. Measurements are recorded at these serial checkups and during acute illness visits if routine well-child visits have been missed[40].

Canada promotes consistent practices by health care providers using current practice guidelines in monitoring child's growth to ensure the health of Canadian children[41]. These guidelines were developed through the collaboration of major Canadian agencies including Dietitians of Canada, The Canadian Paediatric Society, The College of Family Physicians of Canada and Community Health Nurses of Canada[41]. These guidelines recommend evaluation of the growth of all term infants (breastfed or not) and preschoolers, preterm infants (once discharged from neonatal intensive care units) and children with special care needs using growth charts from the WHO Child Growth Standards (birth to 5 years of life)[41,42]. These charts are considered to be international growth standards since they reflect growth patterns of well-fed healthy preschool children from diverse ethnic backgrounds. These guidelines were proposed to replace previously used American growth charts from the Centers for Disease Control and Prevention (CDC)[42]. WHO growth charts are based on a child's gender and age. The age is adjusted for prematurity if required[42]. The measurements show growth trends and can be used to assess nutritional status and identify developmental delays including failure to thrive[13,40].

Overall children grow rapidly from birth to 1-2 years of age. Physical growth of a child refers to an increase not only in body size (length/height and weight) but also in the size of various organs[10,27,43]. Previous studies have shown that the heart doubles in overall size and weight during the first year of life[20]. Lung growth occurs rapidly in the first few months of life doubling in volume in the first 3 to 4 months and quadrupling by the 12th month or life[44]. The right lung is typically heavier than the left one. As well, the studies showed that the lung growth in infancy is very reactive to even minor changes in the general condition of the child and can lag in infants with poor nutritional status[44]. The brain is relatively large in an embryo and fetus, and its weight accounts for approximately 14% of the total body mass at birth. During infancy and childhood, the brain becomes proportionately smaller relative to the total body mass accounting for 2% of body weight

in adulthood[45]. The thymus is relatively large at birth compared to the body weight and further increases in size with advancing age but involutes in early adulthood[46].

Infants proceed through certain developmental stages acquiring more advanced physical and motor skills. A child's development follows a recognized, expected pattern, termed developmental milestones. By the end of the 3rd - 4th month of life, infants usually are able to roll from front to back, control their head and neck movements when sitting, and push with their legs when their feet are in contact with a firm surface[47]. This developmental stage corresponds to the greatest incidence of SIDS cases, which peaks between 1st-2nd and 4th months of age[48]. By 6 months of age, infants typically are able to roll from back to stomach. This coincides with the steady decline of SIDS cases after the age of 6 months[48].

Overall, growth and development follows consistent, predictable patterns and sequences: from simple to complex (simple head movements to finger control) and cephalocaudally (from head to foot, e.g. from head movement to standing and walking)[49]. Proximal to distal development, defined as "inside out growth", starts around 5 months when an infant can first move the torso (center of the body) and roll over before able to control the movements of the extremities, such as walking or grabbing[49]. The rate of development can normally vary between individuals[50].

1.6.2 Factors Affecting Child's Development

There are multiple causes that could cause deviations in a child's growth and development. They can be divided into genetic, environmental, biological, and nutritional factors. These in turn could be divided into modifiable (e.g. child's nutrition) and non-modifiable (e.g. genetic predisposition).

1.6.2.1 Genetic Factors

Genetic influences, such as gender, inherited body size and ethnicity, can predispose an individual to be affected by adverse environmental factors.

Fifty one percent of Ontario and Canadian births are males[3]. In 2012, 53% infant deaths were males[1]. Males have a 1.42-fold increased incidence of sudden infant death

compared to females. Some studies attribute this to more immature sleep-wake patterns in males who have a delay in rapid eye movement sleep development[51, 52]. In addition, males have higher incidence of birth defects and are more vulnerable to reproductive incidents[53]. Other studies found an association between the higher incidence of SIDS in males and a dominant X linked allele[54,55].

Height is a polygenetic inherited trait with environmental influences[56]. Over the last century, body height has been increasing, with children today taller than their parents[56,57]. The increase is attributed to advances in nutrition and treatment of various diseases, and improvement of detrimental socioeconomic factors[58]. Height can also vary significantly based on inherited characteristics. If parents are smaller or larger than normal percentiles, the children tend to follow similar growth trends. This may initially present as a pathological outlier but can be explained by a thorough family history[59,60].

Ethnicity can affect the child's stature. It has been shown that Japanese, Indian and Filipino children are smaller in comparison to children from the United States and Europe[61].

Genetic and inborn metabolic disorders can affect the growth rate of a child. For instance, Down Syndrome is associated with low birth weight and delayed growth[62].

1.6.2.2 Environmental Factors

Environmental factors include: intrauterine exposures and maternal health factors, socioeconomic status, cultural and psychosocial influences, and environmental conditions (e.g. cold or hot climate, high altitude).

Multiple studies have shown that maternal factors such as genetics (as discussed in the preceding section), weight, health and nutrition, all influence birth weight and could impair intrauterine growth[13]. Maternal smoking has been shown to have adverse effects on fetal growth, with 1.75 times increased risk of fetal demise[13]. Maternal substance abuse (alcohol or other drugs) during pregnancy is a well-documented factor causing dose-related growth retardation[63]. Growth retardation has also been linked to maternal hypertension, and maternal congenital heart and respiratory diseases[62,64]. Infants of these

mothers were reported to be very small for gestational age with relatively high brain weight, and low weights of liver, lungs and thymus. In contrast, infants born to diabetic mothers were large for gestational age showing characteristic patterns of increased body measurements and enlarged internal organs with disproportionately large liver, heart and adrenal glands and often a disproportionately smaller brain[62,65]. Other maternal factors influencing fetal growth include young or advanced maternal age, short intervals between recurrent pregnancies, multiple births, non-infectious and infectious diseases[66,67]. Specific pathogens (e.g. *Trichomonas vaginalis*, *Bacteroides* and *Ureaplasma*), have been shown to be associated with premature rupture of membranes and/or preterm labor[68].

The socioeconomic status of a family can affect birth weight and a child's growth and development. Some studies have shown a higher frequency of low-birth weight infants in the lower socioeconomic groups[69–71]. Socioeconomic factors have been attributed to increased infant mortality due to increased risk of poor nutrition, infections and multiple comorbidities[72]. Overcrowding, poor housing quality, single parenting, and inadequate prenatal care have been associated with an increased risk of sudden infant death[73–76].

Some cultural practices, such as overwrapping (swaddling), bed sharing and putting a child in a prone position, have been shown to increase the risk of sudden infant death[77–80]. These practices can be difficult to modify as they impact cultural identity.

Environmental conditions such as temperatures in excess of 29^0C have been shown to increase risk of sudden infant death by 2.78 times[81]. Lower temperatures have also been shown to increase the risk of sudden infant death[82]. Altitude has been shown to associate with increased risk of sudden infant death and incidence of lower birth weight[83–85].

Psychosocial risk factors, such as stress and social environment, have been linked to adverse infant health. For instance, studies have shown that immigration can increase risk of prenatal stress and of preterm births[86–89].

1.6.2.3 Biological Factors

Biological influences, such as birth weight, gestational age at birth, infections and medications, can impact child's growth and development.

Birth weight is one of the most reliable indicators of an infant's health because it has strong implications for health and mortality throughout childhood and adulthood[90–92]. Prematurity has a direct impact on birth weight with future health implications[93].

Acute diseases, such as gastroenteritis, can lead to dehydration and significant weight loss[94]. Chronic disease, such as diabetes mellitus, has been associated with both an increase and decrease in child's weight depending on how well metabolic control is maintained[95]. Lung infections or chronic lung disease can decrease lung capacity and slow overall growth[96]. In addition, medications can have an effect on child's development, for instance, chronic steroid use by an infant has been associated with weight gain[97].

1.6.2.4 Nutritional Factors

An inadequate maternal diet can lead to intrauterine growth retardation and congenital malformations (e.g. spina bifida)[28,98]. Decrease in maternal milk production is associated with decreased growth rate, vitamin and iron deficiency, and cognitive impairment in breastfed infants[99]. Inadequate nutrition can take on many forms, such as poor caloric intact, inadequate caloric absorption, excessive caloric expenditure, or forms of neglect[100]. All of these can lead to a failure to thrive. Overfeeding, as well, can lead to negative lifelong habits of overeating, obesity, and chronic disease[91]. Childhood obesity is linked to poorer health outcomes[101].

1.6.2.5 Prematurity and its Effects on a Child's Growth

Premature neonates have a 120 times higher risk of death in the first 28 days of life and significantly increased risk of short and long-term morbidities as a result of structural and functional immaturity of various organs and systems[102].

Among complications related to prematurity during the first year of life are failure to thrive, respiratory distress syndrome, infections, developmental delay, encephalopathies, prolonged hospital stay, and increased mortality, including sudden death[66,103,104]. The long term effects of prematurity include: increased rate of childhood infections and readmissions to hospital, asthma, learning disabilities and possible mental health

issues[104–106]. In addition, prematurity has been associated with a higher risk of diseases in adulthood including hypertension, diabetes and coronary artery disease, each of which has been linked epidemiologically to a low birth weight[90,91,107].

The patterns of illnesses in preterm children are dependent on degree of prematurity i.e. specific gestational age at birth[13]. Growth and developmental expectations of a preterm child are based on corrected age rather than chronological age as for a term child[108]. It is generally recommended to adjust the age of premature infants for growth measurements and developmental assessments until 2 years of age[108]. Adjusted age is calculated by determining how many weeks premature the birth was and subtracting the number of premature weeks from the chronological age of the child in weeks[109].

1.7 Current References on Autopsied Infant Growth Standards

A pathologist doing a pediatric autopsy will commonly assess a child's developmental stage by measuring various body parameters and organs and comparing these data to standardized parameters using existing charts published in the literature; however, these references have limitations. Some criticisms of the existing reference sources for body measurements and organ weights of infants and neonates include the lack of the normal percentiles, outdated nature of the information, data limited to specific ethnic populations, and difficulties in understanding the data[10–13].

Although, many reference sources exist, both Canadian and international, on body and organ measurements for various groups (fetuses, stillbirths, neonates and infants), there are no updated or Ontario population specific data for children under 1 year of age[12,43,110–117]. In addition, the reference data frequently do not account for the effect of the cause of death in control groups and are lacking any interrelationships between body and organ measurements[115,118]. As well, the reference data range significantly between various sources which can lead to interobserver discrepancies depending on the comparison resource used[113].

1.8 Thesis Objectives and Rational

The first objective of this study is to assess the relative strengths and weaknesses of the currently available autopsy references on infant and neonate body and organ measurements and to develop criteria for the development of a new reference resource. To achieve this goal, a survey of Ontario pathologists doing coroners' pediatric autopsies and a review of the existing literature was conducted.

The second objective is based on the results of the above survey and literature review to create Ontario population-specific organ and body measurement mean charts for infants and neonates and growth graphs for each age category.

The third objective of this study is to determine if groups, based on the cause of death, are different in their body and organ measurements.

The hypothesis is that the differences in the body measurements and organ weights of Ontario neonates and infants will be statistically significant depending on the cause of death according to age and gender.

Chapter 2

2 Survey and Review of Reference Resources Used by Ontario Pathologists

2.1 Methodology

A list of pathologists who do pediatric coroners' autopsies was requested from the Office of the Chief Coroner for Ontario, a branch of the Ministry of Community Safety and Correctional Services (MCSCS). The listing comprised category A and C pathologists from the Ontario Forensic Pathology Service (OFPS). The former category includes pathologists who do any type of coroner's autopsy including pediatric and criminally suspicious cases/homicides. Category C pathologists do pediatric autopsies which are non-criminally suspicious. The contact information for 30 pathologists working in the Ontario provincial and regional forensic pathology units and in teaching and community hospitals was provided. Hard copy packages were sent to the pathologists. Each package consisted of an introductory letter stating the goals of the research, the survey (**Appendix A),** and a return envelope. In addition, an electronic package including the introductory letter and survey was constructed using online electronic survey software (SurveyMonkey). The hard copies and electronic packages were distributed to all 30 pathologists by mail and via an email link. For those who did not respond, a second electronic package was emailed 3 months after the initial submission.

The survey asked the following 6 questions:

1. Do you or your pathologists perform coroners' neonatal (birth to 1 month) or infant (1 month to 1 year) autopsies?

2a. Have you referenced any of the following sources for organ or body measurements?[10–13,43,109,119]

2b. Please provide details (authors, journal, year, volume, page numbers or textbook) for any additional sources.

3. Which of the above sources do you reference most often and why?

4. Are there any limitations of these sources in your opinion?

5. What information would be most helpful for your practice in an Ontario-based study?

6. Would you be interested in receiving a copy of the finished study? If yes, please, provide a delivery preference.

All reference sources, whether provided initially to the surveyed pathologists or added by them, were further assessed based on the following criteria: sample size, statistically significant values, age span of the sampled data, gender differentiation, living vs. autopsied population, and originality (i.e. original data vs. review of pre-existing data). The above criteria were assessed as present or absent. In addition, the year of each publication and origin of the source (the country where the data were collected) were documented.

2.2 Results

Fourteen of 30 Ontario pathologists who do coroners' pediatric autopsies responded to the survey (**Appendix A**).

The responses to question 2a, the utilization frequency by pathologists of the 7 initially cited references in the survey, showed that 2 pathologists referenced Stowens; 6 referenced Stocker and Dehner. and Coppoletta and Wolbach.; 7 referenced Kayser; 8 referenced Schulz et al.; 10 referenced Wigglesworth; and 12 referenced the Centers for Disease Control and Prevention interactive database (CDC)[10–13,43,109,119]. In addition to the 7 references provided, the pathologists identified 13 additional sources in response to question 2b[18,110–117,120–123].

The replies to question 3 are shown in **Figure 2-1**. The references most often used were "Weights of Organs of Fetuses and Infants" by D. M. Schulz, D. A. Giordano and D. H. Schulz (8 pathologists), CDC (6 pathologists), the "Textbook of Fetal and Perinatal Pathology" by J. S. Wigglesworth (5 responders), and "Height and Weight in Human Beings: An Autopsy Report" by K. Kayser (5 responders)[10,12,13,109].

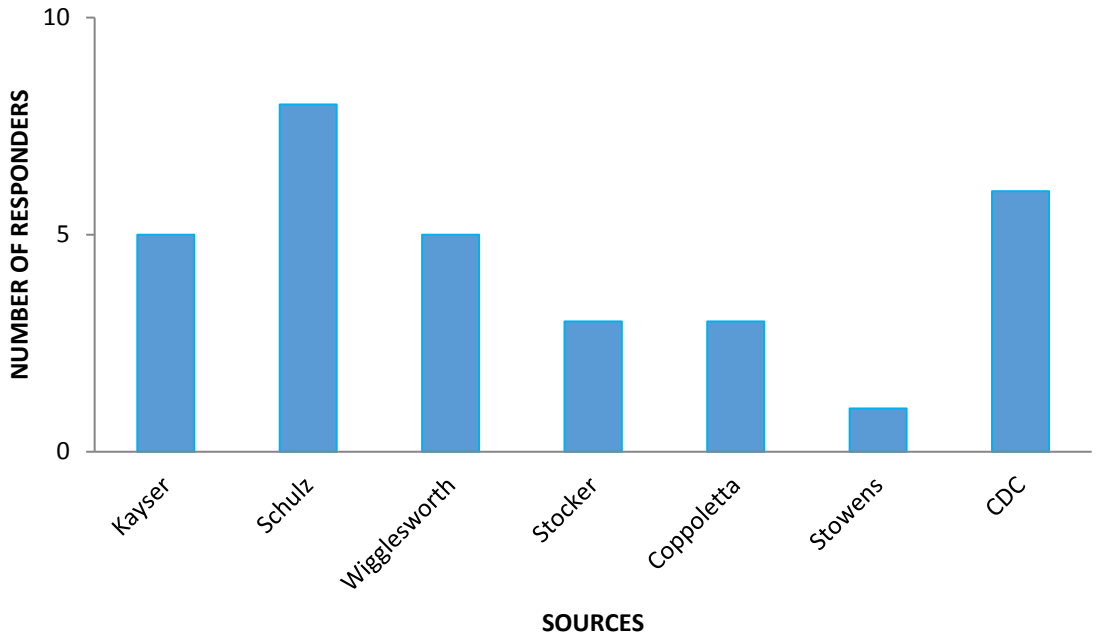

Figure 2-1. Most Frequently Referenced Sources

Results of survey - question 3 "Which of the above sources do you reference most?" Schulz et al (8) and the CDC (6) were the most commonly used by the responding pathologists.

The advantages of sources stated in response to question 3 were: age ranges provided; references readily available and widely used; references most scientific and accurate; standard deviations given; and data combined from multiple sources.

The stated limitations of these publications as noted in survey question 4 were: outdated nature of a database; wide and limited age intervals; data not unique to SIDS/SUDS (Sudden Infant Death Syndrome/Sudden Unexplained Death Syndrome) populations; small sample size; absence of ethnic background information; single reference values (no ranges); standard deviations not given; and difficulty of comparison between various sources.

The pathologists identified 10 features for an ideal reference resource. These features, identified by the responders in survey question 5, included: an up-to-date database with a large sample size; a dataset relevant to the Ontario population; defined controls/standards; provision of standard deviations, confidence intervals and p-values;

gender distinctions; data pertinent to SIDS/SUDS populations; updated demographic/ethnic breakdowns; and an electronically accessible database.

2.3 Discussion

2.3.1 Review of Sources Cited by the Ontario Pathologists

The 20 publications span a period from 1933 to 2010. The oldest reference was by Coppoletta and Wolbach and the most recent was from the CDC[43,109]. Half were published before 2000. **Figure 2-2** illustrates that from 1900 to 2015, only 40% of the references have data collected after 2000, and no sources had data collected beyond 2003. **Table 2-1** shows the assessments of all references based on certain criteria. The reference sources included 11 journal articles, 7 textbooks, a website, and a Master of Science thesis[10–13,18,43,109–117,119–123]. Twelve sources (60%) differentiated genders, 13 (65%) listed actual sample sizes, 18 (90%) provided standard deviations, 11 (55%) used ranges for means, and 7 (35%) included data on statistical significance (e.g. p-values). Seventy percent had 5 or more charts or tables. Of the 20 sources, 11 (55%) were based on original data[10,12,43,110,112–114,116,117,120,123].

Most of the sources, 18 (90%), were based on autopsy observations with 10 of them (56%) based on original data. Of the 10, only 7 included data on children from birth to 12 months of age. Two of these referenced only cardiac data, and one referenced only recumbent body length[110,114,120]. This left only 4 original reference sources for organ and body measurements for infants and neonates (birth to 12 months)[10,12,43,113]. From these, only 2 provided gender distinction and standard deviations or confidence intervals[10,12].

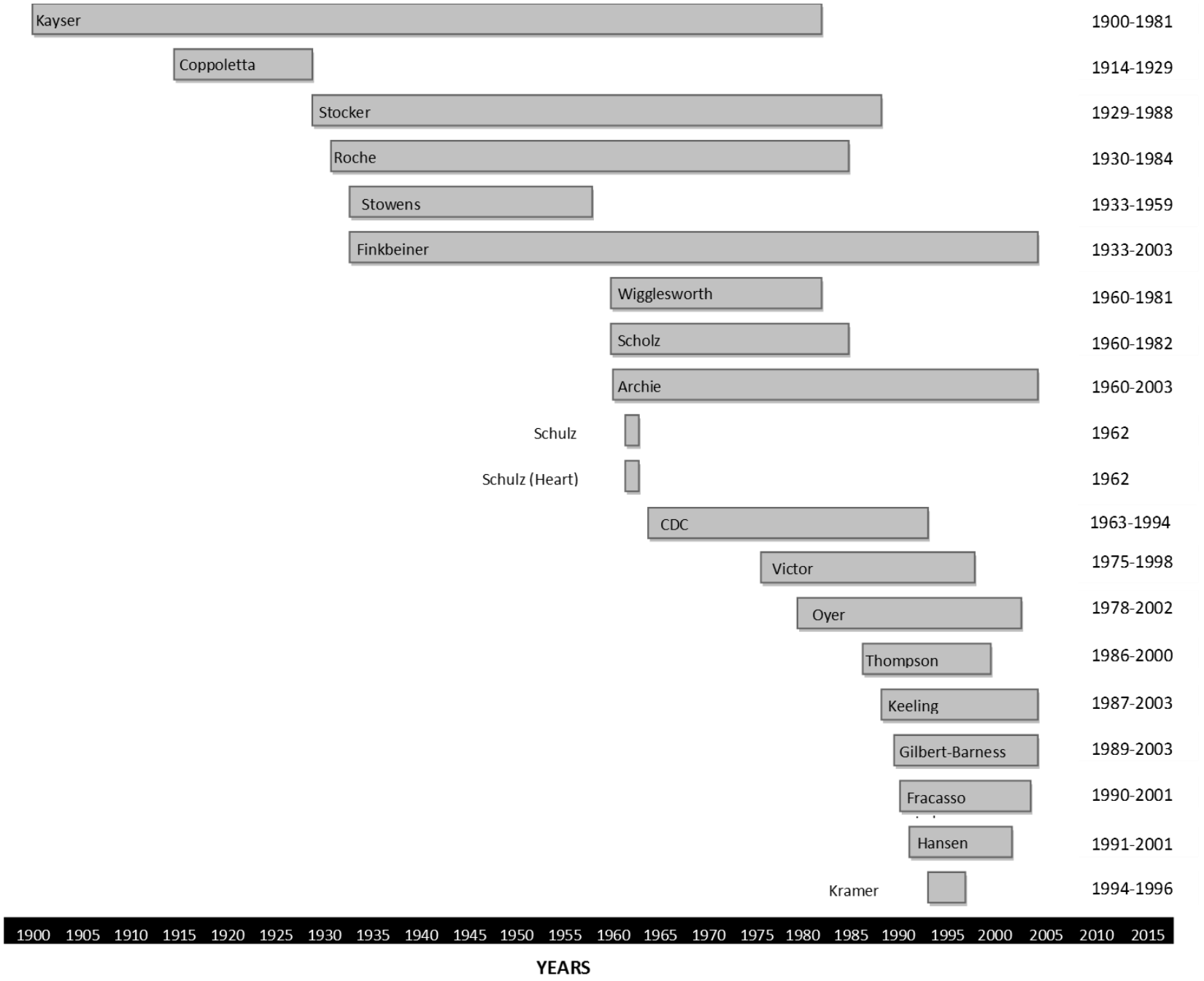

Figure 2-2. Timeline of References

Sources most commonly used by the responding pathologists, depicted by year(s) of data collection, aligned by the oldest initial collection date to the newest.

Table 2-1. Sources Assessed by Proposed Criteria

The assessment of the reference sources according to the criteria proposed by the survey respondents.

SOURCES	YEAR	LOCATION*	SAMPLE SIZE†	AUTOPSIED SAMPLE‡	STANDARD DEVIATIONS§	ORIGINAL DATA**	GENDER DISTINCTION††	SOURCE AGE RANGES‡‡
Archie	2006	Multiple		YES	YES	NO	NO	12 - 45 weeks gestation
CDC	2009	Multiple	8440	NO	YES	NO	YES	birth - 19 years
Coppoletta	1933	United States	155	YES	NO	YES	NO	birth - 12 years
Finkbeiner	2009	Multiple		YES	YES	NO	YES	16 weeks gestation - 86 years
Fracasso	2009	Germany	388	YES	YES	NO	YES	1 - 12 months
Gilbert-Barness	2005	Multiple		YES	YES	NO	YES	24 weeks gestation - 18 years
Oyer	2004	USA	776	YES	YES	YES	NO	15 - 42 weeks gestation
Hansen.	2003	United States	597	YES	YES	YES	NO	12 - 26 weeks gestation
Kayser	1987	Germany	47,523	YES	YES	YES	YES	birth - 99 years
Keeling	2001	Multiple		YES	YES	NO	NO	12 - 43 weeks gestation
Kramer	2001	Canada	676,605	YES	YES	YES	YES	22 - 43 weeks gestation
Roche	1989	United States	504	NO	YES	YES	YES	1 - 12 months
Scholz.	1988	United States	200	YES	YES	YES	YES	birth - 19 years
Schulz.	1962	United States	1339	YES	YES	YES	YES	5 months gestation - 12 months
Schulz (Heart)	1962	United States	1847	YES	YES	YES	YES	5 months gestation - 12 months
Stocker	1940	Multiple		YES	YES	NO	YES	46 days post ovulation - 19 years
Stowens	1959	United States		YES	NO	NO	NO	second lunar month - 5 years
Thompson	2004	United States	453	YES	YES	YES	NO	birth - 12 months
Victor	1999	Canada	2026	YES	YES	YES	YES	18 - 43 weeks gestation
Wigglesworth	1991	United States		YES	YES	NO	NO	12 - 42 weeks gestation

* The country where the data were collected
† Blank fields depict sources where sample size was not provided and/or a compilation of data sources with different sample sizes were used
‡ YES = data collected from autopsied subjects; NO = data collected from living subjects
§ YES = standard deviations were provided; NO = standard deviations were not provided
** YES = authors analyzed original data; NO = authors reviewed data from other sources
†† YES = male and female data were segregated; NO = male and female data were pooled
‡‡ The age span of the sampled data as defined by the source

Growth can be defined as an increase in size over time and, therefore, serial measurements are required for documentation[116]. This is not applicable to autopsy populations since only single observations are available. The definition of normality also poses interpretative challenges since it varies from author to author[111]. Establishing a normal group when faced with variations caused by pathophysiological processes can be difficult[112]. In the present study, a common theme in the 20 cited references was a deficiency in the definition of standard or normal groups. Prior publications identified the inadequacy of the currently available norms[10,43,110]. Various authors have pointed to the lack of statistical information, such as sample size, standard deviations and standard errors in various sources[10,110,112]. Many of the reference sources were lacking a description of exclusion criteria and well-defined control groups[120]. The lack of descriptive information on exclusion criteria can lead to bias[111].

Schulz et al. found the lack of standardization by gender to be common in infant but not in adult studies[10]. Significant differences in norms related to gender were found by some researchers[10,122] and disproven by others, which led to a pooling of pediatric data[43,112,113,115]. Schulz et al. noted that the male brains at 8 months were significantly heavier than female ones[10].

The effect of prematurity on organ and body measurements was proposed as a significant factor[43,113,115]. Fracasso et al. found in their study that heart weights were slightly heavier during the first 3 months, becoming slightly lighter from 6th to 10th months when compared to similar studies[115]. The authors explained these findings by the inclusion of prematurely born neonates and infants in the database, which accounted for the smaller values.

Some studies investigated whether organ weights were different between SIDS and non-SIDS groups[113,115]. No significant differences in organ weights between SIDS and control groups have been identified. Body measurements and organ weights can be affected by maternal and environmental (e.g. smoking) effects on development in utero[113,115]. The systemic effects of disease and pathophysiological processes (e.g. congestion and edema) on organ weights has been noted[12,115]. The validity of excluding single organs affected by disease when assessing other organ weights was previously raised[115].

The present review of the reference sources revealed that organ weights tended to be greater in more recent publications. Lack of complete data did not allow us to verify these observations statistically. This trend can be demonstrated when comparing both Schulz's et al. data collected in 1962 to Coppoletta and Wolbach's data collected during the period of 1914-1929[10,43,110]. The databases in Schulz et al. show an overall increase in organ weights with a 20% increase in heart size. Thompson and Cohle, based on their data collected during 1986-2000, reported a 6-100% increase in various organ weights when compared to one of the aforementioned studies by Schulz et al[10,113]. These differences could be attributed to poorer nutrition and less perinatal care in the past. Thompson and Cohle recommended that new body measurement and organ weight standards needed to be developed using more current data[113]. Fracasso et al. also opined that the earlier published data were not applicable to the modern populations[115]. Although there is no completely satisfactory reference when assessing pediatric growth parameters, utilization of any reference is still a better practice than using none[111,116].

In summary, this part of the study identified and reviewed 20 various types of references for body measurements and organ weights used by Ontario pathologists in the course of their postmortem examinations on infants and neonates. The strengths and weaknesses of the currently available sources were evaluated. Based on the limitations of the current references and criteria suggested for improvements, the present review served as a guide to create a new autopsy-based body measurement and organ weight database for pediatric deaths under 1 year of age. This new reference source used more recent data from the Office of the Chief Coroner for Ontario and involved a larger sample size allowing for statistical relevance. The database aimed to be gender specific and to provide data for specific age intervals.

Chapter 3

3 Research Design for Growth Charts

Data were collected, analyzed and tested to determine if significant relationships were present between the cause of death, age and gender groups. Based on the collected data reference tables were created on body measurements and organ weights, with and without gender distinction.

3.1 Ethics Approval

This research was approved by the Research Ethics Board for Health Sciences Research Involving Human Subjects (Western University) (**Appendix B**) and the Lawson Health Research Institute (**Appendix C**).

3.2 Data Collection

Cases were collected from a database of infant and neonatal deaths that were investigated by Ontario coroners from 2000 to 2010. Only cases where complete postmortem examinations were performed were included in the sample population.

The data were collected and processed according to the research agreement with the Office of the Chief Coroner for Ontario. A data collection sheet (**Appendix D**) was created and completed for each reviewed case. The information was collected from the coroner's investigation statements and reports on postmortem examination commonly including a number of ancillary reports (neuropathological consultation report, toxicology, microbiology, biochemistry, cytogenetic studies etc.). The information was then transferred into an Excel document where blank fields indicated absent data.

Collected data were arranged by the age at the time of death, cause and manner of death. For the purposes of confidentiality, identifying information (including date of birth, date of death and coroner's or autopsy case number) were removed and a random number was assigned to each case.

Cause of death and manner of death for each case were reviewed by re-evaluating specific case information, major findings on gross and microscopic examination, and results of ancillary studies. SIDS cases before 2005, i.e. the year SUDI was defined, were re-classified into the

appropriate category upon review of these cases. Based on this review, cases were subdivided into 3 major groups: SIDS, SUDS and non-SIDS/non-SUDS. SIDS deaths had no anatomical or toxicological cause of death identified in the course of a thorough postmortem examination complemented by ancillary studies, and there were no findings identified to suggest that unsafe sleeping might be a contributing to death factor. SUDS group included cases where cause of death remained unascertained yet unsafe sleeping environment was a potential contributory factor. The remaining cases were included in the third group (non-SIDS/non-SUDS group). This group was further subdivided into several subgroups based on the underlying pathology: congenital abnormalities, metabolic disorders, natural diseases, systemic infections/sepsis, birth asphyxia, accidental deaths, suspicious deaths, and homicides. Accidental deaths incorporated various types of asphyxia including entrapment within a crib, obvious overlaying, hanging, drowning, choking, and fire deaths. The third group (non-SIDS/non-SUDS cases) were further reviewed to select data for a control group. The Control group consisted of pathologically uninvolved organs. Cases were reviewed by me and a staff forensic pathologist. Generally, the Control group was selected from categories 1 and 4 cases according to standardized sudden infant death reporting in Ontario (please see Section 1.3)

The following criteria were used for selecting cases for the Control group. The entire case was excluded, if the child was diagnosed with a pathological condition that usually had systemic effects. The following conditions excluded a case from the study: multiple congenital abnormalities, status after prolonged resuscitation at hospital, systemic infections/sepsis, significant decomposition, generalized body edema, and failure to thrive. In addition, upon the thorough review of the remaining cases, single or multiple organs that showed significant pathological abnormalities (grossly or microscopically) were removed from the Control group data (e.g. lungs in cases diagnosed with pneumonia, brain in cases with hypoxic-ischemic encephalopathy). In cases of traumatic death (whether homicidal or accidental) injured organs were excluded (e.g. brain in craniocerebral trauma, lungs in drowning). Majority of suspicious deaths included in the Control group were cases of head trauma where non-accidental injury was among differential diagnoses and brain was excluded. Cases were excluded from the study when the measurements indicated immaturity based on the stated chronological age, but the gestational age was not provided so term gestation could not be verified. Measurements with obvious typographic errors were removed.

Corrected or adjusted age was calculated for premature infants provided the gestational age at birth was available. Corrected age was calculated based on the following formula:

Corrected age = actual age in weeks – weeks premature.

The infant and neonatal data were further organized by the age groups and growth parameters, such as specific organ weights [heart, lungs (right, left and combined for lungs and the rest of paired organs), kidneys, liver, spleen, pancreas, adrenals, thymus, thyroid, uterus, prostate, testes, and brain], heart measurements (valve circumferences and thickness of each ventricle), and body measurements (body weight, crown-heel length, crown-rump length, head circumference, chest circumference, abdominal circumference, and foot length). The means, standard deviations and sample sizes for each of the above variables were recorded in order to create reference tables.

3.3 Statistical Analysis

All data were distributed into age categories divided into 2-week intervals for the 1st month followed by 4-week intervals from the 4th to 44th week, with the last group including cases from 45th to 52nd weeks of age.

All analyses were performed using the R statistical software (version 3.2.2). The significance level (p-value) was chosen as 0.05 for all the statistical tests in this report. If a p-value obtained from a test statistics was smaller than 0.05, then the corresponding factor had a significant effect on a studied mean value. Linear regression with a backward variable selection method was used to select the factors important in testing the effect of gender, age and cause of death on various measurements. The Akaike Information Criterion (AIC) method was used for variable selection. If the AIC value of modelling an organ weight was lower when a tested factor was removed, then that factor was regarded as important to the organ. In contrast, if the AIC value of modeling an organ weight was not lower when a factor was excluded, then that factor was insignificant and could be removed. The backward selection process was performed using AIC in a Stepwise Algorithm (stepAIC, MASS package). For stepwise backwards selection, the factor with the highest p-value was eliminated in a stepwise process until AIC was minimized.

Unpaired t-test was performed between Females/Males, Control/SIDS, Control/SUDS, and SIDS/SUDS groups using 0.05 as the significance level of calculated probability for each measurement in the given age group. If an observation contained missing values, it was not included in the analysis. When two sample t-test (unpaired t-test) was used, the assumption was made that the two populations were normally distributed. The test for normality (normal distribution of the population) was satisfied. There was no minimal sample size for the t-test to be valid. The tests of gender specific organs were analyzed relative to the age group and cause of death only (uterus, prostate, testes). The effects of all 3 factors (age, gender and cause of death) on the following 16 variables were tested for the following weights: heart, lungs (right, left, combined), kidneys (right, left, combined), liver, spleen, pancreas, adrenals (right, left, combined), brain, whole body weight, and thymus. For a given age group and organ weights, the unpaired t-test to compare the mean weights of males and females was done. If the number of observations (n) for males or females was less than 2 (equal to 0 or 1), then the observations were not included in the analysis.

Chapter 4

4 Results

4.1 Descriptive Statistics

Overall, 1856 infant and neonatal deaths were investigated by Ontario coroners during the period from 2000 to 2010. Of these, complete information was available for 1225 cases. In the remaining 631 cases, either there was no postmortem examination performed, a postmortem report was not available, gender no specified, or exact age in weeks or gender could not be calculated (e.g. no date of birth provided).

Age inclusion was based on the corrected rather than actual, chronological age; therefore, all preterm pediatric deaths where the corrected age was negative (i.e. child who was born prior or at 36 weeks and 6 days gestational age and did not survive long enough to reach term) were excluded (146 cases). The remaining 1079 cases met the inclusion criteria (age and complete data). Upon further reviewing of the "non-SIDS/non-SUDS" group, an additional 179 cases of systemic pathological conditions were excluded, leaving 900 cases to create the present database.

The study population distribution by age (from 0 to 52 weeks) is shown in **Figure 4-1**. Among all the cases investigated by Ontario coroners, male deaths were predominant (56.3% males vs. 41.3% females, 2.4% case with gender unknown). A slightly higher male predominance was observed in the selected 900 cases (59.2 % males and 40.8% females).

Case distribution between the cause of death groups is shown in **Figure 4-2**. Nearly half of the cases (48%) were in the Control group. The SIDS and SUDS groups were respectively 13.6% and 38.4%. Male predominance was slightly more prominent in the SIDS and SUDS groups in comparison to the Control group and was the highest in the SIDS deaths (**Table 4-1**).

Distribution of the SIDS, SUDS and control cases by age and gender is demonstrated in **Figures 4-3** and **Figure 4-4**.

The distribution of body measurements and organ weights is shown in **Tables 4-2** to **4-10**. Growth curves for individual organ weight and body measurement means could be found in **Appendix E (Figures E-1** to **E-3)**.

4.2 Inferential Statistics

The results of a backward selection process using AIC (Akaike Information Criterion) in a stepwise algorithm are shown in **Table 4-11** and **Table 4-12.**

All tested factors (age, gender and cause of death) were important for the following weights: brain, combined lungs, right and left lungs, liver, spleen, combined adrenals, right and left adrenals, combined kidneys, the right and left kidney and thymus. The age and gender but not the cause of death were significant for the body weight and weights of pancreas and heart.

The gender was significant for some organs (heart, kidneys, brain, spleen and body weight) across several age groups, with other organ weights (lungs, liver, pancreas, adrenal glands) being less gender dependent. The effects of gender for each organ in different age groups are shown in **Table 4-13** (p-values in **Appendix F, Table F-1)**.

All organ weights selected by AIC were further assessed for significant differences between the age, gender and cause of death groups using a three way pairwise t-test (between Control and SIDS, Control and SUDS, SIDS and SUDS groups), as shown in **Tables 4-14** to **4-20 (**p-values in **Appendix F, Table F-2** to **Table F-8**). Statistically significant differences between various groups at specific age intervals are shown in **Figures 4-5** to **4-24**.

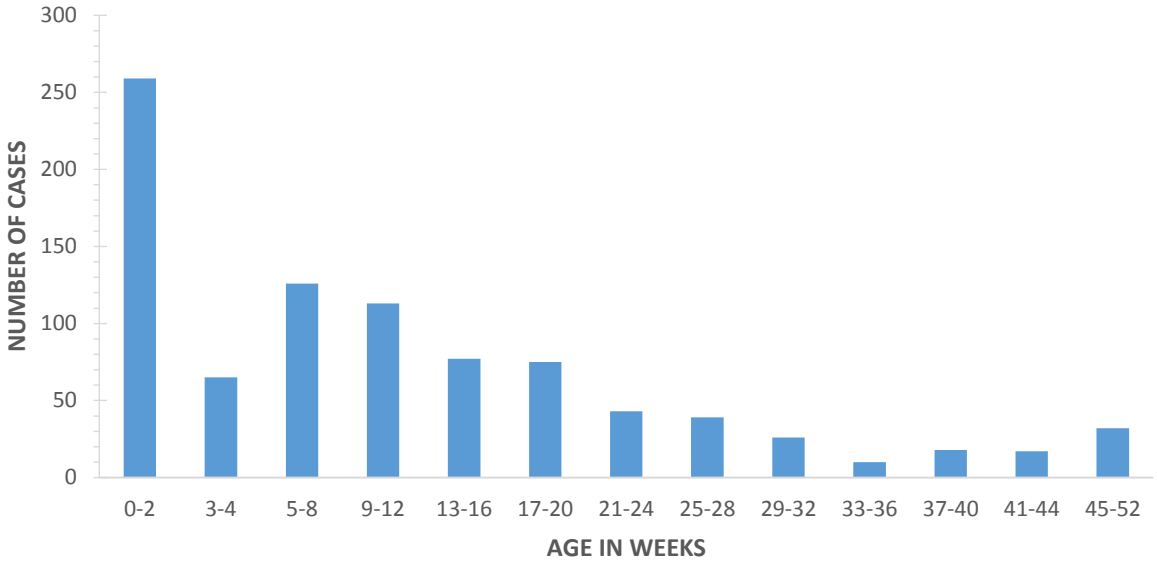

Figure 4-1. Distribution of the Study Population by Age Groups

The distribution of the cases based on age. The highest incidence was during the neonatal period (within the first 28 days after birth) with most of the deaths reported within the first 2 weeks of life. The frequency decreased in older children.

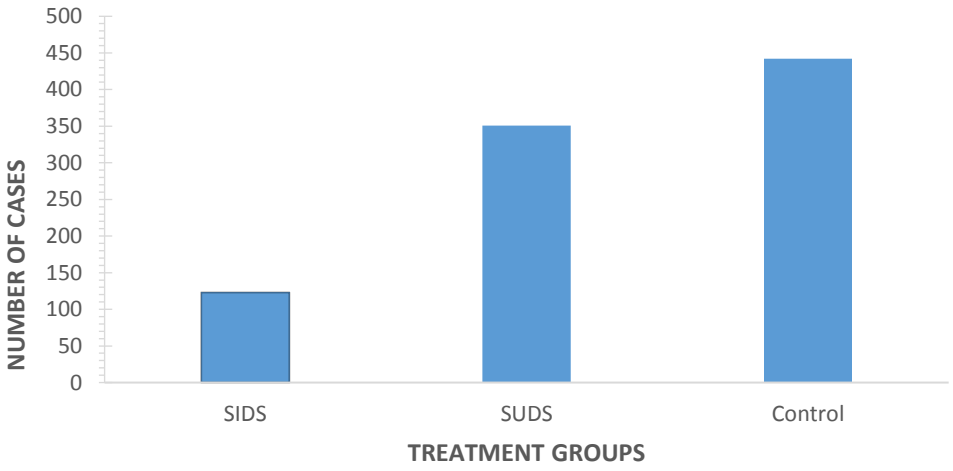

Figure 4-2. Distribution of Cases between the Cause of Death Groups

The distribution of selected cases between the cause of death groups. Nearly half of the cases (48%, n=432) were in the Control group, followed closely by SUDS deaths (38.4%, n=346), and the lowest frequency being SIDS deaths (13.6%, n=122).

Table 4-1. Gender Distribution in the Cause of Death Groups

The distribution of male and female deaths in SIDS, SUDS and Control groups. SIDS deaths showed the highest male predominance. There was a higher male frequency in the SUDS group in comparison with the controls. A chi-square test of goodness of fit (p=0.0720) with Yate`s correction for continuity (p=0.0923) showed no significant differences between the groups. The sample is roughly evenly distributed by percentages among the groups.

CAUSE OF DEATH	MALES	FEMALES	TOTAL
SIDS	82 67.2%	40 32.8%	122 100%
SUDS	209 60.4%	137 39.6%	346 100%
Control	242 56.1%	190 43.9%	432 100%

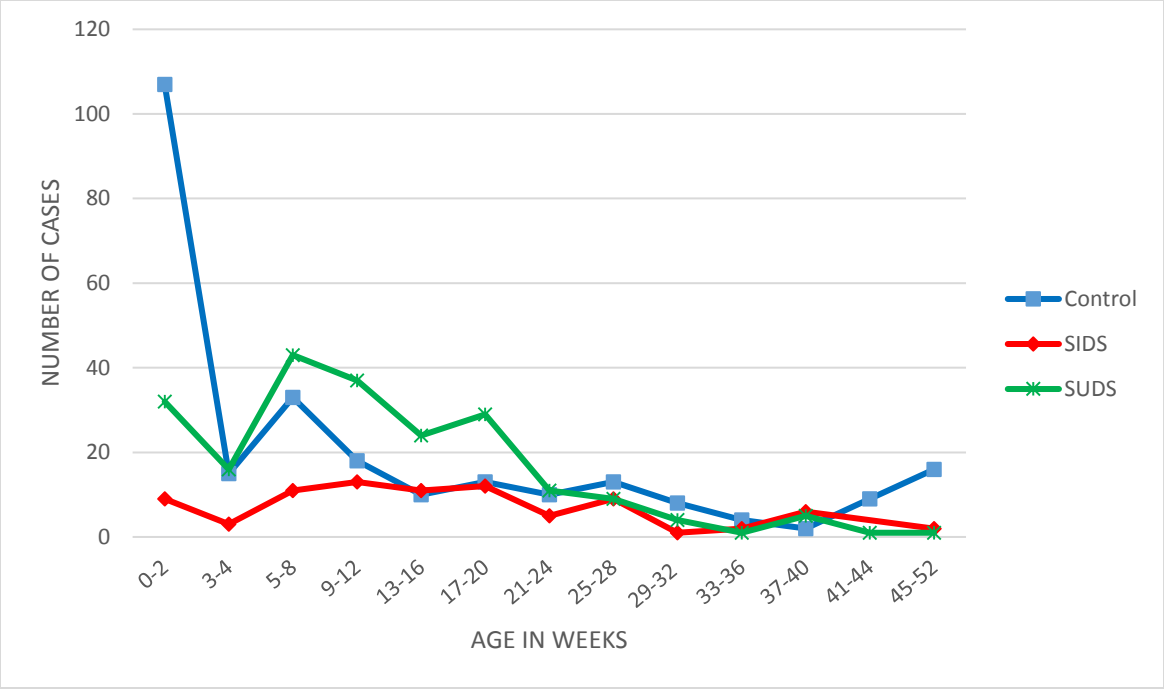

Figure 4-3. Distribution of Male Deaths by Age in Each Cause of Death Group

The figure shows a large variation in the sample size between the cause of death groups for the first 24 weeks. The sample sizes were more constant for the remainder of the 1st year. There was an increase in frequency of SIDS and SUDS deaths between the 1st and 6th month.

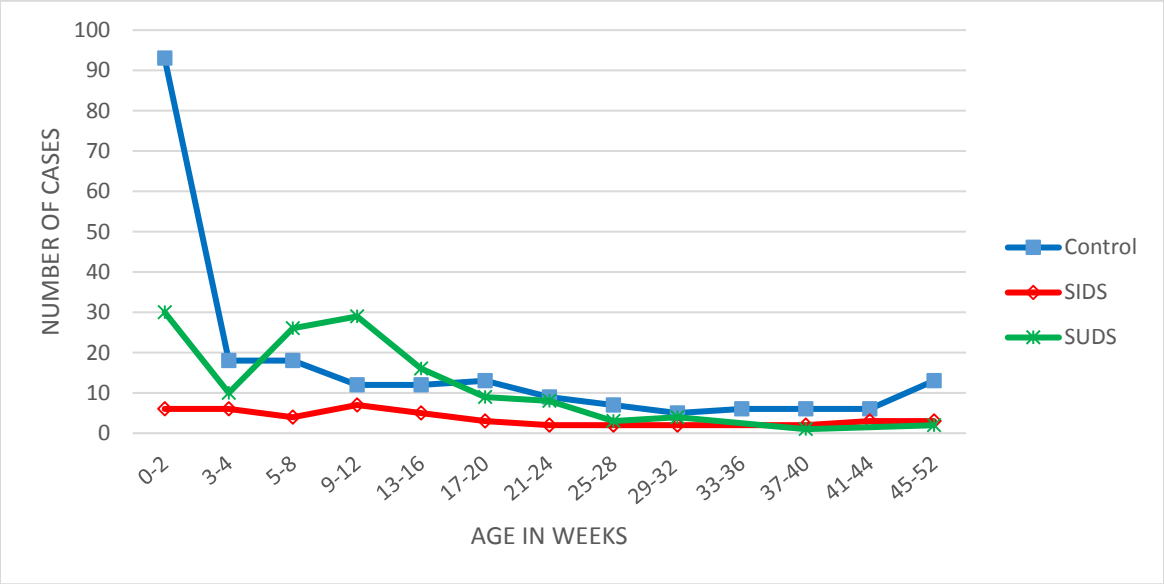

Figure 4-4. Distribution of Female Deaths by Age in Each Cause of Death Group

The figure shows the tendencies similar to the above described for the male deaths.

Table 4-2. Male Body Measurements

Table shows the mean, standard deviation and sample size for each organ by age in weeks. Body weight is provided in grams; the remainder of the measurements in centimeters.

Age (Weeks)		Body Weight	Crown-Heel	Crown-Rump	Head Cir.	Abdomen Cir.	Chest Cir.	Foot Length
0-2	Mean	**3591.97**	**51.37**	**36.39**	**34.98**	**31.99**	**32.89**	**7.75**
	SD	657.75	3.21	2.50	1.94	3.11	3.02	0.64
	n	131	134	71	106	105	107	80
3-4	Mean	**4045.28**	**53.91**	**38.36**	**36.26**	**33.64**	**34.60**	**7.98**
	SD	675.72	3.11	2.07	1.93	4.61	3.31	0.56
	n	28	31	18	29	29	29	21
5-8	Mean	**4685.39**	**56.47**	**40.30**	**38.01**	**36.11**	**36.51**	**8.42**
	SD	686.91	3.11	2.09	1.82	2.96	2.32	0.69
	n	81	80	44	70	65	67	44
9-12	Mean	**5472.20**	**59.06**	**41.47**	**39.67**	**38.97**	**38.41**	**8.55**
	SD	778.84	2.91	2.99	1.35	2.64	2.31	0.55
	n	66	68	40	60	54	56	33
13-16	Mean	**6329.17**	**61.34**	**43.70**	**40.98**	**40.60**	**40.51**	**8.99**
	SD	1007.05	3.64	2.48	1.28	3.78	2.35	0.55
	n	48	48	28	44	40	43	25
17-20	Mean	**7003.19**	**64.19**	**45.37**	**42.65**	**40.91**	**41.81**	**9.31**
	SD	1019.52	4.00	2.69	2.91	3.21	2.79	0.66
	n	47	46	30	44	38	39	29
21-24	Mean	**7230.42**	**65.31**	**45.25**	**42.48**	**43.38**	**42.47**	**9.53**
	SD	940.94	3.15	2.96	1.88	3.38	2.18	0.67
	n	26	27	12	18	17	18	14
25-28	Mean	**7772.17**	**66.64**	**45.92**	**43.19**	**41.79**	**42.33**	**9.44**
	SD	1384.25	2.10	2.27	1.40	3.25	2.17	0.55
	n	29	29	17	26	25	26	21
29-32	Mean	**8331.23**	**69.65**	**48.28**	**44.42**	**42.92**	**42.96**	**9.73**
	SD	1152.27	2.84	1.72	1.99	3.65	2.10	0.63
	n	13	13	9	12	12	12	10
33-36	Mean	**9006.67**	**71.33**	**50.00**	**45.00**	**43.40**	**44.30**	**10.43**
	SD	1165.21	5.09	4.24	1.00	1.34	1.25	0.81
	n	6	6	2	5	5	5	4
37-40	Mean	**8315.00**	**70.47**	**47.80**	**44.81**	**41.13**	**43.26**	**10.10**
	SD	983.87	3.34	3.22	2.26	4.07	2.21	0.56
	n	11	11	7	10	10	10	6
41-44	Mean	**8461.43**	**71.00**	**47.67**	**45.75**	**42.67**	**44.08**	**10.17**
	SD	623.60	3.55	2.89	2.75	3.52	2.29	1.31
	n	7	8	3	6	6	6	4
45-52	Mean	**9635.38**	**75.56**	**49.44**	**46.91**	**45.12**	**46.22**	**11.02**
	SD	1402.55	2.41	1.72	1.42	3.88	3.20	0.47
	n	13	17	8	16	16	16	13

Cir. (circumference)

Table 4-3. Male Organ Weights

Table shows the mean, standard deviation and sample size for each organ by age in weeks. All measurements are in grams.

Age (Weeks)		Heart	R. Lung	L. Lung	R. Kidney	L. Kidney	Liver	Spleen	Pancreas	Adrenals	Thymus	Brain
0-2	Mean	**22.74**	**39.33**	**32.02**	**15.68**	**16.43**	**146.51**	**12.21**	**4.94**	**7.31**	**11.98**	**415.43**
	SD	4.58	8.87	8.51	4.31	4.26	38.65	4.84	1.80	3.81	5.40	58.99
	n	98	48	49	122	121	126	136	99	109	120	60
3-4	Mean	**25.86**	**52.06**	**47.47**	**18.00**	**18.30**	**167.99**	**15.52**	**6.08**	**5.37**	**21.45**	**503.47**
	SD	6.14	11.98	11.72	6.05	4.71	44.00	6.94	2.16	1.74	10.26	60.55
	n	25	21	21	27	27	28	30	26	26	26	20
5-8	Mean	**28.92**	**60.93**	**50.86**	**19.64**	**20.42**	**192.76**	**16.69**	**7.71**	**4.69**	**27.02**	**556.62**
	SD	4.60	11.88	10.46	3.54	4.36	39.35	6.45	6.94	1.67	11.10	61.33
	n	64	62	62	74	73	76	79	60	61	62	60
9-12	Mean	**32.58**	**67.63**	**59.57**	**21.97**	**22.27**	**210.87**	**21.95**	**7.85**	**4.42**	**29.41**	**623.21**
	SD	4.89	12.57	11.95	4.84	4.61	35.87	7.10	2.34	1.70	9.09	62.19
	n	62	47	47	63	63	63	66	53	56	59	54
13-16	Mean	**34.07**	**75.16**	**62.32**	**23.45**	**24.21**	**247.20**	**23.25**	**10.30**	**4.72**	**39.73**	**699.15**
	SD	5.28	12.66	9.67	4.97	4.85	43.29	6.82	3.97	2.00	13.99	80.01
	n	43	39	39	43	43	45	45	39	37	44	42
17-20	Mean	**35.70**	**77.46**	**63.40**	**23.99**	**25.26**	**260.76**	**23.95**	**10.18**	**4.34**	**35.77**	**737.28**
	SD	5.07	15.10	13.96	4.84	5.25	48.53	6.16	3.44	1.48	12.94	154.22
	n	41	34	34	45	44	46	42	32	41	39	34
21-24	Mean	**37.59**	**77.74**	**62.65**	**25.10**	**27.31**	**275.24**	**25.93**	**12.08**	**4.54**	**38.69**	**787.34**
	SD	4.51	18.71	11.73	4.62	5.08	49.70	8.08	3.22	1.07	15.13	103.21
	n	22	20	20	24	25	24	25	19	20	24	21
25-28	Mean	**40.08**	**83.44**	**70.45**	**26.62**	**27.09**	**289.90**	**29.64**	**13.56**	**4.87**	**30.60**	**817.93**
	SD	5.79	17.05	15.29	5.38	5.42	41.27	10.33	5.89	1.57	13.89	75.27
	n	27	18	17	28	28	28	26	23	25	26	22
29-32	Mean	**43.29**	**93.66**	**79.52**	**27.89**	**29.43**	**324.43**	**24.71**	**13.23**	**4.58**	**36.63**	**873.61**
	SD	5.34	20.08	13.74	6.75	6.77	29.14	10.11	2.13	1.44	18.66	62.50
	n	8	5	5	12	12	11	10	11	12	11	8
33-36	Mean	**46.14**	**92.17**	**75.42**	**30.10**	**30.12**	**326.36**	**32.67**	**14.78**	**4.20**	**39.28**	**994.46**
	SD	3.82	18.54	13.61	4.55	3.72	25.87	12.33	4.17	1.00	12.03	59.86
	n	5	4	4	5	5	5	6	6	6	5	5
37-40	Mean	**40.66**	**75.43**	**65.86**	**25.13**	**26.54**	**326.10**	**27.80**	**14.38**	**3.51**	**29.43**	**978.51**
	SD	5.89	22.73	16.79	4.27	5.73	27.99	8.50	2.73	1.00	10.49	78.49
	n	11	9	9	9	9	11	11	10	10	12	9
41-44	Mean	**47.48**	**73.6**	**60.03**	**27.50**	**26.40**	**312.10**	**31.05**	**19.66**	**4.30**	**24.60**	**982.50**
	SD	7.34	13.10	18.14	3.11	2.10	46.87	11.08	4.35	1.02	17.26	179.42
	n	4	3	3	5	5	6	6	5	4	5	4
45-52	Mean	**48.9**	**86.22**	**65.47**	**28.60**	**30.54**	**360.83**	**39.30**	**20.74**	**4.56**	**29.58**	**1058.27**
	SD	5.75	33.41	17.60	5.55	5.73	69.91	16.51	4.97	1.75	11.67	70.41
	n	15	4	4	18	18	17	18	13	15	15	13

R. (right), L. (left)

Table 4-4. Male Heart Measurements

Table shows the mean, standard deviation and sample size for cardiac structures by age in weeks. Heart weight in grams, cardiac valve circumferences in centimeters, ventricular wall thickness in millimeters.

Age (Weeks)		Heart Weight	LV	RV	TV	PV	MV	AV
0-2	Mean	**22.74**	**5.39**	**3.21**	**39.30**	**23.65**	**33.96**	**21.11**
	SD	4.58	1.14	0.83	4.85	3.30	4.21	2.50
	n	98	76	76	81	82	80	81
3-4	Mean	**25.86**	**6.14**	**2.86**	**40.43**	**24.24**	**34.00**	**22.24**
	SD	6.14	1.39	1.37	4.15	3.66	5.02	3.27
	n	25	21	21	21	21	21	21
5-8	Mean	**28.92**	**6.67**	**2.51**	**44.6**	**26.57**	**37.73**	**24.24**
	SD	4.60	1.30	0.76	5.12	3.27	4.25	2.88
	n	64	45	45	50	47	49	50
9-12	Mean	**32.58**	**6.72**	**2.13**	**47.02**	**28.71**	**38.45**	**26.25**
	SD	4.89	0.98	0.62	5.24	4.08	4.14	3.12
	n	62	51	51	51	48	49	51
13-16	Mean	**34.07**	**7.23**	**2.12**	**49.87**	**30.44**	**41.00**	**27.50**
	SD	5.28	1.01	0.54	4.18	3.57	4.47	4.52
	n	43	33	34	35	34	34	34
17-20	Mean	**35.70**	**6.82**	**2.20**	**50.62**	**29.64**	**41.04**	**26.81**
	SD	5.07	1.22	0.44	5.34	3.73	3.91	3.35
	n	41	28	28	26	25	26	26
21-24	Mean	**37.59**	**7.20**	**2.33**	**52.31**	**31.25**	**43.56**	**29.13**
	SD	4.51	1.37	0.62	5.53	4.36	4.10	3.36
	n	22	15	15	16	16	16	15
25-28	Mean	**40.08**	**7.32**	**2.37**	**53.59**	**32.26**	**43.00**	**30.17**
	SD	5.79	1.04	0.68	4.66	2.97	5.09	4.43
	n	27	22	23	22	23	23	23
29-32	Mean	**43.29**	**6.83**	**2.22**	**58.00**	**37.29**	**46.57**	**31.00**
	SD	5.34	1.22	0.44	5.13	3.30	2.82	3.87
	n	8	9	9	7	7	7	7
33-36	Mean	**46.14**	**7.80**	**2.10**	**55.00**	**35.40**	**47.80**	**31.20**
	SD	3.82	1.79	0.55	4.90	2.30	3.03	1.30
	n	5	5	5	5	5	5	5
37-40	Mean	**40.66**	**7.33**	**1.83**	**55.10**	**34.70**	**44.30**	**30.90**
	SD	5.89	1.32	0.35	4.56	5.19	4.76	3.96
	n	11	9	9	10	10	10	10
41-44	Mean	**47.48**	**8.25**	**2.75**	**58.00**	**38.00**	**51.50**	**34.50**
	SD	7.34	1.26	1.50	6.78	4.24	5.07	4.20
	n	4	4	4	4	4	4	4
45-52	Mean	**48.90**	**8.00**	**2.54**	**59.46**	**36.31**	**48.62**	**31.77**
	SD	5.75	0.82	0.52	3.20	4.21	2.75	2.17
	n	15	13	13	13	13	13	13

LV (left ventricle), RV (right ventricle), TV (tricuspid valve), PV (pulmonary valve), MV (mitral valve), AV (aortic valve)

Table 4-5. Female Body Measurements

Table shows the mean, standard deviation and sample size for each organ by age in weeks. Body weight is provided in grams; the remainder of the measurements in centimeters.

Age (Weeks)		Body Weight	Crown-Heel	Crown-Rump	Head Cir.	Abdomen Cir.	Chest Cir.	Foot Length
0-2	Mean	**3496.25**	**51.13**	**35.76**	**34.31**	**31.77**	**32.89**	**7.73**
	SD	681.26	2.62	2.27	1.84	3.27	2.66	0.56
	n	118	119	69	97	93	95	70
3-4	Mean	**3905.71**	**52.73**	**36.67**	**35.35**	**33.24**	**33.24**	**7.58**
	SD	595.45	2.98	2.38	2.08	4.53	2.94	0.53
	n	31	34	20	28	28	28	21
5-8	Mean	**4525.15**	**55.83**	**39.29**	**37.14**	**36.01**	**36.36**	**8.20**
	SD	654.67	3.29	2.02	1.71	2.37	2.26	0.73
	n	42	43	27	36	32	34	26
9-12	Mean	**4987.36**	**57.65**	**40.04**	**38.49**	**37.39**	**37.58**	**8.22**
	SD	720.19	3.24	2.31	1.54	3.74	2.68	0.54
	n	42	44	25	35	36	36	23
13-16	Mean	**5777.63**	**60.84**	**42.38**	**39.91**	**39.13**	**39.15**	**8.83**
	SD	984.79	2.85	4.38	1.45	3.47	2.51	0.56
	n	27	29	17	23	21	22	15
17-20	Mean	**6357.17**	**63.72**	**44.47**	**40.79**	**39.33**	**39.77**	**9.08**
	SD	721.52	3.55	2.78	1.86	3.05	1.94	0.56
	n	23	25	16	24	23	23	16
21-24	Mean	**6381.47**	**65.00**	**45.58**	**41.27**	**39.14**	**40.14**	**9.30**
	SD	1086.61	3.43	3.80	2.17	2.44	2.54	0.52
	n	15	15	6	11	11	11	8
25-28	Mean	**7131.11**	**65.05**	**44.50**	**41.94**	**38.69**	**40.31**	**9.33**
	SD	1088.40	3.72	1.94	1.01	2.07	1.60	0.61
	n	9	10	7	9	8	8	6
29-32	Mean	**8086.73**	**68.50**	**48.33**	**44.00**	**44.25**	**43.75**	**9.66**
	SD	813.82	2.52	4.37	1.33	4.02	1.57	0.86
	n	11	11	6	10	10	10	8
33-36	Mean	**8339.00**	**70.88**	**50.00**	**47.00**	**49.25**	**44.00**	**9.35**
	SD	988.54	4.37	0	1.73	1.77	4.36	0.21
	n	2	4	2	3	2	3	2
37-40	Mean	**7962.50**	**69.60**	**47.33**	**45.62**	**40.33**	**40.83**	**10.45**
	SD	938.45	3.51	4.73	1.11	1.53	1.61	0.53
	n	4	5	3	4	3	3	4
41-44	Mean	**9023.33**	**71.67**	**46.92**	**43.94**	**42.92**	**44.00**	**10.75**
	SD	898.73	4.12	2.13	1.72	2.65	2.63	0.35
	n	6	9	6	7	6	7	2
45-52	Mean	**8810.71**	**73.72**	**48.11**	**45.20**	**43.75**	**44.30**	**10.54**
	SD	1003.64	1.74	3.32	2.15	3.78	2.21	1.14
	n	14	12	9	10	10	10	7

Cir. (circumference)

Table 4-6. Female Organ Weights

Table shows the mean, standard deviation and sample size for each organ by age in weeks. All measurements are in grams.

Age (Weeks)		Heart	R. Lung	L. Lung	R. Kidney	L. Kidney	Liver	Spleen	Pancreas	Adrenals	Thymus	Brain
0-2	Mean	**21.29**	**35.95**	**30.58**	**14.49**	**14.92**	**154.85**	**10.88**	**4.65**	**7.55**	**10.76**	**397.53**
	SD	4.80	10.17	8.71	3.69	3.70	41.18	4.23	1.93	3.63	5.23	51.11
	n	86	47	47	104	101	113	118	89	96	103	53
3-4	Mean	**22.37**	**45.81**	**40.65**	**16.39**	**17.17**	**151.91**	**13.00**	**5.90**	**4.29**	**20.43**	**460.23**
	SD	3.77	12.78	9.65	3.73	3.95	23.20	3.85	1.94	1.32	6.62	57.41
	n	25	21	21	28	28	29	33	25	27	26	28
5-8	Mean	**27.43**	**58.54**	**51.08**	**17.97**	**18.37**	**191.32**	**16.01**	**6.12**	**4.31**	**23.37**	**525.04**
	SD	4.80	13.50	12.65	3.86	3.67	32.73	5.92	2.54	2.18	8.46	61.64
	n	33	33	33	40	40	42	42	30	33	38	33
9-12	Mean	**28.79**	**62.17**	**52.59**	**18.74**	**19.02**	**197.20**	**16.91**	**7.18**	**3.74**	**27.13**	**589.03**
	SD	4.48	11.06	11.36	3.54	3.77	32.86	6.15	2.77	1.39	8.76	54.39
	n	41	36	36	37	37	40	43	33	33	36	40
13-16	Mean	**31.88**	**66.85**	**58.45**	**20.23**	**21.39**	**221.24**	**19.69**	**8.98**	**4.11**	**32.00**	**666.35**
	SD	8.44	11.76	11.38	4.33	5.38	43.81	7.57	2.29	1.22	11.00	70.40
	n	24	20	20	27	27	25	26	20	24	26	24
17-20	Mean	**32.32**	**71.85**	**62.63**	**22.36**	**23.43**	**228.67**	**21.37**	**10.38**	**3.99**	**32.16**	**692.35**
	SD	4.38	8.29	10.93	5.28	5.74	45.27	6.14	3.81	1.49	11.04	56.75
	n	21	14	13	20	20	25	25	20	20	17	15
21-24	Mean	**33.51**	**70.81**	**63.30**	**22.38**	**22.95**	**255.48**	**22.23**	**9.53**	**3.36**	**27.84**	**824.89**
	SD	3.83	10.04	10.62	3.98	4.99	38.01	5.86	2.76	1.35	12.29	61.48
	n	11	9	9	14	14	14	12	11	11	14	9
25-28	Mean	**34.59**	**80.83**	**67.53**	**20.37**	**20.61**	**262.49**	**21.02**	**11.00**	**3.64**	**29.39**	**784.99**
	SD	4.67	8.51	7.83	5.88	4.85	26.53	5.79	2.70	0.99	8.19	90.94
	n	8	6	6	7	7	9	9	8	5	7	7
29-32	Mean	**40.93**	**83.22**	**65.76**	**26.42**	**29.60**	**314.39**	**26.32**	**14.67**	**3.44**	**35.36**	**899.70**
	SD	8.21	21.66	20.28	6.41	7.54	51.40	6.91	3.81	1.32	12.55	45.73
	n	9	5	5	10	10	10	10	9	6	10	7
33-36	Mean	**38.67**	**56.00**	**47.00**	**23.00**	**26.00**	**256.85**	**31.53**	**14.90**	**4.83**	**40.40**	**-**
	SD	8.33	-	-	-	-	46.88	13.51	7.21	1.61	-	-
	n	3	1	1	1	1	2	3	2	3	1	-
37-40	Mean	**45.20**	**100.00**	**68.50**	**26.86**	**28.78**	**320.05**	**29.70**	**15.40**	**4.90**	**25.24**	**893.40**
	SD	2.31	0	0.71	2.57	2.84	35.44	10.96	5.05	0.81	7.30	118.22
	n	3	2	2	5	5	4	5	3	4	5	5
41-44	Mean	**46.94**	**80.80**	**77.37**	**27.69**	**29.68**	**341.60**	**30.70**	**11.53**	**3.36**	**28.76**	**960.13**
	SD	6.97	18.11	20.2	7.12	5.78	87.66	11.86	4.77	1.01	4.27	93.90
	n	7	3	3	9	9	8	8	6	7	5	7
45-52	Mean	**43.00**	**88.21**	**72.13**	**29.62**	**29.56**	**348.82**	**34.62**	**15.16**	**4.77**	**33.39**	**964.66**
	SD	4.38	18.91	16.14	6.22	5.30	51.59	8.01	3.96	3.13	9.80	78.88
	n	11	9	9	12	12	12	12	9	11	10	10

R. (right), L. (left)

Table 4-7. Female Heart Measurements

Table shows the mean, standard deviation and sample size for cardiac structures by age in weeks. Heart weight in grams, cardiac valve circumferences in centimeters, ventricular wall thickness in millimeters.

Age (Weeks)		Heart Weight	LV	RV	TV	PV	MV	AV
0-2	Mean	**21.29**	**5.06**	**2.97**	**38.68**	**23.36**	**32.76**	**20.47**
	SD	4.80	1.02	0.93	4.61	3.20	4.69	2.66
	n	86	69	69	69	70	70	70
3-4	Mean	**22.37**	**5.81**	**2.67**	**38.54**	**23.58**	**31.67**	**21.33**
	SD	3.77	1.54	0.66	3.58	3.88	4.52	2.96
	n	25	21	21	24	24	24	24
5-8	Mean	**27.43**	**6.21**	**2.47**	**43.86**	**25.93**	**35.83**	**23.48**
	SD	4.80	1.07	0.84	4.62	3.73	3.78	2.97
	n	33	28	29	29	29	29	29
9-12	Mean	**28.79**	**6.62**	**2.27**	**45.97**	**28.12**	**37.47**	**25.06**
	SD	4.48	1.14	0.79	3.89	3.67	5.03	3.48
	n	41	33	32	32	32	32	32
13-16	Mean	**31.88**	**7.10**	**2.14**	**48.40**	**29.65**	**39.11**	**26.35**
	SD	8.44	1.55	0.57	5.55	3.67	4.45	2.46
	n	24	21	21	20	20	19	20
17-20	Mean	**32.32**	**6.41**	**1.94**	**49.82**	**28.47**	**39.82**	**26.12**
	SD	4.38	1.37	0.56	3.49	3.52	3.15	3.20
	n	21	17	17	17	17	17	17
21-24	Mean	**33.51**	**7.22**	**2.19**	**52.80**	**31.20**	**42.30**	**28.40**
	SD	3.83	0.83	0.53	4.39	2.78	1.95	3.50
	n	11	9	8	10	10	10	10
25-28	Mean	**34.59**	**6.33**	**2.00**	**52.00**	**30.67**	**40.5**	**26.67**
	SD	4.67	0.82	0	3.41	5.43	2.95	5.61
	n	8	6	6	6	6	6	6
29-32	Mean	**40.93**	**7.50**	**2.44**	**53.50**	**32.62**	**45.00**	**29.62**
	SD	8.21	1.60	0.62	5.37	3.16	3.02	2.56
	n	9	8	8	8	8	8	8
33-36	Mean	**38.67**	**9.00**	**2.00**	**53.00**	**30.50**	**45.50**	**27.50**
	SD	8.33	1.41	1.41	9.90	4.95	6.36	3.54
	n	3	2	2	2	2	2	2
37-40	Mean	**45.20**	**7.50**	**4.00**	**55.00**	**38.00**	**43.5**	**32.50**
	SD	2.31	0.71	1.41	0	4.24	2.12	3.54
	n	3	2	2	2	2	2	2
41-44	Mean	**46.94**	**7.60**	**2.40**	**50.67**	**32.80**	**45.00**	**31.00**
	SD	6.97	0.89	0.55	10.58	3.83	3.61	2.37
	n	7	5	5	6	5	5	6
45-52	Mean	**43.00**	**7.22**	**1.94**	**53.89**	**33.00**	**45.00**	**31.00**
	SD	4.38	1.56	0.53	6.03	4.69	3.32	5.05
	n	11	9	9	9	9	9	9

LV (left ventricle), RV (right ventricle), TV (tricuspid valve), PV (pulmonary valve), MV (mitral valve), AV (aortic valve)

Table 4-8. Body Measurements for Both Genders

Table shows the mean, standard deviation and sample size for each organ by age in weeks. Body weight is provided in grams; the remainder of the measurements in centimeters.

Age (Weeks)		Body Weight	Crown-Heel	Crown-Rump	Head Cir.	Abdomen Cir.	Chest Cir.	Foot Length
0-2	Mean	**3543.73**	**51.25**	**36.06**	**34.65**	**31.91**	**32.90**	**7.74**
	SD	671.61	2.96	2.42	1.92	3.19	2.85	0.60
	n	251	255	142	205	199	203	151
3-4	Mean	**3971.95**	**53.29**	**37.47**	**35.81**	**33.45**	**33.93**	**7.78**
	SD	633.16	3.08	2.37	2.03	4.53	3.18	0.58
	n	59	65	38	57	57	57	42
5-8	Mean	**4628.30**	**56.23**	**39.89**	**37.73**	**36.05**	**36.44**	**8.34**
	SD	679.49	3.16	2.11	1.82	2.79	2.30	0.70
	n	125	125	73	108	99	103	71
9-12	Mean	**5294.32**	**58.54**	**40.97**	**39.27**	**38.34**	**38.11**	**8.42**
	SD	793.88	3.11	2.82	1.56	3.20	2.47	0.56
	n	109	113	66	96	90	93	56
13-16	Mean	**6121.57**	**61.15**	**43.18**	**40.61**	**40.10**	**40.05**	**8.93**
	SD	1023.74	3.33	3.31	1.42	3.72	2.47	0.55
	n	76	78	46	67	61	65	40
17-20	Mean	**6775.56**	**63.97**	**44.99**	**41.97**	**40.27**	**41.02**	**9.22**
	SD	977.50	3.83	2.73	2.72	3.21	2.68	0.62
	n	71	72	47	69	62	63	46
21-24	Mean	**6919.83**	**65.20**	**45.36**	**42.02**	**41.71**	**41.58**	**9.45**
	SD	1066.77	3.22	3.15	2.04	3.67	2.55	0.62
	n	41	42	18	29	28	29	22
25-28	Mean	**7553.57**	**66.10**	**45.39**	**42.79**	**40.83**	**41.71**	**9.41**
	SD	1334.95	2.67	2.26	1.45	3.33	2.25	0.55
	n	40	41	26	37	35	36	28
29-32	Mean	**8219.17**	**69.12**	**48.30**	**44.23**	**43.52**	**43.32**	**9.70**
	SD	998.09	2.70	2.91	1.70	3.79	1.88	0.72
	n	24	24	15	22	22	22	18
33-36	Mean	**8735.33**	**71.05**	**49.80**	**45.56**	**44.44**	**43.94**	**10.07**
	SD	1073.51	4.34	2.17	1.59	3.42	2.47	0.84
	n	9	11	5	9	8	9	6
37-40	Mean	**8144.69**	**70.19**	**47.74**	**44.91**	**40.95**	**42.51**	**10.19**
	SD	968.99	3.19	3.29	1.99	3.60	2.31	0.54
	n	16	17	11	15	13	14	11
41-44	Mean	**8697.86**	**71.44**	**47.45**	**44.72**	**42.58**	**43.89**	**10.37**
	SD	758.92	3.67	2.30	2.27	2.95	2.35	0.98
	n	14	18	10	14	13	14	7
45-52	Mean	**9207.78**	**74.80**	**48.74**	**46.25**	**44.60**	**45.48**	**10.86**
	SD	1260.11	2.32	2.70	1.89	3.83	2.97	0.78
	n	27	29	17	26	26	26	20

Cir. (circumference)

Table 4-9. Organ Weights for Both Genders

Table shows the mean, standard deviation and sample size for each organ by age in weeks. All measurements are in grams.

Age (Weeks)		Heart	R. Lung	L. Lung	R. Kidney	L. Kidney	Liver	Spleen	Pancreas	Adrenals	Thymus	Brain
0-2	Mean	**22.03**	**37.66**	**31.31**	**15.16**	**15.76**	**150.06**	**11.56**	**4.80**	**7.43**	**11.37**	**407.04**
	SD	4.73	9.64	8.59	4.08	4.08	40.37	4.61	1.86	3.71	5.34	55.91
	n	185	95	96	227	223	240	256	189	206	225	113
3-4	Mean	**24.11**	**48.94**	**44.06**	**17.18**	**17.73**	**159.81**	**14.20**	**5.99**	**4.82**	**20.94**	**478.24**
	SD	5.34	12.63	11.15	5.03	4.33	35.61	5.64	2.04	1.62	8.56	61.96
	n	50	42	42	55	55	57	63	51	53	52	48
5-8	Mean	**28.40**	**60.19**	**50.81**	**18.97**	**19.66**	**192.20**	**16.52**	**7.18**	**4.53**	**25.77**	**545.92**
	SD	4.66	12.39	11.15	3.75	4.20	36.78	6.22	5.82	1.85	10.32	63.00
	n	99	97	97	116	115	120	123	92	96	101	95
9-12	Mean	**31.14**	**65.26**	**56.54**	**20.83**	**21.14**	**205.85**	**19.96**	**8.34**	**4.17**	**28.65**	**610.82**
	SD	5.09	12.17	12.13	4.67	4.61	35.16	7.12	7.45	1.61	9.01	64.29
	n	104	83	83	101	101	104	110	87	89	96	95
13-16	Mean	**33.34**	**72.35**	**61.01**	**22.21**	**23.09**	**238.11**	**22.08**	**9.85**	**4.48**	**36.13**	**686.68**
	SD	6.58	12.89	10.35	4.92	5.18	44.64	7.29	3.53	1.73	13.38	77.28
	n	68	59	59	71	71	71	72	59	62	72	67
17-20	Mean	**34.49**	**75.80**	**63.19**	**23.42**	**24.65**	**249.38**	**22.87**	**10.17**	**4.22**	**34.47**	**721.49**
	SD	5.06	13.49	12.94	4.99	5.40	49.20	6.26	3.57	1.47	12.39	132.57
	n	63	49	48	66	65	72	68	53	62	57	50
21-24	Mean	**36.23**	**75.59**	**62.85**	**24.10**	**25.74**	**267.96**	**24.73**	**11.15**	**4.12**	**34.69**	**798.61**
	SD	4.66	16.64	11.21	4.54	5.41	46.22	7.56	3.26	1.29	14.95	93.25
	n	33	29	29	38	39	38	37	30	31	38	30
25-28	Mean	**38.33**	**80.86**	**68.13**	**24.82**	**25.19**	**280.79**	**26.93**	**12.70**	**4.58**	**29.88**	**806.54**
	SD	6.19	16.17	14.33	6.25	6.27	40.18	10.03	5.23	1.57	12.56	79.80
	n	37	26	25	37	37	39	37	33	32	35	30
29-32	Mean	**42.04**	**88.44**	**72.64**	**27.22**	**29.50**	**319.65**	**25.52**	**13.88**	**4.20**	**36.02**	**885.79**
	SD	6.90	20.45	17.87	6.48	6.96	40.49	8.47	3.01	1.47	15.66	55.05
	n	17	10	10	22	22	21	20	20	18	21	15
33-36	Mean	**43.82**	**84.94**	**69.74**	**28.36**	**29.37**	**299.04**	**31.03**	**14.14**	**4.41**	**41.33**	**994.46**
	SD	6.31	22.79	17.33	4.79	3.41	46.13	11.88	4.62	1.17	11.0	59.86
	n	9	5	5	7	7	8	10	9	9	7	5
37-40	Mean	**41.92**	**77.24**	**64.14**	**26.50**	**28.05**	**324.49**	**28.39**	**14.50**	**3.91**	**28.91**	**948.11**
	SD	5.50	23.46	16.25	4.63	5.46	28.92	9.00	3.07	1.12	9.83	99.41
	n	15	12	12	15	15	15	16	14	14	18	14
41-44	Mean	**46.81**	**78.79**	**68.09**	**27.95**	**29.11**	**333.07**	**31.43**	**15.19**	**3.66**	**26.20**	**969.12**
	SD	6.52	14.04	17.98	5.78	5.32	71.37	10.92	5.80	1.03	11.55	117.10
	n	12	7	7	15	15	15	15	12	12	11	12
45-52	Mean	**46.40**	**87.60**	**70.08**	**29.42**	**30.47**	**359.16**	**37.84**	**18.74**	**4.70**	**31.14**	**1017.57**
	SD	5.92	22.77	16.16	6.11	5.68	63.79	13.72	5.34	2.34	10.69	86.61
	n	26	13	13	31	31	30	31	23	27	26	23

R. (right), L. (left)

Table 4-10. Heart Measurements for Both Genders

Table shows the mean, standard deviation and sample size for cardiac structures by age in weeks. Heart weight in grams, cardiac valve circumferences in centimeters, ventricular wall thickness in millimeters.

Age (Weeks)		Heart Weight	LV	RV	TV	PV	MV	AV
0-2	Mean	**22.03**	**5.23**	**3.10**	**39.01**	**23.52**	**33.40**	**20.81**
	SD	4.73	1.10	0.88	4.74	3.25	4.47	2.59
	n	185	145	145	150	152	150	151
3-4	Mean	**24.11**	**5.98**	**2.76**	**39.42**	**23.89**	**32.76**	**21.76**
	SD	5.34	1.46	1.07	3.93	3.75	4.85	3.11
	n	50	42	42	45	45	45	45
5-8	Mean	**28.40**	**6.52**	**2.48**	**44.30**	**26.40**	**36.94**	**23.99**
	SD	4.66	1.22	0.78	4.88	3.43	4.18	2.88
	n	99	75	76	81	78	80	81
9-12	Mean	**31.14**	**6.68**	**2.19**	**46.65**	**28.49**	**38.15**	**25.80**
	SD	5.09	1.03	0.69	4.75	3.89	4.54	3.27
	n	104	85	84	84	81	82	84
13-16	Mean	**33.34**	**7.19**	**2.12**	**49.44**	**30.24**	**40.44**	**27.16**
	SD	6.58	1.23	0.54	4.74	3.62	4.56	3.92
	n	68	55	56	56	55	54	55
17-20	Mean	**34.49**	**6.65**	**2.12**	**50.39**	**29.30**	**40.55**	**26.61**
	SD	5.06	1.27	0.51	4.65	3.71	3.60	3.27
	n	63	46	46	44	43	44	44
21-24	Mean	**36.23**	**7.21**	**2.28**	**52.50**	**31.23**	**43.08**	**28.84**
	SD	4.66	1.18	0.58	5.04	3.77	3.44	3.36
	n	33	24	23	26	26	26	25
25-28	Mean	**38.33**	**7.00**	**2.27**	**52.83**	**31.71**	**42.35**	**29.16**
	SD	6.19	1.11	0.60	4.57	3.56	4.66	4.78
	n	37	30	31	30	31	31	31
29-32	Mean	**42.04**	**7.15**	**2.32**	**55.60**	**34.80**	**45.73**	**30.27**
	SD	6.90	1.41	0.53	5.58	3.93	2.94	3.20
	n	17	17	17	15	15	15	15
33-36	Mean	**43.82**	**8.12**	**2.19**	**54.12**	**34.00**	**46.88**	**30.12**
	SD	6.31	1.55	0.75	5.41	3.38	3.56	2.36
	n	9	8	8	8	8	8	8
37-40	Mean	**41.92**	**7.50**	**2.21**	**54.69**	**35.00**	**43.85**	**30.77**
	SD	5.50	1.24	0.99	4.19	4.90	4.34	3.90
	n	15	12	12	13	13	13	13
41-44	Mean	**46.81**	**7.90**	**2.50**	**54.18**	**35.60**	**48.30**	**32.73**
	SD	6.52	0.99	0.97	9.29	4.65	5.14	3.50
	n	12	10	10	11	10	10	11
45-52	Mean	**46.40**	**7.68**	**2.30**	**57.18**	**34.95**	**47.14**	**31.45**
	SD	5.92	1.21	0.59	5.25	4.61	3.44	3.54
	N	26	22	22	22	22	22	22

LV (left ventricle), RV (right ventricle), TV (tricuspid valve), PV (pulmonary valve), MV (mitral valve), AV (aortic valve)

Table 4-11. Akaike Information Criterion (AIC) Backward Selection

AIC model selection based on information theory. The lower the AIC value the stronger the model. (E=exponential power, positive or negative).

	Age	Gender	Cause of Death
Heart	1.60E-153	1.05E-10	4.62E-01
Lungs	4.19E-94	3.85E-04	9.91E-08
R. Lung	3.50E-88	2.07E-04	2.82E-07
L. Lung	8.73E-81	9.74E-03	1.49E-07
Kidneys	1.20E-105	1.86E-09	3.08E-02
R. Kidney	6.92E-98	3.24E-08	2.61E-02
L. Kidney	1.39E-102	7.36E-09	1.23E-01
Liver	5.21E-89	7.02E-04	1.80E-02
Spleen	6.28E-114	6.66E-07	8.97E-03
Pancreas	4.43E-89	7.02E-04	3.46E-01
Adrenals	2.50E-37	9.12E-02	5.03E-08
R. Adrenal	1.42E-32	1.82E-01	1.19E-07
L. Adrenal	7.59E-36	6.76E-02	7.74E-07
Brain	5.75E-224	2.83E-06	1.32E-03
Body	3.34E-288	7.61E-08	4.08E-01
Thymus	3.071E-102	9.535E-05	6.953E-14

Table 4-12. P-values for Akaike Information Criterion

AIC value for each individual variable based on asymptotic theory (large sample theory). "0" p-values represent values less than 0.000.

	Age	Gender	Cause of Death
Heart	0	0	0.46
Lungs	0	0	0
R. Lung	0	0	0
L. Lung	0	0.01	0
Kidneys	0	0	0.03
R. Kidney	0	0	0.03
L. Kidney	0	0	0.12
Liver	0	0.01	0.02
Spleen	0	0	0.01
Pancreas	0	0	0.35
Adrenals	0	0.09	0
R. Adrenal	0	0.18	0
L. Adrenal	0	0.07	0
Brain	0	0	0
Body	0	0	0.41
Thymus	0	0	0

Table 4-13. Effect of Gender on Individual Organ and Body Weight for Different Age Groups

The table shows how gender affects the weights of various organs and whole body weight. Significant relationships between the gender and specific organ or body weight are labelled as "1" ($p<0.05$). For all variables, "1" represents male organ heavier than female except the adrenals at age of 37-40 weeks. Instances with no statistical relationship are labelled as "0" (see **Appendix F** for p-values).

Age in weeks	Heart	Lungs	R.Lung	L.Lung	Kidneys	R.Kidney	L.Kidney	Liver	Spleen	Pancreas	Adre	R.Adre	L.Adre	Brain	Body
0-2	1	0	0	0	1	1	1	0	1	0	0	0	0	0	0
3-4	1	0	0	1	0	0	0	0	0	0	1	1	1	1	0
5-8	0	0	0	0	1	1	1	0	0	0	0	0	0	1	0
9-12	1	1	1	1	1	1	1	0	1	0	0	0	1	1	1
13-16	0	1	1	0	1	1	1	1	1	0	0	0	0	0	1
17-20	1	0	0	0	0	0	0	1	0	0	0	0	0	0	1
21-24	1	0	0	0	1	0	1	0	0	1	1	1	0	0	1
25-28	1	0	0	0	1	1	1	0	1	0	0	0	0	0	0
29-32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33-36	0	-	-	-	-	-	-	1	0	0	0	0	0	-	0
37-40	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
41-44	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
45-52	1	0	0	0	0	0	0	0	0	1	0	0	0	1	0

R. (right), L. (left), Adre. (adrenal)

Table 4-14. Combined Lung Weight Correlated to Cause of Death

The table shows statistically significant differences in combined lung weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	**1**	**1**	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	**1**	**1**	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	-	0	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	0	**1**	0
5-8	0	0	0
9-12	**1**	**1**	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	**1**	**1**	**1**
29-32	-	-	0
33-36	-	-	-
37-40	-	-	-
41-44	0	-	-
45-52	0	0	0

COMBINED GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	**1**	**1**	0
5-8	0	**1**	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	0	0	0
45-52	0	0	0

Table 4-15. Combined Kidney Weight Correlated to Cause of Death

The table shows statistically significant differences in combined kidney weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	**1**
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	-	-	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	**1**	0
5-8	0	0	0
9-12	0	0	**1**
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	-	-	-
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

COMBINED GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	**1**
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

Table 4-16. Liver Weight Correlated to Cause of Death

The table shows statistically significant differences in liver weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	**1**	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	**1**	0
37-40	0	0	0
41-44	-	**1**	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	**1**	0	0
3-4	0	**1**	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	-	-	-
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

BOTH GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	**1**	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	**1**	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	**1**	0	0
41-44	0	0	0
45-52	0	0	0

Table 4-17. Brain Weight Correlated to Cause of Death

The table shows statistically significant differences in brain weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	-	0	-
33-36	0	0	0
37-40	0	0	0
41-44	-	0	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	0	0	0
5-8	0	0	0
9-12	**1**	**1**	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	-	-	0
33-36	-	-	-
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

COMBINED GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	**1**
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	**1**	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	0	0	0
45-52	0	0	0

Table 4-18. Spleen Weight Correlated to Cause of Death

The table shows statistically significant differences in spleen weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	**1**
9-12	0	0	0
13-16	**1**	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	-	-	0
41-44	-	0	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	-	-	-
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

COMBINED GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	0	0
3-4	0	0	0
5-8	0	**1**	**1**
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	0	0	0
45-52	0	0	0

Table 4-19. Combined Adrenal Weight Correlated to Cause of Death

The table shows statistically significant differences in combined adrenals weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	0	0	0
5-8	0	0	0
9-12	0	0	0
13-16	0	0	**1**
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	-	0	-
45-52	0	**1**	**1**

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	**1**	**1**	0
3-4	0	0	0
5-8	0	0	0
9-12	0	**1**	**1**
13-16	0	**1**	**1**
17-20	0	**1**	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	-	-	-
37-40	0	-	-
41-44	0	-	-
45-52	0	0	0

BOTH GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	**1**	**1**	0
3-4	0	0	0
5-8	0	0	0
9-12	0	**1**	**1**
13-16	**1**	0	**1**
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	**1**	0
41-44	0	0	0
45-52	0	0	0

Table 4-20. Thymus Weight Correlated to Cause of Death

The table shows statistically significant differences in thymus weights depending on the cause of death, across different age groups, for each gender separately and combined. Significant relationship between the groups are labeled as "1" ($p<0.05$). Instances with no statistical relationship are labeled as "0" (p-values are provided in **Appendix F**).

MALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	**1**
3-4	**1**	**1**	0
5-8	0	**1**	0
9-12	0	0	0
13-16	0	0	0
17-20	0	**1**	0
21-24	**1**	**1**	0
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	-	0	-
45-52	0	0	0

FEMALES	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	0	0	0
5-8	0	**1**	0
9-12	0	0	0
13-16	0	0	0
17-20	0	0	0
21-24	0	0	0
25-28	0	0	0
29-32	0	0	0
33-36	-	-	-
37-40	0	0	0
41-44	0	-	-
45-52	0	0	0

COMBINED GENDERS	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0	**1**	0
3-4	**1**	**1**	0
5-8	**1**	**1**	0
9-12	0	0	0
13-16	0	0	0
17-20	0	**1**	0
21-24	**1**	**1**	**1**
25-28	0	0	0
29-32	0	0	0
33-36	0	0	0
37-40	0	0	0
41-44	0	**1**	0
45-52	0	0	0

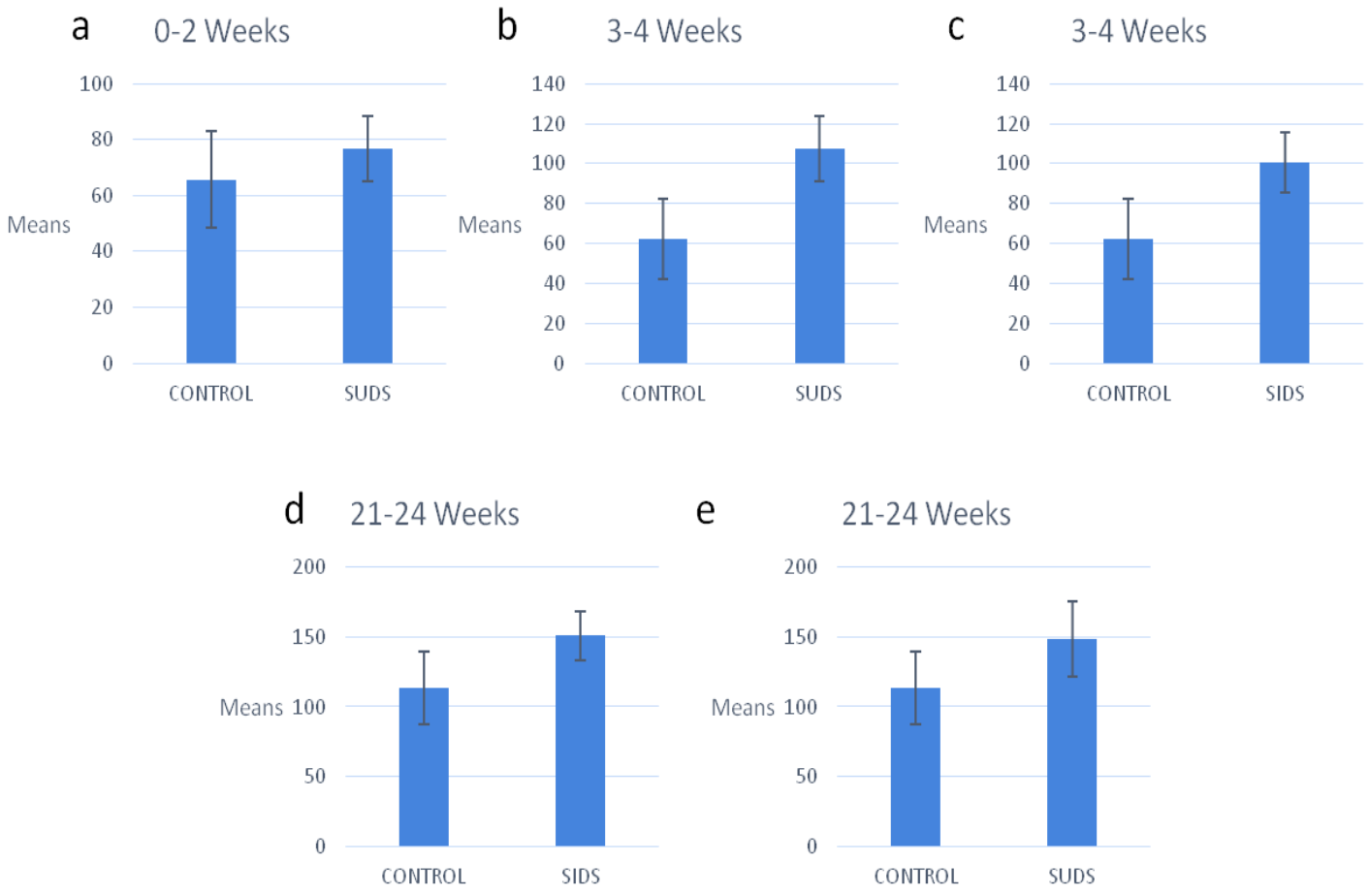

Figure 4-5. Difference in Combined Male Lung Weights between the Cause of Death Groups

The figure shows significant differences in the means of combined male lung weights at specific age intervals between the cause of death groups:

(**a**). Control (n=24) and SUDS (n=22) at 0-2 weeks; (p=0.0196);
(**b**). Control (n=3) and SUDS (n=14) at 3-4 weeks; (p=0.0004);
(**c**). Control (n=3) and SIDS (n=5) at 3-4 weeks; (p=0.005);
(d). Control (n=5) and SIDS (n=5) at 21-24 weeks; (p=0.0298);
(**e**). Control (n=5) and SUDS (n=11) at 21-24 weeks; (p=0.0189).

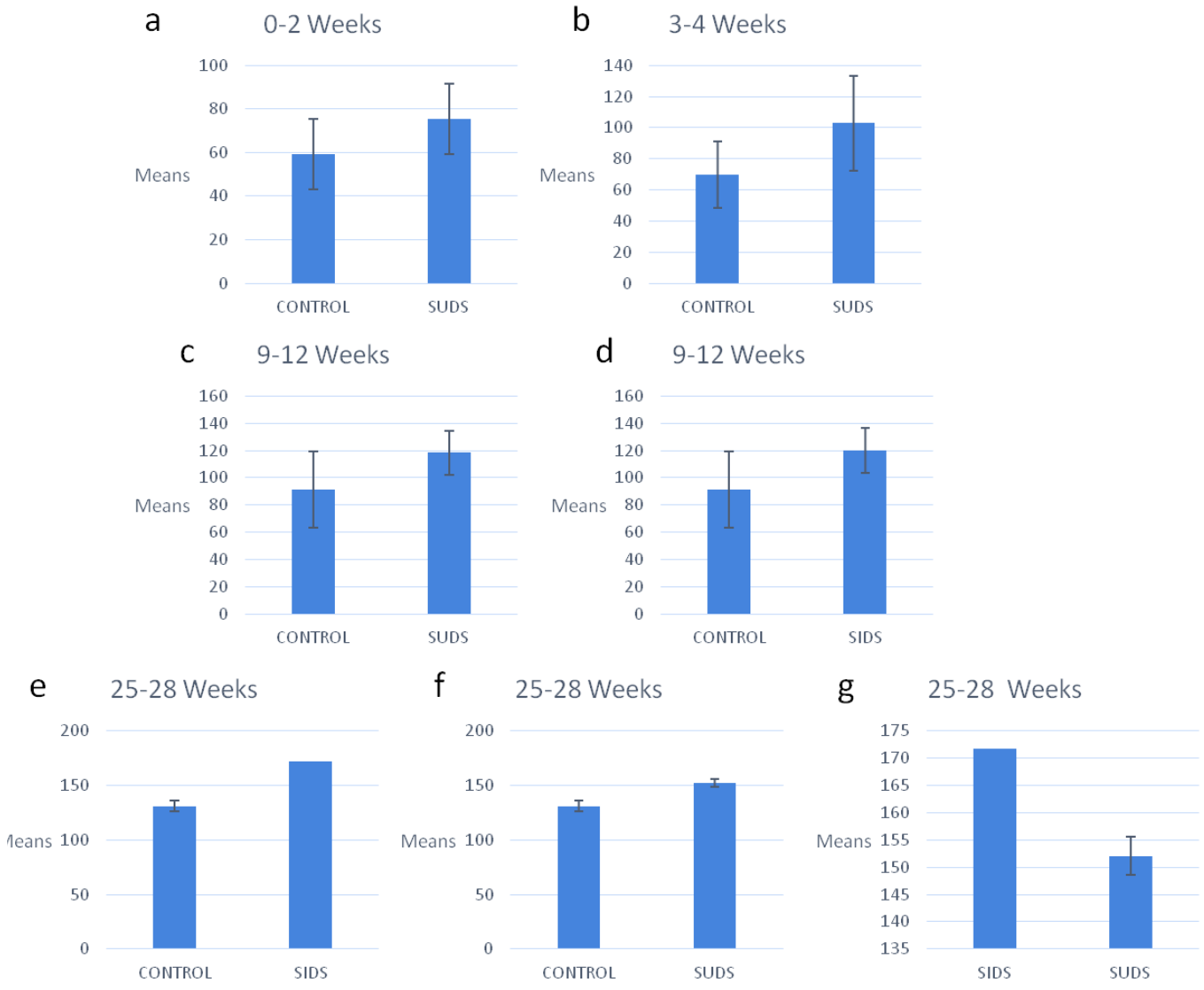

Figure 4-6. Difference in Combined Female Lung Weights between the Cause of Death Groups

The figure shows significant differences in the means of combined female lung weights at specific age intervals between the cause of death groups:

(**a**). Control (n=31) and SUDS (n=18) at 0-2 weeks; (p=0.0018);
(**b**). Control (n=8) and SUDS (n=12) at 3-4 weeks; (p=0.0129);
(**c**). Control (n=5) and SUDS (n=25) at 9-12 weeks; (p=0.00135);
(d). Control (n=5) and SIDS (n=6) at 9-12 weeks; (p=0.0045);
(**e**). Control (n=2) and SIDS (n=1) at 25-28 weeks; (p=0.040);
(**f**). Control (n=2) and SUDS (n=3) at 25-28 weeks; (p=0.0113);
(**g**). SIDS (n=1) and SUDS (=3) at 25-28 weeks; (p=0.0255).

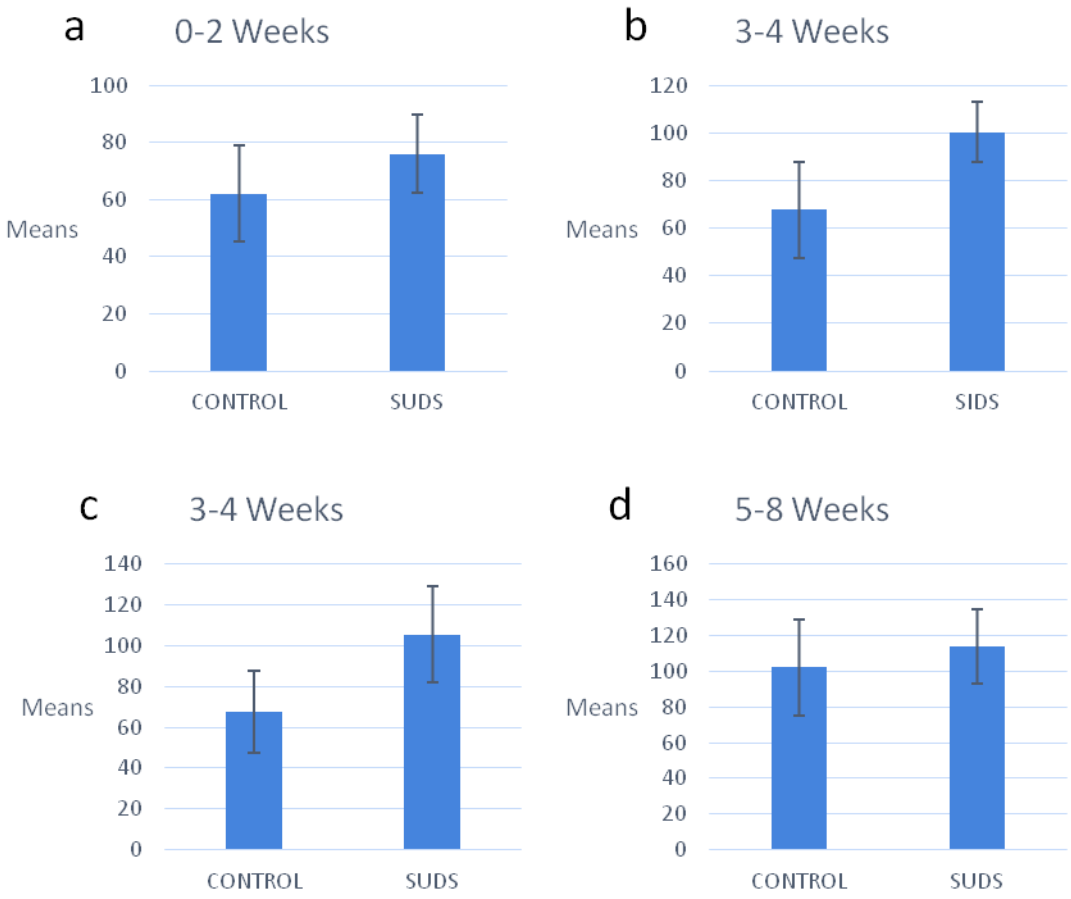

Figure 4-7. Difference in Combined Lung Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of combined lung weights at specific age intervals between the cause of death groups (for both genders combined):

(a). Control (n=55) and SUDS (n=40) at 0-2 weeks; (p=0.0001);
(b). Control (n=11) and SIDS (n=7) at 3-4 weeks; (p=0.0029);
(c). Control (n=11) and SUDS (n=26) at 3-4 weeks; (p=0.0000);
(d). Control (n=20) and SUDS (n=66) at 5-8 weeks; (p=0.0396).

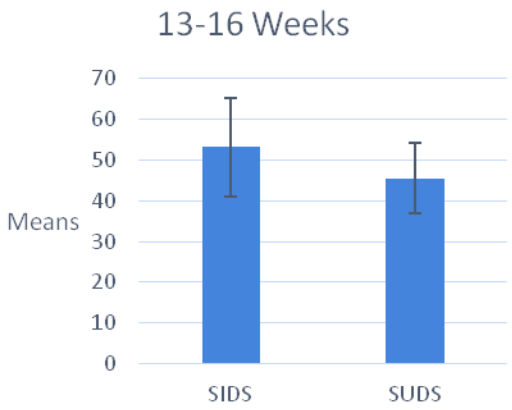

Figure 4-8. Difference in Combined Kidney Weights between the Cause of Death Groups (Males)

The figure shows significant differences in the means of combined kidney weights between the cause of death groups (for males):
SIDS (n=11) and SUDS (n=25) at 13-16 weeks; (p=0.0284).

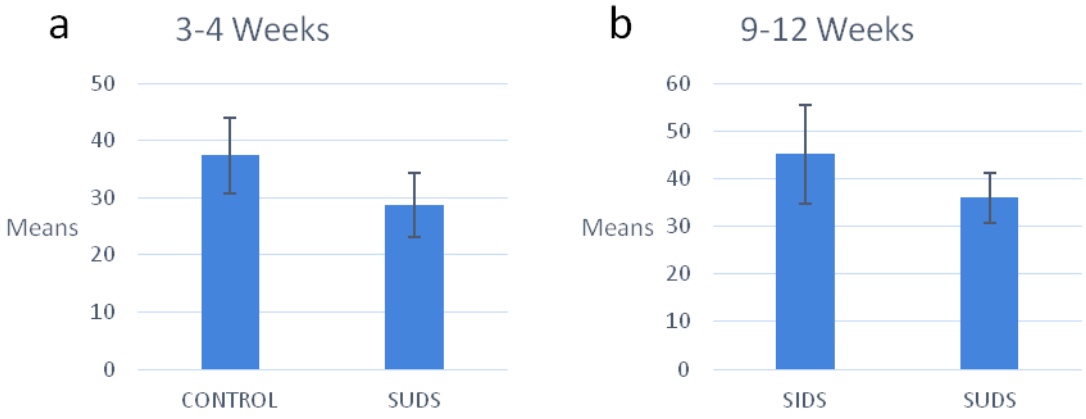

Figure 4-9. Difference in Combined Kidney Weights between the Cause of Death Groups (Females)

The figure shows significant differences in the means of combined kidney weights at specific age intervals between the cause of death groups (for females):

(a). Control (n=14) and SUDS (n=11) at 3-4 weeks; (p=0.0026);
(b). SIDS (n=6) and SUDS (n=26) at 9-12 weeks; (p=0.0026).

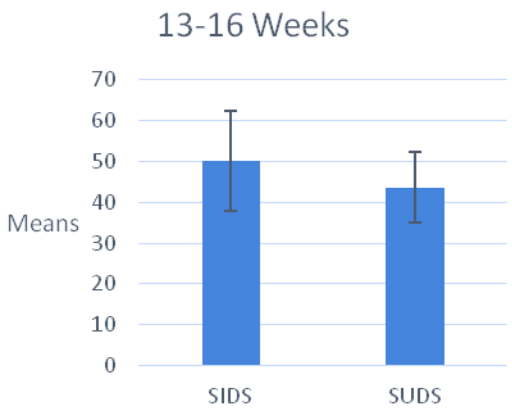

Figure 4-10. Difference in Combined Kidney Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of combined kidney weights between the cause of death groups (for both genders combined):
SIDS (n=14) and SUDS (n=40) at 13-16 weeks; (p=0.0382).

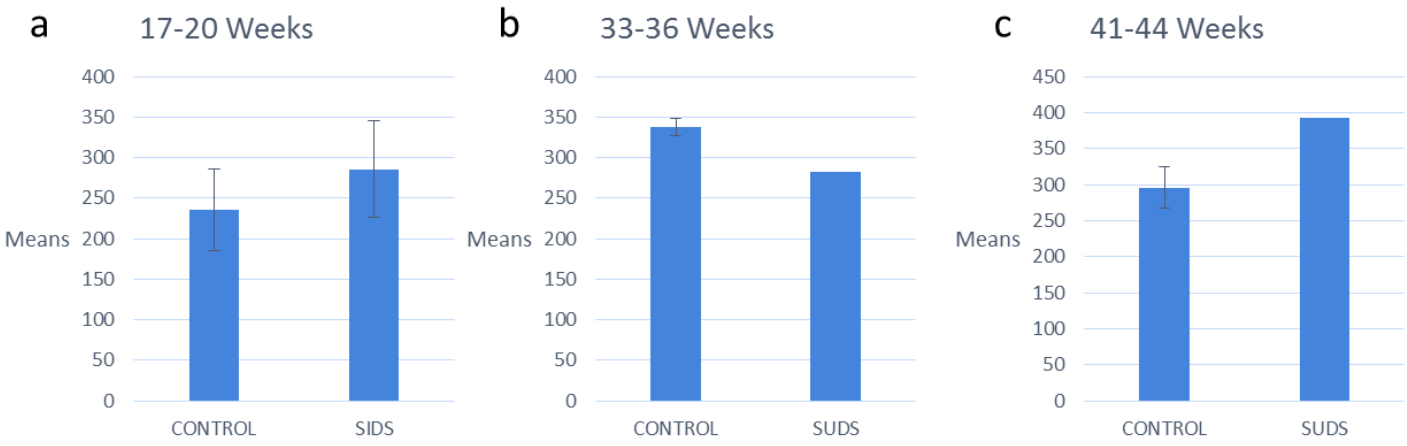

Figure 4-11. Difference in Male Liver Weights between the Cause of Death Groups

The figure shows significant differences in the means of liver weights at specific age intervals between the cause of death groups (for males):

(a). Control (n=11) and SIDS (n=10) at 17-20 weeks; (p=0.0168);
(b). Control (n=3) and SUDS (n=5) at 33-36 weeks; (p=0.0460);
(c). Control (n=5) and SUDS (n=1) at 41-44 weeks; (p=0.0385).

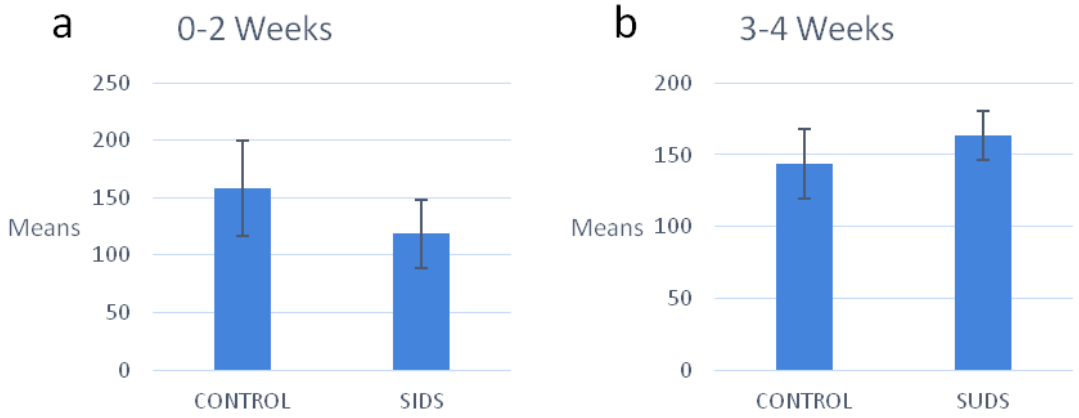

Figure 4-12. Difference in Female Liver Weights between the Cause of Death Groups

The figure shows significant differences in the means of liver weights at specific age intervals between the cause of death groups (for females):

(a). Control (n=80) and SIDS (n=6) at 0-2 weeks of age; (p=0.02170;
(b). Control (n=16) and SUDS (n=11) at 3-4 weeks of age; (p=0.0301).

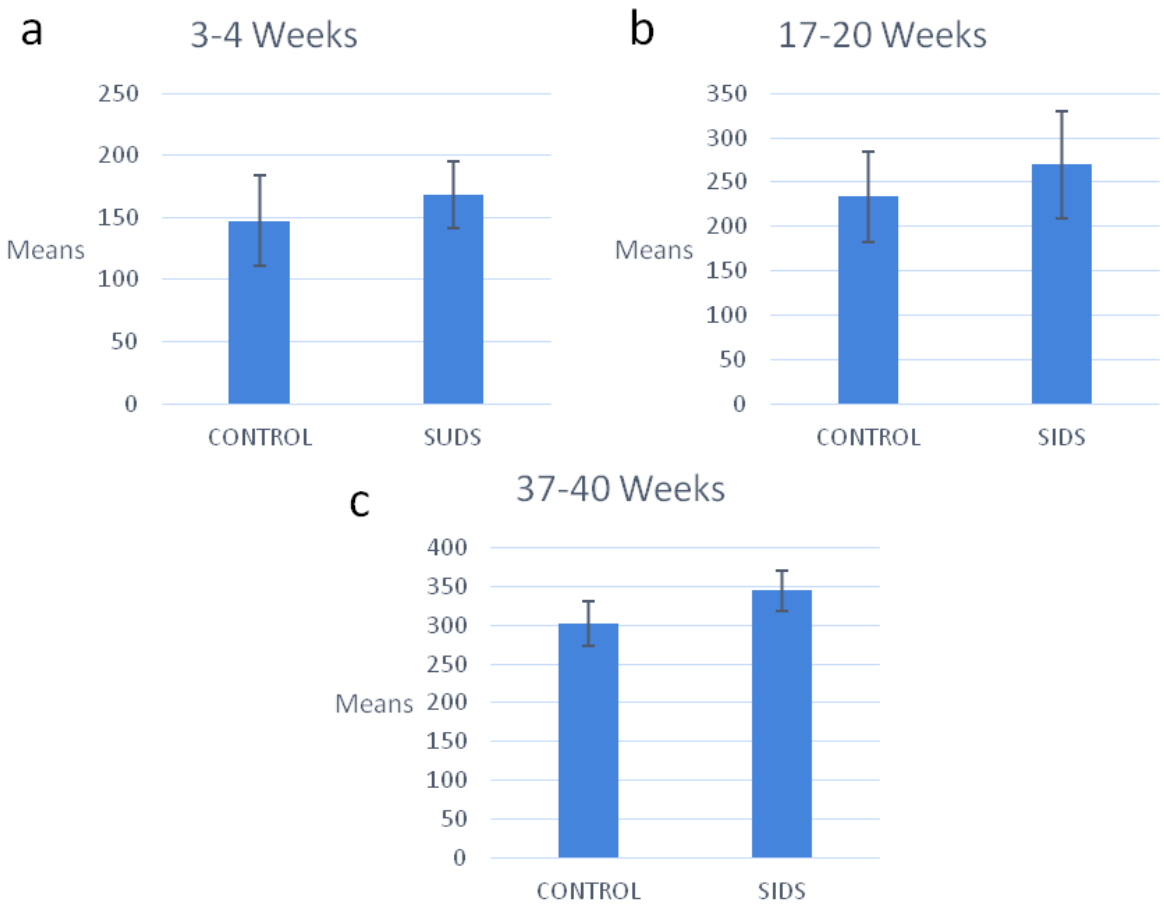

Figure 4-13. Difference in Liver Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of liver weights at specific age intervals between the cause of death groups (for both genders combined):

(a). Control (n=26) and SUDS (n=24) at 3-4 weeks; (p=0.0386);
(b). Control (n=22) and SIDS (n=13) at17-20 weeks; (p=0.0376);
(c). Control (n=3) and SIDS (n=6) at 37-40 weeks; (p=0.0294).

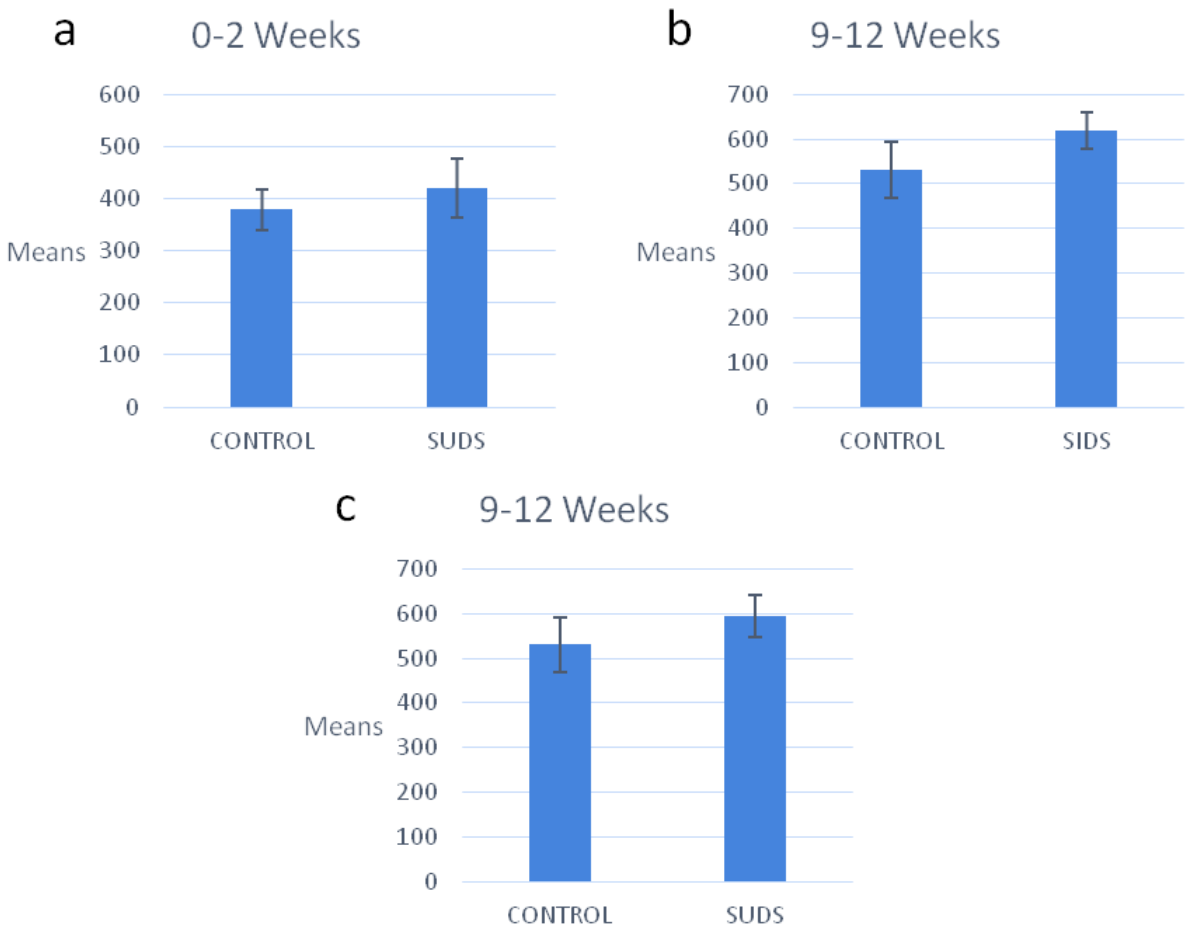

Figure 4-14. Difference in Female Brain Weights between the Cause of Death Groups

The figure shows significant differences in the means of brain weights at specific age intervals between the cause of death groups (for females):

(a). Control (n=24) and SUDS (n=23) at 0-2 weeks; (p=0.0051);
(b). Control (n=6) and SIDS (n=7) at 9-12 weeks; (p=0.0021);
(c). Control (n=6) and SUDS (n=27) at 9-12 weeks; (p=0.0056).

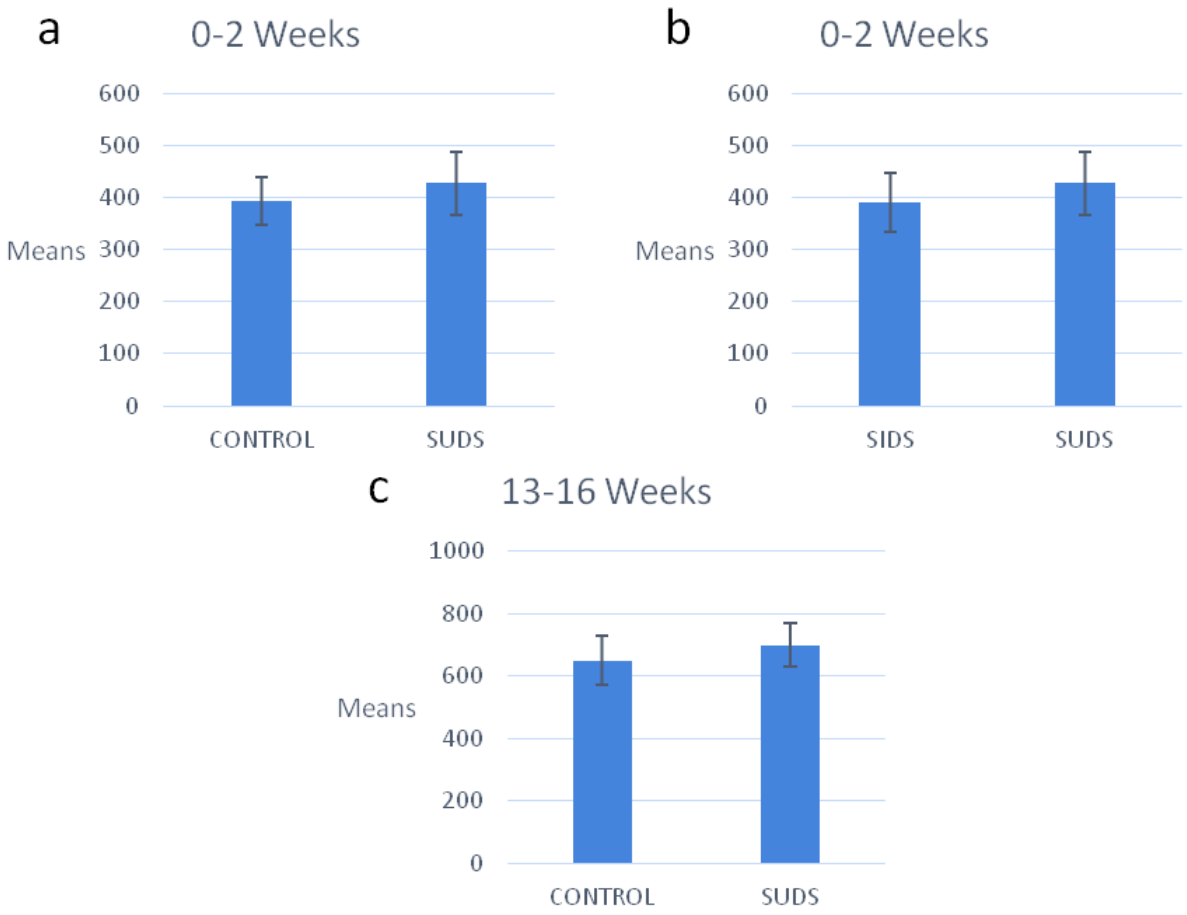

Figure 4-15. Difference in Brain Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of brain weights at specific age intervals between the cause of death groups (for both genders combined):

(a). Control (n=53) and SUDS (n=48) at 0-2weeks; (p=0.0014);
(b). SIDS (n=12) and SUDS (n=48) at 0-2 weeks; (p=0.0400);
(c). Control (n=14) and SUDS (n=39) at 13-16 weeks; (p=0.0410).

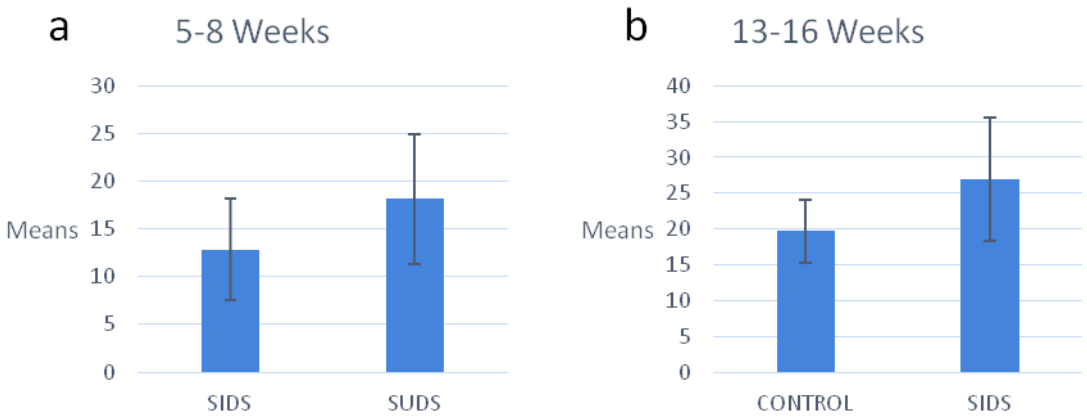

Figure 4-16. Difference in Male Spleen Weights between the Cause of Death Groups

The figure shows significant differences in the means of spleen weights at specific age intervals between the cause of death groups (for males):

(a). SIDS (n=9) and SUDS (n=43) at 5-8 weeks; (p=0.0243);
(b). Control (n=9) and SIDS (n=11) at 13-16 weeks; (p=0.0169).

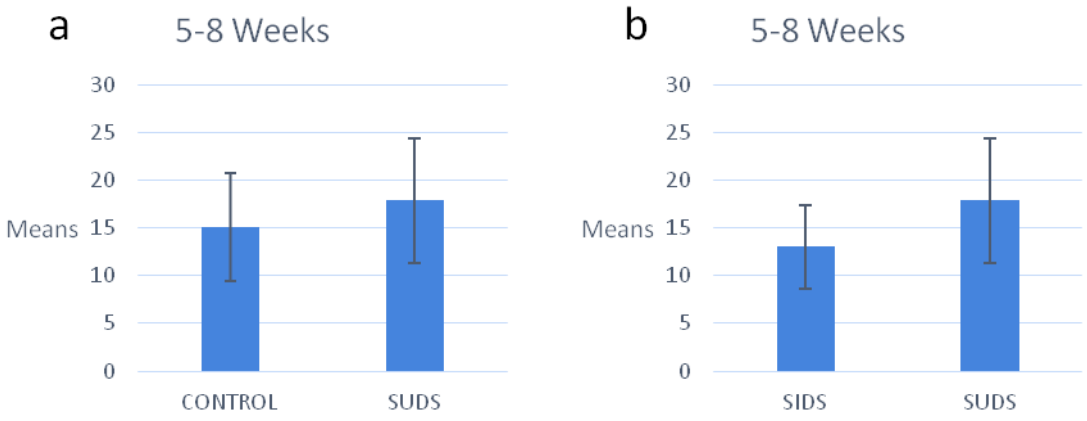

Figure 4-17 Difference in Spleen Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of spleen weights at specific age intervals between the cause of death groups (both genders combined):

(a). Control (n=39) and SUDS (n=69) at 5-8 weeks; (p=0.0249);
(b). SIDS (n=13) and SUDS (n=69) at 5-8 weeks; (p=0.0097).

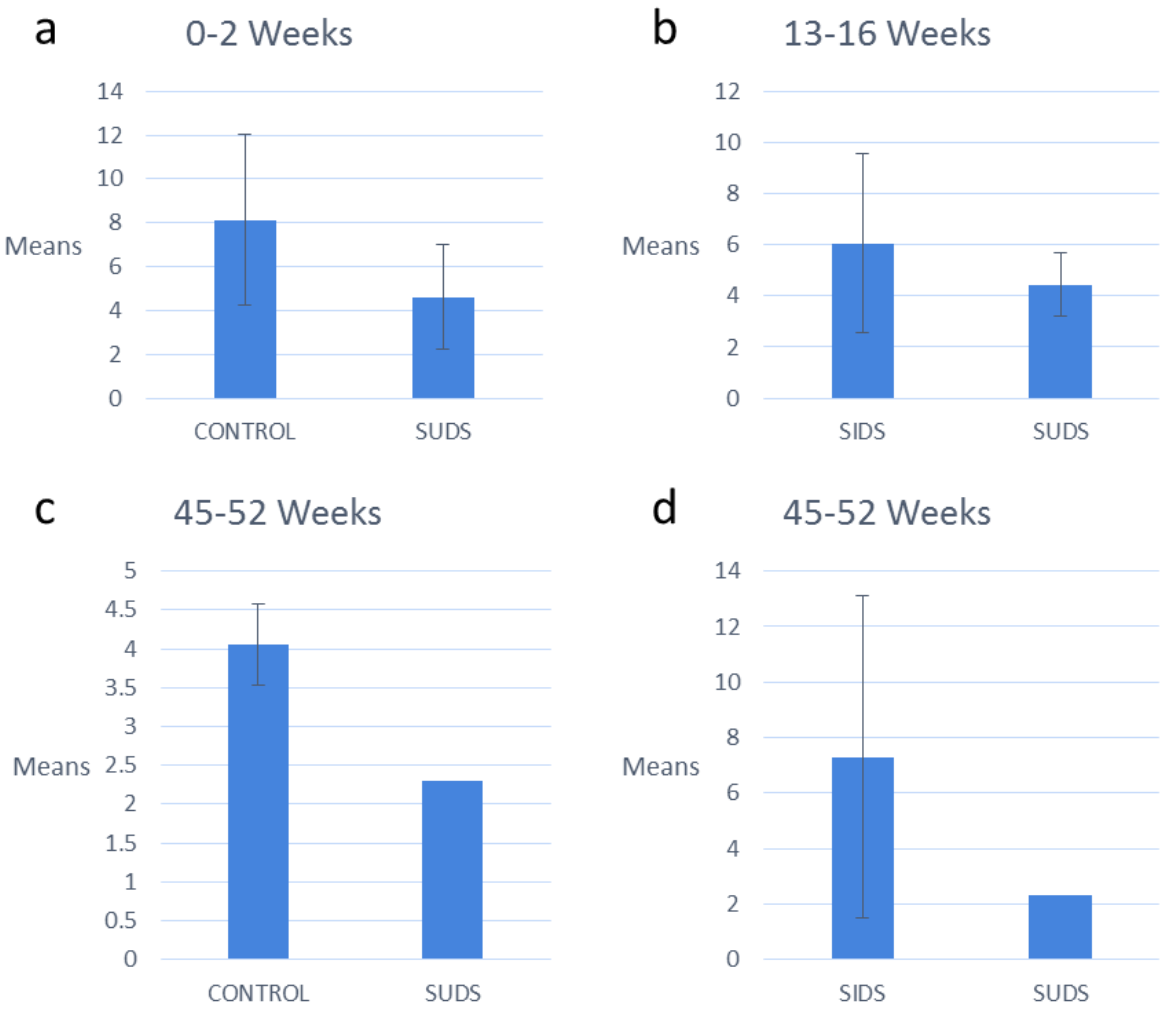

Figure 4-18. Difference in Male Combined Adrenal Weights between the Cause of Death Groups

The figure shows significant differences in the means of combined adrenal weights at specific age intervals between the cause of death groups (for males):

(a). Control (n=80) and SUDS (n=23) at 0-2 weeks; (p=0.0001);
(b). SIDS (n=8) and SUDS (n=23) at 13-16 weeks; (p=0.0468);
(c). Control (n=12) and SUDS (n=1) at 45-52 weeks; (p=0.0460);
(d). SIDS (n=2) and SUDS (n=1) at 45-52 weeks; (p=0.0265).

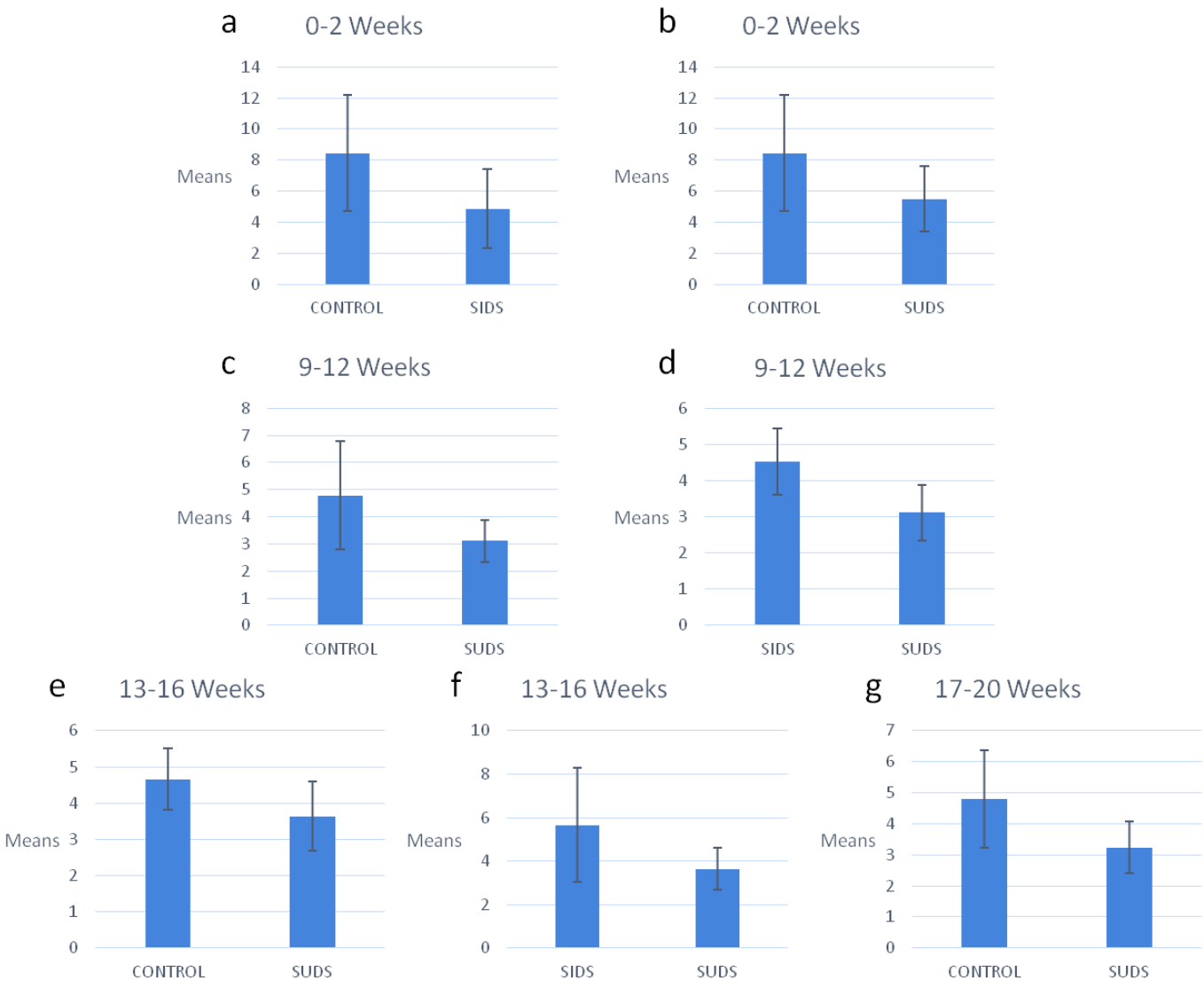

Figure 4-19. Difference in Female Combined Adrenal Weights between the Cause of Death Groups

The figure shows significant differences in the means of combined adrenal weights at specific age intervals between the cause of death groups (for females):

(a). Control (n=68) and SIDS (n=5) at 0-2 weeks; (p=0.0247);
(b). Control (n=68) and SUDS (n=23) at 0-2 weeks; (p=0.0005);
(c). Control (n=8) and SUDS (n=20) at 9-12 weeks; (p=0.0024);
(d). SIDS (n=5) and SUDS (n=20) at 9-12 weeks; (p=0.0257);
(e). Control (n=7) and SUDS (n=15) at 13-16 weeks; (p=0.0483);
(f). SIDS (n=2) and SUDS (n=15) at 13-16 weeks; (p=0.0206);
(g). Control (n=10) and SUDS (n=8) at 17-20 weeks; (p=0.0210).

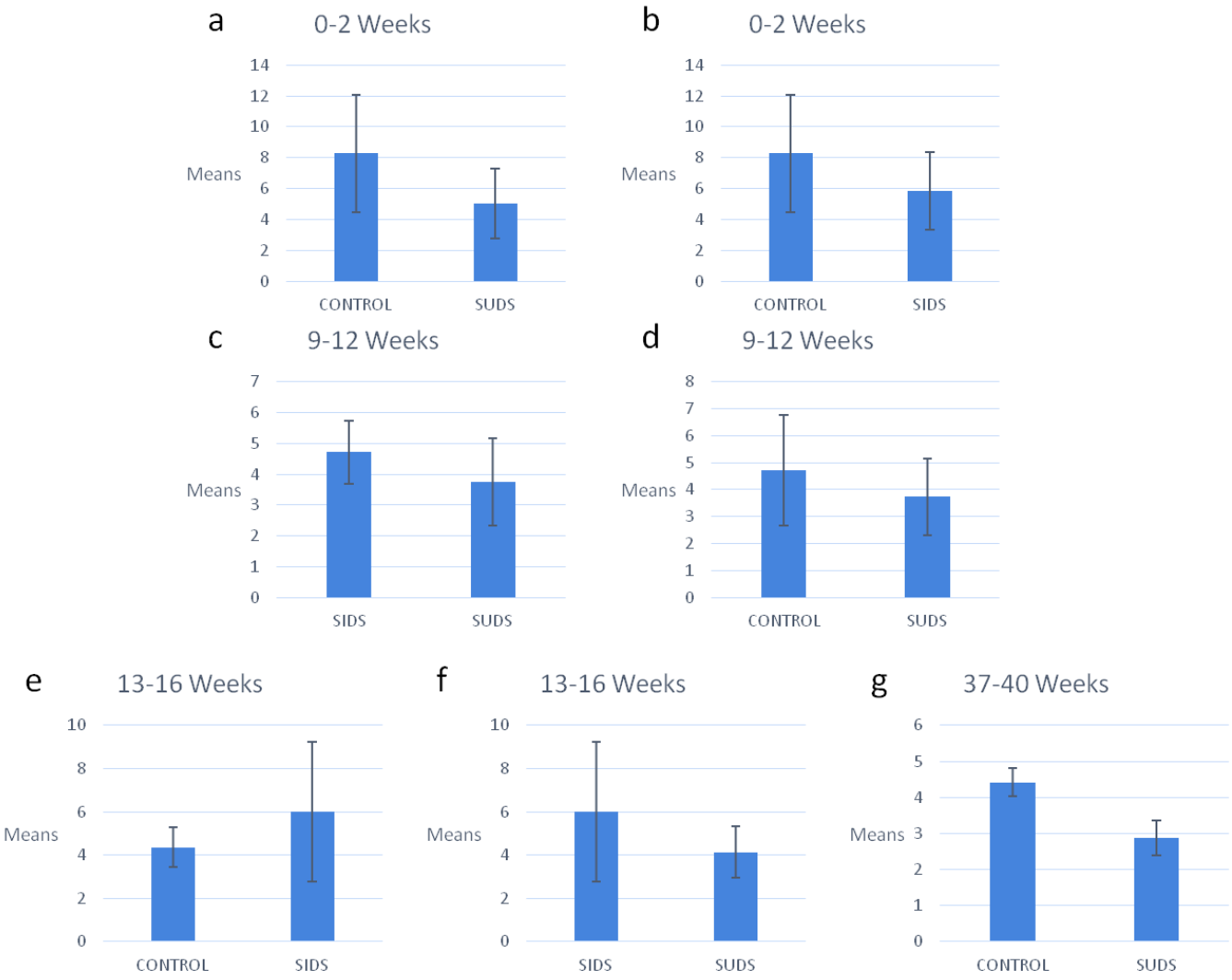

Figure 4-20. Difference in Combined Adrenal Weights between the Cause of Death Groups (Genders Combined)

The figure shows significant differences in the means of combined adrenal weights at specific age intervals between the cause of death groups (for both genders combined):

(a). Control (n=148) and SUDS (n=46) at 0-2 weeks; (p=0.00000);
(b). Control (n=148) and SIDS (n=11) at 0-2 weeks; (p=0.0259);
(c). SIDS (n=15) and SUDS (n=50) at 9-12 weeks; (p=0.0376);
(d). Control (n=24) and SUDS (n=50) at 9-12 weeks; (p=0.0130);
(e). Control (n=13) and SIDS (n=10) at 13-16 weeks; (p=0.0221);
(f). SIDS (n=10) and SUDS (n=38) at 13-16 weeks; (p=0.0024);
(g). Control (n=4) and SUDS (n=4) at 37-40 weeks; (p=0.0453).

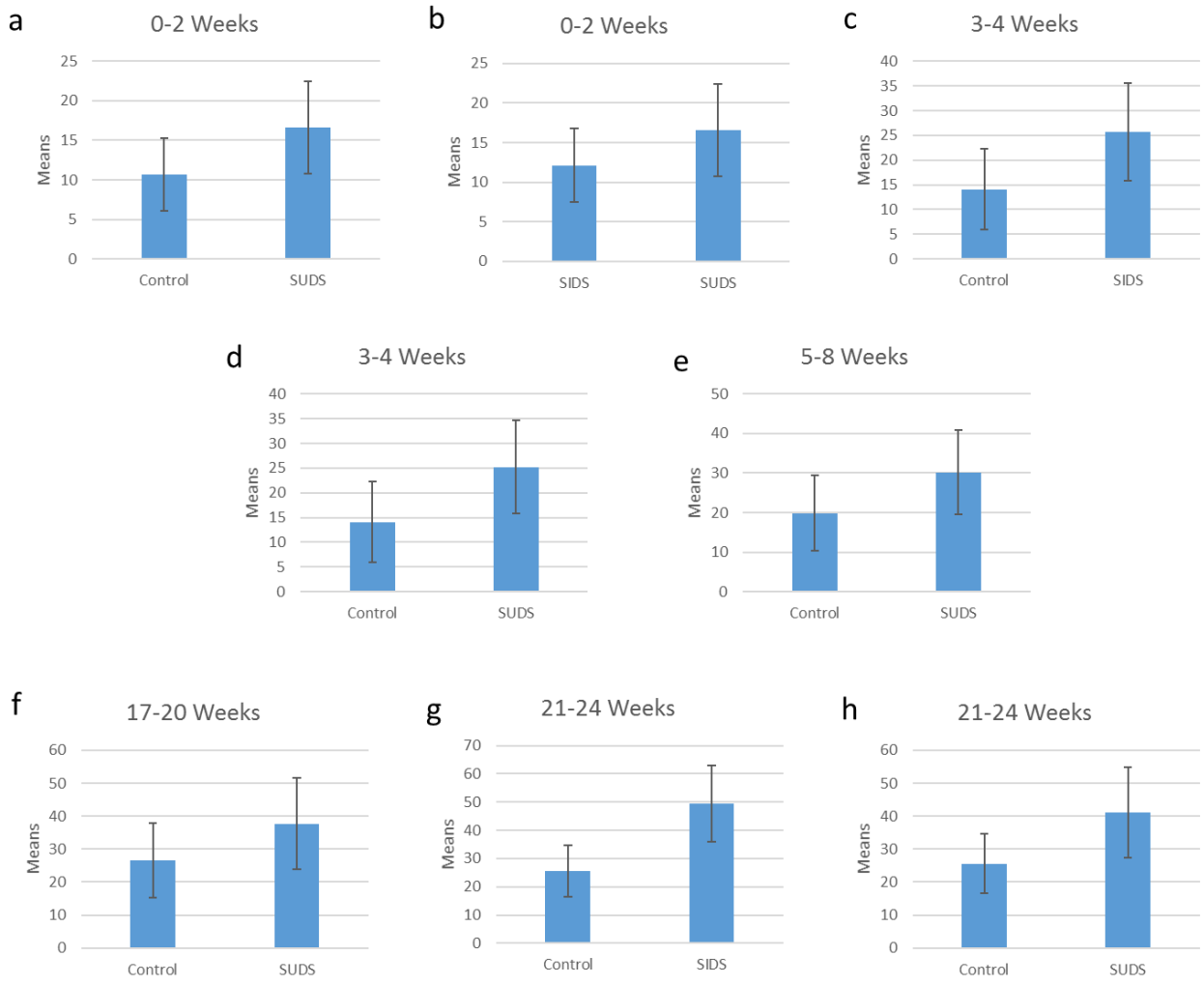

Figure 4-21. Differences in Male Thymus Weights between the Causes of Death Groups

The figure shows significant differences in the means of thymus weights at specific age intervals between the cause of death groups (for males):

(a). Control (n=88) and SUDS (n=25) at 0-2 weeks; (p=0.0000);
(b). SIDS (n=7) and SUDS (n=25) at 0-2 weeks; (p=0.0348);
(c). Control (n=9) and SIDS (n=4) at 3-4 weeks; (p=0.0432);
(d). Control (n=9) and SUDS (n=13) at 3-4 weeks; (p=0.0093);
(e). Control (n=15) and SIDS (n=25) at 5-8 weeks; (p=0.0019);
(f). Control (n=7) and SUDS (n=11) at 17-20 weeks; (p=0.00463);
(g). Control (n=7) and SIDS (n=6) at 21-24 weeks; (p=0.0026);
(h). Control (n=7) and SUDS (n=5) at 21-24 weeks; (p=0.0178).

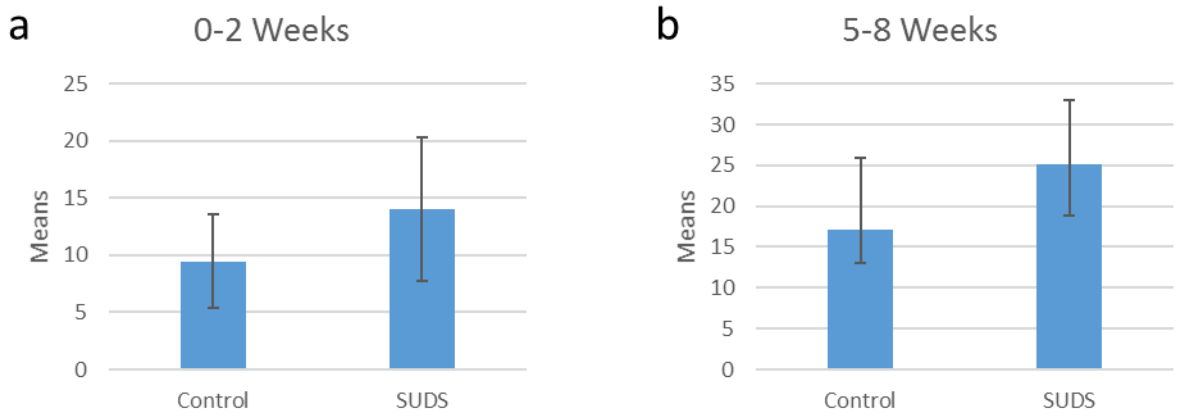

Figure 4-22. Differences in Female Thymus Weights between the Causes of Death Groups

The figure shows significant differences in the means of thymus weights at specific age intervals between the cause of death groups (for females):

(a). Control (n=72) and SUDS (n=25) at 0-2 weeks; (p=0.0001);
(b). Control (n=9) and SUDS (n=25) at 5-8 weeks; (p=0.0138).

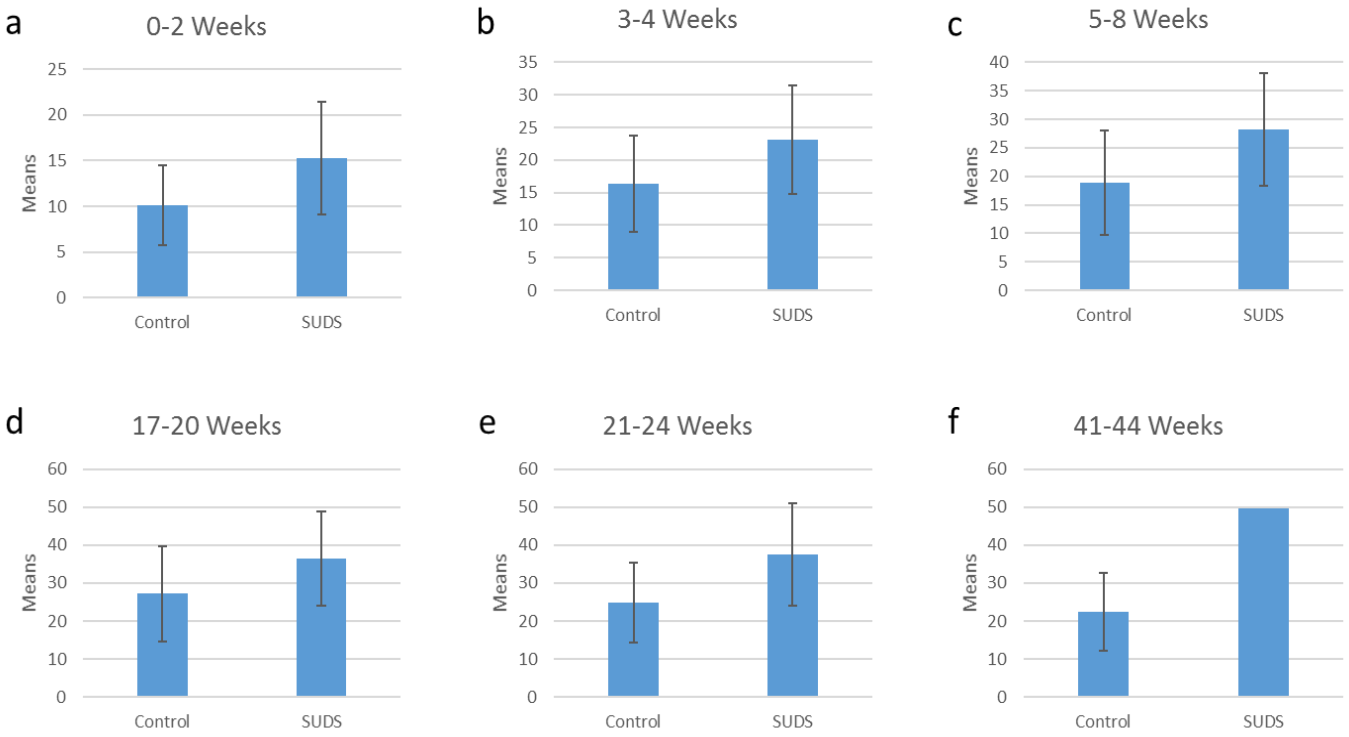

Figure 4-23. Differences in Thymus Weights between Cause of the Death Groups (Genders Combined, SUDS-Controls)

The figure shows significant differences in the means of thymus weights at specific age intervals between the SUDS and Control groups (for both genders combined):

(a). Control (n=160) and SUDS (n=25) at 0-2 weeks; (p=0.00000);
(b). Control (n=19) and SUDS (n=13) at 3-4 weeks; (p=0.0067);
(c). Control (n=24) and SUDS (n=38) at 5-8 weeks; (p=0.0001);
(d). Control (n=11) and SUDS (n=21) at 17-20 weeks; (p=0.0318);
(e). Control (n=15) and SUDS (n=16) at 21-24 weeks; (p=0.0060);
(f). Control (n=7) and SUDS (n=1) at 41-44 weeks; (p=0.0327);

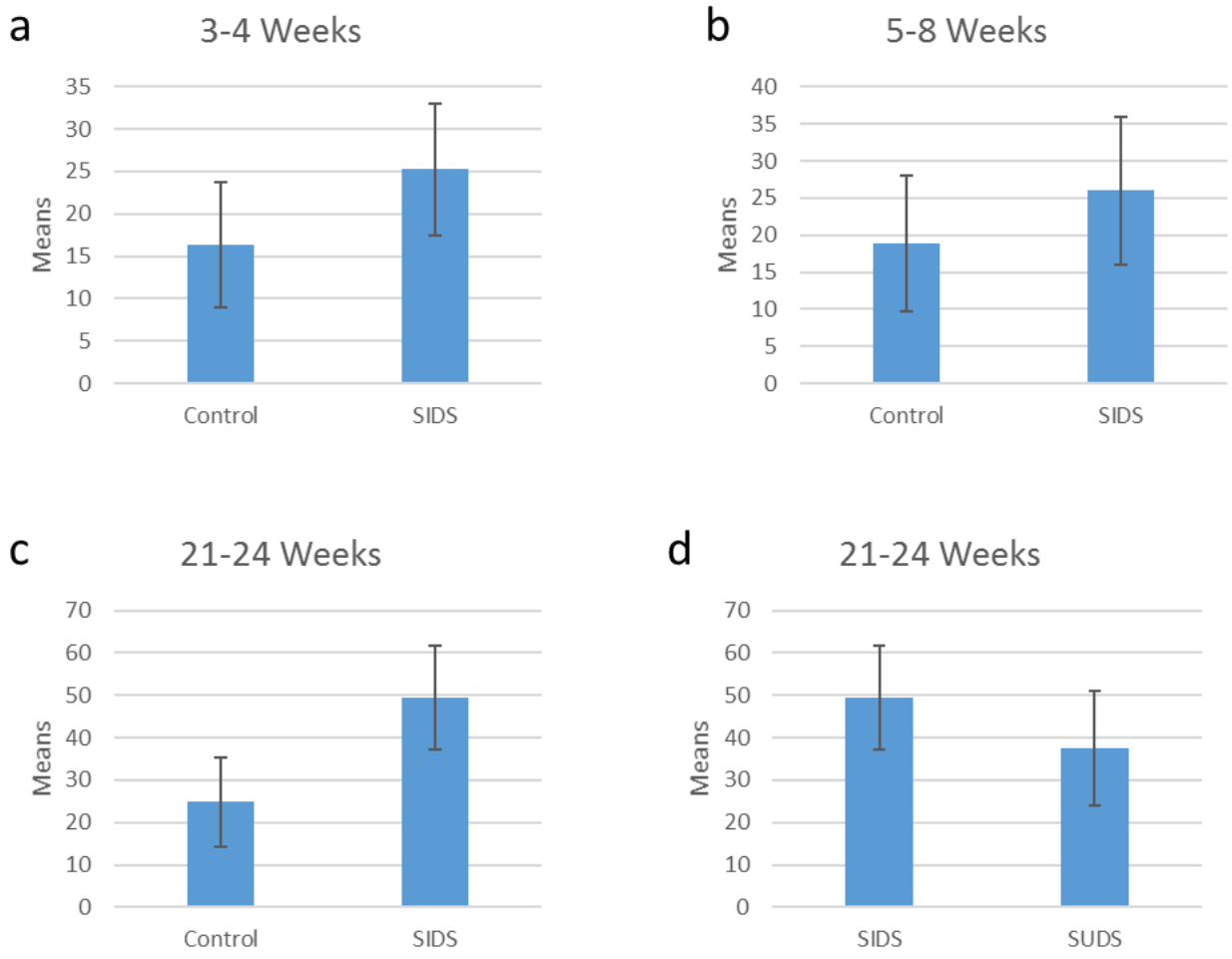

Figure 4-24. Differences in Thymus Weights between Cause of the Death Groups (Genders Combined, SIDS-Controls and SIDS-SUDS)

The figure shows significant differences in the means of thymus weights at specific age intervals between the cause of death groups (for both genders combined):

(a). Control (n=19) and SIDS (n=7) at 3-4 weeks; (p=0.0145);
(b). Control (n=24) and SIDS (n=13) at 5-8 weeks; (p=0.0339);
(c). Control (n=15) and SIDS (n=7) at 21-24 weeks; (p=0.0001);
(d). SIDS (n=7) and SUDS (n=16) at 21-24 weeks; (p=0.0398).

Chapter 5

5 Discussion

5.1 Review of Reference Resources Used by Ontario Pathologists

The objectives of the initial phase of the study were to assess the relative strengths and weaknesses of the currently available references for infant and neonate body and organ measurements used by pathologists in Ontario and to establish criteria for the development of a new reference resource. To achieve this goal, a survey of Ontario pathologists, who do coroners' pediatric autopsies, was conducted. Fourteen responders used 20 publications as references for body and organ measurements. Of all the cited sources, only 2 had all the features regarded by the pathologists as ideal for a reference source; however, both of these sources were based on older data[10,12]. These "ideal" features included: accessibility to the source; larger sample size; defined control population; statistical analyses, and gender distinctions. The results of this part of the study were used to guide the development of a new reference, based on data from the Office of the Chief Coroner for Ontario, to enhance measurement standards for pediatric autopsy practice.

5.2 Body and Organ Measurement Charts

The next objective of this study was to create Ontario population-specific organ and body measurement mean charts for infants and neonates and growth graphs for each gender. As a child grows, hyperplasia (increase in number of cells) accounts for the increase of organ and overall body size[45,124]. In the present study, most organ weights and body measurements gradually increased with age consistent with normal development of a child (**Appendix E, Figures E-1** and **E-2)**[37]. Relative to the infants aged 33-36 weeks, males and females showed decreases for most body measurements and body weights at 37-40 weeks; at this age range, male infants also had relatively smaller organs by weight **(Tables 4.2, 4.4, 4.5, Figures 5-4** to **5-7, E-1** and **E-2).** These trends could be attributed to smaller sample sizes or other confounding factors, such as cessation of breast feeding.

Most paired organs tend to show a symmetric increase with age indicating a normal growth pattern[45], which was seen in most organs in this study. The adrenal glands were an exception **(Figures 5-2** and **5-3**). Combined adrenal weight in males and females demonstrated initial decline during the first 12 weeks of life and later stabilized around 4-6 grams **(Tables 4-3** and **4-6)**. In Schulz's et al study, combined adrenal weight was fairly constant during the first year of life, ranging about 4.5 to 6.0 grams[10]. The initial decline in adrenal weight, found in the present study, can be related to the rapid regression of the fetal cortex at birth. The fetal cortex makes up to 80% of newborn adrenal gland and disappears almost completely by the age of 1st year[125]. The adrenal weight is more likely to be a subject of interobserver variability as it can be affected by the dissection techniques used by individual pathologists and their assistants. The inclusion of an excess periadrenal adipose tissue results in a greater recorded weight of an adrenal gland. Some factors that affect adrenal weight (e.g. cortical lipid depletion due to fetal stress in maternal chorioamnionitis[126]) cannot be assessed retrospectively, such as in the present study.

The thymus was the other organ that did not demonstrate steady growth instead showing a relatively erratic growth pattern **(Figures 5-2** and **5-3**). In the present study, the thymic weight increased from approximately 10 grams at birth to 30 grams by the end of the 1st year **(Tables 4-3** and **4-6)**. Similar growth patterns were observed for both genders. The thymic growth pattern was contrary to other studies that reported a gradual increase in weight reaching its near-maximum of 30 grams by 2 years of age[46,127]. In the present study, the thymus weight was found to be greater than that reported by Schulz et al, for both genders[10].

Overall, there are very limited reference sources on thymic weight. A number of factors are recognized that influence its size, for many of which it is difficult to account in retrospective studies. For instance, some studies showed a strong correlation between breast feeding and thymic weight[128,129]. In the exclusively formula-fed infants the thymus was less than half the size of the thymus in the breastfed infants, irrespective of body weight, length, gender or previous/current illness[128–131]. Acute thymic involution is a common response to stress from a prenatal (e.g. maternal chorioamnionitis) or postnatal event (e.g. infection or malnutrition in a child)[45]. The heavier weights observed for the thymus in the present study could be that there was less involution due to physical stressors (e.g. disease, malnutrition) in a more modern

population[132]. Considering that in the cases studied, the gland was normal based on the microscopic examination provided, the finding could also be attributed to accelerated thymic growth or selection bias (including cases with true thymic hyperplasia)[133].

The size disparity between male and female organ and body measurements has been reported in some studies[10,27,122]. A number of studies showed no significant differences in norms related to gender [43,112,113,115]. The present study showed some of male organs statistically larger than those of females across some age groups **(Table 4-13)**, especially heart and kidneys. The female adrenal glands, at age of 37-40 weeks, were larger than male counterparts; however, the female sample size for this age group was small (n=4) comparing to that of males (n=10), likely increasing the mean range.

The data on body weights and length when compared to previously published showed overall similar growth trends. The body weight doubled by 5 months of age and tripled by the end of the 1st year of life, as expected[37,39]. Comparison of the study population weights to a normal living population (WHO and CDC data) showed more similarity to CDC growth charts[109,134] **(Figures 5-4** and **5-5)**. For some age groups (over 20 weeks of age) the weights were lower than both WHO and CDC data which could be attributed to the smaller sample sizes for these older age groups. Both, this study and the CDC body weights were slightly lower when compared to the WHO standards. This is not surprising considering that the WHO standard source is a concept of what the norm should be in a healthy full-term infant with optimum nutrition and favorable socioeconomic conditions[135,136]. The WHO standards, as well, are based on a more diverse comparison population since the data from multiple countries are included[42,134].

The population body lengths in the present study showed an expected increase by about 25 cm during the 1st year of life (from the birth length of approximately 50 cm) and were comparable to other published data[37]**(Figures 5-6** and **5-7)**. In the present study, there was a similar tendency in head circumference growth with an exception of a “spike” in 33-36-week-old females likely related to a small size of this age group (n=3) **(Figures 5-8** and **5-9)**.

The specific organ weights of the studied population were similar to Fracasso, Vennemann et al, and the non-SIDS Thompson and Cohle data[113,115](**Figure 5-1**). The organ weights were consistently heavier than those reported by Coppoletta and Wolbach with an exception of combined kidney weights[43]**(Figure 5-1**). The organ weights were slightly higher than those published by Schulz et al, and Kayser[10,12]**(Figures 5-2** and **5-3)**. One more recent study had reported a 6% to 100% increase in individual organ weights in comparison to the Schulz et al 1962 data and attributed it to growing public awareness of healthy lifestyle, improved pre- and postnatal care, and improved medical investigations and nutrition[10,113].

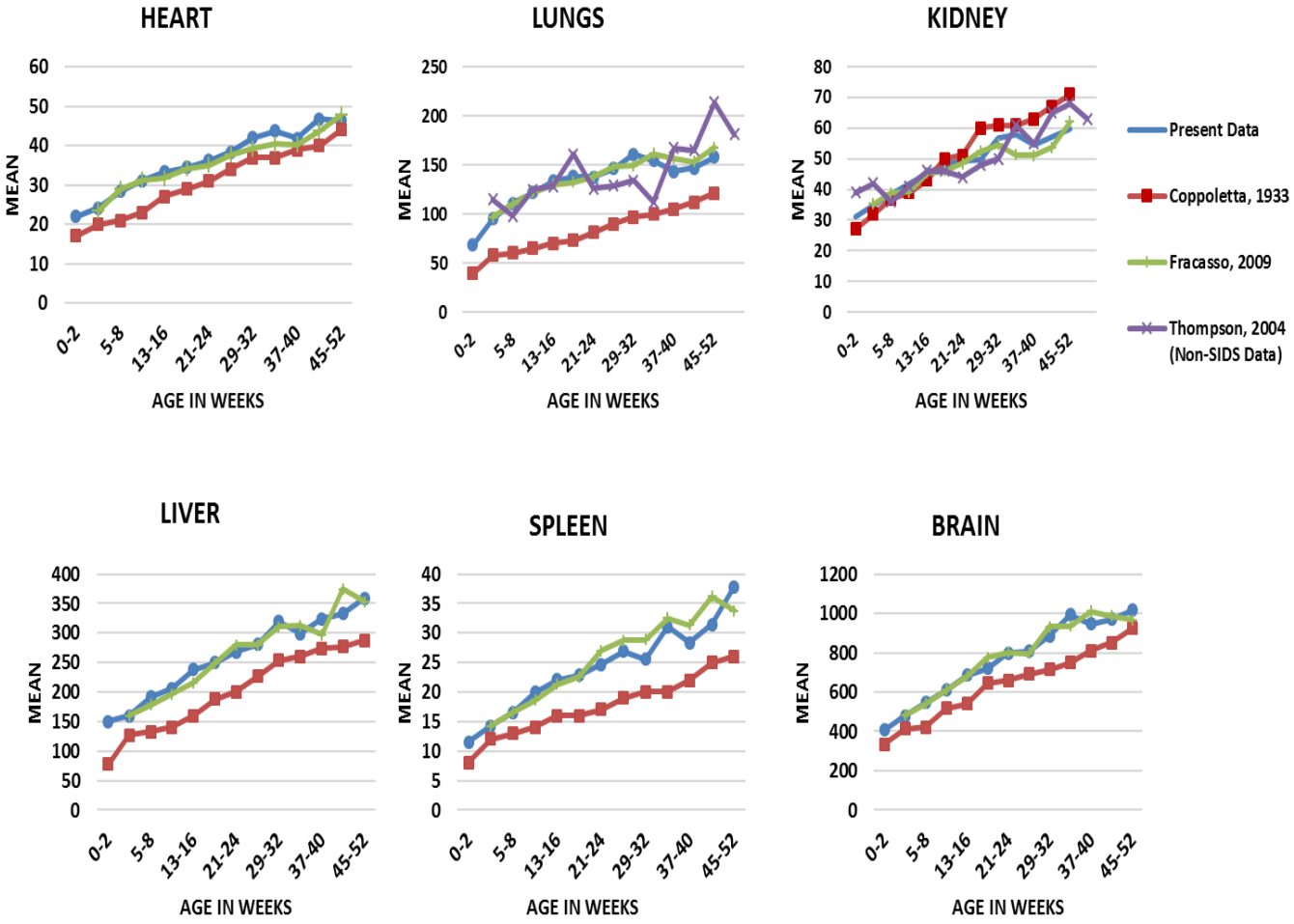

Figure 5-1. Present Data Compared to Previously Published (Combined Genders)

The specific organ weights of the studied population were similar to Fracasso et al. and non-SIDS Thompson and Cohle data. The weights were consistently heavier than those reported by Coppoletta and Wolbach with an exception of combined kidney weights. All weights in grams.

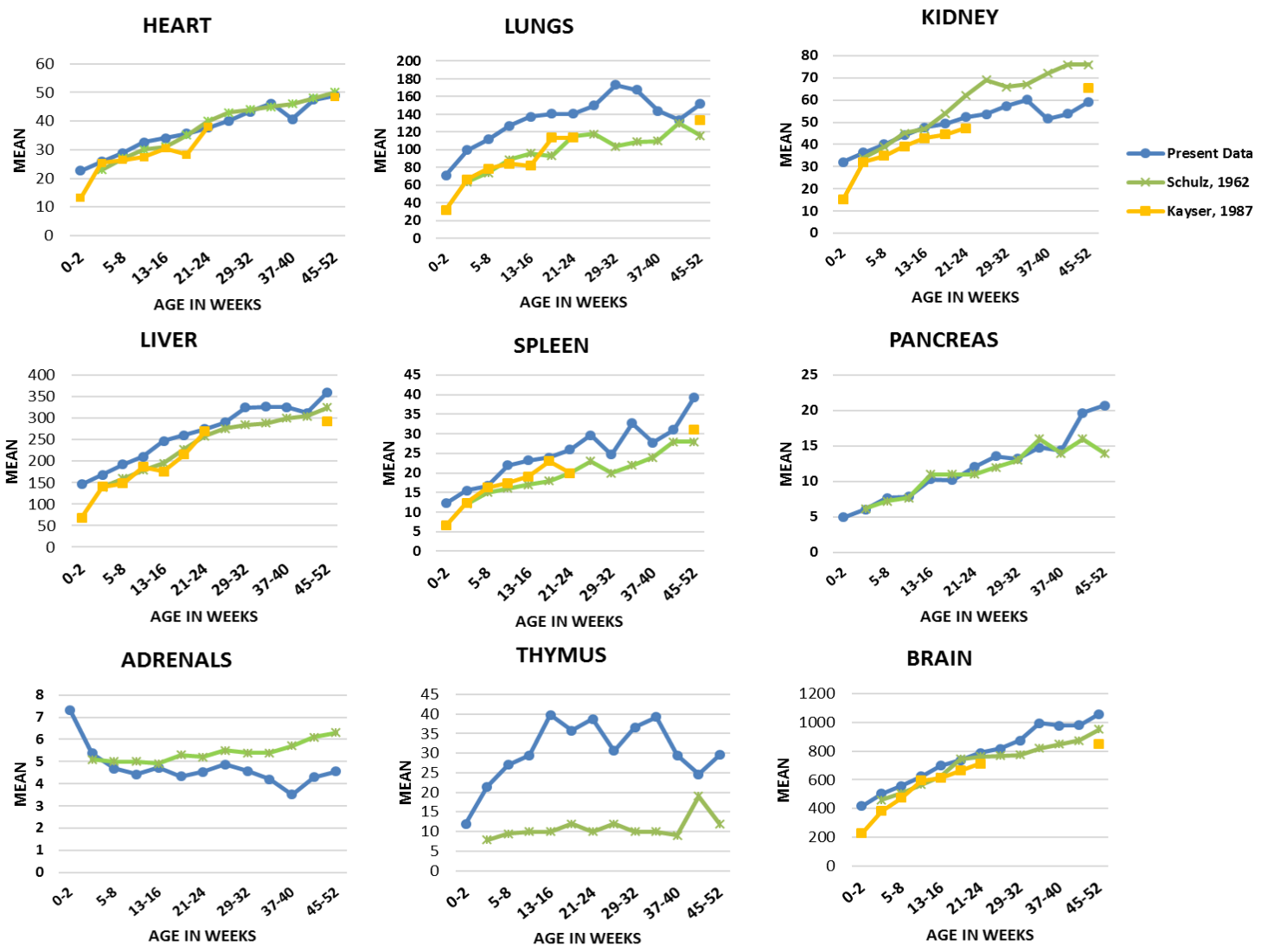

Figure 5-2. Present Study Data Compared to Previously Published Literature (Male Deaths)

The male organ weight means for adrenals and thymus differ from the previously published Schulz's et al. data. The present means for combined lung weights are larger than Kayser's data. The present data closely follows the curves for the remaining organs. All weights in grams.

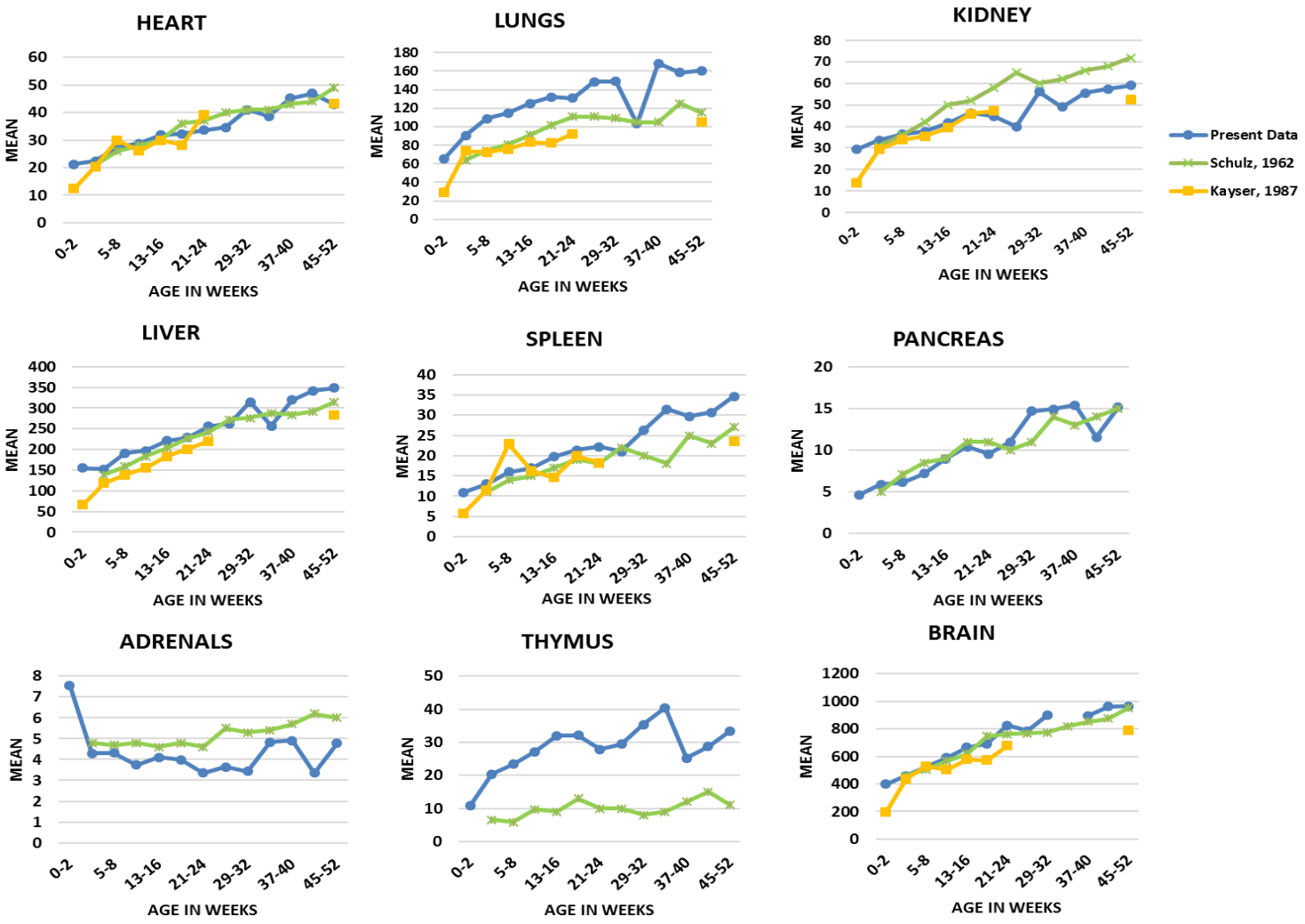

Figure 5-3. Present Data Compared to Previously Published (Female Deaths)

The female thymus and combined lung mean weights in this study were much higher than those published by Schulz et al. and Kayser while those for kidneys and adrenals were smaller. The other mean organ weights were slightly higher than those published by Schulz et al. and Kayser. All weights in grams.

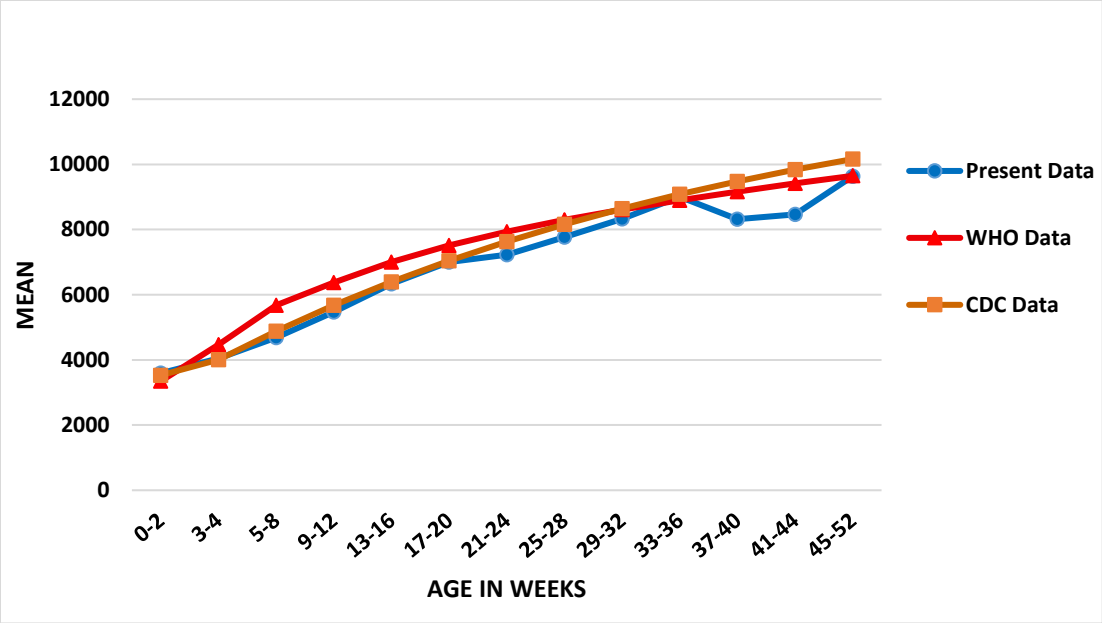

Figure 5-4. Male Body Weight Compared to the CDC and WHO Standards

Comparison of the study population male body weights to a normal living population (WHO and CDC data) shows more similarity to CDC growth charts. For some age groups over 20 weeks the weights are lower than both CDC and WHO standards. Both, this study and CDC body weights are slightly lower than WHO standards.

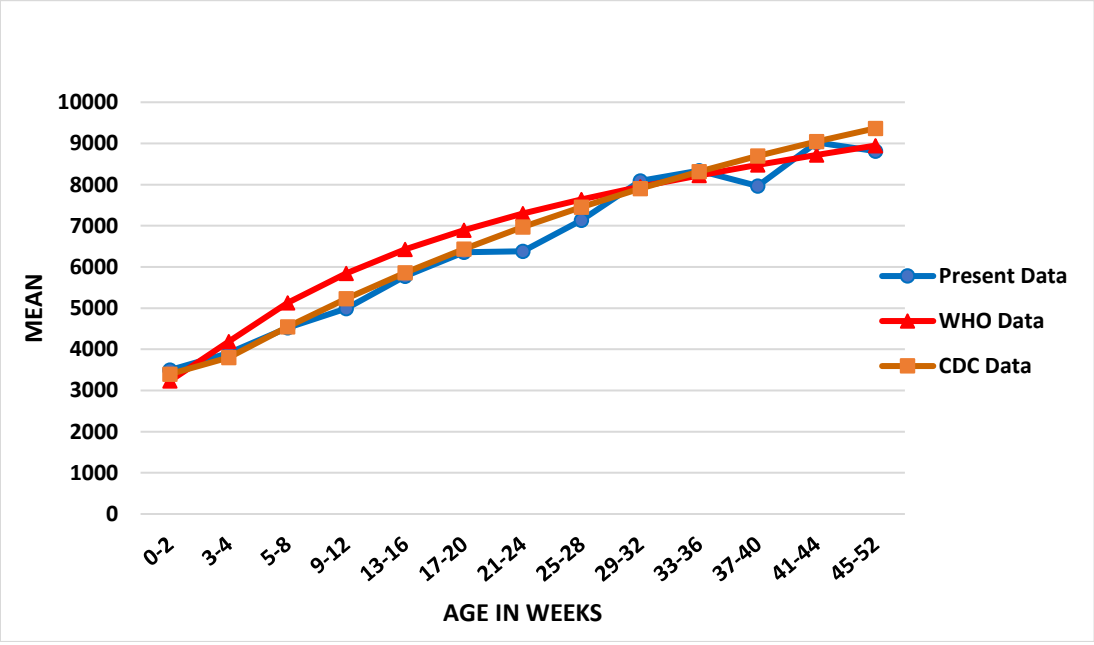

Figure 5-5. Female Body Weight Compared to the CDC and WHO Standards

Comparison of the study population female body weights to a normal living population (WHO and CDC) shows similar tendency as in the studied male population (see Figure 5-4).

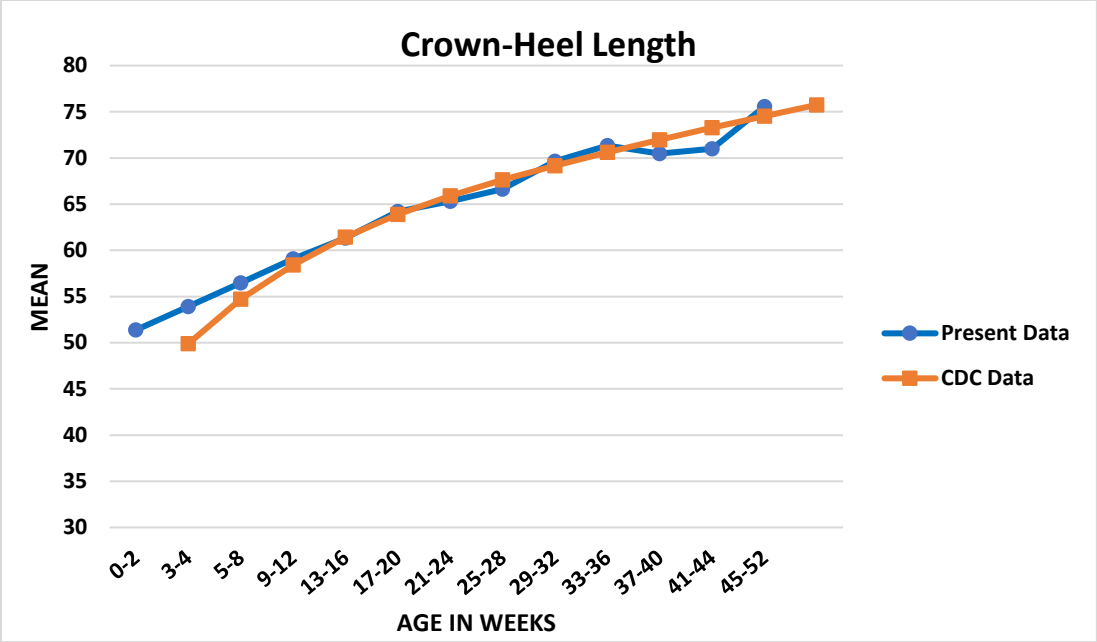

Figure 5-6. Crown-Heel Length Compared to the CDC Data (Male Deaths)

Comparison of the study population male crown-heel length to a normal living population (CDC) shows similar growth tendencies.

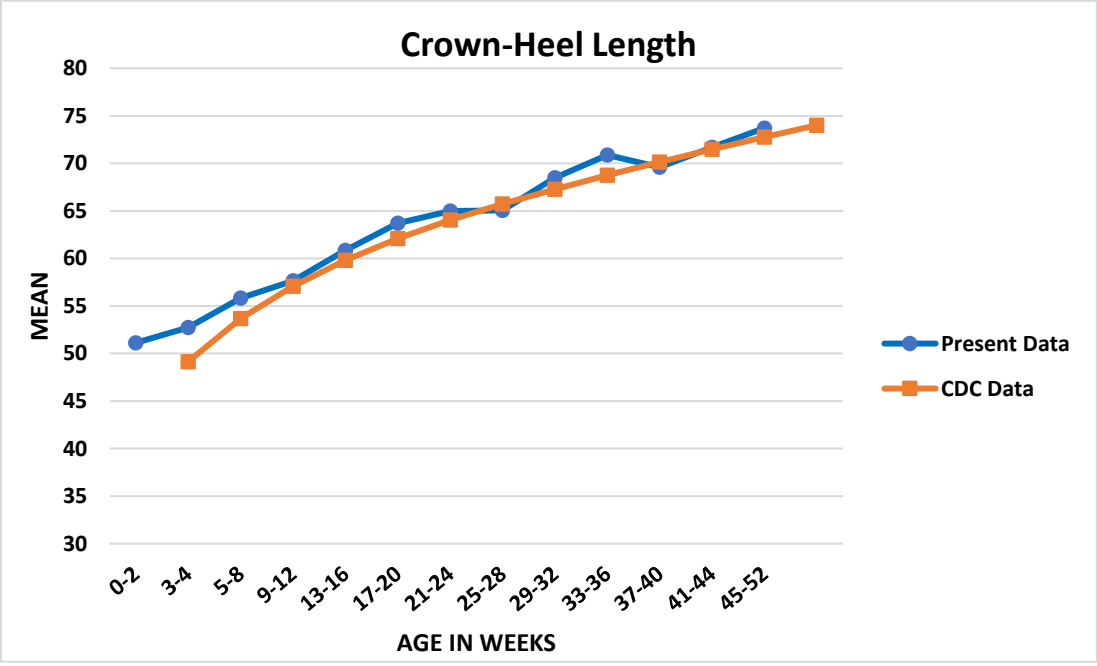

Figure 5-7. Crown-Heel Length Compared to the CDC Data (Female Deaths)

Comparison of the study population female crown-heel length to a normal living population (CDC) shows similar growth tendencies.

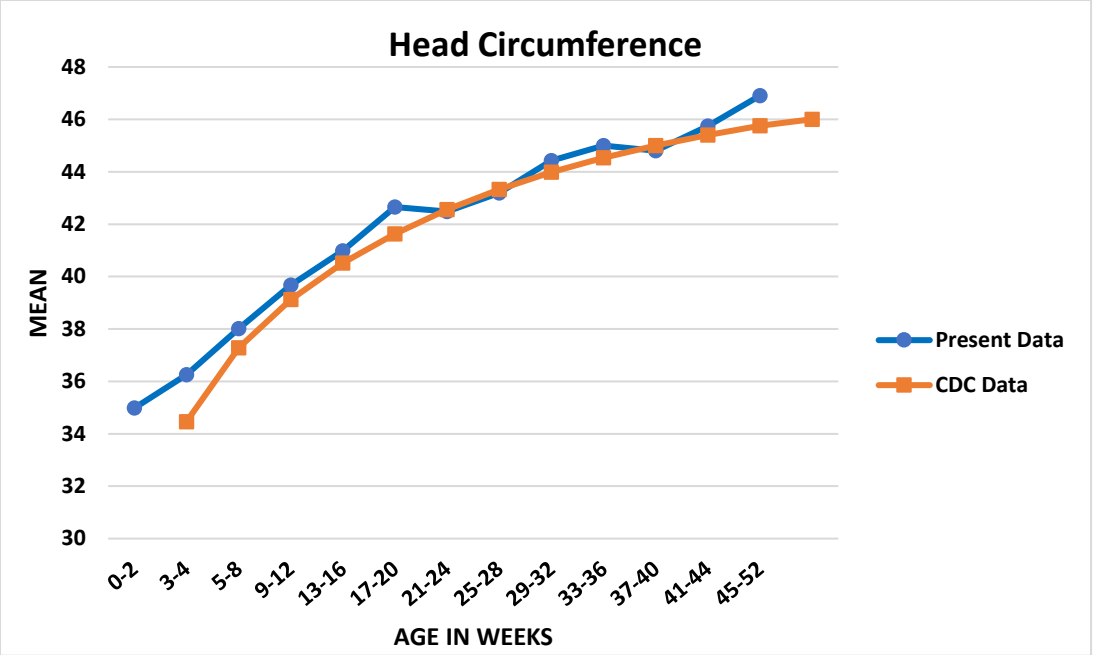

Figure 5-8. Head Circumference Compared to the CDC Data (Male Deaths)

Comparison of the study population head circumference to a normal living population (CDC) shows similar growth tendencies in males.

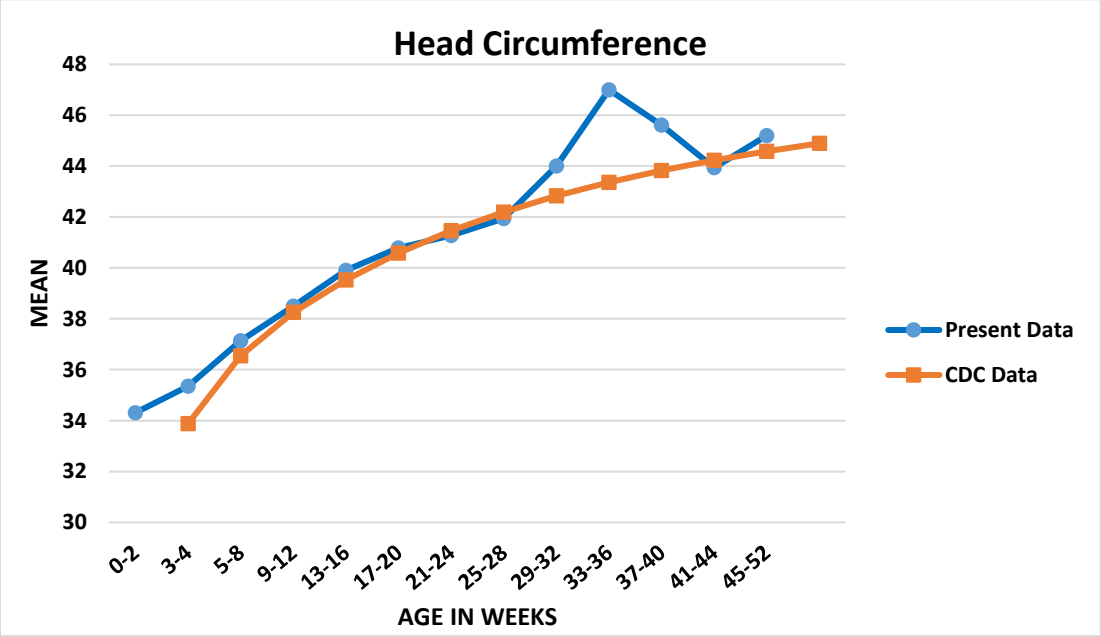

Figure 5-9. Head Circumference Compared to the CDC Data (Female Deaths)

Comparison of the female head circumference to a normal living population (CDC) shows similar growth tendencies with an exception of a "spike" at 33-36 weeks.

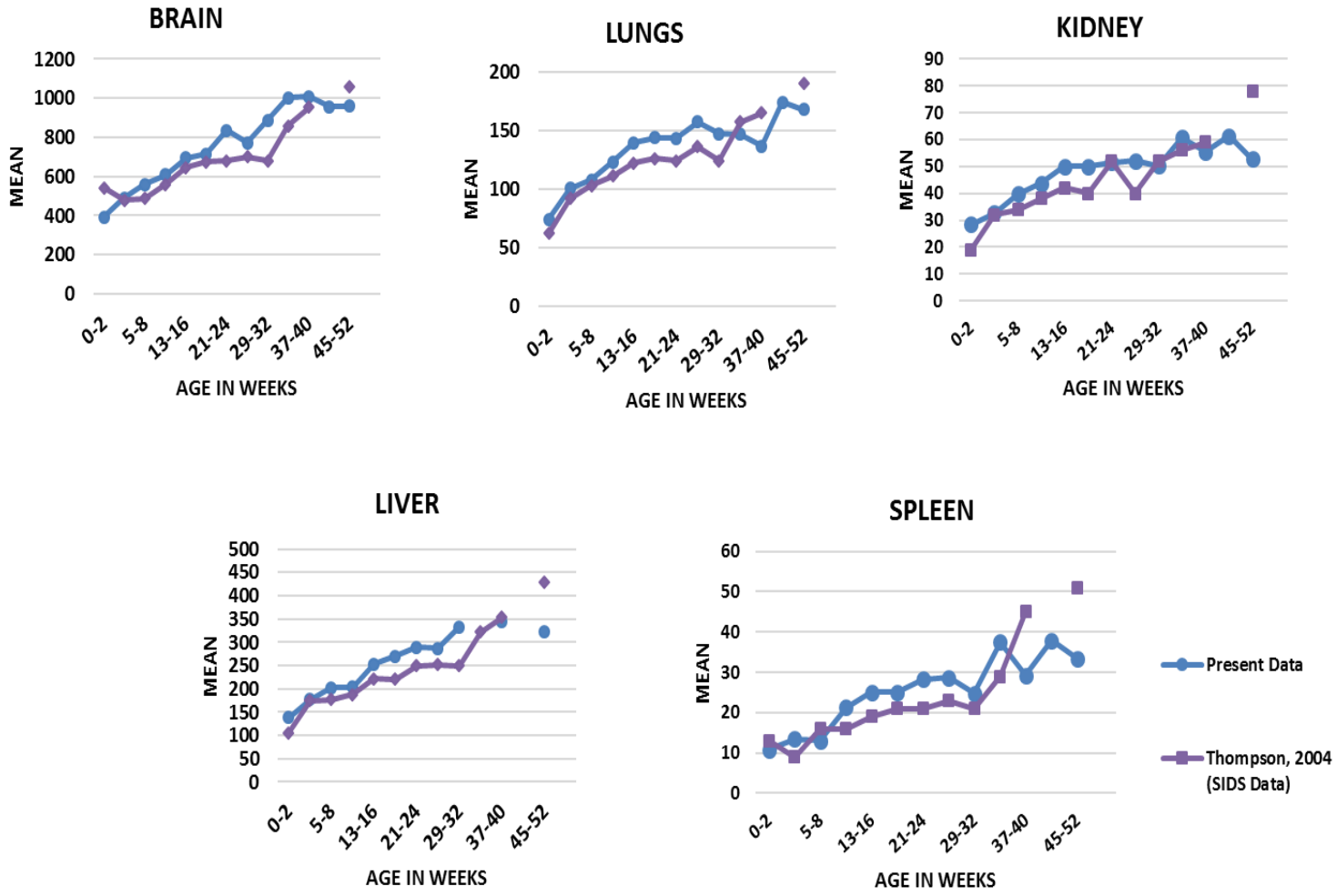

Figure 5-10. SIDS Data Compared to Previously Published Thompson and Cohle's Data (Combined Genders)

The individual organ weights in the SIDS group were similar to the data on SIDS deaths in the Thompson and Cohle's study. All weights in grams.

5.3 Body and Organ Measurements Correlated to Cause of Death

The final objective of this study was to determine if groups, based on the cause of death (SIDS, SUDS and Control groups), were different in their body and organ measurements, when accounted for age and gender.

Sudden Infant Death Syndrome is generally a diagnosis of exclusion when any anatomical, toxicological, metabolic etc. causes of death have been ruled out in the course of thorough multidisciplinary investigations. The incidence of reported SIDS varies considerably partly due to the variable use of terminology and death certification in different death investigation systems. Statistics Canada reported SIDS in 2.8% of all infant deaths in 2012[134]. According to 2014 CDC data, SIDS was the cause of 7% of infant deaths in the United States[137,138]. Ontario had recently adopted a more strict definition of SIDS excluding any case which had an unsafe sleeping environment and a background of adverse socioeconomic factors. As a result of the strict application of the definition of SIDS, of the 70 cases reviewed by the Ontario Death Under Five Committee in 2013, no SIDS cases were identified[22]. In nearly half (51%) of the cases reviewed by the committee, death occurred in the presence of sleep associated circumstances, and in less than 3% social risk factors were present (without sleep-associated circumstances).

For the purpose of this study, the cases in the database were classified as SIDS when the sleeping environment appeared safe and SUDS when any adverse sleep circumstances (e.g. unsafe sleeping surface, bed sharing with an adult) were identified. Of the 900 cases assessed, approximately 14% were classified as SIDS and 38% as SUDS. The SIDS frequency is higher than the Canadian SIDS data since it relates to a selected autopsied population only rather than infant mortality overall. The SIDS data is certainly higher than the more recent Ontario data, reflecting both the decrease in SIDS incidence and more strict definitions/guidelines in Ontario pediatric death investigations.

Strict categorization of infant deaths allows the development of strategies for further research and pediatric death prevention. Although the etiology of SIDS has yet to be identified, multiple theories have been put forth as possible mechanisms in SIDS deaths, including but

not limited to: apnea, overheating, inflammatory mechanisms, immunizations, long Q-T syndrome and other arrhythmias, seizure disorders, and complications of prematurity[48,83,139–146]. According to some studies, various metabolic abnormalities have been detected in 10% of SIDS deaths[147]. Some studies emphasized a potential role of respiratory viruses in SIDS and reported their presence in 20-45% of sudden infant deaths[148–151].

Common autopsy findings in SIDS deaths include petechial hemorrhages (e.g. pleural and thymic), pulmonary congestion and edema, effusions in various body cavities, fatty changes in the liver, positive respiratory samples for viruses or bacteria (without microscopic findings of significant infection)[152–158].

The subject of organ weights and body measurements in SIDS cases has been discussed in several previous studies, and the data are rather controversial. Some studies found no difference in the body measurements/organ weights between the SIDS and normal populations[27,113,115,159]. Other studies reported significant differences in various parameters possibly indicating a disturbance of normal growth patterns of vital organs in SIDS cases[160–163].

One study reported SIDS body weights being lower than in normal infants[160]. Another study has identified a poor postnatal weight gain to be independently associated with an increased risk of SIDS[164]. The crown-rump length and head circumference were shown not to be associated with an increased risk of SIDS[163,165].

Some studies found the brain, lungs, liver and thymus to be significantly heavier in SIDS deaths compared to the normal population[160,162,166]. Another study identified a pattern of abnormal relative size of the brain, heart, liver, and kidneys[167]. The increase in the weights of these organs relative to the total body weight among SIDS victims was approximately 3 times the increase among controls in the first year of life[167]. In contrast, the adrenal glands in SIDS infants have been shown to be smaller than normal[160,168]. Other studies showed no significant weight differences between SIDS and control infants for kidneys or pancreas[27,169].

Overall, a large number of statistically significant relationships were identified in the present study based on the cause of death, age and gender. However, number of cases in each age group had dropped significantly after 6 months of age. As a result, inferences cannot be made

from most of the relationships in the older age groups (after 25-28 weeks) due to small sample sizes. The decline in the incidence of infant deaths after 6 months reflects the natural history of SIDS with the highest incidence of death between the 1st and 6th of an infant's life[170]. SUDS incidence had decreased after 6 months, as well, due to increased physical mobility of an infant who around that age usually is able to roll, sit on his/her own, and control the upper body and arms[47]. This increased mobility lessened the risks of an unsafe sleeping environment.

The organ weights in the SIDS group in the present study were similar to the data on SIDS deaths in Thompson and Cohle's study (**Figure 5-10)**[113].

In the present study, there was no difference between the groups in relation to the body weight, heart and pancreas weights **(Tables 4-11** and **4-12)**. A study by Siebert and Hass based on 500 autopsies, reported SIDS mean body weights generally below the 50th percentile when compared to living infants[160]. The heart weights in this study showed a marginally significant increase above published norms.

From birth to the 12th week of life, the combined lung weight means were greater in SUDS than in SIDS group with the latter showing greater means than the Control group (SUDS>SIDS>Control) **(Appendix G, Table G-1)**. An exception was the combined female lung weight in 9-12 weeks age group (SIDS>SUDS>Control). From the 12th to 24th week, the female lungs showed similar tendencies being heavier in SUDS than in SIDS group, while the male lungs were heavier in SIDS group in comparison to SUDS group. The tendencies were proven statistically significant for both genders separately and combined for the age from birth to 4 weeks, females in 9-12 weeks group and males in 21-24 weeks group **(Table 4-14, Figures 4-5** to **4-7)**. Heavier lung weight in the SUDS group is most likely related to the effects of unsafe sleeping environment[171]. Although exact cause and manner of death in this group are undetermined, asphyxia is considered as potential mechanism of death since unsafe sleep factors (e.g. bed sharing, cluttered crib) might interfere with an infant's breathing and/or cause entrapment, overlaying, or suffocation. Pulmonary congestion and edema are very common findings in asphyxial deaths[171,172].

SIDS lungs were heavier than controls for all age groups and both genders, except in females in 13-16 and 21-24 weeks age groups; however, each of these groups had small sample size **(Appendix G, Table G-1)**. These observations were statistically significant for 3-4-week-old males and both genders combined, 9-12-week-old females and 21-24-week-old males **(Table 4-14, Figure 4-5** to **4-7)**. Although exact mechanisms of SIDS deaths are uncertain, some studies reported pulmonary congestion and edema and minor microscopic inflammatory infiltrates in the lungs of SIDS victims[160,173].

One study reported SIDS kidneys to be smaller than controls and hypothesized that delayed kidney growth may be an indicator of increased risk of SIDS in infants under 1 year[174]. Another study has found reduced glomerular numbers in SIDS subjects with both normal and low birth weights[175]. In the present study, there was no significant difference between SIDS and control kidney weights for all age groups and both genders (separately and combined) **(Table 4-15, Figures 4-8** to **4-10)**. SUDS kidneys were significantly lighter than SIDS for females at 9-12 weeks and for males and genders combined at 13-16 weeks. The SUDS kidneys were significantly lighter than controls in females at 3-4 weeks. One study reported that low birth weight was associated not only with small kidneys at birth and decreased nephron numbers but with impaired kidney growth in early childhood. The study suggested that intrauterine growth had a regulatory influence on nephron formation and renal function in humans reaching beyond the neonatal period[176]. Some studies reported decreased kidney weight in cases of prenatal hypoxia[177,178].

There was no difference between SIDS and SUDS liver weights for all age groups and both genders (**Table 4-16)**. Although the mean liver weights were higher in SIDS and SUDS groups when compared to the controls for most age groups below 25 weeks (for each gender separately and combined) **(Appendix G, Table G-3)**. The difference was significant for: SUDS vs. Control for females and genders combined at 3-4 weeks and SIDS vs. Control for males and genders combined for 17-20 weeks **(Figures 4-11** to **4-13)**. Common causes of hepatomegaly in children under 1 year of age who die include hepatic congestion and fatty changes. Both are nonspecific findings and have been reported in autopsies of SIDS and SUDS infants[160]. Increased liver weight in SIDS deaths could be, as well, due to undiagnosed fatty acid oxidation or other metabolic disorders[179,180]. Postmortem diagnosis of fatty acid

oxidation might be difficult. True prevalence of these cases among SIDS is unknown. Female SIDS livers in this study were significantly smaller than controls during the first 2 weeks of life **(Figure 4-12)**, a finding of uncertain significance.

Male brains showed no weight difference between the age groups and cause of death groups. SUDS brains were significantly heavier than controls in females younger than 2 weeks and for combined genders in this age group **(Table 4-17, Figures 4-14** and **4-15)**. In 9-12 weeks age group, both SIDS and SUDS female brains were significantly heavier than controls **(Figure 4-14)**. Heavier brains in infants who died in unsafe sleeping environment could be related to hypoxic-ischemic effects of asphyxia on the brain leading to cerebral edema[172,181,182]. The role of brain weight in etiology of SIDS is controversial. One study showed a trend towards higher brain-body weight ratios in SIDS infants, which, however, failed to reach significance[165]. In another study, brain weights in SIDS cases were significantly greater than published norms[160].

SIDS spleens showed a tendency of being smaller than controls at 0-8 weeks and larger than controls at 9-28 weeks for males, females and combined genders (except 13-20-week-old females who showed smaller than controls spleens) **(Appendix G, Table G-5)**. Only for the 13-16 weeks age male group SIDS>Control relationship was proven to be significant **(Table 4-18, Figure 4-16**). SUDS spleens showed a tendency of being larger than controls in males and genders combined at 0-16 and 21-24 weeks and smaller than controls at 17-20 weeks **(Appendix G, Table G-5)**. The SUDS>Control and SUDS>SIDS relationships were proven to be significant for 5-8 weeks for combined gender group **(Figure 4-17)**. SUDS spleens tended to be larger than controls in 0-2- and 5-12-week-old females and smaller than controls in 3-4-week and 13-24-week-old females **(Appendix G, Table G-5)**. None of female relationships reached the established significance level.

Splenomegaly (increased spleen size/weight) can be attributed to undiagnosed infections, increased blood flow (hyperemia), reduced venous flow (congestion) or coexistent liver disease. In some animal models, excessive polycythemic response to hypoxic exposure was linked to profound splenic erythropoiesis[183,184]. Hypoxic mechanisms arising from an unsafe sleep environment in SUDS could be responsible for splenic enlargement. In addition, around

5-8 weeks of life, an infant receives his/her first immunization (including *Diphtheria*, *Tetanus*, *Pertussis*, *Polio*, *Haemophilus Influenzae* type B, Pneumococcal Conjugate 13, and Rotavirus vaccines)[185]. The spleen at this age shows an increase in size/weight due to an immune reaction to the above vaccines[186]. This could explain larger spleens after 9 weeks of age in the present study.

Overall, the mean values for combined adrenal glands in SUDS cases were smaller than controls for all age groups (below 25 weeks) when genders were combined and for most of the age groups for males and females **(Appendix G, Table G-6)**. This relationship was significant ($p<0.05$) for combined genders at 0-2 and 9-12 weeks age groups, for 0-2 week-old males and females and for 9-20-week-old females **(Figures 4-18** to **4-20)**.

At 13-16 weeks, the mean values for combined adrenal glands in SIDS group were greater than controls, for either gender **(Appendix G, Table G-6)**. The tendency was significant when the genders were combined **(Table 4-19, Figure 4-20)**. In 0-2-weeks age group, SIDS deaths showed smaller adrenals than in controls (relationship was significant for females and genders combined). Although in the remaining age groups, the SIDS means for the adrenals showed a tendency of being smaller than the controls, these differences did not reach the pre-established significance level.

The authors in one study found a uniform decrease in adrenal weights, but their calculated slopes of linear regressions were low, hampering statistical analysis[160]. Another study of 146 SIDS cases found a normal maturation of the adrenal glands in SIDS cases[187]. Although some morphological alterations were noted (e.g. a focal lipid depletion in the zona fasciculata, hyperemia, siderosis, and calcifications), they were similar to the control cases, and none of them explained the sudden death of the infants in this series.

Small (hypoplastic) adrenal glands are seen in cases of congenital adrenal hypoplasia. This condition can cause acute adrenal insufficiency resulting in a sudden death. Frequently, no specific pathological changes are found at autopsy, and diagnosis is confirmed with genetic testing[188–190]. This condition typically presents in infancy and more commonly affects males

since one variant is X-linked[191,192]. Some of the lower adrenal weights in the present SIDS cases could represent undiagnosed cases of congenital adrenal hypoplasia.

A subset of SIDS adrenals is this study (age group 13-16 weeks) was heavier than controls. Some of larger adrenal glands could represent cases of undiagnosed congenital adrenal hyperplasia (CAH). The latter is reported as cause of unexplained infant death resembling SIDS. CAH can present with adrenal crisis characterized by cardiovascular collapse typically in the first month of life or more rarely in mid infancy[168]. Cases of CAH can be identified by metabolic screening. While the classical salt-wasting form is easier to diagnose in females (by characteristic ambiguous genitalia), male infants have normal appearing external genitalia at birth and are more likely to be undiagnosed. Chronic stress is another condition which was shown to induce adrenal hyperplasia and hypertrophy in specific-zone distribution leading to increased adrenal weight[132].

Adrenal glands in SUDS group were smaller than SIDS adrenals in 9-12 and 13-16-weeks age groups for genders combined **(Figure 4-20)**. It coincides with a peak in SUDS deaths **(Figures 4-3** and **4-4)**. The possible explanation is that the children in an unsafe sleep environment might be predisposed to sudden death because their smaller adrenals have impaired reserves to respond to stress.

Overall, the mean values for thymus in both SIDS and SUDS groups were greater than controls for all age groups (below 25 weeks) for either gender and genders combined [with an exception of 13-16-week-old female SIDS cases: their thymuses were smaller than controls but sample size for this group was small (n=3)]. **(Appendix G, Table G-7)**. SUDS>Control relationship was significant ($p<0.05$) for combined genders and males at 0-8 and 17-24 weeks age groups, for 0-2- and 5-8-week-old females **(Table 4-20** and **Figures 4-21** to **4-24)**. SIDS>Controls relationship was proven significant for combined genders at age of 3-8 and 21-24 weeks and 3-4- and 21-24-week-old males. For 0-2 week-old males, SUDS thymuses were significantly heavier than SIDS **(Figure 4-21)**.

Some studies reported thymic weight in SIDS cases to be greater than in controls[115,160,166]. Another study found no difference between SIDS and control thymuses[113]. The older concept

of status tymico-lymphaticus (pathological enlargement of thymus in SIDS cases) is long abandoned. One study suggested that thymic size in SIDS infants who were usually previously healthy was more representative of the living infant population than weights in infants dying of other causes who may have been exposed to various thymolytic factors[11]. It is possible that the control thymuses in this study were smaller for the same reasons.

5.4 Limitations

The retrospective nature of this study meant that the standardized case data pertaining to detailed information about the circumstances of a child's demise, and the associated social and maternal history were sometimes lacking. This deficiency could potentially lead to an underestimation of the role of adverse sleeping environments and socioeconomic factors in the deaths of the infants studied.

In addition, a lack of uniform autopsy dissection techniques and measuring equipment used at different sites in Ontario could inadvertently result in an interobserver variability in recording various measurements. Measurements with fairly standard measuring techniques and not requiring dissections (e.g. body length and various body circumferences), showed less interobserver variability and smaller standard deviations. Lack of documentation of specific measurements reduced sample sizes for some organs and affected statistical analyses. For example, pancreatic weights were documented in 672 cases, thyroid weights in 163 cases and body lengths in 890 of 900 cases. The variability of histological sampling of organs and diagnostic interpretation meant that disease and/or pathophysiological processes affecting organ weights could not always be assessed.

The third major limitation of this study was the sample size, especially evident in the older age groups. Further assessment with a larger sample size particularly in the 6-month to 1-year age groups would provide a better understanding of the overall trends.

Although, an attempt was made to create a reliable control group limiting it to the cases or individual organs uninvolved by any pathological process, such standardization is suboptimal in the context of a retrospective study. A prospective study with standardized autopsy

techniques and documentation would assure a more strict selection process. Moreover, the simple elimination of the affected/deceased organ from the database was previously criticized as artificial since it did not take into account the systemic implications of the illness[115]. In this study, an attempt was made to carefully evaluate individual organs and to exclude all organs apparently affected by pathological processes, whether related or unrelated to the cause of death. A control group based on healthy infants who died rapidly as a result of accidents or homicides with no resuscitation might be a better alternative in standardizing organ weights, but the prevalence of these manners of death in the first year of life is very low.

Chapter 6

6 Conclusions

Although Canada has significantly reduced infant mortality over the last few decades, the rate continues to be relatively high considering the country's level of socioeconomic development. Sudden death in infants is a major mortality category in children younger than 1 year. Ontario recently adopted a more strict defintion of SIDS, which excludes unsafe sleep environoments and adverse socioeconomic factors. If these factors are evident during a death investigation, then the case can be classified as SUDS. This new infant death categorization assists in the standardization of classifying the cause and manner of death as well as death prevention. In the present study, over one third of the deaths were SUDS and about 14% were SIDS.

The first objective of the present study was to assess the currently available autopsy references on infant and neonate body and organ measurements. A survey of Ontario pathologists and literature review revealed that many of the currently used reference resources were outdated, contained small sample sizes, had limited age intervals, and lacked statistical information. Many reference sources were lacking well-defined control groups and descriptions of exclusion criteria.

The second objective of this study was to create Ontario population-specific organ and body measurement mean charts for infants and neonates as well as growth graphs for each age category. Based on the review of the strengths and weaknesses of the currently available reference sources, a new reference resource for the body and organ measurements of neonates and infants has been developed. This resource is based on an Ontario population database derived from the Office of the Chief Coroner. The database consists of a larger sample size with defined control groups, provision of standard deviations, p-values, and gender distinctions.

When compared to previously published literature, data in the present study showed similar growth trends, although organ weights tended to be heavier than in the older series. In contrast, adrenal glands diminished in size in the first 3 months of life, and thymus weight,

although increasing, was more erratic in its growth. The body weight and length data had more similarities to the CDC than the WHO growth standards.

The third objective of the study was to determine if there were any differences in the body and organ measurements based on the cause of death. Overall, a number of statistically significant relationships were identified based on the cause of death, age, and gender. The size disparity between male and female organs was most significant for the heart and kidneys across most of the age groups. The tendencies in growth patterns between SIDS, SUDS, and Control groups demonstrated somewhat complex patterns across various age groups and between the genders. There was no difference between the cause of death groups in relation to the weight of the body, heart or pancreas. The lungs, brain, liver, spleen and thymus tended to be heavier in SIDS and SUDS cases compared to the Control group, while adrenal glands and kidneys had a tendency of being smaller.

Heavier lung weights in SUDS cases were likely related to the effects of unsafe sleeping environments where asphyxia with resultant pulmonary edema was among the potential mechanisms of death. Heavier lung weights in SIDS cases could be related to terminal pulmonary congestion and edema or undiagnosed natural disease. Cerebral edema in settings of an unsafe sleeping environment could explain heavier brain weights in some SUDS cases. Increased liver weights in SIDS and SUDS groups could be attributed to hepatic congestion, hypoxia- induced fatty changes or undiagnosed fatty acid oxidation, and other metabolic disorders. Lower kidney weights in both SIDS and SUDS groups could be related to renal growth restriction in the settings of intrauterine hypoxia or effects of prematurity. Although there was a tendency for SIDS and SUDS thymus weights to be heavier, this trend could be relative, because the thymus in the control infants could have involuted secondary to natural disease.

The data revealed that SUDS cases for both genders peaked in the approximately 5-16-weeks age group. In the analysis of organ weights, the adrenal glands were smaller in the 9-16-weeks age group. This suggests that a child placed in an unsafe sleeping environment may be less able to deal with consequent physical stress in this setting. Also of interest was that children aged 5-8 weeks had relatively enlarged spleens in the SUDS group. Hypoxic

mechanisms arising from usafe sleeping conditions could be responsible for splenic enlargement.

This study further emphasized the need for standardization of the classification as well as investigative and autopsy approaches to sudden infant deaths, specifically SIDS and SUDS cases with adverse sleep and social environments. Further standardization of pediatric autopsy practice will assist in the advancement of more refined research on the causes and mechanisms of sudden death in young children.

References

1. Statistics Canada, Canadian Vital Statistics B and DD. *Deaths: Table 4-1 — Deaths by Age Group and Geography — Both Sexes*.; 2012.
2. World Health Association. Children: reducing mortality. WHO. http://www.who.int/mediacentre/factsheets/fs178/en/. Published 2016. Accessed June 8, 2016.
3. Statistics Canada. Table 051-0013. *Table - 051-0013 - Estimates of Births, by Sex, Canada, Provinces and Territories. CANSIM (Database).*; 2015.
4. The Conference Board of Canada. Infant Mortality. http://www.conferenceboard.ca/hcp/details/health/infant-mortality-rate.aspx. Published 2016. Accessed June 8, 2016.
5. Statistics Canada. *Deaths – 2009 Deaths by Age Group and Geography — Both Sexes Statistics Canada – Catalogue No . 84F0211X Deaths – 2009 Table 4-1 – Continued Deaths by Age Group and Geography — Both Sexes Statistics Canada – Catalogue No . 84F0211X*.; 2012.
6. Government of Canada PHA of C. Safe Sleep for Your Baby brochure - Public Health Agency of Canada. March 2010. http://www.phac-aspc.gc.ca/hp-ps/dca-dea/stages-etapes/childhood-enfance_0-2/sids/ssb_brochure-eng.php. Accessed January 11, 2016.
7. Government of Canada PHA of C. Joint Statement on Safe Sleep: Preventing Sudden Infant Deaths in Canada - Public Health Agency of Canada. June 2011. http://www.phac-aspc.gc.ca/hp-ps/dca-dea/stages-etapes/childhood-enfance_0-2/sids/jsss-ecss-eng.php. Accessed January 11, 2016.
8. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? *Lancet*. 2005;365(9462):891-900.
9. Bryce J, Boschi-Pinto C, Shibuya K, Black R. WHO estimates of the causes of death in children. *Lancet*. 2005;365(9465):1147-1152.
10. Schulz DM, Giordano DA, Schulz DH. Weights of organs of fetuses and infants. *Arch Pathol*. 1962;74:244-250.
11. Stocker J, Dehner L. *Pediatric Pathology.* 2nd Editio. Philadelphia: Lippincott Williams & Wilkins; 1940.
12. Kayser K. *Height and Weight in Human Beings: Autopsy Report*. (Oldenbourg, ed.). Munich: Verlag für angewandte Wissenschaften; 1987.
13. Wigglesworth J. *Textbook of Fetal and Perinatal Pathology*. Boston: Blackwell Scientific Publication; 1991.
14. American Academy of Pediatrics Task Force on Sudden Infant Death Syndrome. The changing concept of sudden infant death syndrome: diagnostic coding shifts, controversies regarding the sleeping environment, and new variables to consider in reducing risk. *Pediatrics*. 2005;116(5):1245-1255.
15. Gilbert-Barness E. *Potter's Pathology of the Fetus, Infant, and Child*. Mosby Elsevier; 2007.
16. Loughrey CM, Preece MA, Green A. Sudden unexpected death in infancy (SUDI). *J Clin Pathol*. 2005;58(1):20-21.
17. Côté A, Russo P, Michaud J. Sudden unexpected deaths in infancy: what are the causes? *J Pediatr*. 1999;135(4):437-443.
18. Gilbert-Barness E, Spicer DE, Steffensen TS. *Handbook of Pediatric Autopsy Pathology*. Totowa, NJ: Humana Press; 2005.
19. Willinger M, James LS, Catz C. Defining the sudden infant death syndrome (SIDS): deliberations

of an expert panel convened by the National Institute of Child Health and Human Development. *Pediatr Pathol*. 1991;11(5):677-684.

20. Moini J. *Introduction to Pathology for the Physical Therapist Assistant*. Boston: Jones & Bartlett Learning; 2013.

21. Office of the Chief Coroner. Paediatric Death Review Committee and Deaths Under Five Committee Annual Report 2015. http://www.mcscs.jus.gov.on.ca/english/Deathinvestigations/OfficeChiefCoroner/Publicationsreports/PDRC_2015.html. Published 2015. Accessed January 21, 2016.

22. Office of the Chief Coroner for Ontario. *Paediatric Death Review Committee and Deaths Under Five Committee Annual Report 2013*. http://www.mcscs.jus.gov.on.ca/sites/default/files/content/mcscs/docs/ec163306.pdf. Accessed June 8, 2016.

23. Ministry of Community Safety & Correctional Services. Death Investigation. http://www.mcscs.jus.gov.on.ca/english/DeathInvestigations/Ourcommitment/DI_Strat_plan_15_20.html. Published 2016. Accessed June 8, 2016.

24. Ministry of Community Safety and Correctional Services. Common questions about death investigations. http://www.mcscs.jus.gov.on.ca/english/DeathInvestigations/CommonQuestionsAboutCoronersInvestigations/OCC_common_questions.html. Accessed January 11, 2016.

25. The Honourable Stephen T. Goudge. *Inquiry into Pediatric Forensic Pathology in Ontario*. Toronto; 2008.

26. Forensic Pathology Unit Office of the Chief Coroner. *Guideline On Autopsy Practice for Sudden Unexpected Deaths of Infant and Children Under 5 Years*. Toronto; 2014.

27. Pryce JW, Bamber AR, Ashworth MT, Kiho L, Malone M, Sebire NJ. Reference ranges for organ weights of infants at autopsy: results of (greater than) 1,000 consecutive cases from a single centre. *BMC Clin Pathol*. 2014;14(1):18.

28. Block RW, Krebs NF, American Academy of Pediatrics Committee on Child Abuse and Neglect, American Academy of Pediatrics Committee on Nutrition. Failure to thrive as a manifestation of child neglect. *Pediatrics*. 2005;116(5):1234-1237. http://www.ncbi.nlm.nih.gov/pubmed/16264015. Accessed June 8, 2016.

29. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems 10th Revision*.; 2010.

30. Center for Disease Control and Prevention. *Medical Examiners' and Coroners' Handbook on Death Registration and Fetal Death Reporting*.; 2003.

31. Ministry of Community Safety and Correctional Services. 2013 Report. http://www.mcscs.jus.gov.on.ca/english/DeathInvestigations/office_coroner/PublicationsandReports/PDRC/2013Report/PDRC_2013.html#25. Accessed January 12, 2016.

32. Ministry of Community Safety and Correctional Services. 2014 Report. http://www.mcscs.jus.gov.on.ca/english/DeathInvestigations/office_coroner/PublicationsandReports/PDRC/2014Report/PDRC_2014.html. Accessed January 21, 2016.

33. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. *Lancet*. 2012;379(9832):2162-2172.

34. Reddy UM, Bettegowda VR, Dias T, Yamada-Kushnir T, Ko C-W, Willinger M. Term pregnancy: a period of heterogeneous risk for infant mortality. *Obstet Gynecol*. 2011;117(6):1279-1287.

35. The American College of Obstetricians and Gynecologists Committee on Obstetric Practice Society for Maternal-Fetal Medicine. AGOC Committee Opinion No 579: Definition of term pregnancy. *Obstet Gynecol*. 2013;122(5):1139-1140.

36. Barfield WD. Standard terminology for fetal, infant, and perinatal deaths. *Pediatrics*. 2011;128(1):177-181.

37. Burdi A, Huelke D, Snyder R, Lowrey G. Infants and children in the adult world of automobile safety design: pediatric and anatomical considerations for design of child restraints. *J Biomech*. 1969;2(3):267-280.

38. Flaherman VJ, Schaefer EW, Kuzniewicz MW, Li SX, Walsh EM, Paul IM. Early weight loss nomograms for exclusively breastfed newborns. *Pediatrics*. 2015;135(1):16-23.

39. Krogman W. *Growth of Man*. Uitgeverij Dr. W. Junk; 1941.

40. Khadilkar V, Khadlikar A, Choudhury P, Agarwal K, Ugar D, Shah N. IAP growth monitoring guidelines for children from birth to 18 years. *Indian Pediatr*. 2007;44(3):187-197.

41. Dietitians of Canada, Canadian Paediatric Society, The College of Family Physcians of Canada, Canada CHN of. Promoting optimal monitoring of child growth in Canada: Using the new World Health Organization growth charts - Executive Summary. *Paediatr Child Health*. 2010;15(2):77-83.

42. Dietitians of Canada and Canadian Paediatric Society. *A Health Professional's Guide for Using the WHO Growth Charts for Canada*.; 2014.

43. Coppoletta JM, Wolbach SB. Body length and organ weights of infants and children: a study of the body length and normal weights of the more important vital organs of the body between birth and twelve years of age. *Am J Pathol*. 1933;9(1):55-70.

44. Engel S. Growth of the lung in healthy and sick infants. *Arch Dis Child*. 1935;17(89):41-48.

45. Cole TJ. Growth and organ development. *Adv Exp Med Biol*. 2009;639:1-13. http://www.ncbi.nlm.nih.gov/pubmed/19227530. Accessed May 11, 2016.

46. Kendall MD, Johnson HR, Singh J. The weight of the human thymus gland at necropsy. *J Anat*. 1980;131(Pt 3):483-497.

47. Grenier D, Leduc D. *Well Beings: A Guide to Health in Child Care*. 3rd Editio. (Leduc D, ed.). Canadian Paediatric Society/Societe canadienne de pediatrie; 2015.

48. Leach CEA, Blair PS, Fleming PJ, et al. Epidemiology of SIDS and explained sudden infant deaths. *Pediatrics*. 1999;104(4):e43.

49. Nucci L. *Nice Is Not Enough: Facilitating Moral Development*. 1st Editio. Merrill: Prentice Hall; 2009.

50. Patterson C. *Child Development*. Boston: McGraw-Hill Higher Education; 2008.

51. Mitchell E, Stewart A. Gender and the sudden infant death syndrome. *Acta Paediatr*. 2008;86(8):854-856. http://doi.wiley.com/10.1111/j.1651-2227.1997.tb08611.x. Accessed June 10, 2016.

52. Cornwell AC. Sex differences in the maturation of sleep/wake patterns in high risk for SIDS infants. *Neuropediatrics*. 1993;24(1):8-14. http://www.ncbi.nlm.nih.gov/pubmed/8474614. Accessed June 13, 2016.

53. Davis DL, Gottlieb MB, Stampnitzky JR. Reduced ratio of male to female births in several industrial countries: a sentinel health indicator? *JAMA*. 1998;279(13):1018-1023.

54. Mage DT, Donner M. The X-linkage hypotheses for SIDS and the male excess in infant mortality. *Med Hypotheses*. 2004;62(4):564-567. http://linkinghub.elsevier.com/retrieve/pii/S0306987704000088. Accessed June 13, 2016.

55. Mage DT, Donner M. A unifying theory for SIDS. *Int J Pediatr*. 2009;2009:1-10. http://www.hindawi.com/journals/ijpedi/2009/368270/. Accessed June 13, 2016.

56. Silventoinen K, Sammalisto S, Perola M, et al. Heritability of adult body height: a comparative

study of twin cohorts in eight countries. *Twin Res*. 2003;6(5):399-408. http://www.journals.cambridge.org/abstract_S1369052300004001. Accessed June 10, 2016.

57. Silventoinen K. Determinants of variation in adult body height. *J Biosoc Sci*. 2003;35(2):263-285.

58. Kuh D, Wadsworth M. Parental height: childhood environment and subsequent adult height in a national birth cohort. *Int J Epidemiol*. 1989;18(3):663-668. http://ije.oxfordjournals.org/cgi/doi/10.1093/ije/18.3.663. Accessed June 10, 2016.

59. Nwosu BU, Lee MM. Evaluation of short and tall stature in children. *Am Fam Physician*. 2008;78(5):597-604.

60. Lee JM, Appugliese D, Coleman SM, et al. Short stature in a population-based cohort: social, emotional, and behavioral functioning. *Pediatrics*. 2009;124(3):903-910. http://www.ncbi.nlm.nih.gov/pubmed/19706592. Accessed June 13, 2016.

61. Eveleth PB. Population Differences in Growth: Environmental and Genetic Factors. In: *Human Growth*. Boston, MA: Springer US; 1979:373-394.

62. Cameron N, Demerath EW. Critical periods in human growth and their relationship to diseases of aging. *Am J Phys Anthropol*. 2002;Suppl 35:159-184.

63. Doberczak TM, Thornton JC, Bernstein J, Kandall SR. Impact of maternal drug dependency on birth weight and head circumference of offspring. *Am J Dis Child*. 1987;141(11):1163-1167.

64. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation*. 2001;104(5):515-521.

65. Naeye RL. Infants of diabetic mothers: a quantitative, morphologic study. *Pediatrics*. 1965;35:980-988.

66. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;371(9606):75-84.

67. Muglia L, Katz M. The enigma of spontaneous preterm birth. *N Engl J Med*. 2010;362(6):529-535.

68. Minkoff H, Grunebaum AN, Schwarz RH, et al. Risk factors for prematurity and premature rupture of membranes: A prospective study of the vaginal flora in pregnancy. *Am J Obstet Gynecol*. 1984;150(8):965-972.

69. Hughes D, Simpson L. The role of social change in preventing low birth weight. *Future Child*. 1995;5(1):87-102.

70. Fedrick J, Adelstein P. Factors associated with low birth weight of infants delivered at term. *Br J Obstet Gynaecol*. 1978;85(1):1-7.

71. Paneth N, Wallenstein S, Kiely JL, Susser M. Social class indicators and mortality in low birth weight infants. *Am J Epidemiol*. 1982;116(2):364-375.

72. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet*. 2003;361(9376):2226-2234.

73. Spencer N, Logan S. Sudden unexpected death in infancy and socioeconomic status: a systematic review. *J Epidemiol Community Health*. 2004;58(5):366-373.

74. Valdés-Dapena MA. Sudden infant death syndrome: a review of the medical literature 1974-1979. *Pediatrics*. 1980;66(4):597-614.

75. Byard RW. *Sudden Death in Infancy, Childhood, and Adolescence*. 2nd Editio. Cambridge: Cambridge University Press; 2004.

76. Cage RA, Foster J. Overcrowding and infant mortality: a tale of two cities. *Scott J Polit Econ*. 2002;49(2):129-149.

77. van Sleuwen BE, Engelberts AC, Boere-Boonekamp MM, Kuis W, Schulpen TWJ, L'Hoir MP.

Swaddling: a systematic review. *Pediatrics*. 2007;120(4):e1097-e1106.

78. Abel S, Park J, Tipene-Leach D, Finau S, Lennan M. Infant care practices in New Zealand: a cross-cultural qualitative study. *Soc Sci Med*. 2001;53(9):1135-1148.

79. McKenna JJ. Sudden infant death syndrome in cross-cultural perspective: is infant-parent cosleeping protective? *Annu Rev Anthropol*. 1996;25(1):201-216. http://www.annualreviews.org/doi/abs/10.1146/annurev.anthro.25.1.201. Accessed June 9, 2016.

80. Ball HL, Volpe LE. Sudden infant death syndrome (SIDS) risk reduction and infant sleep location – Moving the discussion forward. *Soc Sci Med*. 2013;79(1):84-91. http://linkinghub.elsevier.com/retrieve/pii/S0277953612002924. Accessed June 10, 2016.

81. Auger N, Fraser WD, Smargiassi A, Kosatsky T. Ambient heat and sudden infant death: a case-crossover study spanning 30 years in Montreal, Canada. *Environ Health Perspect*. 2015;123(7):712-716.

82. Ponsonby AL, Jones ME, Lumley J, Dwyer T, Gilbert N. Climatic temperature and variation in the incidence of sudden infant death syndrome between the Australian states. *Med J Aust*. 1992;156(4):246-248, 251.

83. Katz D, Shore S, Bandle B, Niermeyer S, Bol KA, Khanna A. Sudden infant death syndrome and residential altitude. *Pediatrics*. 2015;135(6):1442-1449.

84. Kohlendorfer U, Kiechl S, Sperl W. Living at high altitude and risk of sudden infant death syndrome. *Arch Dis Child*. 1998;79(6):506-509. http://adc.bmj.com/cgi/doi/10.1136/adc.79.6.506. Accessed June 10, 2016.

85. Barkin RM, Hartley MR, Brooks JG. Influence of high altitude on sudden infant death syndrome. *Pediatrics*. 1981;68(6):891-892.

86. Dressler WW, Oths KS, Gravlee CC. Race and ethnicity in public health research: models to explain health disparities. *Annu Rev Anthropol*. 2005;34:231-252.

87. Kleinman J, Fingerhut L, Prager K. Differences in infant mortality by race nativity status and other maternal characteristics. *Am J Dis Child*. 1991;145(2):194-199.

88. Zambrana RE, Scrimshaw SC, Collins N, Dunkel-Schetter C. Prenatal health behaviors and psychosocial risk factors in pregnant women of Mexican origin: the role of acculturation. *Am J Public Health*. 1997;87(6):1022-1026.

89. Morales LS, Lara M, Kington RS, Valdez RO, Escarce JJ. Socioeconomic, cultural, and behavioral factors affecting Hispanic health outcomes. *J Health Care Poor Underserved*. 2002;13(4):477-503.

90. Curhan GC, Willett WC, Rimm EB, Spiegelman D, Ascherio AL, Stampfer MJ. Birth weight and adult hypertension, diabetes mellitus, and obesity in US men. *Circulation*. 1996;94(12):3246-3250. http://circ.ahajournals.org/cgi/doi/10.1161/01.CIR.94.12.3246. Accessed June 10, 2016.

91. Li Y, Ley SH, Tobias DK, et al. Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. *BMJ*. 2015;351(11):h3672.

92. Cosmi E, Fanelli T, Visentin S, et al. Consequences in infants that were intrauterine growth restricted. *J Pregnancy*. 2011:1-6. http://www.hindawi.com/journals/jp/2011/364381/. Accessed June 10, 2016.

93. Fenton TR. A new growth chart for preterm babies: Babson and Benda's chart updated with recent data and a new format. *BMC Pediatr*. 2003;3:13.

94. Isolauri E, Juntunen M, Wiren S, Vuorinen P, Koivula T. Intestinal permeability changes in acute gastroenteritis: effects of clinical factors and nutritional management. *J Pediatr Gastroenterol Nutr*. 1989;8(4):466-473.

95. Daneman D, Frank M, Perlman K, Wittenberg J. The infant and toddler with diabetes: challenges

of diagnosis and management. *Paediatr Child Health*. 1999;4(1):57-63.

96. World Health Organization. *Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses*. 2nd Editio. Geneva: World Health Organization; 2013.

97. Razavi Z, Sanginabadi M. Linear growth arrest without weight gain due to overuse of topical clobetasol. *Oman Med J*. 2014;29(6):454-457. http://www.ncbi.nlm.nih.gov/pubmed/25584165. Accessed June 13, 2016.

98. Groenen PM, van Rooij IA, Peer PG, Ocké MC, Zielhuis GA, Steegers-Theunissen RP. Low maternal dietary intakes of iron, magnesium, and niacin are associated with spina bifida in the offspring. *J Nutr*. 2004;134(6):1516-1522.

99. Walker SP, Wachs TD, Gardner JM, et al. Child development: risk factors for adverse outcomes in developing countries. *Lancet*. 2007;369(9556):145-157.

100. Cole SZ, Lanham J. Failure to Thrive: An Update. *Am Fam Physician*. 2011;83(7):829-834.

101. Swallen KC, Reither EN, Haas SA, Meier AM. Overweight, obesity, and health-related quality of life among adolescents: the National Longitudinal Study of Adolescent Health. *Pediatrics*. 2005;115(2):340-347. http://www.ncbi.nlm.nih.gov/pubmed/15687442. Accessed June 13, 2016.

102. Romero R, Mazor M, Munoz H, Gomez R, Galasso M, Sherer DM. The preterm labor syndrome. *Ann N Y Acad Sci*. 1994;734:414-429.

103. Volpe JJ. The encephalopathy of prematurity--brain injury and impaired brain development inextricably intertwined. *Semin Pediatr Neurol*. 2009;16(4):167-178. http://linkinghub.elsevier.com/retrieve/pii/S1071909109000631. Accessed June 13, 2016.

104. Eichenwald EC, Stark AR. Management and outcomes of very low birth weight. *N Engl J Med*. 2008;358(16):1700-1711.

105. Vanderbilt D, Gleason MM. Mental health concerns of the premature infant through the lifespan. *Pediatr Clin North Am*. 2011;58(4):815-832.

106. Schlotz W, Phillips DI. Fetal origins of mental health: evidence and mechanisms. *Brain Behav Immun*. 2009;23(7):905-916.

107. Barker D, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. *Lancet*. 1986;1(8489):1077-1081. http://linkinghub.elsevier.com/retrieve/pii/S0140673686913401. Accessed June 10, 2016.

108. Center for Disease Control and Prevention. *Guidelines for Growth Charts and Gestational Age Adjustment for Premature Infants and Children Up To The Age Of 24 Months*.; 2000.

109. Center for Disease Control and Prevention. *Growth Charts*.; 2009. http://www.cdc.gov/growthcharts/percentile_data_files.htm. Accessed December 7, 2015.

110. Schulz DM, Giordano DA. Hearts of infants and children. Weights and measurements. *Arch Pathol*. 1962;74:464-471.

111. Archie JG, Collins JS, Lebel RR. Quantitative standards for fetal and neonatal autopsy. *Am J Clin Pathol*. 2006;126(2):256-265.

112. Hansen K, Sung CJ, Huang C, Pinar H, Singer DB, Oyer CE. Reference values for second trimester fetal and neonatal organ weights and measurements. *Pediatr Dev Pathol*. 2003;6(2):160-167.

113. Thompson WS, Cohle SD. Fifteen-year retrospective study of infant organ weights and revision of standard weight tables. *J Forensic Sci*. 2004;49(3):575-585.

114. Roche AF, Guo S, Moore WM. Weight and recumbent length from 1 to 12 mo of age: reference data for 1-mo increments. *Am J Clin Nutr*. 1989;49(4):599-607.

115. Fracasso T, Vennemann M, Pfeiffer H, Bajanowski T. Organ weights in cases of sudden infant death syndrome: a German study. *Am J Forensic Med Pathol*. 2009;30(3):231-234.

116. Kramer MS, Platt RW, Wen SW, et al. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics*. 2001;108(2):E35.

117. Victor JC. *Ontario Organ Growth Standards for Perinatal Autopsy [Dissertation]*. London ON: University of Western Ontario; 1999.

118. Mitropoulos G, Scurry J, Cussen L. Organ weight/bodyweight ratios: growth rates of fetal organs in the latter half of pregnancy with a simple method for calculating mean organ weights. *J Paediatr Child Health*. 1992;28(3):236-239.

119. Stowens D. *Pediatric Pathology*. Baltimore: Williams & Wilkins; 1959.

120. Scholz DG, Kitzman DW, Hagen PT, Ilstrup DM, Edwards WD. Age-related changes in normal human hearts during the first 10 decades of life. Part I (Growth): A quantitative anatomic study of 200 specimens from subjects from birth to 19 years old. *Mayo Clin Proc*. 1988;63(2):126-136.

121. Keeling J. *Fetal and Neonatal Pathology 3rd Edition*. New York: Springer; 2003.

122. Finkbeiner WE, Ursell PC, Davis RL. *Autopsy Pathology: A Manual and Atlas*. Philadelphia: Churchill Livingstone; 2009.

123. Oyer CE, Sung CJ, Friedman R, et al. Reference values for valve circumferences and ventricular wall thicknesses of fetal and neonatal hearts. *Pediatr Dev Pathol*. 2004;7(5):499-505.

124. Prentice A, Paul A, Prentice A, Black A, Cole T, Whitehead R. Cross-Cultural Differences in Lactational Performance. In: *Human Lactation 2*. Boston, MA: Springer US; 1986:13-44.

125. Folligan K, Bouvier R, Targe F, Morel Y, Trouillas J. Development of the human adrenal glands. *Ann Endocrinol (Paris)*. 2005;66(4):325-332.

126. de Sa DJ. Adrenal changes in chorioamnionitis. *Arch Dis Child*. 1974;49(2):149-151.

127. Crelin ES. *Functional Anatomy of the Newborn*. New Haven and London: Yale University Press; 1973.

128. Hasselbalch H, Jeppesen D, Engelmann M, Michaelsen K, Nielsen M. Decreased thymus size in formula-fed infants compared with breastfed infants. *Acta Paediatr*. 1996;85(9):1029-1032. http://doi.wiley.com/10.1111/j.1651-2227.1996.tb14211.x. Accessed May 11, 2016.

129. Hasselbalch H, Engelmann MD, Ersboll AK, Jeppesen DL, Fleischer-Michaelsen K. Breast-feeding influences thymic size in late infancy. *Eur J Pediatr*. 1999;158(12):964-967.

130. Gui J, Mustachio LM, Su D-M, Craig RW. Thymus size and age-related thymic involution: early programming, sexual dimorphism, progenitors and stroma. *Aging Dis*. 2012;3(3):280-290.

131. Toti P, De Felice C, Stumpo M, et al. Acute thymic involution in fetuses and neonates with chorioamnionitis. *Hum Pathol*. 2000;31(9):1121-1128. http://www.humanpathol.com/article/S0046817700565976/fulltext. Accessed May 11, 2016.

132. Ulrich-Lai YM, Figueiredo HF, Ostrander MM, Choi DC, Engeland WC, Herman JP. Chronic stress induces adrenal hyperplasia and hypertrophy in a subregion-specific manner. *Am J Physiol Endocrinol Metab*. 2006;291(5):E965-E973.

133. Kim H-J, Jang S-H, Park J-S, et al. A case of true thymic hyperplasia in the mediastinum with ectopic thymus in the neck. *Korean J Pediatr*. 2006;49(9):996-999.

134. World Health Organization. The WHO Child Growth Standards. *WHO*. 2006. http://www.who.int/childgrowth/standards/en/. Accessed June 27, 2016.

135. Kuczmarski R, Ogden C, Guo S, et al. 2000 CDC Growth Charts for the United States: Methods and Development. *Vital Heal Stat 11*. 2002;(246):1-190. http://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf. Accessed June 23, 2016.

136. Use and interpretation of anthropometric indicators of nutritional status. WHO Working Group. *Bull World Health Organ*. 1986;64(6):929-941.

137. Statistics Canada. Table 102-0562- Leading causes of death, infant, by sex, Canada, annual. CANSIM (database). http://www5.statcan.gc.ca/cansim/pick-choisir. Accessed June 27, 2016.

138. Center for Disease Control and Prevention. National Vital Statistics System-Compressed Mortality, 1999-2014 Request. 2014. http://wonder.cdc.gov/cmf-ICD10.html. Accessed June 27, 2016.

139. Mitchell EA. What is the mechanism of SIDS? Clues from epidemiology. *Dev Psychobiol*. 2009;51(2):215-222.

140. Rohde MC, Corydon TJ, Hansen J, et al. Heat stress and sudden infant death syndrome—stress gene expression after exposure to moderate heat stress. *Forensic Sci Int*. 2013;232(1-3):16-24.

141. Hoffman H, Damus K, Hillman L, Krongrad E. Risk factors for SIDS. Results of the National Institute of Child Health and Human Development SIDS cooperative epidemiological study. *Ann N Y Acad Sci*. 1988;533:13-30.

142. Grasmeyer S, Madea B. Myocardial apoptosis and SIDS. *Forensic Sci Int*. 2015;246:1-5.

143. Campuzano O, Allegue C, Sarquella-Brugada G, et al. The role of clinical, genetic and segregation evaluation in sudden infant death. *Forensic Sci Int*. 2014;242:9-15.

144. Berul CI, Perry JC. Contribution of long-QT syndrome genes to sudden infant death syndrome: is it time to consider newborn electrocardiographic screening? *Circulation*. 2007;115(3):294-296.

145. Miller ER, Moro PL, Cano M, Shimabukuro TT. Deaths following vaccination: what does the evidence show? *Vaccine*. 2015;33(29):3288-3292.

146. Sturner WQ. Can baby organs be donated in all forensic cases? Proposed guidelines for organ donation from infants under medical examiner jurisdiction. *Am J Forensic Med Pathol*. 1995;16(3):215-218.

147. Bonham JR, Downing M. Metabolic deficiencies and SIDS. *J Clin Pathol*. 1992;45(11 Suppl):33-38.

148. Garcia M, Beby-Defaux A, Lévêque N. Respiratory viruses as a cause of sudden death. *Expert Rev Anti Infect Ther*. 2016;14(4):359-363.

149. Weber MA, Hartley JC, Ashworth MT, Malone M, Sebire NJ. Virological investigations in sudden unexpected deaths in infancy (SUDI). *Forensic Sci Med Pathol*. 2010;6(4):261-267.

150. Desmons A, Terrade C, Boulagnon C, et al. Post-mortem diagnosis, of cytomegalovirus and varicella zoster virus co-infection by combined histology and tissue molecular biology, in a sudden unexplained infant death. *J Clin Virol*. 2013;58(2):486-489.

151. Burger MC, Dempers JJ, de Beer C, et al. Profiling the approach to the investigation of viral infections in cases of sudden unexpected death in infancy in the Western Cape Province, South Africa. *Forensic Sci Int*. 2014;239:27-30.

152. Guntheroth WG. Sudden infant death syndrome (crib death). *Am Heart J*. 1977;93(6):784-793.

153. Risse M, Weiler G. Differential diagnosis SIDS/non-SIDS on the basis of histological findings of petechial thymus hemorrhages. *Forensic Sci Int*. 1989;43(1):1-7.

154. Berry PJ. Pathological findings in SIDS. *J Clin Pathol*. 1992;45(11 Suppl):11-16.

155. Krous HF. The microscopic distribution of intrathoracic petechiae in sudden infant death syndrome. *Arch Pathol Lab Med*. 1984;108(1):77-79.

156. Rajs J, Hammarquist F. Sudden infant death in Stockholm. A forensic pathology study covering ten years. *Acta Paediatr Scand*. 1988;77(6):812-820.

157. Molz G, Brodzinowski A, Bär W, Vonlanthen B. Morphologic variations in 180 cases of sudden

infant death and 180 controls. *Am J Forensic Med Pathol*. 1992;13(3):186-190.

158. Helweg-Larsen K. Sudden, unexplained infant death--sudden infant death syndrome. Forensic pathological aspects. *Ugeskr Laeger*. 1992;154(49):3477-3482.

159. Råsten-Almqvist P, Eksborg S, Rajs J. Heart weight in infants--a comparison between sudden infant death syndrome and other causes of death. *Acta Paediatr*. 2000;89(9):1062-1067.

160. Siebert JR, Haas J. Organ Weights in Sudden Infant Death Syndrome. *Fetal Pediatr Pathol*. 1994;14(6):973-985.

161. Kelmanson IA. Differences in somatic and organ growth rates in infants who died of sudden infant death syndrome. *J Perinat Med*. 1992;20(3):183-188.

162. Falck G, Rajs J. Brain weight and sudden infant death syndrome. *J Child Neurol*. 1995;10(2):123-126.

163. Kadhim H, Sébire G, Khalifa M, et al. Incongruent cerebral growth in sudden infant death syndrome. *J Child Neurol*. 2005;20(3):244-246.

164. Blair PS, Nadin P, Cole TJ, et al. Weight gain and sudden infant death syndrome: changes in weight z scores may identify infants at increased risk. *Arch Dis Child*. 2000;82(6):462-469.

165. Elliott JA, Vink R, Jensen L, Byard RW. Brain weight-body weight ratio in sudden infant death syndrome revisited. *Med Sci Law*. 2012;52(4):207-209.

166. Goldwater PN. Sudden infant death syndrome: a critical review of approaches to research. *Arch Dis Child*. 2003;88(12):1095-1100.

167. Little BB, Kemp PM, Bost RO, Snell LM, Peterman MA. Abnormal allometric size of vital body organs among sudden infant death syndrome victims. *Am J Hum Biol*. 2000;12(3):382-387.

168. Gassner HL, Toppari J, Quinteiro González S, Miller WL. Near-miss apparent SIDS from adrenal crisis. *J Pediatr*. 2004;145(2):178-183.

169. Weber MA, Pryce JW, Ashworth MT, Malone M, Sebire NJ. Histological examination in sudden unexpected death in infancy: evidence base for histological sampling. *J Clin Pathol*. 2012;65(1):58-63.

170. American Academy of Pediatrics. Committee on Child Abuse and Neglect. American Academy of Pediatrics: Distinguishing sudden infant death syndrome from child abuse fatalities. *Pediatrics*. 2001;107(2):437-441.

171. Schnitzer PG, Covington TM, Dykstra HK. Sudden unexpected infant deaths: sleep environment and circumstances. *Am J Public Health*. 2012;102(6):1204-1212.

172. Randall BB, Paterson DS, Haas EA, et al. Potential asphyxia and brainstem abnormalities in sudden and unexpected death in infants. *Pediatrics*. 2013;132(6):e1616-e1625.

173. Krous HF. Sudden infant death syndrome: pathology and pathophysiology. *Pathol Annu*. 1984;19 Pt 1:1-14.

174. Kelmanson IA. Evidence for retarded kidney growth in sudden infant death syndrome. *Pediatr Nephrol*. 1996;10(6):683-686.

175. Hinchliffe SA, Howard C V, Lynch MR, Sargent PH, Judd BA, van Velzen D. Renal developmental arrest in sudden infant death syndrome. *Pediatr Pathol*. 13(3):333-343.

176. Schmidt I, Chellakooty M, Boisen KA, et al. Impaired kidney growth in low-birth-weight children: distinct effects of maturity and weight for gestational age. *Kidney Int*. 2005;68(2):731-740.

177. Tang J, Zhu Z, Xia S, et al. Chronic hypoxia in pregnancy affected vascular tone of renal interlobar arteries in the offspring. *Sci Rep*. 2015;5:9723.

178. Farahani R, Kanaan A, Gavrialov O, et al. Differential effects of chronic intermittent and chronic constant hypoxia on postnatal growth and development. *Pediatr Pulmonol*. 2008;43(1):20-28.

179. Leslie ND, Valencia CA, Strauss AW, Connor J, Zhang K. *Very Long-Chain Acyl-Coenzyme A Dehydrogenase Deficiency*. University of Washington, Seattle; 1993.

180. Boles RG, Buck EA, Blitzer MG, et al. Retrospective biochemical screening of fatty acid oxidation disorders in postmortem livers of 418 cases of sudden death in the first year of life. *J Pediatr*. 1998;132(6):924-933.

181. Randall BB, Wadee SA, Sens MA, et al. A practical classification schema incorporating consideration of possible asphyxia in cases of sudden unexpected infant death. *Forensic Sci Med Pathol*. 2009;5(4):254-260.

182. Task Force on Sudden Infant Death Syndrome, Moon RY. SIDS and other sleep-related infant deaths: expansion of recommendations for a safe infant sleeping environment. *Pediatrics*. 2011;128(5):1030-1039.

183. Kam HY, Ou LC, Thron CD, Smith RP, Leiter JC. Role of the spleen in the exaggerated polycythemic response to hypoxia in chronic mountain sickness in rats. *J Appl Physiol*. 1999;87(5):1901-1908.

184. Kubanek B, Ferrari L, Tyler WS, Howard D, Jay S, Stohlman F. Regulation of erythropoiesis. 23. Dissociation between stem cell and erythroid response to hypoxia. *Blood*. 1968;32(4):586-596.

185. Publicly Funded Immunization Schedule for Ontario-October 2015. http://www.health.gov.on.ca/en/pro/programs/immunization/docs/immunization_schedule.pdf. Published 2015. Accessed June 29, 2016.

186. Siegrist C-A. The challenges of vaccine responses in early life: selected examples. *J Comp Pathol*. 2007;137:S4-S9.

187. Pérez-Platz U, Saeger W, Dhom G, Bajanowski T. The pathology of the adrenal glands in sudden infant death syndrome (SIDS). *Int J Legal Med*. 1994;106(5):244-248.

188. Kyritsi EM, Sertedaki A, Chrousos G, Charmandari E. Familial Or Sporadic Adrenal Hypoplasia Syndrome. In: Endotext INC, ed. *Endotext*. South Dartmouth; 2000.

189. Loureiro M, Reis F, Robalo B, Pereira C, Sampaio L. Adrenal hypoplasia congenita: a rare cause of primary adrenal insufficiency and hypogonadotropic hypogonadism. *Pediatr Rep*. 2015;7(3):5936.

190. Achermann JC, Vilain EJ. *X-Linked Adrenal Hypoplasia Congenita*. Seattle: GeneReviews; 2001.

191. Habiby RL, Boepple P, Nachtigall L, Sluss PM, Crowley WF, Jameson JL. Adrenal hypoplasia congenita with hypogonadotropic hypogonadism: evidence that DAX-1 mutations lead to combined hypothalmic and pituitary defects in gonadotropin production. *J Clin Invest*. 1996;98(4):1055-1062.

192. Uttley WS. Familial congenital adrenal hypoplasia. *Arch Dis Child*. 1968;43(232):724-730.

Appendices

Appendix A Autopsy Body and Organ References Survey

Autopsy Body and Organ References Survey

1) Do you or your pathologists perform Coroners' neonatal (Birth – 1 month) or infant (1 month -1 year) autopsies? Please circle the appropriate response Yes or No

2) Have you referenced any of the following sources for organ or body measurements? Please provide details (Authors, Journal, Year, Volume, Page #s or Textbook) for any additional sources.

- ☐ Kayser K. **Height and weight in human beings**; Autopsy report. Munich: Oldenbourg, 1987.51
- ☐ Schulz DM, Giordano DA, Schulz DH. **Weights of Organs of Fetuses and Infants**. Arch Pathol 1962; 74:244
- ☐ Sung CJ, Singer DB, Winggleworth JS. **Fetal growth and maturation: with standards for body and organ development**. In: Winggleworth JS, Singer DB, eds. Textbook of Fetal and Perinatal Pathology, 2nd ed. Boston. Blackwell Scientific Publications, Sung CJ, Singer DB, Winggleworth JS. 1998; 8-40
- ☐ Stocker JT, Dehner LP. **Pediatric Pathology** 2nd ed. Philadelphia. Lippincott Williams and Wilkins. 1940.
- ☐ Coppoletta JM, Wolback SB. **Body length and organ weights in infants and children: Study of body lengths and normal weights of more important vital organs and body between birth and 12 years of age.** Am J Pathol 1933;9:55-70
- ☐ Stowens D. **Pediatric Pathology**. Baltimore. The Williams and Wilkins Co. 1959
- ☐ Centers for Disease Control (CDC) http://www.cdc.gov/growthcharts/percentile_data_files.htm
- ☐ Other (Please specify) _____
- ☐ _____
- ☐ _____
- ☐ _____
- ☐ _____

3) Which of the above sources do you reference most often and why? _____
_____
_____
_____

4) Are there any limitations of these sources in your opinion?
_____
_____
_____
_____

Appendix B The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects Approval

Re-issued

Western Research

Research Ethics

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Michael Shkrum
File Number:102845
Review Level: Delegated
Approved Local Adult Participants:0
Approved Local Minor Participants:0
Protocol Title: Ontario Growth Standards for Neonates and Infants: An Autopsy Retrospective Study
Department & Institution: Schulich School of Medicine and Dentistry\Pathology,London Health Sciences Centre
Sponsor:
Ethics Approval Date: August 22, 2012 **Expiry Date:**April 30, 2016
Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Western University Protocol		

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

Janice Sutherland (jsutherl@uwo.ca)	Grace Kelly (grace.kelly@uwo.ca)	Shantel Walcott (swalcot@uwo.ca)

This is an official document. Please retain the original in your files.

Appendix C Lawson Health Research Institute Approval

LAWSON HEALTH RESEARCH INSTITUTE

FINAL APPROVAL NOTICE

RESEARCH OFFICE REVIEW NO.: R-12-373

PROJECT TITLE: Ontario Growth Standards for Neonates and Infants: An Autopsy Retrospective Study

PRINCIPAL INVESTIGATOR: Dr. Michael Shkrum

DATE OF REVIEW BY CRIC: August 30, 2012

Health Sciences REB#: 102845

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and the project:

Was Approved

PLEASE INFORM THE APPROPRIATE NURSING UNITS, LABORATORIES, ETC. BEFORE STARTING THIS PROTOCOL. THE RESEARCH OFFICE NUMBER MUST BE USED WHEN COMMUNICATING WITH THESE AREAS.

Dr. David Hill
V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Research Office Review Number and should be directed to Sherry Paiva, CRIC Liaison, Lawson Health Research Institute, 750 Baseline Road, East, Suite 300.

cc: Administration

Appendix D Data Collection Sheet

Data Collection Sheet

Demographics

Age at Death-_____
Date of Death-_____
Location-_____
Sex-_____
Birth Weight-_____

Lengths

Crown-Rump-_____
Crown-Heel-_____
Head Cir.-_____
Abdomen Cir.-_____
Chest Cir.-_____
Foot Lengths-_____
Inner Canthal-_____
Outer Canthal-_____

Weights

Body-_____
Brain-_____
Thymus-_____
Heart-_____
- Tricuspid-_____
- Pulmonary-_____
- Mitral-_____
- Aortic-_____
- Right Ventricle-_____
- Left Ventricle-_____

Lungs-_____
- Right-_____
- Left-_____

Liver-_____
Pancreas-_____
Spleen-_____
Adrenals-_____
- Right-_____
- Left-_____

Kidneys-_____
- Right-_____
- Left-_____

Uterus/Prostate-_____
Testes-_____
Thyroid-_____

Cultures

Blood Cultures-_____
Lung Cultures-_____
CSF Cultures-_____
Nasopharyngeal swabs-_____

Ancillary Testing

MCAD-_____
Blood Spot DOB-_____
Blood Spot DOD-_____
Bile Spot-_____
DNA-_____
Cytogenetic-_____
EM-_____
Toxicology-_____
_____

Vitreous

Glucose-_____
Sodium-_____
Potassium-_____
Chloride-_____
Creatinine-_____
Urea-_____
Ketones-_____

Skeletal Survey-_____
_____

Gross Examination-_____
_____

Microscopic Examination-_____
_____

Cause and Manner of Death-_____
_____
_____
_____
_____

Appendix E Growth Curves for Individual Organs and Body Measurements

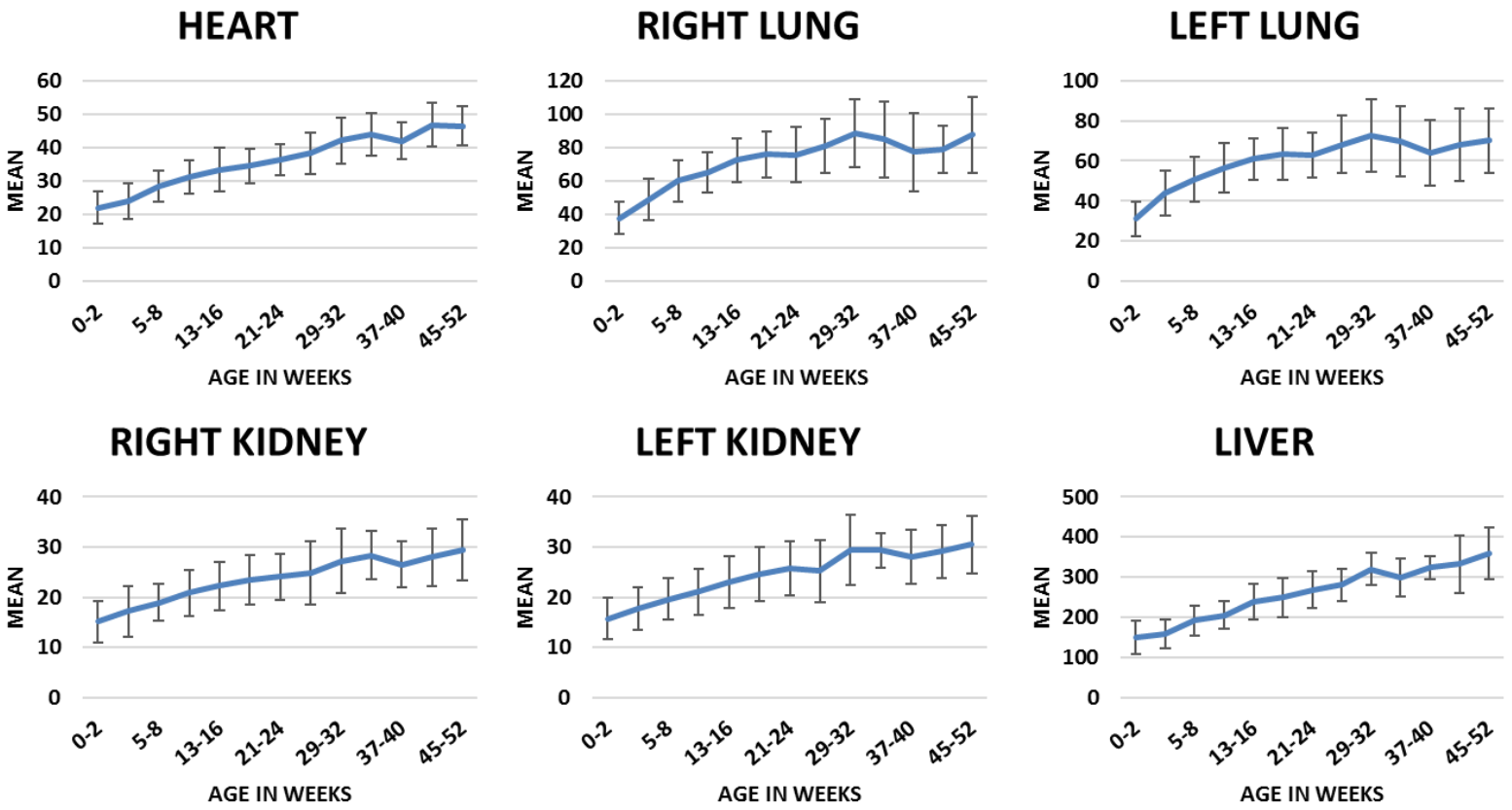

Figure E-1. Growth Curves for Individual Organs

Mean individual organ weights in grams plotted by age in weeks. Weights gradually increased with age consistent with normal development of a child.

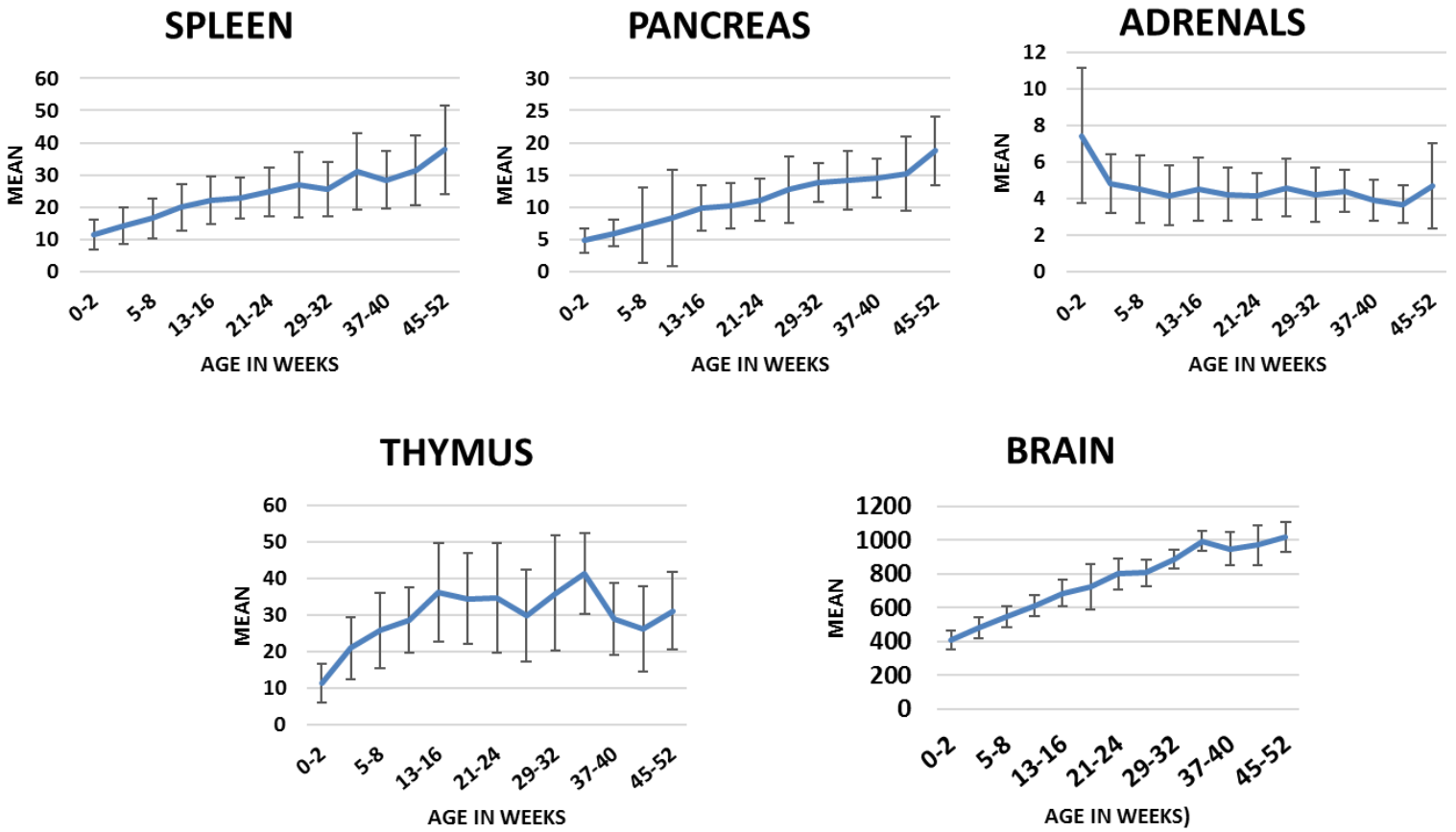

Figure E-2. Growth Curves for Individual Organs

Mean individual organ weights in grams plotted by age in weeks. Most weights gradually increased with age consistent with normal development of a child, except thymus and adrenal glands.

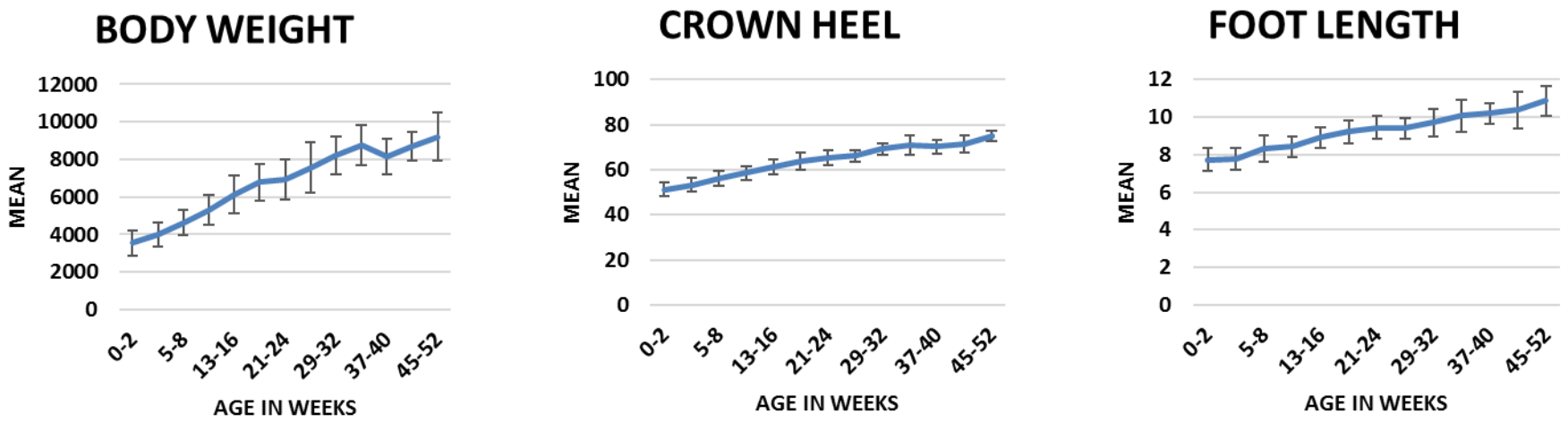

Figure E-3. Growth Curves for Individual Body Measurements

Means of body measurements plotted by age in weeks (weight in grams, crown-heel and foot length in centimeters). The body measurements gradually increased with age consistent with normal development of a child.

Appendix F P-values

Table F-1. P-values for the Effect of Gender on Individual Organ and Body Weight for Different Age Groups

Of the 56 significant relationships ($p<0.05$), 44 were at age less than 25 weeks.

AGE	Heart	Lungs	R.Lung	L.Lung	Kidneys	R.Kidney	L.Kidney	Liver	Spleen	Pancreas	Adrenals	R.Adrenal	L.Adrenal	Brain	Body
0-2	0.0376	0.0909	0.0867	0.4147	0.0103	0.0277	0.0056	0.1077	0.0214	0.2859	0.6524	0.6675	0.7325	0.0895	0.2607
3-4	0.0191	0.2462	0.1099	0.0458	0.2614	0.2372	0.3389	0.0885	0.0764	0.7602	0.0139	0.0246	0.0168	0.0155	0.4025
5-8	0.141	0.4942	0.3773	0.927	0.0099	0.0214	0.0133	0.8403	0.5709	0.2276	0.351	0.4274	0.3099	0.0198	0.2151
9-12	0.0001	0.0108	0.0424	0.0086	0.0003	0.0006	0.0004	0.0544	0.0002	0.2338	0.0525	0.1551	0.0205	0.0067	0.0016
13-16	0.195	0.0369	0.0176	0.1754	0.0118	0.0074	0.026	0.0195	0.0457	0.1778	0.1839	0.3199	0.1222	0.0996	0.0246
17-20	0.0119	0.2657	0.1975	0.8587	0.2508	0.2267	0.2136	0.0082	0.1017	0.8415	0.3999	0.4365	0.3612	0.2809	0.0083
21-24	0.0152	0.3291	0.308	0.8876	0.0185	0.0741	0.0138	0.2079	0.1664	0.0359	0.0124	0.019	0.088	0.3207	0.0122
25-28	0.0196	0.9093	0.7247	0.6627	0.0016	0.0108	0.0069	0.071	0.0242	0.2489	0.106	0.2289	0.0771	0.3453	0.2127
29-32	0.5006	0.329	0.4521	0.2446	0.8225	0.6081	0.9548	0.5837	0.682	0.2992	0.1265	0.316	0.0562	0.3794	0.5616
33-36	0.1244	-	-	-	-	-	-	0.0449	0.903	0.9773	0.4807	0.0724	0.2582	-	0.4993
37-40	0.2256	0.3926	0.1766	0.8356	0.3869	0.4294	0.4348	0.7342	0.7096	0.6452	0.0297	0.0448	0.0515	0.1291	0.5459
41-44	0.9074	0.4328	0.6066	0.3308	0.5683	0.9565	0.251	0.4715	0.9561	0.0169	0.1713	0.2337	0.0784	0.7881	0.2114
45-52	0.009	0.7221	0.8919	0.517	0.9934	0.6413	0.6372	0.6176	0.3709	0.011	0.8263	0.7883	0.8911	0.0068	0.0894

R. (right). L. (left),

Table F-2. P-Values – Difference in Combined Lung Weights between the Cause of Death Groups

P-values distribution for the combined lung weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.16	0.0018	0.6954
3-4	0.163	0.0129	0.892
5-8	0.7942	0.196	0.4299
9-12	0.0135	0.0045	0.8478
13-16	0.5286	0.8495	0.4114
17-20	0.9547	0.2869	0.2419
21-24	0.6797	0.8558	0.79
25-28	0.004	0.0113	0.0255
29-32	0.9439	-	-
33-36	-	-	-
37-40	-	-	-
41-44	0.4887	-	-
45-52	0.3374	0.2422	0.7321

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.2095	0.0196	0.9621
3-4	0.005	0.0004	0.4156
5-8	0.4864	0.1029	0.6026
9-12	0.9398	0.579	0.6123
13-16	0.9979	0.2925	0.1479
17-20	0.0817	0.1598	0.2806
21-24	0.0298	0.0189	0.8528
25-28	0.2489	0.3062	0.8276
29-32	0.4209	0.658	0.5485
33-36	0.4573	0.4404	0.9652
37-40	0.9342	0.6857	0.6018
41-44	-	0.2405	-
45-52	0.9084	0.9549	0.9594

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0502	0.0001	0.7397
3-4	0.0029	0.0000	0.5812
5-8	0.4991	0.0396	0.3664
9-12	0.171	0.0627	0.8209
13-16	0.5759	0.6394	0.2091
17-20	0.0703	0.1152	0.5073
21-24	0.1087	0.0564	0.993
25-28	0.0972	0.1582	0.6787
29-32	0.2895	0.4869	0.4999
33-36	0.8406	0.8149	0.9781
37-40	0.5082	0.8683	0.5642
41-44	0.0902	0.186	0.8337
45-52	0.3602	0.3285	0.891

Table F-3. P-Values – Difference in Combined Kidney Weights between the Cause of Death Groups

P-values distribution for the combined kidney weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0983	0.9802	0.1186
3-4	0.316	0.0026	0.2936
5-8	0.2095	0.1445	0.7039
9-12	0.0638	0.5306	0.0026
13-16	0.3942	0.3579	0.7746
17-20	0.1674	0.0684	0.7659
21-24	0.7107	0.5122	0.921
25-28	0.3515	0.6072	0.5231
29-32	0.1085	0.2077	0.5814
33-36	-	-	-
37-40	0.5436	0.9398	0.6534
41-44	0.551	-	-
45-52	0.7234	0.327	0.6084

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.8904	0.1215	0.524
3-4	0.3687	0.7798	0.4665
5-8	0.8052	0.7118	0.9778
9-12	0.5545	0.756	0.6954
13-16	0.1453	0.808	0.0284
17-20	0.2474	0.4581	0.548
21-24	0.5877	0.8407	0.6862
25-28	0.2714	0.1271	0.7196
29-32	0.9557	0.5161	0.7531
33-36	0.831	0.366	0.5322
37-40	0.5218	0.6937	0.1452
41-44	-	-	-
45-52	0.1086	0.9678	0.2959

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.21	0.2099	0.5882
3-4	0.1936	0.0782	0.9134
5-8	0.4146	0.3374	0.8012
9-12	0.9346	0.193	0.2086
13-16	0.1843	0.5772	0.0382
17-20	0.8014	0.5711	0.4459
21-24	0.5083	0.8657	0.5965
25-28	0.8966	0.2829	0.4008
29-32	0.2934	0.8496	0.3819
33-36	0.9293	0.5192	0.561
37-40	0.8589	0.2354	0.1477
41-44	0.3542	-	-
45-52	0.1648	0.3566	0.7976

Table F-4. P-Values – Difference in Liver Weights between the Cause of Death Groups

P-values distribution for the liver weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0217	0.4884	0.0684
3-4	0.54	0.0301	0.5784
5-8	0.1812	0.0641	0.8336
9-12	0.249	0.6191	0.3389
13-16	0.6748	0.3957	0.9637
17-20	0.6102	0.8876	0.676
21-24	0.351	0.8595	0.437
25-28	0.8652	0.8215	0.9855
29-32	0.3169	0.6361	0.6024
33-36	-	-	-
37-40	0.4648	0.9521	0.4898
41-44	0.4984	-	-
45-52	0.6849	0.3266	0.2792

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.5826	0.8218	0.5325
3-4	0.207	0.3308	0.5835
5-8	0.3776	0.8191	0.4401
9-12	0.6966	0.3118	0.1679
13-16	0.5931	0.8186	0.3593
17-20	0.0168	0.1199	0.1777
21-24	0.2704	0.585	0.4839
25-28	0.904	0.6483	0.7432
29-32	0.4764	0.2367	0.987
33-36	0.9447	0.046	0.0689
37-40	0.1016	0.3568	0.1696
41-44	-	0.0385	-
45-52	0.3693	0.991	0.5824

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.2268	0.5564	0.4068
3-4	0.0555	0.0386	0.589
5-8	0.1539	0.2606	0.4453
9-12	0.7615	0.3768	0.6347
13-16	0.1258	0.464	0.2851
17-20	0.0376	0.1688	0.2625
21-24	0.0975	0.4495	0.2803
25-28	0.5968	0.517	0.9343
29-32	0.6013	0.7654	0.4687
33-36	0.6022	0.6969	0.4884
37-40	0.0294	0.455	0.0595
41-44	0.2117	0.2908	0.8056
45-52	0.2836	0.5756	0.2275

Table F-5. P-Values – Difference in Brain Weights between the Cause of Death Groups

P-values distribution for the brain weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.9404	0.0051	0.0797
3-4	0.5654	0.512	0.813
5-8	0.6988	0.4027	0.9281
9-12	0.0021	0.0056	0.2316
13-16	0.4235	0.28	0.9381
17-20	0.4111	0.2654	0.954
21-24	0.6032	0.1349	0.3811
25-28	0.4979	0.5178	0.2442
29-32	-	-	0.5758
33-36	-	-	-
37-40	0.4669	0.7548	0.4152
41-44	0.9263	-	-
45-52	0.7476	0.6676	0.5192

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.9516	0.0581	0.2271
3-4	0.7691	0.406	0.738
5-8	0.1834	0.085	0.8615
9-12	0.5819	0.2996	0.1356
13-16	0.297	0.1281	0.7027
17-20	0.5835	0.7943	0.6838
21-24	0.0716	0.1961	0.4604
25-28	0.2048	0.7621	0.2732
29-32	-	0.8765	-
33-36	0.8404	0.6642	0.8429
37-40	0.3867	0.0948	0.1483
41-44	-	0.7009	-
45-52	0.5652	0.2794	0.2281

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.9504	0.0014	0.04
3-4	0.3662	0.1818	0.9318
5-8	0.1522	0.0829	0.7219
9-12	0.3441	0.0872	0.6481
13-16	0.1226	0.041	0.8829
17-20	0.949	0.8048	0.7406
21-24	0.1747	0.6	0.3285
25-28	0.2206	0.9016	0.1402
29-32	0.8355	0.7466	0.9533
33-36	0.8404	0.6642	0.8429
37-40	0.2341	0.7588	0.1232
41-44	0.9635	0.4888	0.5038
45-52	0.182	0.7452	0.214

Table F-6. P-Values – Difference in Spleen Weights between the Cause of Death Groups

P-values distribution for the spleen weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.6849	0.1325	0.2641
3-4	0.83	0.1885	0.5798
5-8	0.9116	0.0864	0.214
9-12	0.0519	0.1513	0.3045
13-16	0.5549	0.6455	0.7556
17-20	0.4161	0.8948	0.4664
21-24	0.3907	0.8151	0.3301
25-28	0.7814	0.7418	0.6293
29-32	0.5272	0.06	0.1701
33-36	-	-	-
37-40	0.3016	0.0851	0.2748
41-44	0.209	-	-
45-52	0.5407	0.5889	0.9408

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.7944	0.7541	0.6893
3-4	0.8959	0.2395	0.2955
5-8	0.2491	0.1117	0.0243
9-12	0.5783	0.3285	0.8451
13-16	0.0169	0.2109	0.0918
17-20	0.1818	0.8952	0.0921
21-24	0.124	0.1674	0.6969
25-28	0.9915	0.8959	0.9133
29-32	0.8653	0.5582	0.8107
33-36	0.9372	0.1153	0.1687
37-40	-	-	0.7315
41-44	-	0.3669	-
45-52	0.8381	0.0632	0.0888

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.6432	0.2625	0.3221
3-4	0.8392	0.6293	0.5973
5-8	0.2914	0.0249	0.0097
9-12	0.1741	0.2086	0.639
13-16	0.0704	0.5175	0.1364
17-20	0.2739	0.9644	0.2241
21-24	0.0625	0.194	0.4153
25-28	0.7314	0.9581	0.7014
29-32	0.6848	0.0821	0.2868
33-36	0.7993	0.1074	0.154
37-40	0.3553	0.3175	0.8968
41-44	0.1762	0.2487	0.783
45-52	0.6318	0.1985	0.1663

Table F-7. P-Values – Difference in Combined Adrenal Weights between the Cause of Death Groups

P-values distribution for the combined adrenal weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0247	0.0005	0.7133
3-4	0.3841	0.8578	0.3268
5-8	0.6856	0.513	0.3579
9-12	0.7094	0.0024	0.0257
13-16	0.2614	0.0483	0.0206
17-20	0.0829	0.021	0.7831
21-24	0.6767	0.2853	0.5835
25-28	0.8193	0.7315	0.6467
29-32	0.7262	0.7634	0.9272
33-36	-	-	-
37-40	0.0927	-	-
41-44	0.3277	-	-
45-52	0.1469	0.5933	0.1785

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.3299	0.0001	0.2098
3-4	0.4233	0.4337	0.1672
5-8	0.2128	0.1256	0.7814
9-12	0.8751	0.3062	0.2984
13-16	0.0542	0.6192	0.0468
17-20	0.8494	0.907	0.7466
21-24	0.5458	0.2197	0.5811
25-28	0.4067	0.3736	0.9971
29-32	0.6115	0.4355	0.3612
33-36	0.4214	0.3089	0.1876
37-40	0.8518	0.2827	0.1487
41-44	-	0.609	-
45-52	0.3267	0.046	0.0265

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0259	0.0000	0.4901
3-4	0.6889	0.6926	0.4997
5-8	0.1928	0.4494	0.3877
9-12	0.9801	0.013	0.0376
13-16	0.0221	0.6608	0.0024
17-20	0.2938	0.2625	0.8438
21-24	0.9478	0.6027	0.7025
25-28	0.5558	0.6614	0.8629
29-32	0.5474	0.8841	0.5002
33-36	0.597	0.2769	0.2331
37-40	0.7853	0.0453	0.0506
41-44	0.6997	0.9539	0.8415
45-52	0.2662	0.6479	0.7869

Table F-8. P-Values – Difference in Thymus Weights between the Cause of Death Groups

P-values distribution for the thymus weights between the cause of death groups for males, females and combined genders. Significance threshold of $p < 0.05$.

Female	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.1029	0.0001	0.6088
3-4	0.1655	0.3490	0.4072
5-8	0.0582	0.0138	0.7558
9-12	0.0544	0.3935	0.1067
13-16	0.6072	0.5815	0.3662
17-20	1.0000	0.4103	0.5296
21-24	0.0643	0.4056	0.1515
25-28	0.9646	0.9702	0.9382
29-32	0.2506	0.3699	0.7146
33-36	-	-	-
37-40	0.6574	0.1513	0.2920
41-44	0.7592	-	-
45-52	0.9177	0.8937	0.8591

Male	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.4383	0.0000	0.0348
3-4	0.0432	0.0093	0.9237
5-8	0.1831	0.0019	0.2561
9-12	0.7055	0.1575	0.4452
13-16	0.1152	0.1694	0.6363
17-20	0.0630	0.0463	0.9425
21-24	0.0026	0.0178	0.2083
25-28	0.8296	0.6725	0.5173
29-32	0.6093	0.4910	0.9251
33-36	0.5525	0.8671	0.7135
37-40	0.4037	0.5119	0.7508
41-44	-	0.0943	-
45-52	0.5792	0.4229	0.7327

All	Control-SIDS	Control-SUDS	SIDS-SUDS
0-2	0.0967	0.0000	0.0660
3-4	0.0145	0.0067	0.5350
5-8	0.0339	0.0001	0.4553
9-12	0.1641	0.1756	0.6766
13-16	0.0715	0.0929	0.6187
17-20	0.0630	0.0318	0.9824
21-24	0.0001	0.0060	0.0398
25-28	0.8191	0.6990	0.5357
29-32	0.2673	0.2749	0.8207
33-36	0.4551	0.8523	0.6414
37-40	0.1565	0.1750	0.9773
41-44	0.3849	0.0327	0.1307
45-52	0.5720	0.7790	0.8276

Appendix G Raw Data

The following tables demonstrate descriptive statistics (mean, standard deviations and sample sizes) for the individual organs that showed significant weight differences in relationship to cause of death, age and gender (by Backward Selection stepAIC). Means are given in grams. “-“ represents no data.

Table G-1. Lung Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	59.38	65.69	62.13
0-2	SD	16.03	17.38	16.78
0-2	n	31	24	55
3-4	Mean	69.82	62.26	67.76
3-4	SD	21.12	19.93	20.1
3-4	n	8	3	11
5-8	Mean	97.27	104.11	102.05
5-8	SD	34.02	24.61	27.01
5-8	n	6	14	20
9-12	Mean	91.22	123.76	111.25
9-12	SD	27.95	31.1	33.11
9-12	n	5	8	13
13-16	Mean	125.04	143.46	134.25
13-16	SD	9.89	24.08	19.89
13-16	n	5	5	10
17-20	Mean	121.8	99.3	114.3
17-20	SD	25.74	-	22.36
17-20	n	2	1	3
21-24	Mean	133.55	113.46	122.39
21-24	SD	14.75	26.4	23.28
21-24	n	4	5	9
25-28	Mean	131.1	123.6	127.35
25-28	SD	5.09	40.87	24.17
25-28	n	2	2	4
29-32	Mean	-	196	196
29-32	SD	-	-	-
29-32	n	-	1	1
33-36	Mean	103	189.9	160.93
33-36	SD	-	30.97	54.74
33-36	n	1	2	3
37-40	Mean	168.5	132.5	156.5
37-40	SD	0.71		20.79
37-40	n	2	1	3
41-44	Mean	127	116.9	120.27
41-44	SD	-	16.26	12.89
41-44	n	1	2	3
45-52	Mean	142.65	146	143.77
45-52	SD	36.66	86.27	47.93
45-52	n	4	2	6

SIDS		Female	Male	Combined
0-2	Mean	71.72	76.4	74.06
0-2	SD	19.14	22.88	19.69
0-2	n	4	4	8
3-4	Mean	100.1	100.58	100.44
3-4	SD	2.26	15.25	12.49
3-4	n	2	5	7
5-8	Mean	101.56	110.55	107.55
5-8	SD	10.93	21.57	18.66
5-8	n	4	8	12
9-12	Mean	119.85	124.61	122.83
9-12	SD	16.39	23.96	20.97
9-12	n	6	10	16
13-16	Mean	113.5	143.49	139.2
13-16	SD	10.61	19.22	20.97
13-16	n	2	12	14
17-20	Mean	122.73	149.89	143.62
17-20	SD	14.48	28.44	27.99
17-20	n	3	10	13
21-24	Mean	124.95	150.84	143.44
21-24	SD	2.9	17.52	19.12
21-24	n	2	5	7
25-28	Mean	171.76	155.11	156.96
25-28	SD	-	30.64	29.19
25-28	n	1	8	9
29-32	Mean	147.63	145.4	147.07
29-32	SD	50.93	-	41.6
29-32	n	3	1	4
33-36	Mean	-	146.5	146.5
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	-	136.49	136.49
37-40	SD	-	59.83	59.83
37-40	n	-	4	4
41-44	Mean	173.75	-	173.75
41-44	SD	36.84	-	36.84
41-44	n	2	-	2
45-52	Mean	170	161.3	167.82
45-52	SD	30.61	-	25.37
45-52	n	3	1	4

SUDS		Female	Male	Combined
0-2	Mean	75.27	76.8	76.11
0-2	SD	16.21	11.76	13.77
0-2	n	18	22	40
3-4	Mean	102.88	107.75	105.5
3-4	SD	30.31	16.35	23.44
3-4	n	12	14	26
5-8	Mean	112.43	114.75	113.87
5-8	SD	24.39	19.18	21.15
5-8	n	25	41	66
9-12	Mean	118.26	128.97	124.27
9-12	SD	16.28	21.36	19.87
9-12	n	25	32	57
13-16	Mean	127.21	132.69	130.65
13-16	SD	24.67	20.14	21.74
13-16	n	13	22	35
17-20	Mean	137.02	138.74	138.22
17-20	SD	17.15	26.11	23.5
17-20	n	10	23	33
21-24	Mean	130.47	148.3	143.55
21-24	SD	31.95	26.97	28.37
21-24	n	4	11	15
25-28	Mean	152.07	151.43	151.6
25-28	SD	3.52	34.48	28.89
25-28	n	3	8	11
29-32	Mean	151	174.83	165.3
29-32	SD	42.43	35.62	35.42
29-32	n	2	3	5
33-36	Mean	-	144.1	144.1
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	-	151.76	151.76
37-40	SD	-	18.82	18.82
37-40	n	-	5	5
41-44	Mean	-	167.1	167.1
41-44	SD	-	-	-
41-44	n	-	1	1
45-52	Mean	181.25	153.5	172
45-52	SD	34.29	-	29.06
45-52	n	2	1	3

Table G-2. Kidney Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	29.65	32.75	31.39
0-2	SD	7.81	8.53	8.34
0-2	n	70	89	159
3-4	Mean	37.39	37.76	37.54
3-4	SD	6.6	13.85	9.98
3-4	n	14	10	24
5-8	Mean	33.4	39.63	37.68
5-8	SD	6.48	6.85	7.26
5-8	n	11	24	35
9-12	Mean	37.94	45.06	43.51
9-12	SD	5.29	12.18	11.34
9-12	n	5	18	23
13-16	Mean	44.34	46.53	45.3
13-16	SD	12.21	5.35	9.6
13-16	n	9	7	16
17-20	Mean	51.71	46.82	49.02
17-20	SD	11.96	9.4	10.63
17-20	n	9	11	20
21-24	Mean	46.36	51.11	48.58
21-24	SD	10.35	11.25	10.67
21-24	n	8	7	15
25-28	Mean	36.1	57.69	52.71
25-28	SD	4.26	6.22	11.03
25-28	n	3	10	13
29-32	Mean	66.83	55.23	58.71
29-32	SD	21.43	11.77	15.03
29-32	n	3	7	10
33-36	Mean	49	63.03	59.52
33-36	SD	-	8.69	9.98
33-36	n	1	3	4
37-40	Mean	56.4	49.4	54.65
37-40	SD	4.06	-	4.82
37-40	n	3	1	4
41-44	Mean	55.43	53.9	54.74
41-44	SD	14.07	4.43	10.37
41-44	n	6	5	11
45-52	Mean	61.35	60.57	60.84
45-52	SD	13.23	10.42	11.18
45-52	n	8	15	23

SIDS		Female	Male	Combined
0-2	Mean	24.5	32.27	28.38
0-2	SD	7.63	13	10.94
0-2	n	6	6	12
3-4	Mean	33.23	32.02	32.54
3-4	SD	8.52	6.95	6.98
3-4	n	3	4	7
5-8	Mean	38.73	40.43	39.81
5-8	SD	7.19	6.01	6.16
5-8	n	4	7	11
9-12	Mean	45.17	42.96	43.74
9-12	SD	10.35	8.04	8.66
9-12	n	6	11	17
13-16	Mean	38.8	53.14	50.07
13-16	SD	3.63	11.99	12.24
13-16	n	3	11	14
17-20	Mean	40.25	51.7	49.94
17-20	SD	3.18	12.44	12.18
17-20	n	2	11	13
21-24	Mean	43.6	54.17	51.52
21-24	SD	11.6	11.09	11.45
21-24	n	2	6	8
25-28	Mean	48.99	52.44	52.05
25-28	SD		11.76	11.06
25-28	n	1	8	9
29-32	Mean	48.27	56.1	50.23
29-32	SD	4.31	-	5.26
29-32	n	3	1	4
33-36	Mean	-	60.6	60.6
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	53	56.06	55.55
37-40	SD	-	10.25	9.26
37-40	n	1	5	6
41-44	Mean	61.23	-	61.23
41-44	SD	10.28	-	10.28
41-44	n	3	-	3
45-52	Mean	57.95	47.5	52.73
45-52	SD	4.31	5.8	7.34
45-52	n	2	2	4

SUDS		Female	Male	Combined
0-2	Mean	29.69	29.85	29.77
0-2	SD	5.24	6.25	5.72
0-2	n	25	26	51
3-4	Mean	28.77	36.5	32.96
3-4	SD	5.55	8.23	8.01
3-4	n	11	13	24
5-8	Mean	37.25	40.34	39.19
5-8	SD	7.39	7.99	7.86
5-8	n	25	42	67
9-12	Mean	36.01	44.22	40.66
9-12	SD	5.18	7.6	7.78
9-12	n	26	34	60
13-16	Mean	40.55	45.57	43.69
13-16	SD	8.37	8.62	8.77
13-16	n	15	25	40
17-20	Mean	42.64	49.52	47.37
17-20	SD	8.91	8.36	8.99
17-20	n	10	22	32
21-24	Mean	42.82	52.09	49.2
21-24	SD	5.72	8.43	8.7
21-24	n	5	11	16
25-28	Mean	40.65	50.74	47.86
25-28	SD	13.6	11.1	12.26
25-28	n	4	10	14
29-32	Mean	53.73	61.27	57.5
29-32	SD	6.19	18.28	13.26
29-32	n	4	4	8
33-36	Mean	51.4	51.4	-
33-36	SD	-	-	-
33-36	n	1	1	-
37-40	Mean	56	45.13	47.85
37-40	SD	5.43	7.01	-
37-40	n	1	3	4
41-44	Mean	-	-	-
41-44	SD	-	-	-
41-44	n	0	0	-
45-52	Mean	51.7	61	54.8
45-52	SD	1.84	5.52	-
45-52	n	2	1	3

Table G- 3. Liver Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	158.47	146.45	152.04
0-2	SD	41.83	40.63	41.51
0-2	n	80	92	172
3-4	Mean	143.73	153.87	147.63
3-4	SD	24.45	51.55	36.61
3-4	n	16	10	26
5-8	Mean	174.89	189.92	185.45
5-8	SD	32.97	52.97	47.95
5-8	n	11	26	37
9-12	Mean	188.99	205.5	200.25
9-12	SD	47.51	49.85	48.61
9-12	n	7	15	22
13-16	Mean	211.54	246.53	228.11
13-16	SD	43.12	44.3	46.09
13-16	n	10	9	19
17-20	Mean	231.83	235.32	233.58
17-20	SD	54.94	50.57	51.56
17-20	n	11	11	22
21-24	Mean	249.56	261.09	255.32
21-24	SD	45.8	58.22	50.68
21-24	n	7	7	14
25-28	Mean	260.09	286.22	277.51
25-28	SD	26.63	39.56	37.03
25-28	n	5	10	15
29-32	Mean	294.95	335.4	319.22
29-32	SD	61.36	27.87	46.08
29-32	n	4	6	10
33-36	Mean	256.85	337.67	305.34
33-36	SD	46.88	10.69	50.66
33-36	n	2	3	5
37-40	Mean	307.6	290.8	302
37-40	SD	39.03	29.25	-
37-40	n	2	1	3
41-44	Mean	323.68	296.12	309.9
41-44	SD	107.17	28.81	75.39
41-44	n	5	5	10
45-52	Mean	344.51	366.87	358.74
45-52	SD	59.1	73.98	68.36
45-52	n	8	14	22

SIDS		Female	Male	Combined
0-2	Mean	118.52	154.86	138.08
0-2	SD	29.95	47.87	43.3
0-2	n	6	7	13
3-4	Mean	153.95	185.14	176.23
3-4	SD	23.97	53.09	46.97
3-4	n	2	5	7
5-8	Mean	200.3	203.53	202.54
5-8	SD	39.08	47.01	43.1
5-8	n	4	9	13
9-12	Mean	209.7	200.07	203.62
9-12	SD	36.96	29.09	31.54
9-12	n	7	12	19
13-16	Mean	226.35	256.95	252.58
13-16	SD	72.62	53.11	54
13-16	n	2	12	14
17-20	Mean	216	285.75	269.65
17-20	SD	13	59.74	60.34
17-20	n	3	10	13
21-24	Mean	280.5	292.88	289.79
21-24	SD	57.28	25.55	31.11
21-24	n	2	6	8
25-28	Mean	266	288.61	286.35
25-28	SD	25.05	24.68	-
25-28	n	1	9	10
29-32	Mean	339.37	311.7	332.45
29-32	SD	55.08	47.05	-
29-32	n	3	1	4
33-36	Mean	336.7	336.7	-
33-36	SD	-	-	-
33-36	n	1	1	-
37-40	Mean	361	341.6	344.83
37-40	SD	27.55	25.88	-
37-40	n	1	5	6
41-44	Mean	371.47	371.47	-
41-44	SD	42.26	42.26	-
41-44	n	3	3	-
45-52	Mean	327	316	321.5
45-52	SD	4.24	50.06	29.69
45-52	n	2	2	4

SUDS		Female	Male	Combined
0-2	Mean	152.19	144.53	148.36
0-2	SD	38.23	29.23	33.93
0-2	n	27	27	54
3-4	Mean	163.45	172.25	168.22
3-4	SD	17.28	33.41	27.06
3-4	n	11	13	24
5-8	Mean	196.68	192.2	193.98
5-8	SD	30.63	26	27.79
5-8	n	27	41	68
9-12	Mean	196.05	216.71	208.05
9-12	SD	27.4	30.52	30.79
9-12	n	26	36	62
13-16	Mean	227.92	242.58	237.43
13-16	SD	43.28	38.5	40.27
13-16	n	13	24	37
17-20	Mean	228.97	261.96	251.88
17-20	SD	42.5	38.12	41.83
17-20	n	11	25	36
21-24	Mean	253.76	274.62	268.1
21-24	SD	18.72	54.71	46.78
21-24	n	5	11	16
25-28	Mean	265.33	295.28	287.79
25-28	SD	36.95	57.52	53.27
25-28	n	3	9	12
29-32	Mean	315.33	311.15	312.94
29-32	SD	38.89	31.71	31.81
29-32	n	3	4	7
33-36	Mean	282.1	282.1	-
33-36	SD	-	-	-
33-36	n	1	1	-
37-40	Mean	304	317.66	315.38
37-40	SD	22.33	20.74	-
37-40	n	1	5	6
41-44	Mean	392	392	-
41-44	SD	-	-	-
41-44	n	1	1	-
45-52	Mean	387.85	366	380.57
45-52	SD	25.67	22.1	-
45-52	n	2	1	3

Table G-4. Brain Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	379.61	402.85	392.33
0-2	SD	39.34	48.87	45.9
0-2	n	24	29	53
3-4	Mean	451.22	486.58	462.39
3-4	SD	53.63	83.39	64.3
3-4	n	13	6	19
5-8	Mean	505.43	529.52	521.91
5-8	SD	62.44	69.46	66.57
5-8	n	6	13	19
9-12	Mean	529.92	613.69	588.55
9-12	SD	62.67	62.85	72.72
9-12	n	6	14	20
13-16	Mean	639.94	657.77	648.86
13-16	SD	79.28	83.98	79
13-16	n	7	7	14
17-20	Mean	666.36	760.99	717.98
17-20	SD	63.94	58.24	75.98
17-20	n	5	6	11
21-24	Mean	865.13	726.13	772.47
21-24	SD	49.34	132.35	128.01
21-24	n	3	6	9
25-28	Mean	764.95	840.4	821.54
25-28	SD	148.42	97.61	105.7
25-28	n	2	6	8
29-32	Mean	-	877.48	877.48
29-32	SD	-	84.51	84.51
29-32	n	-	4	4
33-36	Mean	-	981	981
33-36	SD	-	79.54	79.54
33-36	n	-	3	3
37-40	Mean	877	1075	926.5
37-40	SD	133.15	-	147.04
37-40	n	3	1	4
41-44	Mean	963.4	955.67	960.09
41-44	SD	82.48	209.68	134.44
41-44	n	4	3	7
45-52	Mean	964.52	1055.13	1026.82
45-52	SD	106.68	71.05	91
45-52	n	5	11	16

SIDS		Female	Male	Combined
0-2	Mean	381.25	401.27	391.26
0-2	SD	36.07	74.81	56.96
0-2	n	6	6	12
3-4	Mean	477.3	499.8	490.8
3-4	SD	21.64	45.11	35.86
3-4	n	2	3	5
5-8	Mean	525.5	567.81	558.41
5-8	SD	27.58	56.03	52.9
5-8	n	2	7	9
9-12	Mean	619.36	599.07	607.94
9-12	SD	40.39	27.32	34.04
9-12	n	7	9	16
13-16	Mean	680.17	699.24	694.84
13-16	SD	141.94	78.72	89.86
13-16	n	3	10	13
17-20	Mean	707.5	715.7	714.33
17-20	SD	45.96	271.12	245.65
17-20	n	2	10	12
21-24	Mean	836.25	835.42	835.62
21-24	SD	52.68	74.06	65.68
21-24	n	2	6	8
25-28	Mean	682	785.43	772.5
25-28	SD	-	66.1	71.29
25-28	n	1	7	8
29-32	Mean	887.07	-	887.07
29-32	SD	32.62	-	32.62
29-32	n	3	-	3
33-36	Mean	-	1002	1002
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	1014	1005.5	1007.2
37-40	SD	-	69.83	60.59
37-40	n	1	4	5
41-44	Mean	955.77	-	955.77
41-44	SD	127.26	-	127.26
41-44	n	3	-	3
45-52	Mean	943.33	1011	960.25
45-52	SD	53.26	-	55.1
45-52	n	3	1	4

SUDS		Female	Male	Combined
0-2	Mean	420.48	433.43	427.23
0-2	SD	57.34	63.42	60.3
0-2	n	23	25	48
3-4	Mean	466.6	513.68	488.18
3-4	SD	65.72	52.84	63.58
3-4	n	13	11	24
5-8	Mean	529.71	563.46	550.48
5-8	SD	64.06	58.38	62.37
5-8	n	25	40	65
9-12	Mean	594.31	634.52	615.8
9-12	SD	47.15	67.61	61.88
9-12	n	27	31	58
13-16	Mean	676.6	710.7	698.46
13-16	SD	47.28	78.82	70.45
13-16	n	14	25	39
17-20	Mean	704.81	741.37	730.12
17-20	SD	55.48	75.92	71.25
17-20	n	8	18	26
21-24	Mean	789.02	796.1	793.92
21-24	SD	64.11	87.32	78.24
21-24	n	4	9	13
25-28	Mean	820.75	828.22	825.92
25-28	SD	60.74	64.96	61.22
25-28	n	4	9	13
29-32	Mean	909.17	869.75	889.46
29-32	SD	56.52	43.97	51.4
29-32	n	4	4	8
33-36	Mean	-	1027.3	1027.3
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	822	927.4	906.32
37-40	SD	-	63.22	72.24
37-40	n	1	4	5
41-44	Mean	-	1063	1063
41-44	SD	-	-	-
41-44	n	-	1	1
45-52	Mean	997	1140	1044.67
45-52	SD	36.77	-	86.56
45-52	n	2	1	3

Table G-5. Spleen Descriptive Statistics by Cause of Death Groups

Control		Female	Male	Combined
0-2	Mean	10.59	12.17	11.45
0-2	SD	4.37	5.26	4.93
0-2	n	85	102	187
3-4	Mean	13.86	14.03	13.93
3-4	SD	4.36	6.44	5.19
3-4	n	16	11	27
5-8	Mean	13.85	15.66	15.1
5-8	SD	6	5.58	5.69
5-8	n	12	27	39
9-12	Mean	13.97	20.61	18.32
9-12	SD	5.24	6.95	7.08
9-12	n	10	19	29
13-16	Mean	20.89	19.69	20.29
13-16	SD	8.96	4.45	6.89
13-16	n	9	9	18
17-20	Mean	21.94	23.24	22.56
17-20	SD	7.83	7.16	7.36
17-20	n	11	10	21
21-24	Mean	21.8	21.99	21.91
21-24	SD	7.01	6.04	6.21
21-24	n	6	8	14
25-28	Mean	21.49	29.4	27.14
25-28	SD	7.96	11.87	11.22
25-28	n	4	10	14
29-32	Mean	21.34	23.4	22.78
29-32	SD	5.64	12.04	10.23
29-32	n	3	7	10
33-36	Mean	31.53	36.48	34.36
33-36	SD	13.51	9.67	10.71
33-36	n	3	4	7
37-40	Mean	23.17	-	23.17
37-40	SD	6.17	-	6.17
37-40	n	3	0	3
41-44	Mean	26.42	29	27.71
41-44	SD	10.04	11.05	10.04
41-44	n	5	5	10
45-52	Mean	35.75	37.78	37.02
45-52	SD	7.4	15.07	12.58
45-52	n	9	15	24

SIDS		Female	Male	Combined
0-2	Mean	9.87	11.67	10.84
0-2	SD	4.88	3.62	4.17
0-2	n	6	7	13
3-4	Mean	13.33	13.54	13.46
3-4	SD	4.51	3.93	3.83
3-4	n	3	5	8
5-8	Mean	13.47	12.86	13.05
5-8	SD	0.98	5.33	4.39
5-8	n	4	9	13
9-12	Mean	19.89	22.13	21.25
9-12	SD	7	10.81	9.34
9-12	n	7	11	18
13-16	Mean	17.77	26.96	24.99
13-16	SD	10.04	8.57	9.35
13-16	n	3	11	14
17-20	Mean	18.53	26.93	24.99
17-20	SD	3.14	5.31	6.03
17-20	n	3	10	13
21-24	Mean	26.3	28.82	28.19
21-24	SD	5.8	7.86	7.09
21-24	n	2	6	8
25-28	Mean	23.61	29.46	28.73
25-28	SD	-	8.19	7.86
25-28	n	1	7	8
29-32	Mean	24.53	25.5	24.77
29-32	SD	8.22	-	6.73
29-32	n	3	1	4
33-36	Mean	-	37.4	37.4
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	33	28.67	29.29
37-40	SD	-	9.93	9.22
37-40	n	1	6	7
41-44	Mean	37.83	-	37.83
41-44	SD	12.98	-	12.98
41-44	n	3	-	3
45-52	Mean	31.5	35.35	33.42
45-52	SD	14.85	21.14	15.08
45-52	n	2	2	4

SUDS		Female	Male	Combined
0-2	Mean	12	12.5	12.25
0-2	SD	3.55	3.32	3.42
0-2	n	27	27	54
3-4	Mean	11.96	17.4	14.68
3-4	SD	3.06	7.97	6.54
3-4	n	14	14	28
5-8	Mean	17.4	18.14	17.86
5-8	SD	6.03	6.83	6.51
5-8	n	26	43	69
9-12	Mean	17.23	22.61	20.35
9-12	SD	5.98	5.84	6.43
9-12	n	26	36	62
13-16	Mean	19.33	22.9	21.62
13-16	SD	6.59	6.07	6.42
13-16	n	14	25	39
17-20	Mean	21.58	22.93	22.48
17-20	SD	4.94	5.88	5.54
17-20	n	11	22	33
21-24	Mean	20.85	27.23	25.53
21-24	SD	4.36	9	8.4
21-24	n	4	11	15
25-28	Mean	19.9	30.05	26.93
25-28	SD	4.68	11.15	10.59
25-28	n	4	9	13
29-32	Mean	31.4	28.9	30.57
29-32	SD	3.79	1.56	3.28
29-32	n	4	2	6
33-36	Mean	-	12.7	12.7
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	46	26.76	29.97
37-40	SD	-	7.39	10.27
37-40	n	1	5	6
41-44	Mean	-	41.3	41.3
41-44	SD	-	-	-
41-44	n	-	1	1
45-52	Mean	30.7	70	50.35
45-52	SD	-	-	27.79
45-52	n	1	1	2

Table G-6. Adrenal Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	8.45	8.14	8.28
0-2	SD	3.74	3.88	3.81
0-2	n	68	80	148
3-4	Mean	4.33	5.51	4.87
3-4	SD	0.73	1.8	1.43
3-4	n	12	10	22
5-8	Mean	4.02	5.16	4.83
5-8	SD	1.34	1.92	1.83
5-8	n	9	22	31
9-12	Mean	4.78	4.69	4.72
9-12	SD	1.99	2.12	2.04
9-12	n	8	16	24
13-16	Mean	4.66	4	4.36
13-16	SD	0.84	0.93	0.91
13-16	n	7	6	13
17-20	Mean	4.81	4.33	4.56
17-20	SD	1.57	1.61	1.57
17-20	n	10	11	21
21-24	Mean	3.69	5.02	4.24
21-24	SD	1.56	1.43	1.6
21-24	n	7	5	12
25-28	Mean	3.6	5.31	4.88
25-28	SD	1.31	1.43	1.55
25-28	n	3	9	12
29-32	Mean	2.87	4.44	4.26
29-32	SD	-	1.14	1.18
29-32	n	1	8	9
33-36	Mean	4.83	4.25	4.5
33-36	SD	1.61	0.91	1.17
33-36	n	3	4	7
37-40	Mean	4.53	4.1	4.42
37-40	SD	0.42	-	0.4
37-40	n	3	1	4
41-44	Mean	3.1	4.5	3.62
41-44	SD	1.11	1.15	1.27
41-44	n	5	3	8
45-52	Mean	4.05	4.49	4.32
45-52	SD	0.52	1.56	1.28
45-52	n	7	12	19

SIDS		Female	Male	Combined
0-2	Mean	4.87	6.67	5.85
0-2	SD	2.56	2.42	2.53
0-2	n	5	6	11
3-4	Mean	3.57	6.35	5.16
3-4	SD	0.86	2.1	2.16
3-4	n	3	4	7
5-8	Mean	3.48	4.26	3.97
5-8	SD	0.46	1.15	1.01
5-8	n	4	7	11
9-12	Mean	4.52	4.8	4.71
9-12	SD	0.91	1.09	1.01
9-12	n	5	10	15
13-16	Mean	5.65	6.06	5.98
13-16	SD	2.62	3.52	3.23
13-16	n	2	8	10
17-20	Mean	2.95	4.2	3.97
17-20	SD	1.34	0.74	0.93
17-20	n	2	9	11
21-24	Mean	3.2	4.6	4.2
21-24	SD	0.99	0.93	1.1
21-24	n	2	5	7
25-28	Mean	3.21	4.63	4.45
25-28	SD	-	1.29	1.29
25-28	n	1	7	8
29-32	Mean	3.65	3.6	3.63
29-32	SD	1.91	-	1.35
29-32	n	2	1	3
33-36	Mean	-	5.2	5.2
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	6	3.9	4.25
37-40	SD	-	1.17	1.35
37-40	n	1	5	6
41-44	Mean	4	-	4
41-44	SD	0.14	-	0.14
41-44	n	2	-	2
45-52	Mean	7.3	3.3	5.7
45-52	SD	5.8	0.85	4.67
45-52	n	3	2	5

SUDS		Female	Male	Combined
0-2	Mean	5.49	4.61	5.05
0-2	SD	2.1	2.4	2.27
0-2	n	23	23	46
3-4	Mean	4.43	4.92	4.68
3-4	SD	1.8	1.56	1.67
3-4	n	12	12	24
5-8	Mean	4.61	4.45	4.51
5-8	SD	2.63	1.54	2.01
5-8	n	20	32	52
9-12	Mean	3.12	4.15	3.74
9-12	SD	0.77	1.61	1.42
9-12	n	20	30	50
13-16	Mean	3.64	4.44	4.13
13-16	SD	0.95	1.24	1.19
13-16	n	15	23	38
17-20	Mean	3.24	4.4	4.08
17-20	SD	0.82	1.68	1.57
17-20	n	8	21	29
21-24	Mean	2.4	4.27	3.96
21-24	SD	0.14	0.95	1.13
21-24	n	2	10	12
25-28	Mean	4.2	4.63	4.58
25-28	SD	-	1.95	1.84
25-28	n	1	9	10
29-32	Mean	3.5	5.27	4.38
29-32	SD	1.51	2.37	2.02
29-32	n	3	3	6
33-36	Mean	-	3	3
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	-	2.88	2.88
37-40	SD	-	0.49	0.49
37-40	n	-	4	4
41-44	Mean	-	3.7	3.7
41-44	SD	-	-	-
41-44	n	-	1	1
45-52	Mean	2.3	8	5.15
45-52	SD	-	-	4.03
45-52	n	1	1	2

Table G- 7. Thymus Descriptive Statistics by Cause of Death Groups

CONTROL		Female	Male	Combined
0-2	Mean	9.45	10.65	10.11
0-2	SD	4.12	4.6	4.42
0-2	N	72	88	160
3-4	Mean	18.39	14.08	16.35
3-4	SD	6.3	8.18	7.38
3-4	N	10	9	19
5-8	Mean	17.16	19.85	18.84
5-8	SD	8.7	9.57	9.16
5-8	N	9	15	24
9-12	Mean	23.27	27.06	26.07
9-12	SD	8.25	10	9.54
9-12	N	6	17	23
13-16	Mean	30.05	32.11	30.95
13-16	SD	12.71	12.73	12.33
13-16	N	9	7	16
17-20	Mean	28.5	26.44	27.19
17-20	SD	16.35	11.31	12.57
17-20	N	4	7	11
21-24	Mean	24.1	25.57	24.79
21-24	SD	12.13	9.06	10.46
21-24	N	8	7	15
25-28	Mean	29.28	29.96	29.82
25-28	SD	3.71	20.19	17.85
25-28	N	2	8	10
29-32	Mean	27.7	32.18	30.69
29-32	SD	16.81	21.99	19.44
29-32	N	3	6	9
33-36	Mean	40.4	42.43	41.92
33-36	SD	-	15.22	12.47
33-36	n	1	3	4
37-40	Mean	21.73	20.7	21.48
37-40	SD	5.49	-	4.51
37-40	n	3	1	4
41-44	Mean	28.17	18.32	22.54
41-44	SD	5.48	11.61	10.25
41-44	n	3	4	7
45-52	Mean	33.27	30.99	31.83
45-52	SD	11.8	12.63	12.05
45-52	n	7	12	19

SIDS		Female	Male	Combined
0-2	Mean	12.87	12.14	12.48
0-2	SD	6.62	4.69	5.42
0-2	n	6	7	13
3-4	Mean	24.6	25.73	25.24
3-4	SD	6.02	9.88	7.83
3-4	n	3	4	7
5-8	Mean	26.45	25.74	25.96
5-8	SD	6.02	10.46	9.06
5-8	n	4	9	13
9-12	Mean	33.05	28.43	30.16
9-12	SD	12.66	6.22	9.05
9-12	n	6	10	16
13-16	Mean	26.63	42.73	39.51
13-16	SD	6.25	14.67	14.8
13-16	n	3	12	15
17-20	Mean	28.5	38.04	36.57
17-20	SD	17.68	9.86	10.95
17-20	n	2	11	13
21-24	Mean	48.7	49.43	49.33
21-24	SD	-	13.46	12.29
21-24	n	1	6	7
25-28	Mean	28.7	28.4	28.43
25-28	SD	-	10.41	9.74
25-28	n	1	8	9
29-32	Mean	40.77	43.7	41.5
29-32	SD	8.08	-	6.76
29-32	n	3	1	4
33-36	Mean	-	30	30
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	25	31.23	30.34
37-40	SD	-	10.32	9.71
37-40	n	1	6	7
41-44	Mean	29.65	-	29.65
41-44	SD	3.18	-	3.18
41-44	n	2	-	2
45-52	Mean	32	25.7	27.8
45-52	SD	-	3.82	4.53
45-52	n	1	2	3

SUDS		Female	Male	Combined
0-2	Mean	14.01	16.6	15.3
0-2	SD	6.31	5.82	6.15
0-2	n	25	25	50
3-4	Mean	21.04	25.22	23.13
3-4	SD	6.88	9.38	8.34
3-4	n	13	13	26
5-8	Mean	25.12	30.16	28.16
5-8	SD	7.83	10.65	9.88
5-8	n	25	38	63
9-12	Mean	26.62	30.96	29.1
9-12	SD	7.34	9.27	8.7
9-12	n	24	32	56
13-16	Mean	32.4	40.41	37.54
13-16	SD	8.12	13.77	12.55
13-16	n	14	25	39
17-20	Mean	34.16	37.7	36.48
17-20	SD	8.43	13.93	12.29
17-20	n	11	21	32
21-24	Mean	29.66	41.17	37.57
21-24	SD	9.6	13.8	13.49
21-24	n	5	11	16
25-28	Mean	29.62	32.87	31.94
25-28	SD	11.38	11.13	10.86
25-28	n	4	10	14
29-32	Mean	37.05	41.52	39.29
29-32	SD	12.2	16.31	13.55
29-32	n	4	4	8
33-36	Mean	-	39.1	39.1
33-36	SD	-	-	-
33-36	n	-	1	1
37-40	Mean	36	29.02	30.18
37-40	SD	-	12.05	11.15
37-40	n	1	5	6
41-44	Mean	49.7	49.7	49.7
41-44	SD	-	-	-
41-44	n	-	1	1
45-52	Mean	34.5	20.5	29.83
45-52	SD	4.95	-	8.81
45-52	n	2	1	3

Curriculum Vitae

AUDREY-ANN M EVETTS

WORK EXPERIENCE:

2008-Current **Pathologists' Assistant, London Health Sciences Center**, London, Ontario
-Performing duties associated with autopsy and surgical grossing
-Teaching graduate students and residents
-Assisting funeral homes and religious communities
-Member of the Safety and Social Committees
-Involvement in departmental policy development
-Involvement in Ontario lab accreditation committees
-Basic training on voice recognition software dictation

EDUCATION

2013 - Current **MSc. Pathology** Candidate, Western University, London, ON
Thesis Title: Body and Organ Measurements in Neonates and Infants: An Autopsy Study
Thesis Supervisors: Dr. E. Tugaleva and Dr. M. Shkrum

2005 - 2008 **MSc. Pathology**, University of Manitoba, Winnipeg, MB
Thesis Title: Gross Assessment of Colonic Abnormalities with Particular Focus on Diverticular Disease and Polyps: An Autopsy Study
Thesis Advisor: Dr. C. Littman

2001 – 2005 **BSc. Biological Sciences with Honors,** *Forensic Science***,** Laurentian University, Sudbury ON

TEACHING

2008 – Current **Pathologists' Assistant Mentor, London Health Sciences Center**
-Providing guidance and instructions on postmortem examination techniques and surgical dissections
-Practical evaluation of student's theoretical knowledge and practical skills

ABSTRACTS AND PUBLICATIONS

2016 A Evetts, Dr. M Shkrum, Dr. E Tugaleva
"Postmortem Body and Organ Measurements in Neonates and Infants: A Review of Reference Resources Used by Ontario Pathologists (Part 1)"
Am J Forensic Med Pathol, Accepted for Publication, 2016

2016 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. C Dean,
"Ontario Growth Standards for Infants: A Retrospective Autopsy Study"
Abstract - 67th Annual Meeting of the Canadian Association of
Pathologist – Pathologist Assistant Section, Vancouver, BC

2016 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. C Dean,
"Ontario Growth Standards for Infants: A Retrospective Autopsy Study"
Abstract - London Health Research Day,

2014 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. J Koval,
"Ontario Growth Standards for Neonates and Infants: An Autopsy Retrospective Study"
Abstract - London Health Research Day

RESEARCH PRESENTATIONS

2016 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. C Dean,
"Ontario Growth Standards for Infants: A Retrospective Autopsy Study"
Poster, 67th Annual Meeting of the Canadian Association of
Pathologist – Pathologist Assistant Section Poster Presentation, Vancouver, BC

2013-2015 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. C Dean,
"Ontario Growth Standards for Neonates and Infants. An Autopsy Retrospective Study."
Poster, Annual Pathology Research Day, London, ON

2012-2014 A Evetts, Dr. M Shkrum, Dr. E Tugaleva, Dr. Z Khan, Dr. J Koval
"Ontario Growth Standards for Neonates and Infants: An Autopsy Retrospective Study"
Journal Club January 2012, Canada, Ontario, London

AWARDS

2016 Award Best Poster "Ontario Growth Standards for Infants: A Retrospective Autopsy Study"
67th Annual Meeting of the Canadian Association of Pathologist Vancouver, BC

2016 Dr. Fredrick Winnet Luney Graduate Research Award
Enhancing graduate training and promoting students to present their graduate research work at scientific meetings and pursue research-related activities

2016 Pathology and Laboratory Medicine Support Staff Continuing Education Award
Continuing education award for laboratory members

2012-2014 London Laboratory Services Groups Award
Continuing education award for laboratory members

2012 Diane Y Stewart Endowed Scholarship Award
Professional development for hospital support staff

SOCIETIES AND MEMBERSHIPS

Canadian Association of Pathologists-Association Canadienne des Pathologistes (CAP-ACP)

Western Society of Graduate Students – Western University

Alumni Associations, University of Manitoba and Laurentian University