A Comparison Study of Hospitalization Characteristics and Predictors for Inpatients with Down's Syndrome With and Without Aging Diseases in The United States

By Susan Banas

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A Comparison Study of Hospitalization Characteristics and Predictors for Inpatients with Down's Syndrome With and Without Aging Diseases in The United States

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ABSTRACT

BACKGROUND: Down's syndrome is one of the most common genetic diseases that causes a disability to their hosts. The prevalence of this disability is reported in approximately one per seven hundred births and is influenced by several factors such as the age of the mother and environment of the pregnancy. Approximately ninety five percent of the cases are related to an abnormal addition of chromosome 21. There is a relationship to the translocation of certain genetic chromosomes. One example is the Robertsonian chromosomal abnormality. It is associated with the fusion of up to four percent of the chromosomes in Down's syndrome patients. The main defects and abnormalities found in patients with Down's syndrome are congenital deformity, heart disease and abnormal functions of the respiratory tract. These deformities negatively influence the life span and survival rates of the patients. The abnormal physiological functions of their body organs increase the need for healthcare professionals to manage the complications and mortality of the disease.

METHOD: The study implemented a cross sectional design to achieve the objectives of the present study. The data was downloaded and extracted, with permission, from the Nationwide Inpatient Sample (NIS). A total of 58,438 patients with Down's syndrome were admitted to hospitals in the United States between the years of 2007-2012. The main variables of the NIS dataset involved non-clinical and clinical information. The non-clinical information included the patients' demographic information, financial statuses, hospital information, length of stay and total charges. The clinical information involved the patients' health status, comorbidities, number of procedures, healthcare services and mortality. The Statistical Package for the Social Sciences (SPSS) version 22 was used to analyze the data for the present study. All outcomes with a p-value of less than 0.05 were found to be significant. Multinomial logistic regression and multiple linear regressions (dummy method) were the appropriate statistical tests utilized to determine the predictors of the study outcomes.

RESULTS: The descriptive analysis of the present study revealed the highest incidences of the patient socio-demographic information were those who were younger than thirty years of age (55.2%), White (53.8%), Male (53.9%), on Medicare (36.7%) and had a household income in the 0-25th percentile (27.5%). The patients' medical information showed the highest comorbidity with hypothyroidism (23.5%), fluid-electrolyte disorders (20.9%) and neurological disorders (14.2%). The incidence of mortality for Down's syndrome patients was 2.9%. The mean (± SD) for the length of hospital stay and total charges are 7.34 (±12.605) days and $53678.26 (±120800.0) respectively. The admission of Down's syndrome patients with Alzheimer's disease was higher than those with Parkinson's disease. The overall mortality showed a higher incidence with Alzheimer's than with Parkinson's disease (9.1% vs. 0.7%). The incidence of mortality increased with dementia and cardiac malformation by 13.49% and 7.78%, respectively. A significant association was found between Down's syndrome complications and Parkinson's disease in terms of atlantoaxial instability by 12.77%. The risk factors for the length of stay for Down's syndrome only were congestive heart failure, fluid and electrolyte disorders and weight loss. The Down's syndrome patients with Parkinson's and Alzheimer's diseases presented drug abuse and weight loss as the main risk factors for the length of hospital stay. The number of

procedures is the predictor with the highest effect on total charges for Down's syndrome patients. It is followed by coagulopathy and congestive heart failure. The predictors of total charges for Down's syndrome patients with Parkinson's and Alzheimer's diseases presented drug abuse and the number of procedures as the main risk factors. The number of procedures showed the highest incidence of mortality for Down's syndrome patients, followed by fluid and electrolyte disorders and age categories. In Down's syndrome patients the risk factor with the highest incidence of mortality was pulmonary circulation disorder. The risk factor with the highest incidence of mortality was neurological disorders for Parkinson's and Alzheimer's diseases respectively.

CONCLUSION: Several factors were observed to increase the high risk of mortality, total charges and length of stay for Down's syndrome patients included in the present study. The comorbidities can increase the costs and mortality. These are considered as serious risks for the patients' outcome. The patients with Down's syndrome showed little difference in the type and severity of risk factors between those with and without aging diseases. Although the mortality is higher with numerous risk factors in Down's syndrome patients with Alzheimer's disease, the severity of risk factors is higher with Parkinson's disease. This is because of the complications that result from the Down's syndrome related diseases. It will require more attention from the government, clinicians and researchers to manage the preventable risk factors to minimize the incidence of mortality and control the costs of therapy and health services administered to Down's syndrome patients with and without aging diseases.

CHAPTER I

INTRODUCTION

1.1 Background of Down's syndrome

Down's syndrome is a common genetic disease that causes a disability to their hosts. The prevalence of this disability was reported in approximately one per seven hundred births. It is influenced by several factors such as the age of the mother and the environment during their pregnancy (Centers for Disease Control and Prevention, 2006; Cocchi et al., 2010; Mégarbané et al., 2009). The most common cause of Down's syndrome is the abnormality of a genetic formation. Approximately ninety five percent of the cases were related to the abnormal addition of chromosome 21. They are also related to the translocation of genetic chromosomes such as Robertsonian. Robertsonian is associated to the fusion of chromosomes in four percent of Down's syndrome patients (Mutton, Alberman, & Hook, 1996; Zhu et al., 2013). The main defects and abnormalities found in patients with Down's syndrome are congenital deformity, congenital heart diseases and abnormal functions of the respiratory tract. These deformities negatively influence the life span and survival rates of the patients. However, the rise in the age limit for patients diagnosed with Down's syndrome in the last decade has increased due to the development of medical interventions and improvements in healthcare services (Day, Strauss, Shavelle, & Reynolds, 2005; Rasmussen, Wong, Correa, Gambrell, & Friedman, 2006). This chapter includes the historical background of Down's syndrome, pathophysiology and etiology of Down's syndrome, epidemiology of Down's syndrome, goals and objectives of the present study, research hypotheses, statement of the problem, definition of terms and the importance of the study.

1.2 Historical background of Down's syndrome

Down's syndrome was first discovered twenty five hundred years ago in an area located between Colombia and Ecuador (Mégarbané et al., 2009). Martinez-Frias reported the first identification of the disorder and the clinical relationship between Trisomy 21 and the incidence of Alzheimer's disease. This was identified in six hundred patients in Mexico between the fifteenth and sixteenth century (Martinez-Frias, 2005). In the year 1846, a psychiatrist by the name of Esquirol differentiated between the psychological disorders and Trisomy 21 related to the mental ability and the retardation that is induced by Down's syndrome (Mégarbané et al., 2009).

Down's syndrome is named after the British physician, John Langdon Down. He was the first individual to describe the disorder in 1866. This syndrome was originally known as 'Mongolism'. However, the term was not accepted, and it was changed to 'Down's syndrome' in the year 1970. Dr. Down diagnosed a common symptom of the patients which is having an 'up-slanted eye'. In 1950, Professor Jerome Lejeune, a French physician of genetics, discussed the chromosome structure changes observed in patients diagnosed with Down's syndrome. He discovered that one of the main reasons for the disease was a change in the chromosomes during pregnancy. A high prevalence of Down's syndrome was found in the individuals who were born from mothers older than thirty-five years of age. His research group identified serum markers as an early sign and prediction for this illness. Several investigational studies have been done which have highlighted the common problems and obstacles that patients endure during their lifetime. In the United States during the first half of the twentieth century, the care of patients with Down's syndrome was considered a priority for society. This is because the loss of care for these individuals by their families caused psychological and health issues (Goplerud, 1999; The National Association for Down's Syndrome, 2018).

There were numerous terms utilized before and after the initial diagnosis of Down's syndrome. The terms depended on the type, symptom, classification and scientist who diagnosed and approved the common characteristics of the disease. Figure 1 depicts the terminology and time period related to the disease. The term 'Mongolism' scientifically ended its' use in the year 1980. This term was replaced with 'Down's syndrome'. However, there are other terms which have been utilized in scientific studies such as 'Langdon Down's and 'Trisomy'. The present studies utilize the terminology of 'Down's syndrome' for this illness.

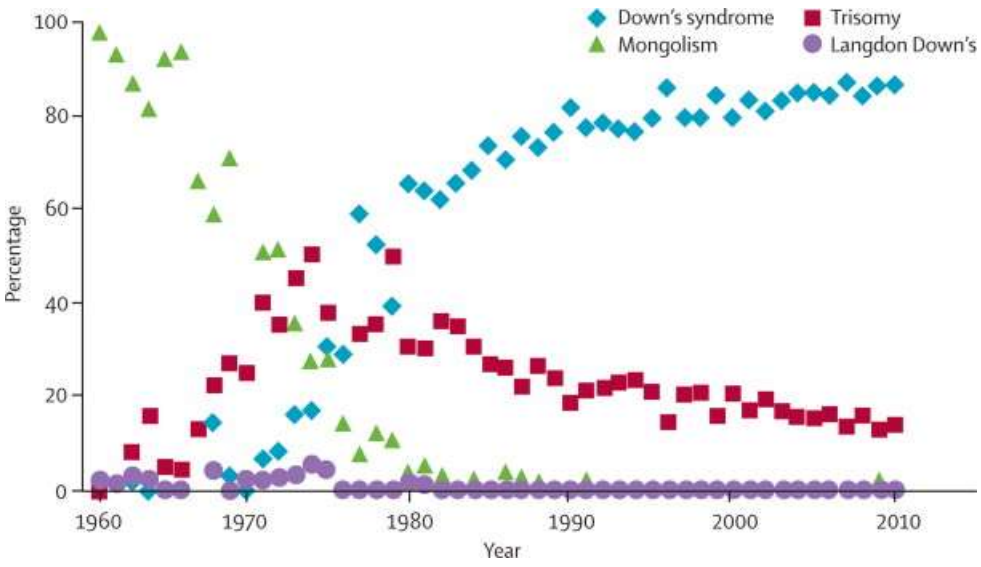


Figure 1 Terminology Terms of Down's syndrome - Adapted from (Rodríguez-Hernández & Montoya, 2011)

1.3 Pathophysiology and etiology of Down's syndrome

Down's syndrome is a genetic disease impacted by the abnormal changes found in chromosome 21. Transient myeloproliferative disorder is the hematopoietic disorder that influences approximately ten percent of the neonates with Down's syndrome. The abnormal mutations of the GATA1 gene is considered one of the main reasons for the change in the histological and physiological structures. The mutations influence the balance of the organ and body functionality. These changes are believed to be the reasons for diseases such as megakaryoblastic leukemia or autoimmune disorders. The GATA1 mutant genesis is associated to the pluripotent stem cells found in a normal healthy subject. These cells are responsible for the reproduction of the human embryonic hematopoietic. The cells have an impact on the growth and formation of organs and body tissue and are an indicator for the development of Down's syndrome in a newborn baby (Yoko et al., 2014).

The primary etiologies of Down's syndrome, as reported by literature, are attributed to several theories. The first theory is the change and mutation that occurs in the copy of the human chromosome 21 (Has 21). This mutation causes the chromosome to be small in length (Antonarakis, Lyle, Dermitzakis, Reymond, & Deutsch, 2004). The second theory related to this disease is known as the Robertsonian translocation of chromosomes. The changes in the chromosome cause an incomplete clone which will prompt an imbalance in the length of the arms. The third theory is related to the mosaicism of Down's syndrome. This concept is related to errors in the protein strips which cause a division in the body organs and tissues (Asim, Kumar, Muthuswamy, Jain, & Agarwal, 2015).

One of the main clinical pathophysiological results of Down's syndrome is the coexistence of several conditional diseases. These diseases include morphological abnormalities such as heart defects, leukemia, hypertension, gastrointestinal disorders and Alzheimer's disease. Figure 2 describes the main diseases and disorders which are induced by the genetic changes found in patients diagnosed with Down's syndrome.

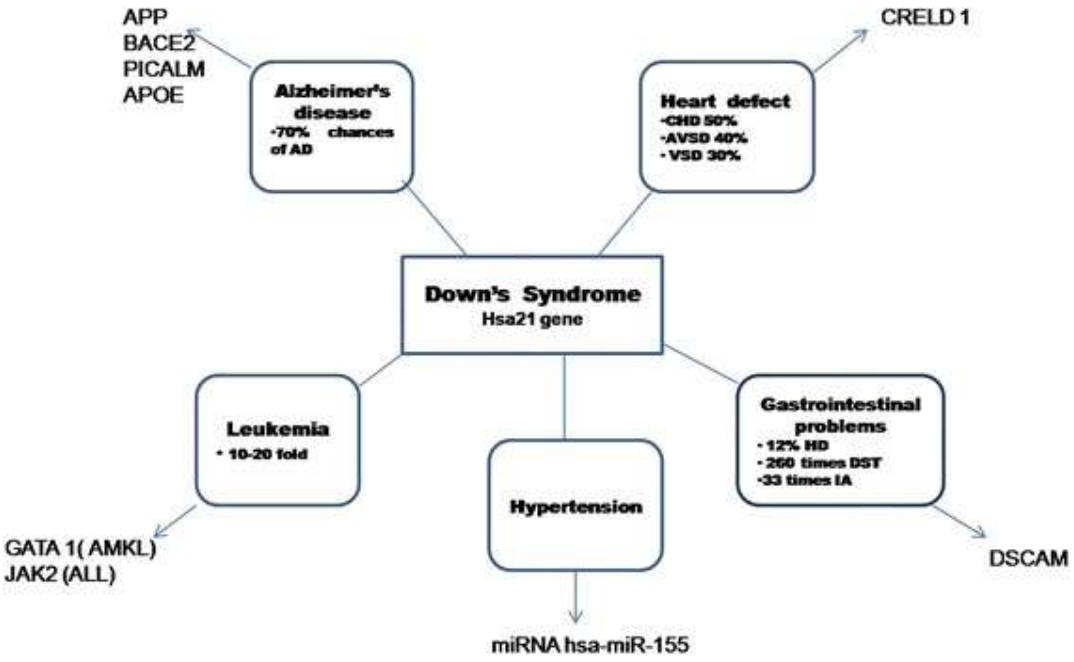


Figure 2 Abnormal genes and related diseases of Down's syndrome (Asim et al., 2015)

1.4 Epidemiology of Down's syndrome

A high prevalence of Down's syndrome is recorded among individuals living in different regions, countries and ethnicities in the world. According to the statistics from 'The National Down's Syndrome Society', the number of patients in the United States diagnosed with the disease ranges from between three hundred forty to four hundred thousand individuals (Presson et al., 2013). Researchers have estimated that the rate of birth defects due to the disease is 10.3 per ten thousand between the years of 1979-2003 in this country (Shin et al., 2009) The prevalence of Down's syndrome in other

worldwide countries is as follows: (per thousand) 13.1 in Ireland, 7.7 in the Netherlands and 6.1 in the United Kingdom and Wales (De Graaf et al., 2011).

The more recent reports have stated that the incidence of birth defects for patients diagnosed with Down's syndrome in the United States is 8.3 per ten thousand. This is especially true for individuals who are of an age that is younger than nineteen years (Besser, Shin, Kucik, & Correa, 2007). The occurrence of Down's syndrome is dependent on the maternal age. But the prevalence of the disease is changeable based on the type and severity of the risk factors (Presson et al., 2013). There is an increase in the percentage of patients diagnosed with the disease which has caused a higher percentage of mortality (Carothers, Hecht, & Hook, 1999).

1.5 Goals and Objectives

The main objectives of this study are to determine the following elements:

1. Whether there is a significant association between mortality and the type of aging diseases.
2. Whether there is a significant association between mortality and dementia for aging diseases.
3. Whether there is a significant association between mortality and Down's syndrome complications.
4. Whether there is a significant association between Down's related consequences and aging diseases.
5. Whether there are predictors for length of stay in patients with Down's syndrome.
6. Whether there are predictors for length of stay in patients with Down's syndrome and an aging disease.

7. Whether there are predictors for total charges in patients with Down's syndrome and an aging disease.
8. Whether there are predictors for total charges in patients with Down's syndrome.
9. Whether there are predictors for mortality in patients with Down's syndrome.
10. Whether there are predictors for mortality in patients with Down's syndrome and an aging disease.
11. Whether there is an impact for the predictor interaction on the length of stay of a patient with Down's syndrome.
12. Whether there is an impact for the predictor interaction on the total charges of a patient with Down's syndrome.

1.6 Research hypotheses

Hypothesis 1: There is significant association between mortality and the type of aging disease.

Null Hypothesis: $H0 = H1$

Alternative Hypothesis: $H0 \neq H1$

Hypothesis 2: There is significant association between mortality and dementia for aging diseases.

Null Hypothesis: $H0 = H1$

Alternative Hypothesis: $H0 \neq H1$

Hypothesis 3: There is significant association between mortality and Down's syndrome with cardiac complications.

Null Hypothesis: $H0 = H1$

Alternative Hypothesis: $H0 \neq H1$

Hypothesis 4: There is significant association between Down's syndrome related consequences and aging disease.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 5: There are significant predictors for length of stay in patients with Down's syndrome.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 6: There are significant predictors for length of stay in patients with Down's syndrome diagnosed with Alzheimer's and Parkinson's diseases.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 7: There is significant impact for the predictors' interaction on the total charges for Down's syndrome patients diagnosed with Alzheimer's and Parkinson's diseases.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 8: There are significant predictors for total charges of Down's syndrome only.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 9: There are significant predictors for total charges of Down's syndrome patients with Alzheimer's and Parkinson's diseases.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 10: There is significant impact for the predictors' interaction on the total charges of Down's syndrome patients with Alzheimer's and Parkinson's diseases.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 11: There are significant predictors for mortality of Down's syndrome only.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

Hypothesis 12: There are significant predictors for mortality of Down's syndrome patients with Alzheimer's and Parkinson's diseases.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

1.7 Statement of the problem

A significant impact has been found related to the incidence of Down's syndrome and the medical and social outcomes such as mortality and the patients' quality of life (Haddad, Bourke, Wong, & Leonard, 2018). There have been several studies which have highlighted the adverse outcomes of the disorder. They are as follows: congenital

malformations, cardiovascular disorders, psychological and neurological disabilities. There is a high rate of mortality for patients diagnosed with Down's syndrome (Hithersay et al., 2019; Zhu et al., 2013) in the United States (Yang, Rasmussen, & Friedman, 2002). However, most of the studies were focused on the age of the patient such as an elderly individual versus a child (Bayen, Possin, Chen, Cleret De Langavant, & Yaffe, 2018; Cua, Haque, Santoro, Nicholson, & Backes, 2017; Henderson, Lynch, Wilkinson, & Hunter, 2007).

Numerous studies have theoretically and clinically investigated the association between Down's syndrome and Alzheimer's disease due to common genetic and neurodegenerations (Beacher et al., 2009; Strydom et al., 2018). Parkinson's disease has also been associated to Down's syndrome. However, there are very few clinical studies that have shown the impact on the patients' hospital outcome, especially in the United States (Wisniewski, Bendheim, & Bolton, 1987). There are limited studies that have highlighted the impact and severity of the risk factors and comorbidities on the hospitalization outcomes for patients diagnosed with Down's syndrome with and without the coexistence of an aging disease. For example, seventy five prevent of patients with Down's syndrome have been diagnosed with a cardiovascular or pulmonary disease (Colvin & Yeager, 2017). There is a high rate of mortality, as reported in previous studies, due to the coexistence of aging diseases and comorbidities in the United States. Many expenditures and services are provided for patients with Down's syndrome. This causes a rise in the number of total charges which is considered to be a burden to the families and healthcare environment (Jensen, Taylor, & Davis, 2013). The annual costs are high for the administration of medical services in the United States for inpatients and outpatients diagnosed with Down's syndrome. The costs are $21,842 and $13,594, respectively (Shoffstall et al., 2016). The cost of caring for a child

with Down's syndrome is higher than a normal child by twelve to thirteen times. The cost of caring for a Down's syndrome patient with congenital heart defects was five to seven times greater than for an individual without heart disease (Wilmott, 2008).

1.8 Definition of terms

The definition of medical terms used in this study is illustrated in Table 1.

Table 1 Definitions of terms

Term	Definition
Symptoms	Any medical, physical and/or mental disorders related to a specific disease
Diagnosis	Examination and identification of an illness according to the symptoms and clinical evaluation
Health	Free from any an illness or a disease
Disorder	Abnormality of the body physical or mental status
Medication	Drugs used for a special disorder or disease
Down's syndrome	Congenital disorder of chromosome defects due to abnormal expression and/or mutation
Parkinson's disease	A neurological disorder and aging disease that affects movement and is seen in advanced age
Alzheimer's disease	A neurological disorder and aging disease that causes irreversible brain cell damage
Atlantoaxial instability	Abnormal movement of junctions between the atlas (C1) and axis (C2) due to the abnormality of bone or ligaments
Mortality rate	The number of deaths counted for a specific population per unit of time

1.9 Importance of the study

Down's syndrome is a genetic disease diagnosed by an abnormal miosis and growth in the patient. Some of the complications exhibited in patients diagnosed with the disorder are congenital heart disease, hypertension, respiratory disorders, psychological issues and cognitive disabilities. Aging diseases are impacted by neurodegeneration in the adult patients diagnosed with Down's syndrome. A study has not been produced that has highlighted the comorbidities and risk factors related to the outcomes of length of stay, total charges and mortality in Down's syndrome patients with and without aging diseases. This study has disclosed the findings and results related to hospitals in the United States. It demonstrates the strength and interaction of the risk factors that contribute to the elevation of the consumption of patient health services and the increased burden to healthcare facilities. This study is unique in comparison to previous studies because numerous parameters are evaluated such as hospitalization outcomes, demographics and interactions of the risk factors, comorbidities, the comparison of aging diseases and the complications found in a large sample size of patients diagnosed with Down's syndrome in the United States.

CHAPTER II

LITERATURE REVIEW

2.1 Introduction

Down's syndrome consists of cognitive and physical indicators that result from processing an entire extra chromosome 21 or a piece of the chromosome. It is the most common chromosomal reason of mild to moderate intellectual incapacities. Individuals with the syndrome also have distinctive physical structures such as a flat-looking face (Zhu et al., 2013). Abnormality in anatomical structures and physiological functions trigger the occurrence of fatal risks and comorbidities. This has led to an elevation in the rate of mortality for patients with Down's syndrome. It is an age-related disease and the incidence of mortality will differ based on the stage and severity of the risk factors (Mendiratta, Wei, Dayama, & Li, 2018). There are numerous complications attributed to the disease. The related aging diseases of Alzheimer's and Parkinson's complicate the management therapy plans of patients with Down's syndrome (Colvin & Yeager, 2017; Mégarbané et al., 2009). This chapter includes the reasons, diagnosis, symptoms, risk factors, complications, comorbidities, mortality and impact of aging diseases.

2.2 Risk factors of mortality for Down's syndrome

In the United States, the estimated annual percentages of births and deaths of Down's syndrome patients from the years of 1900 to 2010 varied depending upon the maternal age, regions and state. There was an increase in the number of births during this time period. But, there was a reduction in the mortality rate after the year of 1980 due to the advanced developments of therapy plans. Surgeries were also performed to prolong the lifespan of patients with the disorder. This information is shown below in Figure 3.

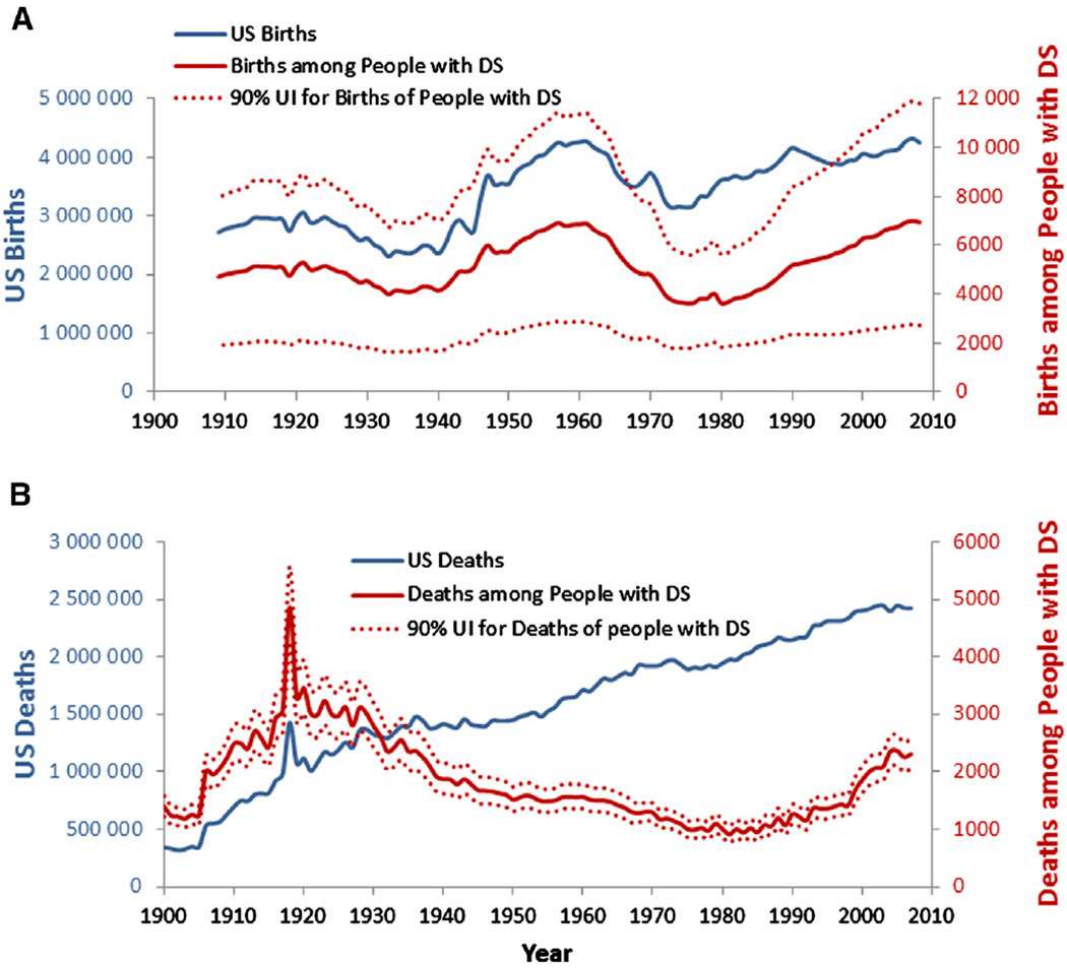


Figure 3 Births and Mortality of Down's syndrome Patients in the United States Between 1900-2010 (Presson et al., 2013)

Numerous factors influence the mortality of Down's syndrome patients. These factors are as follows:

2.2.1 Geographic distribution and country

In recent decades there have been several studies indicating a longer patient survival rate today than in the past for individuals diagnosed with Down's syndrome (Day et al., 2005; E. J. Glasson et al., 2002; Rasmussen et al., 2006). This is due to the developments in technology and science which aid in the prevention of congenital heart

defects for patients with this disease (Gilboa, Salemi, Nembhard, Fixler, & Correa, 2010). The mortality rate of Down's syndrome demonstrated differences based on geographic distributions. There is a lower incidence of mortality observed in the metropolitan areas of the United States (Mendiratta et al., 2018).

2.2.2 Karyotypes of Down's syndrome

There are three types of Down's syndrome as reported by previous studies. They are the standard Trisomy 21, Robertson translation and Mosaic Down's syndrome. According to a study conducted in Denmark, there is a higher survival rate of Down's syndrome patients (with or without congenital heart diseases) found in individuals with standard Trisomy, followed by Robertsonian translocation and Mosaic Down's syndrome (Zhu et al., 2013).

A study in the United States however, indicated a different observation stating that patients with Mosaic Down's syndrome had a higher survival rate than the other areas (Shin, Siffel, & Correa, 2010).

2.2.3 Race: The prevalence of Down's syndrome is different based on the race of patients in the United States. Individuals of the Hispanic race had the highest incidence of negative outcomes and mortality compared to the White and Black non-Hispanic race (Derrington et al., 2013; Sayegh & Knight, 2014).

2.2.4 Age: The median age at death was 3.6 years for the age of 62 years (between 1969 to 1973). Therefore, age is a significant moderator and a trigger factor of mortality and other comorbidities for patients with Down's syndrome. Patients with Down's syndrome are at an increased risk for many different health-related comorbidities as they age including congenital heart defects, pneumonia, infection risk due to immune system problems, leukemias and an enhanced risk of dementia later in life (Englund,

Jonsson, Zander, Gustafsson, & Annerén, 2013). Therefore, the mortality rate will vary between children and elderly patients diagnosed with the disease (Cua et al., 2017).

2.2.5 Gender: The gender plays a role in the incidence of mortality and has an impact on the hospitalization outcomes. Studies have indicated that male patients required more attention and health services than females because of the nature of their body organs and associated comorbidities (Chenbhanich, Wu, Phupitakphol, Atsawarungruangkit, & Treadwell, 2019). However, there have been reports showing a higher mortality rate in females (Mendiratta et al., 2018).

2.2.6 Aging diseases

1) Alzheimer's disease

The main challenge of Alzheimer's disease for patients with Down's syndrome is the duplication of the amyloid precursor protein gene of chromosome 21. This is a result of the triplication of the amyloid precursor protein (APP) gene at 21q21.3. This gene increases the amyloid beta deposition and worsens the cognition abnormality. Therefore, issues related to memory and dementia are noted in approximately eighty eight percent of patients with an advanced age of greater than sixty five years (Doran et al., 2017). However, there are significant variations in the onset of dementia in patients with Down's syndrome (Torr, Strydom, Patti, & Jokinen, 2010). The seizure progression begins at approximately two years after the onset of dementia for more than forty three percent of patients with a previous epilepsy free history. Therefore the Down's syndrome patients may require the use of dementia management therapy (Gholipour, Mitchell, Sarkis, & Chemali, 2017; Sinai et al., 2017). Several studies have demonstrated the relationship between mortality and the incidence of dementia for patients diagnosed with Down's syndrome (Henderson et al., 2007; Hithersay et al., 2019; Yang et al., 2002).

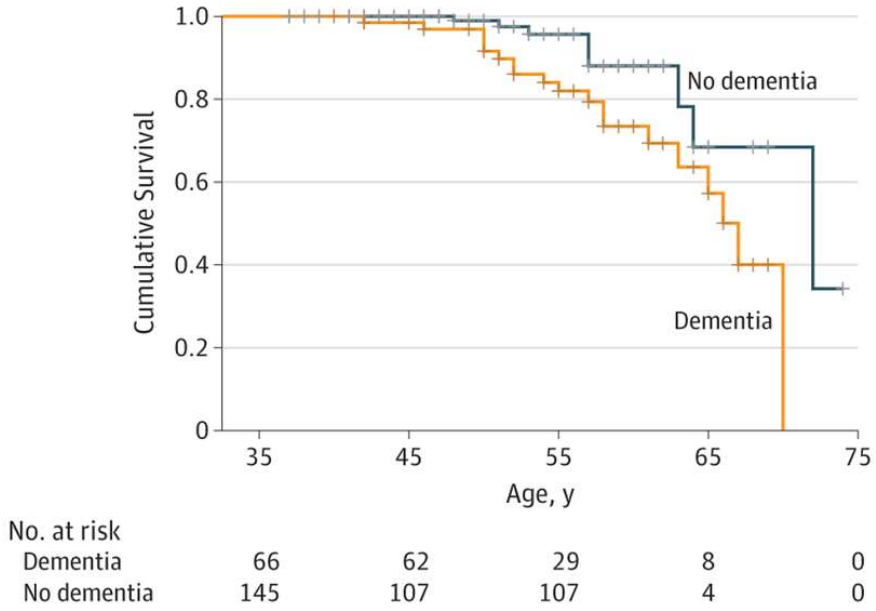


Figure 4 Mortality of Down's syndrome With Dementia (Hithersay et al., 2019)

The complications found in Down's syndrome patients diagnosed with Alzheimer's disease are as follows: (Head, Powell, Gold, & Schmitt, 2012).

1) Hypertension: also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. It causes an increase in the risks of stroke and or the cerebrovascular diseases.
2) Obesity: A condition of being overweight which is higher with females than males and increases the risks of Alzheimer's disease and sleep apnea.
3) Diabetes: Type 1 is the most common form which increases the risk of inflammations.
4) Cardiovascular diseases: conditions that involve narrowed or blocked blood vessels which can lead to intellectual disability and other defects in the functions of cardiac valves especially in children who exhibit a higher percentage than adults.

5) Cerebrovascular diseases: a group of conditions, diseases, and disorders that affect the blood vessels and blood supply to the brain. The direct injury of the brain affects the cognition causing inflammation and hypoperfusion.
6) Head injury: trauma to the scalp, skull, or brain that can lead to an increase in brain injury and the β-amyloid precursor protein.
7) Sleep apnea: a potentially serious sleep disorder in which breathing repeatedly stops and starts. Approximately ninety four percent of patients with sleep apnea have an abnormality of the oxygen intake.
8) Thyroid dysfunction: a medical condition that affects the function of the thyroid gland and is observed in 35-40% of patients with advanced age. Hashimoto's thyroiditis is commonly reported in individuals with Down's syndrome and Alzheimer's disease.
9) Seizures: a sudden, uncontrolled electrical disturbance in the brain. It is commonly reported as a result of the myoclonus epilepsy gene of chromosome 21 where the frequency of seizures increases with age for Down's syndrome patients from 7% to 46%, and to 84% when diagnosed with dementia.

2) Parkinson's disease

The neural degeneration induced by the abnormal growth of organs and cells of Down's syndrome patients is considered a cause for future neural diseases such as Parkinson's disease. There is a strong relationship between Parkinson's disease and Down's syndrome due to the abnormality of distribution and functional disorders found in the Lewy body in substantia nigra. The primary indicators of patients with Lewy body dementia are variations in cognition with a noticeable attention dysfunction. The illness is linked with atypical deposits of a protein called "alpha-synuclein in the brain"

(Uversky, 2007). Approximately twenty percent of patients with Down's syndrome will develop Alzheimer's disease. Therefore, this aging disease may increase the risks of mortality and cause a burden to healthcare (Vee P Prasher & Routhu, 2011). There is a significant relationship among Down's syndrome, Parkinson's and Alzheimer's diseases. Very few studies have stated the impact of the association between Parkinson's disease and Down's syndrome. Some researchers have discussed the idiopathic Parkinson's type which is considered a serious condition due to the abnormal functions of organs that cause defects of growth (Raghavan et al., 1993). The signs of Parkinson's disease may be seen in patients with Down's syndrome which leads to a relationship between these two disorders. Some patients with Down's syndrome take the drug, Levodopa. The drug is used to treat the symptoms of Parkinson's disease or Parkinson's-like symptoms such as shakiness, stiffness or difficulty in walking. Parkinson's disease is seen in patients with Down's syndrome who are of age fifty five years or more (Vieira, 2013).

2.2.7 Comorbidities

Several comorbidities are involved causing a higher incidence of mortality for patients with Down's syndrome. Some examples are pneumonia and lung infections, congenital heart diseases, circulatory illnesses, dementia, epilepsy, ischemic heart disorders and malignancies. However, the contribution of these comorbidities varies between cultures and karyotypes. Pneumonia infections and congenital heart diseases are the most common reasons of mortality in patients with Down's syndrome (Colvin & Yeager, 2017; Englund et al., 2013; Guffroy et al., 2019), as shown in Figure 5.

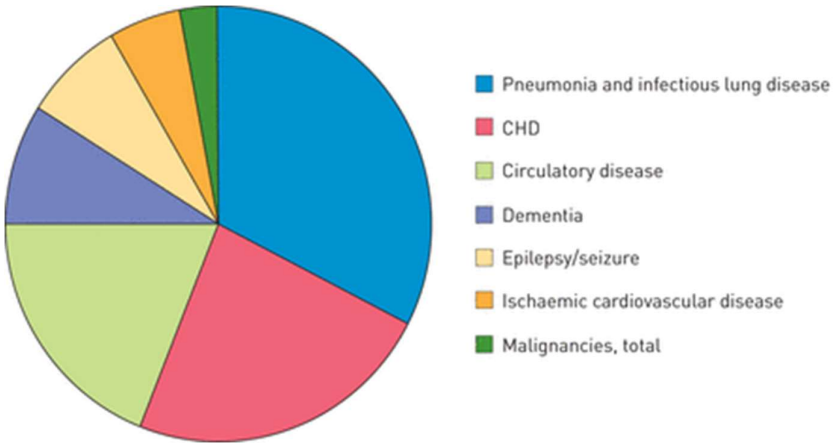


Figure 5 Comorbidities and Mortality in Patients With Down's Syndrome (Colvin & Yeager, 2017)

The mortality induced by the comorbidities varies based on the age groups. For example, the highest incidence of mortality is shown with pneumonia and respiratory diseases for those aged forty years and older as shown in the table below adapted from (Bittles, Bower, Hussain, & Glasson, 2007).

Table 4 Comorbidities and Mortality of Down's syndrome Patients Based on Age (Bittles, Bower, Hussain, & Glasson, 2007)

Cause of death	Childhood and early adulthood (0–18 yr), % (*n*)	Adulthood (19–40 yr), % (*n*)	Senescence (>40 yr), % (*n*)
Congenital heart defects	12.8 (19)	23.1 (9)	0 (0)
Pneumonia and other respiratory infections	33.1 (49)	23.1 (9)	39.6 (44)
Coronary artery disease	1.4 (2)	2.6 (1)	9.9 (11)
Cerebrovascular accidents	1.4 (2)	5.1 (2)	6.3 (7)
Cardiac, renal and respiratory failure	11.5 (17)	10.2 (4)	9.0 (10)
Cancers	3.4 (5)	7.7 (3)	5.4 (6)
Other causes	36.5 (54)	28.2 (11)	29.7 (33)
Total (298 deaths)	100 (148)	100 (39)	100 (111)

2.2.8 Number and type of procedures

The type and number of procedures is considered as another factor that influences the high rate of mortality and hospitalization outcomes. The patients with Down's syndrome often need urgent surgical interventions to save their lives due to the abnormal histological and physiological growth of organs. For example, the most common cardiac procedures of Down's syndrome, as reported by previous studies, are complete AVSD repair, VSD closure, mitral valve repair/replacement, partial AVSD repair, PDA ligation, tetralogy of Fallot repair, ASD closure, coarctation/arch repair, tricuspid valve repair/replacement and a tetralogy of Fallot-AVSD repair. Most of these surgical procedures had a higher mortality rate for patients with Down's syndrome compared to non-Down's syndrome patients (Chauhan S., 2006; Fudge et al., 2010).

2.3 Symptoms of Down's syndrome

The symptoms of Down's syndrome show few differences for a newborn compared to an adult and children (K. K Ostermaier, 2019). The stages of the symptoms are grouped as follows:

a) Newborns: The physical appearances that are seen directly after birth are as listed below:

1) Flattened face
2) Thick layer of skin on the back of neck
3) Eyes slant upwards
4) Weakness of muscle
5) Abnormality of joints
6) Unusual appearance of ears

7) Crease of palms
8) Space between the first and second toes

b) Children and adults: Other symptoms arise for children and adults as they age. These symptoms are noted below:

1) Flattened head in the back
2) Skin fold of eyelids
3) Flattened nose bridge
4) Gap of mouth
5) Abnormal teeth
6) Short neck
7) Short hands
8) Small abnormal ears

2.4 Complications of Down's syndrome

There are several complications that have been reported related to patients with Down's syndrome (Chenbhanich et al., 2019; Colvin & Yeager, 2017; Evans, Dharmar, Meierhenry, Marcin, & Raff, 2014; Frid, Drott, Lundell, Rasmussen, & Annerén, 1999; Goldacre, Wotton, Seagroatt, & Yeates, 2004; Guffroy et al., 2019; Henderson et al., 2007; I.T. & M., 2010; Nader-Sepahi, Casey, Hayward, Crockard, & Thompson, 2005; K. K Ostermaier, 2019; Ram & Chinen, 2011; Rattan, Bansal, & Dhamija, 2016). The complications are as follows:

- **Heart complications:** Approximately fifty percent of newborns with Down's syndrome have a heart defect. Many of the defects are associated with an abnormal structure and function in the walls of the heart chamber. Some of the

defects are as follows: septal defect, patent ductus arteriosus, tetralogy of fallot and congenital valvular disease.

- **Blood complications:** One of most serious blood complications is leukemia which influences the quality of life.
- **Immunity complications:** Immunity is one of the most common difficulties for patients with Down's syndrome. Their immunity levels increase the risk for cancer and infections.
- **Gastrointestinal complications:** Approximately five percent of Down's syndrome patients have digestive problems due to defects found in the gastrointestinal organs. This leads to an increase in gastric surgeries. There is an insufficient synthesis and secretion of hormones induced by several diseases such as Diabetes type 1 and thyroid conditions.
- **Skeletal complications:** Bone and muscle diseases are observed in patients with Down's syndrome. There are gaps and spaces found between the disks of spine, especially in the neck area. The gaps cause severe pain due to pressure on the spine or a move to one side. This complication is called atlantoaxial instability. Neurologic symptoms can occur when the spinal cord or adjoining nerve roots are involved in this complication.
- **Intellectual complications:** Most of the patients with Down's syndrome have issues related to cognition and memory. The disease causes mild to moderate intellectual incapacities.
- **Height and weight:** The patients with Down's syndrome experience a shortness in height, smaller heads and a tendency towards excessive weight.
- **Vision complications:** Vision issues are a common complaint of patients with Down's syndrome. They experience issues when they are nearsighted,

farsighted or have an astigmatism. The risk of cataracts increases as they become older. These patients have problems related to eye movements, glaucoma, retinitis pigmentosa, blindness and keratoconus.

- **Hearing complications:** Up to eighty percent of patients with Down's syndrome experience hearing loss due to structural issues in the ear.
- **Skin problems:** The patients with Down's syndrome are subject to dry and flaky skin issues. The skin problems impact their scalp and cause eczema and thick layers in several areas of the body.
- **Behavior complications:** Several behavioral and psychological complications were seen in patients with Down's syndrome. The complications include hyperactivity, attention deficit, depression, aggressions and autism.
- **Sleep apnea:** The patients diagnosed with Down's syndrome often have a history of disruptive sleep apnea. The present evaluations state that the childhood incidence is approximately fifty to one hundred percent and it is close to one hundred percent in adulthood. Some of the possibilities to handle the condition include upper airway surgery (primarily adenotonsillectomy) and continuous positive airway pressure (CPAP). There are also adjunctive therapies available including nasal steroids, palate expansion and exercises.
- **Fertility complications:** Females diagnosed with Down's syndrome are fertile and can easily become pregnant. Males, however, are usually infertile and have difficulty with sexual activities.

2.5 Diagnosis of Down's syndrome

The diagnosis of Down's syndrome is usually performed during pregnancy. However, the diagnosis can be done after birth by checking the appearance, features and

symptoms of the newborn infant. A scan can also be done to confirm the disease (K. K. Ostermaier, 2019).

2.6 Screening of Down's syndrome

There are four strategies utilized to screen the patients with Down's syndrome. The screening process is usually done in the first and second trimesters of pregnancy (Gilbert et al., 2001).

1) **First trimester screening (10-14 weeks):** Maternal age, nuchal translucency measurement, first trimester double test (PAPP-A, HCG) and first trimester combined test (nuchal translucency and PAPP-A, HCG).
2) **Second trimester screening (15 to 19 weeks):** Maternal age, second trimester double test (AFP, HCG), triple test (AFP, HCG, uE3) and quadruple test (AFP, HCG, uE3, inhibin A).
3) **Integrated test** (First trimester: nuchal translucency, PAPP-A; second trimester: quadruple test).
4) **Prenatal diagnosis:** Amniocentesis (⩾15 weeks), chorionic villus sampling (11-14 weeks), termination, surgical dilatation, evacuation (11 to 13 weeks) and medical termination with mifepristone (⩾14 weeks).

2.7 Identification type of Down's syndrome

Cytogenic analysis is utilized to identify the type of Down's syndrome. These techniques determine whether the diagnosis is related to Trisomy 21, aneuploidies or translocation. There are several advantages and disadvantages that exist for each method which are as follows: (Asim et al., 2015).

1) **Cytogenetics analysis:** This method of analyzing the chromosomes and related abnormalities involves the Giemsa banding of fetal cells. It is appropriate for low income countries. The disadvantages are that it wastes time, has a low detection rate of structure abnormalities and contains a high percentage of errors.
2) **FISH (Fluorescence in situ hybridization):** This method is utilized to understand numerous abnormalities and genetic mutations. It detects the chromosome DNA sequences and uses probes to detect the abnormalities. The disadvantages are that it wastes time and is not applicable for use in pregnant mothers and their fetuses.
3) **QF-PCR (Quantitative fluorescent-polymerase chain reaction):** This method uses fluorescent labeled primers. It is highly reliable, accurate, easily utilized for maternal and fetus purposes and is feasible and faster than other methods. The disadvantages are that it is not applicable for mosaic cases and is difficult to differentiate the results between genders.
4) **Paralogous sequence quantification:** The PCR is used to detect targeted abnormalities in the chromosome. The advantage is that it produces a low amount of errors in the detection of large quantities. The disadvantage is that it is very expensive.
5) **MLPA (multiplex probe ligation assay):** The four phases utilized in this technique are DNA denaturation, hybridization of probe, probe ligation and PCR amplification of the ligated probe. The advantages are that it is a fast and low-cost method. The disadvantages are that it is not detectable when using mosaic methods.

6) **NGS (Next Generation Sequencing):** This method is known for sequencing genomes at high speed. It provides an amplification of the DNA. The advantages are that it is a fast and accurate method. The disadvantages are that it is an expensive and complex technique.

2.8 Biomarkers of Down's syndrome

There are several biomarkers that are used to detect the type of complication and or malformations found in patients with Down's syndrome. It is utilized extensively in patients with aging diseases such as Alzheimer's. The biomarkers are as follows:

1) **AD-type APP mutations: (1) London mutation** (V717I) which detects the disorders related to behavioral, emotional, personality, memory, cognition and seizure types. **(2)** AD-type APP **Swedish mutation** (KM670/671NL): which detects abnormalities related to memory, cognition and seizures.
2) **CAA-type APP mutations: Dutch mutation (**E693Q) and **Italian** (E693K): which detects intracerebral hemorrhage, stroke, memory and cognition abnormalities.
3) **Duplication APP CNVs:** which detects the abnormality related to memory, cognition, seizures, intracerebral hemorrhage and stroke.

2.9 Treatment of Down's syndrome

There has been no specific treatment identified for patients with Down's syndrome. The individuals do take medications for the disease related complications. The prophylaxis action is taken to prevent other serious consequences and reduce the incidence of mortality. However, surgical interventions may be required to overcome the difficulties of complications incurred from invasive procedures related to the cardiac, gastro and

pulmonary areas. Other devices also may be prescribed to the patient such as hearing and vision aids (K. K. Ostermaier, 2019).

2.10 Therapy Animals

Animal-assisted endeavors and therapies have been utilized as a complementary therapy for several medical and psychological situations. Animal-assisted therapy is individually personalized to assist a patient in meeting specific conditions and results. It is executed under the direction of a health care professional and is reviewed on a steady basis as a change occurs in the patient's objectives. An animal-assisted activity is introduced for 'recreation, education, quality, and/or enjoyment to a person's life'. One of the uses is for the treatment of dementia (Yakimicki et al., 2018). Therapy and service animals assist individuals in a mental and physical area. Some of the ways in which the animals aid in mental capacity include lowering anxiety and promoting relaxation. The animals can help with loneliness and provide distractions. The physical attributes include the lowering of blood pressure, a decrease in the number of medications and an increase in motivation (Uclahealth.org, 2019).

Pets can offer both companionship and everyday assistance with regular life activities. A service dog can help individuals with Parkinson's Disease maintain balance while walking or notify someone after a fall. The animals can be trained to assist individuals with the disease move when they have gait freezes or cannot rise from a chair or a fall. Having a pet can also assist with depression (The Michael J. Fox Foundation for Parkinson's Research | Parkinson's Disease, 2019).

Animal Use - Definitions

Classification	Definition
Assistance Animal	Any animal that works, aids, or performs tasks for the benefit of a person with a disability, or provides emotional support that alleviates an identified symptom or effects of a person's disability.
Service Animal	Any dog that is individually trained to do work or perform tasks for the benefit of an individual with a disability, including a physical, sensory, psychiatric, intellectual, or other mental disability. The work or tasks performed by a service animal must be directly related to the disability.
Emotional Support Animal	An emotional support animal can be of any species, the use of which is supported by a qualified physician, psychiatrist or other mental health professional based upon a disability-related need. An ESA does not have to be trained to perform any task.
Therapy Animal	A therapy animal is a type of assisted intervention in which there is a goal directive with the animal meeting specific criteria as an integral part of the treatment process. Animal-assisted therapy is provided in a variety of settings and may be group or individual in nature.

(Avma.org, 2019). Pets can intensify trust and compassion. A dog can "read a person's body language despite the person's inabilities and does not judge". Therapy dogs reduce challenging conduct such as anxiety, hostility, unhappiness and lethargy. In the country of Sweden, therapy schools train dogs and educate handlers. A therapy dog appointment involves the person with dementia, the therapy dog and the trainer. The trainer's capability to be receptive, communicate and work together during the collaboration between the person and the dog is crucial (Swall et al., 2016).

Some of the things that a specially trained dog can do are as follows: retrieve dropped items, open and close the doors, provide notifications that a medication was not taken, offer camaraderie, prevent the individual from getting lost, assist in an emergency such as a fall and lead the individual home if they become lost (Alzu.org, 2019).

CHAPTER III

MATERIAL AND METHODS

3.1 Nationwide inpatient sample data

The data of the Nationwide Inpatient Sample (NIS), as a secondary dataset, is used to achieve the goals of the present study. All permissions and approvals are granted from the people in charge of this issue. The NIS datasets are commonly used by clinicians in the United States and researchers to investigate their main outcomes, especially those related to mortality, length of stay and total charges. The primary patient information found in the NIS are demographic characteristics, hospital information, type of insurance, years and types of admissions and the existence of comorbidities and a diagnosis.

3.2 Data and methods

The NIS dataset utilized in the present study is related to Down's syndrome patients with concurrent aging disorders such as Alzheimer's and Parkinson's disease. The total number of patients with Down's syndrome is 58,438 from 1,050 hospitals representing forty-four states from the years 2007 to 2012. The number of individuals suffering from Parkinson's and Alzheimer's diseases are 1,198 and 2,352 patients respectively. The main variables of the NIS dataset involved non-clinical and clinical information. The non-clinical information included the patients' demographic information, financial statuses, hospital information, length of stay and total charges. The clinical information included the patients' health status, comorbidities, number of procedures, healthcare services and mortality. The codes for the diseases are mentioned in the main webpage of the NIS. These codes were assigned for each disease and diagnosis. However, these

codes also involved other consequences of the disease such as cardiac malformation of Down's syndrome and dementia of aging diseases. All areas of the NIS data were coded based on the nature of the variable. For example, information related to the payments for inpatients were reported as the type of insurance (Medicare, Medicaid and others) and as a categorical variable. The total charges referred to the total amount paid for the medical services. The analysis of the NIS dataset for the present study involved three main phases based on the objectives and hypotheses. The first area was for all Down's syndrome patients, the second area was for Down's syndrome with Alzheimer's disease and the third analysis was for Down's syndrome with Parkinson's disease. There are two types of variables based on their classifications: dependent and independent. The dependent variables in this study are total charges, length of hospital stay and mortality. The independent variables involved the patients' socio-demographic characteristics (age, gender, race... etc.), type of insurance, median household income and comorbidities. SPSS version 22 is used in the analysis of NIS datasets and provides the most appropriate statistical tests with their corresponding assumptions. All results with p values less than 0.05 were considered as significant. The statistical tests used in this study were chi-square, Pearson correlation, multinomial logistic regression and multiple linear regression (dummy method). The filtering stage used in the statistical analysis to determine the variables might influence the mortality of Down's syndrome with aging diseases. Chi-square is used to obtain the significant variables, which are then analyzed in one model utilizing logistic regression. The chi-square test is used to find the association between categorical variables such as gender and mortality. The Pearson correlation test is used to determine the type and strength of correlation between two or more numerical variables. An example is the relationship between the length of stay, total charges and number of procedures. A multinomial logistic

regression test is used to determine the predictors (risk factors) of mortality. The multiple linear regression (dummy method) is used to determine the predictors of length of hospital stay and total charges.

3.3 Data variables, research questions, statistical analysis procedures

The NIS dataset used in the present study covered the patients for the years 2007-2012. All variables involved to achieve the objectives of this study are illustrated in Table 2.

Table 2 Data variables used for the analysis

Study variables	Original variables in NIS	Variables description
AGE	AGE	Age in years; Numerical Variable
MORTALITY	DIED	Patient did not die during hospitalization (DIED=0); Patient died during hospitalization (DIED=1), Categorical Variable
GENDER	FEMALE	Gender of patient FEMALE = 1 is Female; FEMALE= 0 is Male; Categorical Variable
TOTAL CHARGE	TOTCHG	Total charges, Numerical Variable
RACE	RACE	1 = White, 2 = Black, 3 = Hispanic, 4 =Asian/Pacific, 5 = Native Am., 6 = Other; Categorical Variable
INSURANCE TYPE	PAY1	1=Medicare, 2=Medicaid, 3=Private insurance,4=Self-pay,5=No charge,6=Other; Categorical Variable
NUMBER OF PROCEDURES	NPR	The number of procedures performed while patient was hospitalized; Numerical Variable
SOCIO_ ECONOMIC STATUS	ZIPINC_QRTL	Median household income for patient's ZIP Code, 1= 76th to 100th percentile, 2= 26th to 50th percentile, 3= 51st to

		75th percentile, 4= 0-25th percentile; Categorical Variable
COMORBIDITIES	CM_AIDS, CM_ALCOHOL, CM_ANEMDEF, CM_ARTH, CM_BLDLOSS, CM_CHF, CM_CHRNLUNG, CM_COAG, CM_DEPRESS, CM_DM, CM_DMCX, CM_DRUG, CM_HTN_C, CM_HYPOTHY, CM_LIVER, CM_LYMPH, CM_LYTES, CM_METS, CM_NEURO, CM_OBESE, CM_PARA, CM_PERIVASC, CM_PSYCH, CM_PULMCIRC, CM_RENLFAIL, CM_TUMOR, CM_ULCER, CM_VALVE, CM_WGHTLOSS	Acquired immune deficiency syndrome, alcohol abuse, deficiency anemias, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes uncomplicated, diabetes with chronic complications, drug abuse, hypertension , hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease, weight loss; Categorical variable
LENGTH OF STAY	LOS	The number of days patient was hospitalized; Numerical Variable
Number of chronic conditions	NCHRONIC	Number of chronic conditions; Numerical variable

3.4 Study hypotheses and statistical tests

In order to answer the research questions, twelve hypotheses were tested using different statistical tests. All research questions, hypotheses, outcomes, independent variables and statistical tests are illustrated in Table 3.

Table 3 Study hypotheses, research questions and appropriate statistical tests

Research questions	Hypotheses	Independent variables	Outcomes variables	Inferential statistical analysis
Is there association between mortality and type of aging disease	Hypothesis 1	Alzheimer's and Parkinson's disease	Mortality	Chi-square
Is there association between mortality and dementia of aging diseases	Hypothesis 2	Dementia of aging diseases	Mortality	Chi-square
Is there association between mortality and Down's cardiac complications	Hypothesis 3	Down's cardiac malformation	Mortality	Chi-square
Is there association between Down's-related consequences and aging disease	Hypothesis 4	Down's atlantoaxial instability	Parkinson's disease	Chi-square
Are there predictors for length of stay of Down's syndrome only	Hypothesis 5	Patients' information & comorbidities	Length of stay	Multiple linear regression
Are there predictors for length of stay of Down's syndrome patients with Alzheimer's and Parkinson's diseases	Hypothesis 6	Patients' information & comorbidities	Length of stay	Multiple linear regression
Is there any impact for predictors' interaction on the length of stay for Down's syndrome patients with Alzheimer's and Parkinson's diseases	Hypothesis 7	Patients' information & comorbidities	Length of stay	Multiple linear regression
Are there predictors for total charges of Down's syndrome only	Hypothesis 8	Patients' information & comorbidities	Total charges	Multiple linear regression
Are there predictors for total charges of Down's syndrome patients with Alzheimer's and Parkinson's diseases	Hypothesis 9	Patients' information & comorbidities	Total charges	Multiple linear regression

Is there any impact for predictors' interaction on the total charges of Down's syndrome patients with Alzheimer's and Parkinson's diseases	Hypothesis 10	Patients' information & comorbidities	Total charges	Multiple linear regression
Are there predictors for mortality of Down's syndrome only	Hypothesis 11	Patients' information & comorbidities	Mortality	Multiple linear regression
Are there predictors for mortality of Down's syndrome patients with Alzheimer's and Parkinson's diseases	Hypothesis 12	Patients' information & comorbidities	Mortality	Multiple linear regression

The patient information related to Down's syndrome, Alzheimer's disease and Parkinson's disease was extracted from the NIS database after checking the codes and entries of 58,438 patients who visited the hospital for the years 2007-2012. The analysis and results of the present study are fully outlined in the next chapter.

CHAPTER FOUR

RESULTS AND ANALYSIS

4.1 Introduction

This chapter contained the results of the descriptive and statistical analysis. The Statistical Package for the Social Sciences, (SPSS) version 22, was used for the analysis of the NIS dataset for the years 2007-2012. It included 58,438 patients who suffered from Down's syndrome as their main illness with the co-existence of Parkinson's and Alzheimer's diseases. The number of patients who complained of Parkinson's and Alzheimer's diseases was 1,198 and 2,352 patients respectively. The ICD-9-CM codes for the diseases are as follows: Down's syndrome: 7580, 7249 and 7453-7459; Parkinson's disease: 3320, 3321, 7810, 7813, 78199, 7812, 29410, 29411, 2948, and 7843; and Alzheimer's disease: 2900, 29010-29020, 2903, 29040-2909, 3310-3312, 33182, 797, 29410, 2948, 29021, 29411, 7843, 29410, 33189, 7812, and 7998. The results with *p* values less than 0.05 were considered as significant.

4.2 Demographic characteristics and health information

4.2.1 Age

The patients were categorized into age groups, where the highest incidence was observed with those aged as being younger than 30 years old by 55.2%. This was followed by those aged 51-60 years (16.2%) and 41-50 years (12.4%), while the lowest percentages were for patients aged older than 80 years (1.1%) respectively, as shown in Table 5.

Table 5 Patient age groups

Age groups		Frequency	Percent
	≤30	32243	55.2
	31-40	3833	6.6
	41-50	7261	12.4
	51-60	9441	16.2
	61-70	3949	6.8
	71-80	994	1.7
	>80	652	1.1
	Total	58373	99.9
Missing	System	65	0.1
Total		58438	100.0

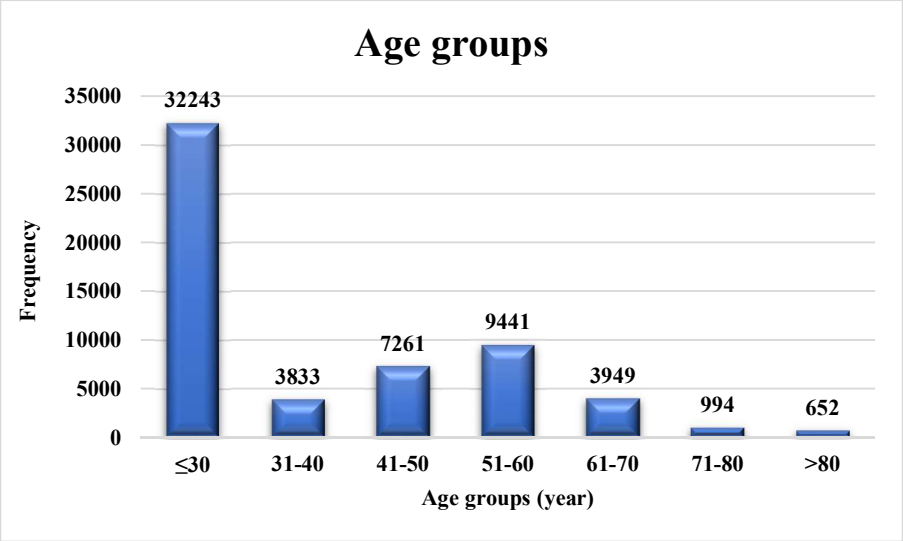


Figure 5 Age groups of Down's syndrome patients

4.2.2 Race

The White race occupied the highest incidence of Down's syndrome patients by 53.8%, followed by the Hispanic race patients (16%), and Black race patients (8.7%), as shown in Table 6.

Table 6 Patients and race groups

Race		Frequency	Percent
	White	31438	53.8
	Black	5079	8.7
	Hispanic	9367	16.0
	Asian or Pacific Islander	1150	2.0
	Native American	375	0.6
	Others	2092	3.6
	Total	49501	84.7
Missing	System	8937	15.3
Total		58438	100.0

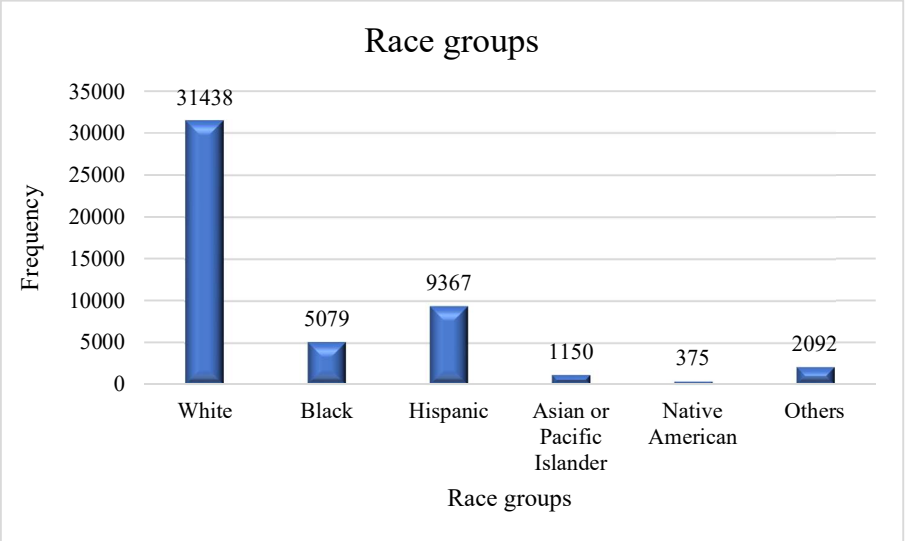


Figure 6 Incidence of Down's syndrome among races

4.2.3 Gender

Males showed a higher incidence of Down's syndrome than females (53.9% vs. 46.0%), as shown in Table 7.

Table 7 Incidence of Down's syndrome between genders

Genders		Frequency	Percent
	Male	31505	53.9
	Female	26885	46.0
	Total	58390	99.9
Missing	System	48	0.1
Total		58438	100.0

4.2.4 Health insurance

Medicare was the main form of health insurance with the highest incidence of 36.7%, followed by 32.1% of Medicaid, and 26.6% of Private (HMO), as shown in Table 8.

Table 8 Down's syndrome and health insurance

Health insurance		Frequency	Percent
	Medicare	21451	36.7
	Medicaid	18760	32.1
	Private including HMO	15569	26.6
	Self-pay	896	1.5
	No charge	96	0.2
	Others	1574	2.7
	Total	58346	99.8
Missing	System	92	0.2
Total		58438	100.0

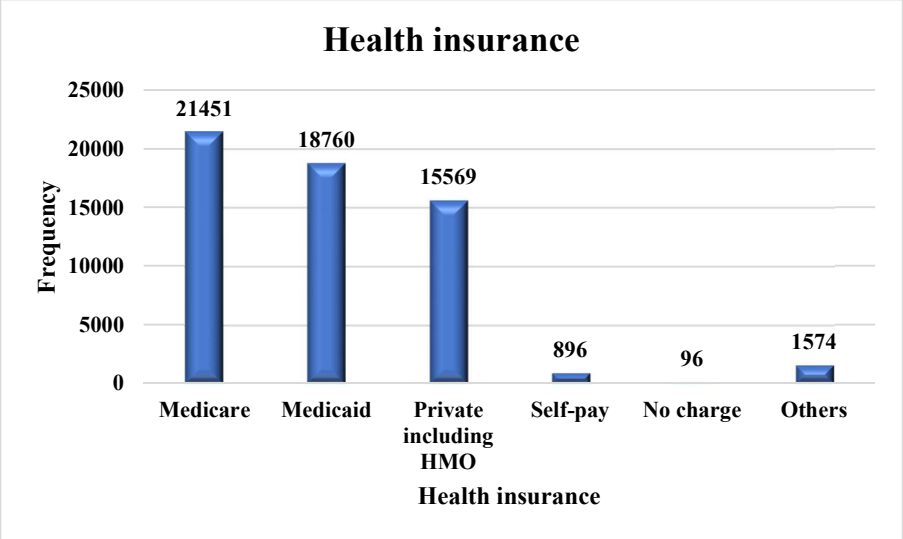


Figure 7 Insurance types of Down's syndrome patients

4.2.5 Patient comorbidities

The highest incidence of comorbidities for Down's syndrome disease patients was observed with hypothyroidism by 23.5%, followed by fluid and electrolyte disorders (20.9%), and other neurological disorders (14.2%), while the comorbidities with the lowest incidence were acquired immune deficiency syndrome (0.03%) and peptic ulcer disease excluding bleeding (0.2%), as shown in Table 9.

Table 9 Down's syndrome and patient comorbidities

Comorbidities	Frequency	Percent
1. Hypothyroidism	13711	23.5
2. Fluid and electrolyte disorders	12192	20.9
3. Other neurological disorders	8319	14.2
4. Hypertension (combine uncomplicated and complicated)	6602	11.3
5. Chronic pulmonary disease	6625	11.3
6. Deficiency anemias	5854	10.0
7. Diabetes, uncomplicated	3871	6.6
8. Obesity	3698	6.3
9. Congestive heart failure	3470	5.9
10. Valvular disease	2827	4.8
11. Depression	2615	4.5
12. Coagulopathy	2582	4.4
13. Renal failure	2225	3.8
14. Weight loss	2145	3.7
15. Pulmonary circulation disorders	2163	3.7
16. Psychoses	1319	2.3
17. Paralysis	1357	2.3
18. Liver disease	749	1.3
19. Peripheral vascular disorders	618	1.1
20. Diabetes with chronic complications	521	.9
21. Rheumatoid arthritis/collagen vascular diseases	528	.9

22. Drug abuse	416	.7
23. Chronic blood loss anemia	299	.5
24. Alcohol abuse	233	.4
25. Solid tumor without metastasis	175	.3
26. Metastatic cancer	149	.3
27. Lymphoma	70	.1
28. Acquired immune deficiency syndrome	15	.03
29. Peptic ulcer disease excluding bleeding	12	.02

4.2.6 Mortality

The incidence of mortality for Down's syndrome patients was approximately 2.9%, as shown in Table 10.

Table 10 Mortality of Down's syndrome patients

Mortality		Frequency	Percent
	did not die during hospitalization	56715	97.1
	died during hospitalization	1683	2.9
	Total	58398	99.9
Missing	System	40	.1
Total		58438	100.0

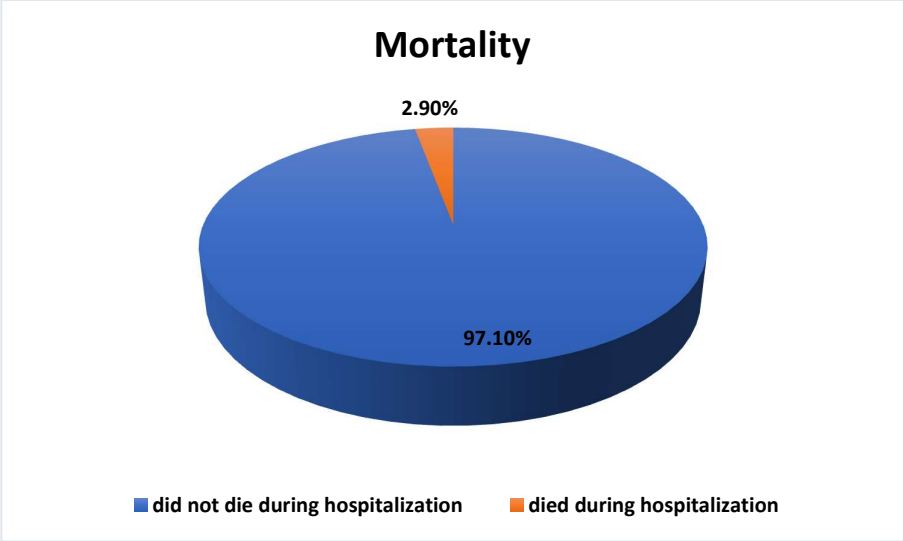


Figure 8 Mortality of the Down's syndrome patient

4.2.7 Length of stay and total charge

The mean (±SD) length of stay for patients with Down's syndrome was 7.34 (±12.605) days. The mean (±SD) total cost was $53678.26 (±$120800), as shown in Table 11.

Table 11 Length of hospital stay and total charge of Down's syndrome patients

Parameters	Mean	Median	± SD	Skewness	Kurtosis
Length of hospital stay (days)	7.34	4.00	12.605	7.953	112.755
Total cost ($)	53678.26	20823.00	120800.0	9.575	156.505

4.2.8 Median household income

Four levels of the median household income were observed in this study. They are as follows: 0-25th percentile, 26th to 50th percentile, 51st to 75th percentile and 76th to 100th percentile. The percentages of median income of Down's syndrome patients are as follows: 27.5%, 25.1%, 24.2% and 20.8% for the 0-25th percentile, 26th to 50th percentile, 51st to 75th percentile, and 76th to 100th percentile respectively, as shown in Table 12.

Table 12 Median household income of Down's syndrome patients

Levels of household income		Frequency	Percent
	0-25th percentile	16079	27.5
	26th to 50th percentile	14653	25.1
	51st to 75th percentile	14167	24.2
	76th to 100th percentile	12163	20.8
	Total	57062	97.6
Missing	System	1376	2.4
Total		58438	100.0

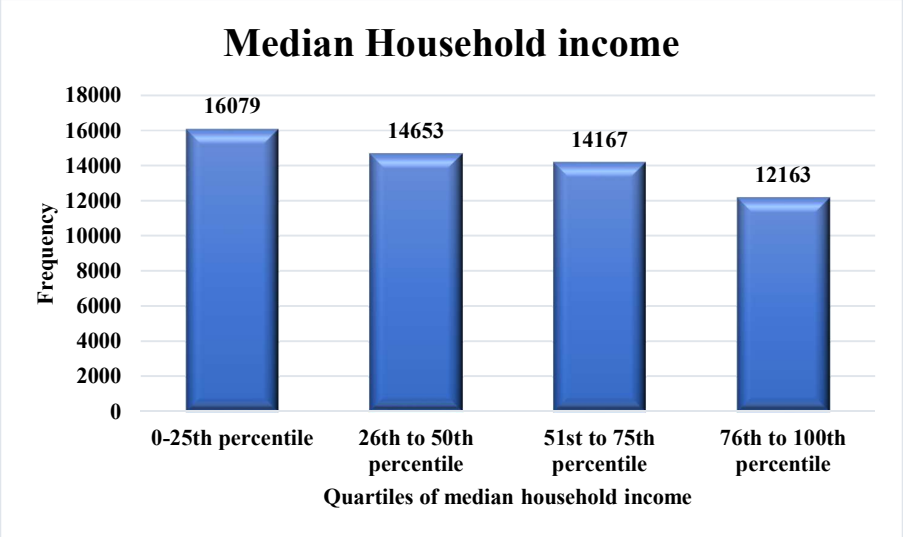


Figure 9 Median household incomes of Down's syndrome patients

4.2.9 Years of hospital admission

This study involved all patients admitted to hospitals in the United States from the years 2007-2012. The highest percentage for admission of Down's syndrome patients was observed in the year 2010 (17.5%), followed by year 2011 (16.9%) and 2009 (16.8%), as shown in Table 13.

Table 13 Hospital admissions of Down's syndrome patients between years 2007-2012

Year	Frequency	%
2007	9442	16.2
2008	9379	16.0
2009	9813	16.8
2010	10243	17.5
2011	9870	16.9
2012	9691	16.6

Figure 10 depicts the percentage of Down's syndrome patients with Parkinson's and Alzheimer's disease admitted to the hospital. Steady increments were observed with admissions to the hospitals from the lowest incidence in the year 2007 to the highest incidence in the year 2012. These diseases had an increase in the percentage of admissions through the years. However, the admission of Down's syndrome patients diagnosed with Alzheimer's disease had a higher percentage than Parkinson's disease.

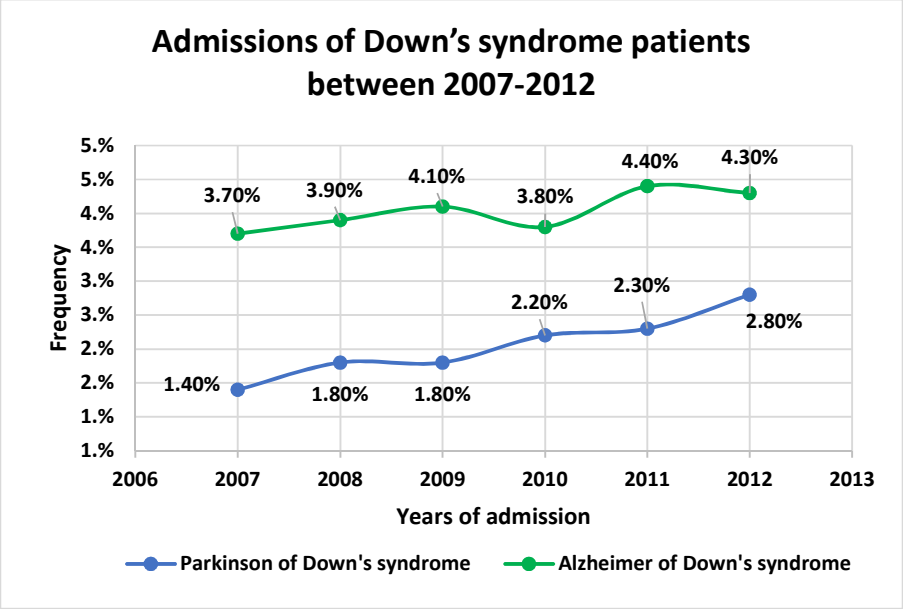


Figure 10 Admissions of Down's syndrome patients with Alzheimer's and Parkinson's diseases

4.2.10 Number of procedures and number of chronic diseases

The mean (±SD) number of procedures for patients with Down's syndrome is 1.77 (±2.691). The mean (±SD) number of chronic diseases is 4.26 (±2.623), as shown in Table 14.

Table 14 Number of procedures and number of chronic diseases of Down's syndrome patients

Parameters	Mean	Median	± SD	Skewness	Kurtosis
Number of chronic diseases	4.26	4.00	2.623	.985	.945
Number of procedures	1.77	1.00	2.691	2.816	12.805

4.3 Parkinson's and Alzheimer's diseases and demographic characteristics of the Down's syndrome patient

4.3.1 Gender

The Down's syndrome female patients had a higher incidence of Alzheimer's disease compared to the males (4.2% vs. 3.8%), while the incidence of Parkinson's disease was higher with males (2.1%) than of females (1.9%), as shown in Figure 11.

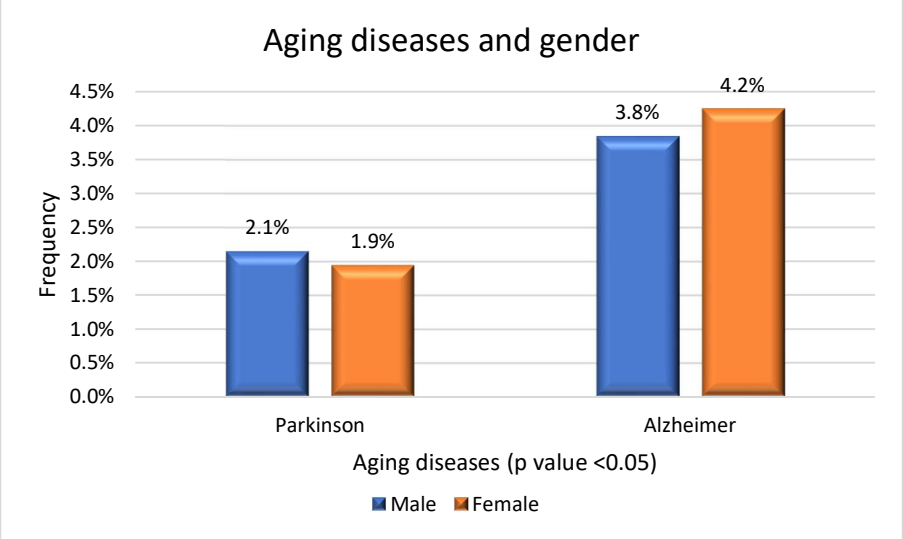


Figure 11 Aging diseases and gender of Down's syndrome patients

4.3.2 Insurance company

Private and Medicare insurance had the highest incidences for Down's syndrome patients with aging diseases. Private including HMO insurance showed the highest incidence (13.9%) for Down's syndrome patients. There was a higher incidence of patients with Alzheimer's than with Parkinson's disease (13.9% vs. 1.2%). Medicare is the second highest insurance with higher incidences for Alzheimer's disease than for Parkinson's disease (6.1% vs. 2.8%), as shown in Figure 12.

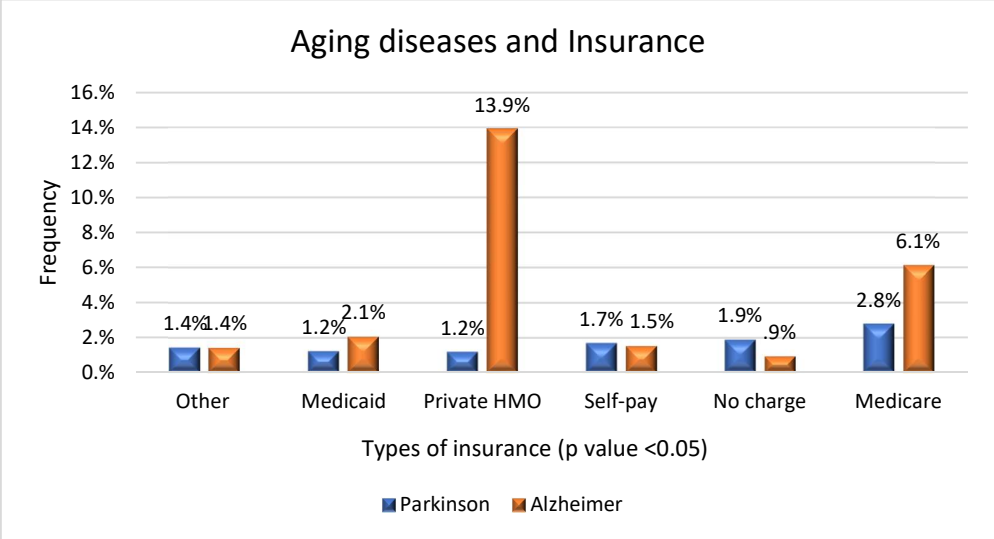


Figure 12 Aging diseases and insurance type of Down's syndrome patients

4.3.3 Race

Down's syndrome patients of the White race occupied a higher incidence of admission than other races with aging diseases. White race patients with Alzheimer's disease had a higher incidence than Parkinson's disease (5.6% vs. 2.3%). Black is the second highest race for the Down's syndrome patient where the individuals with Alzheimer's disease had a higher incidence than Parkinson's disease (2.1% vs. 1.9), as shown in Figure 13.

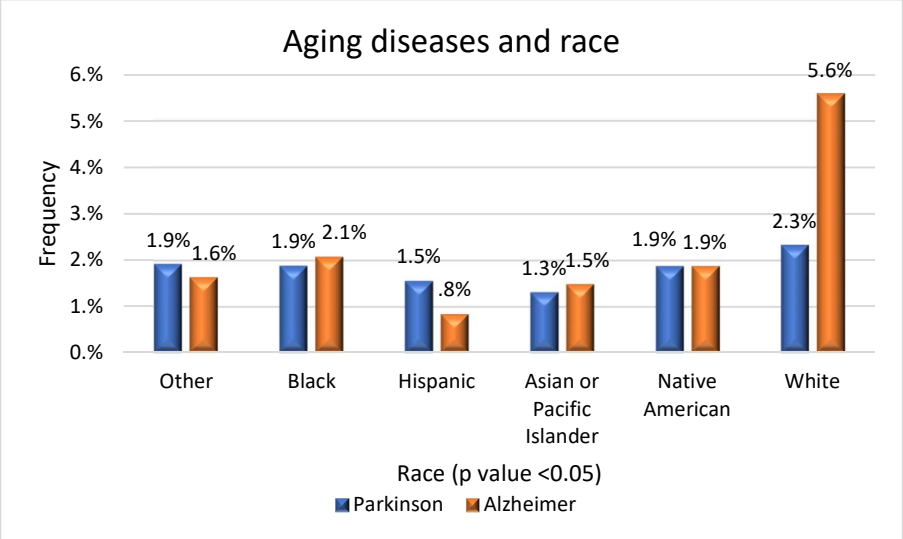


Figure 13 Aging diseases and race of Down's syndrome patients

4.3.4 Household income

Down's syndrome patients with aging diseases had the highest incidence of admission with household income in the 76th-100th percentile. There was a higher incidence with Alzheimer's disease than Parkinson's disease (5.2% vs. 2.3%). The income percentile of 51th-75th showed the second higher incidence for Down's syndrome with aging diseases. A higher incidence was obtained with the Alzheimer's patient than Parkinson's disease (4.2% vs. 2%), as shown in Figure 14.

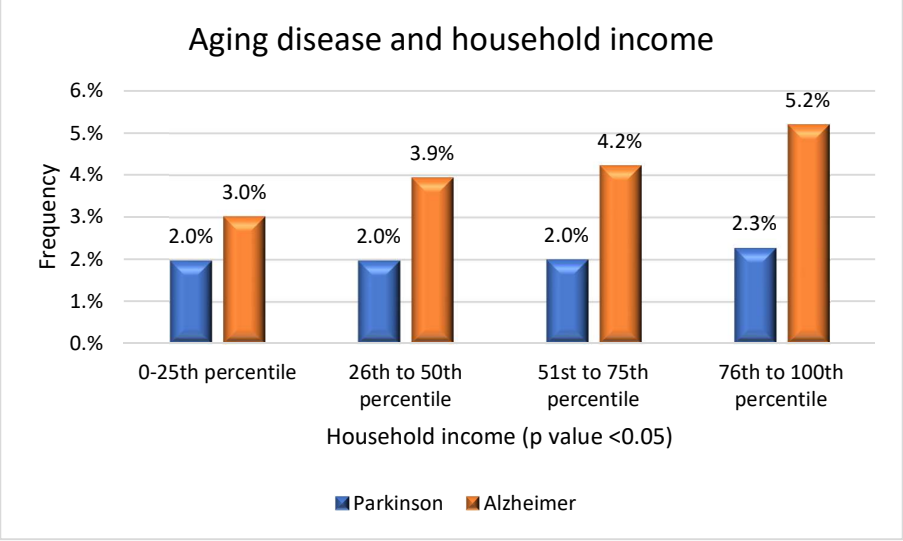


Figure 14 Aging diseases and household income of Down's syndrome patients

4.3.5 Age groups

Down's syndrome patients and age groups had the highest incidence with elderly individuals. Patients with aging diseases aged 61-70, older than 80 years and ages 51-60 showed the highest incidences of admissions (14.4% vs. 2.9%, 8.1% vs. 8.1%, and 13.3% vs. 2.9%, respectively). However, patients with Alzheimer's disease showed higher incidences of admission than Parkinson's disease, except for those aged older than 80 years, as shown in Figure 15.

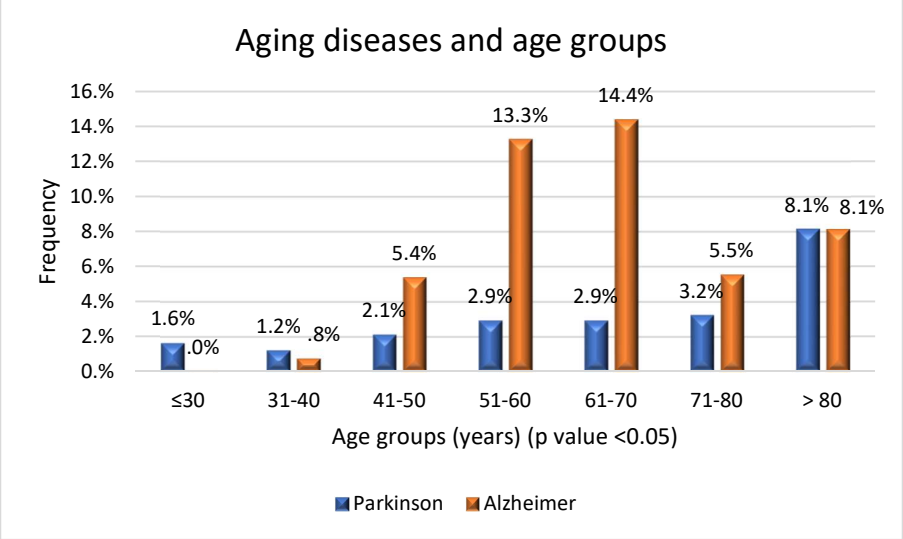


Figure 15 Aging diseases and age groups of Down's syndrome patients

4.4 Mortality incidence of Down's syndrome patients

4.4.1 Mortality and aging diseases (Hypothesis 1)

There was a significant association found between mortality and aging diseases. For Down's syndrome patients, a higher incidence of mortality was reported for those with Alzheimer's disease by 9.1%, while there was a lower incidence for those with Parkinson's disease (0.7%). More than 70% of Alzheimer's disease patients were subjected to mortality compared to 25% with Parkinson's disease, as shown in Figure 16.

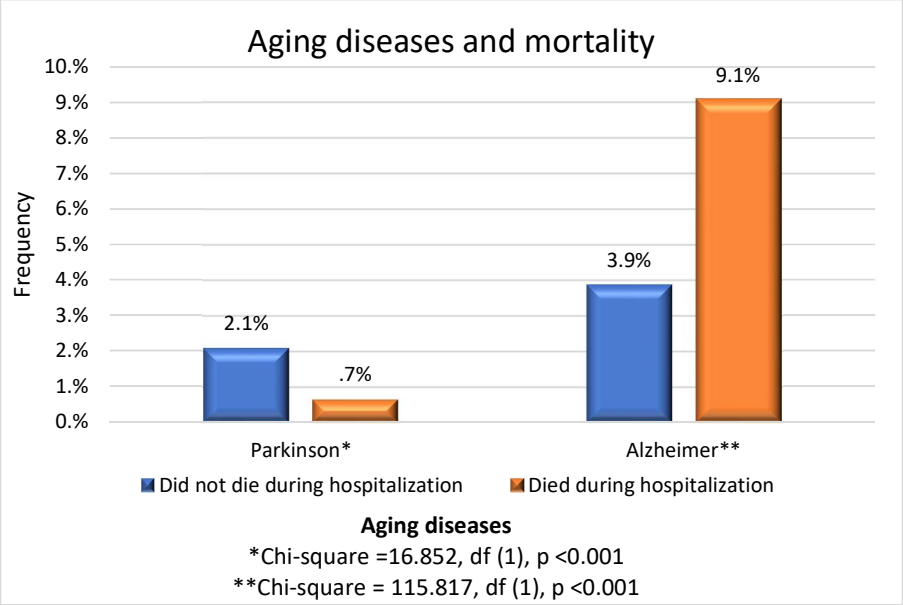


Figure 16 Mortality of Down's syndrome with aging diseases

4.4.2 Mortality and dementia (Hypothesis 2)

There is a significant association between mortality and the existence of dementia for aging diseases in Down's syndrome patients. The incidence of mortality for Down's syndrome patients with dementia of aging diseases was 13.49% compared to the 5.93% without mortality, as shown in Figure 17.

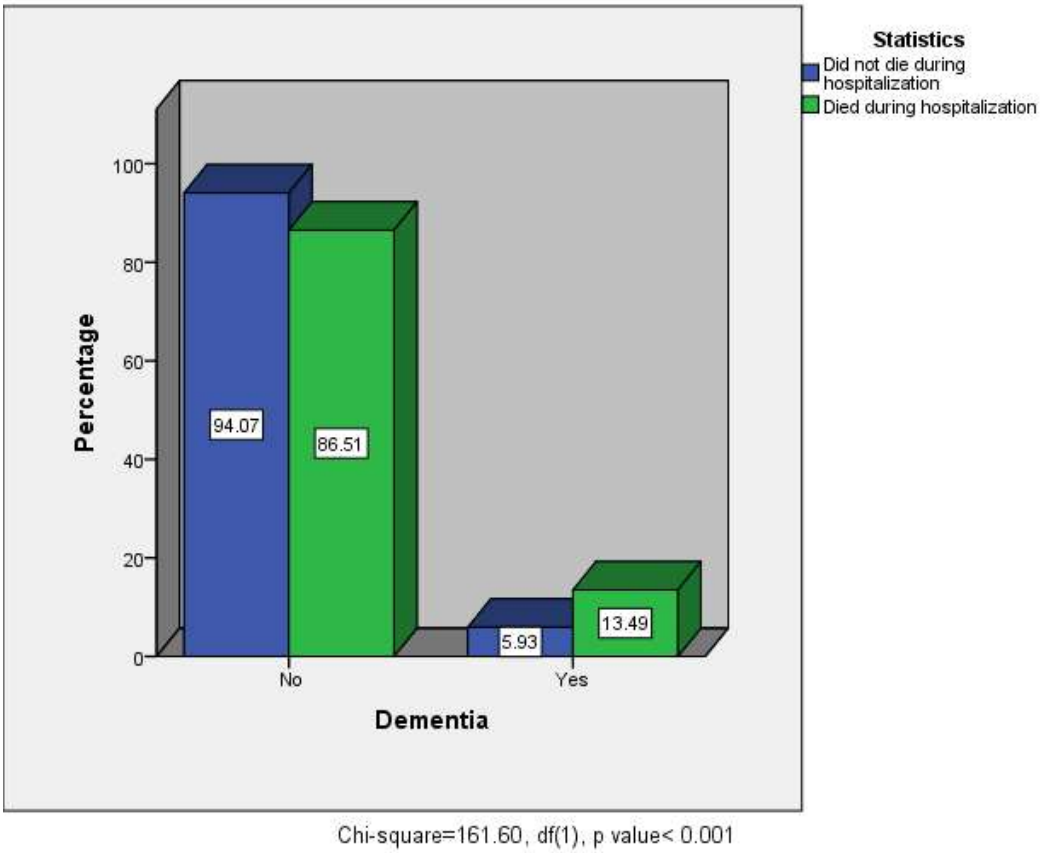


Figure 17 Mortality and Dementia of Down's syndrome patients

4.4.3 Mortality and Down's syndrome cardiac malformation (Hypothesis 3)

There is a significant association found between mortality and cardiac malformation related to Down's syndrome. There is a higher incidence of mortality observed for patients with Down's cardiac malformation by 7.78%, as shown in Figure 18.

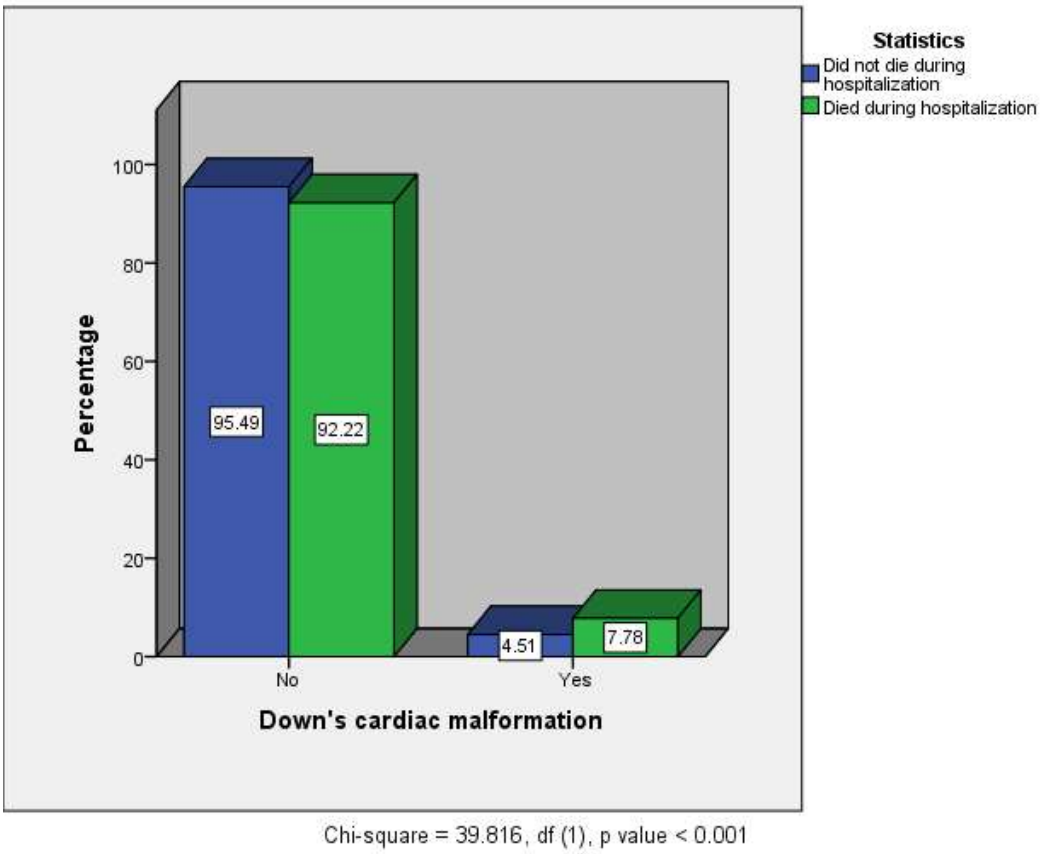
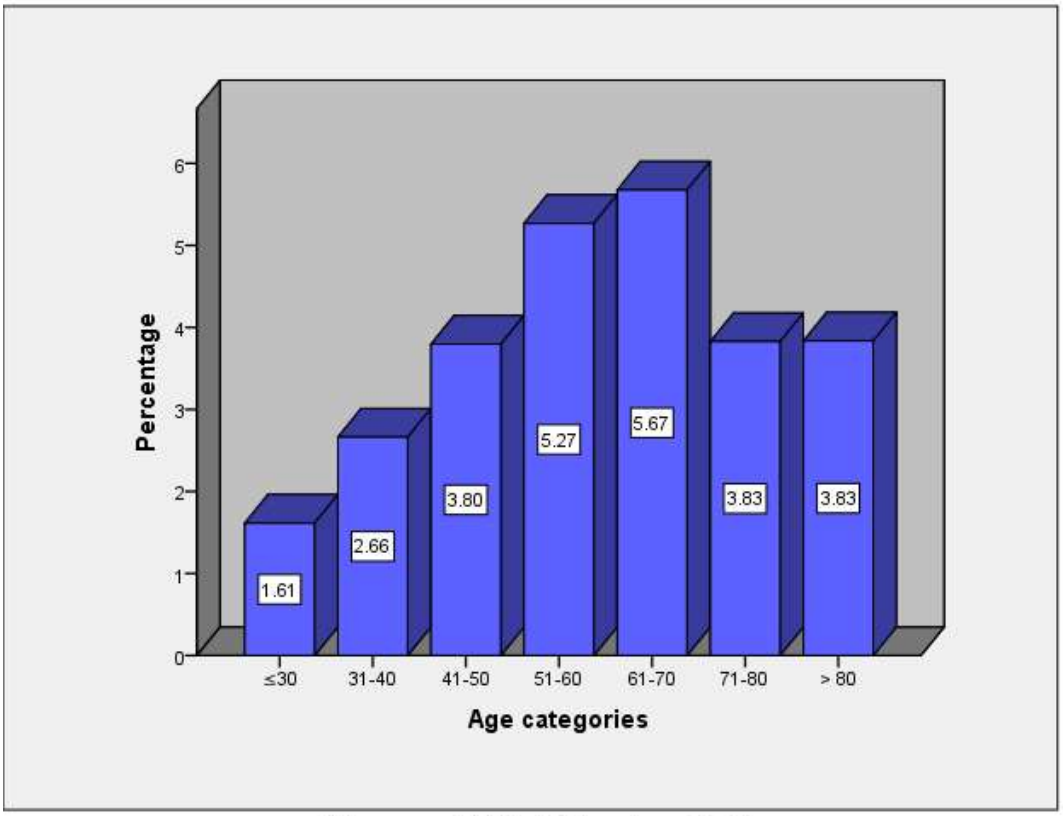


Figure 18 Mortality and Down's cardiac malformation

4.4.4 Mortality and age groups

There is a significant association found between the age groups and mortality of Down's syndrome patients. The highest incidence was observed for those aged 61-70 years (5.67%), followed by 51-60 years (5.27%) and 71-80 years and older than 80 years (3.83% each) as shown in Figure 19.



Chi-square = 514.79, df (6), p value < 0.001

Figure 19 Mortality and age categories

4.4.5 Mortality and gender

There is no significant association found between the mortality of Down's syndrome patients and gender. However, there is a higher incidence observed with females than males as shown in Figure 20.

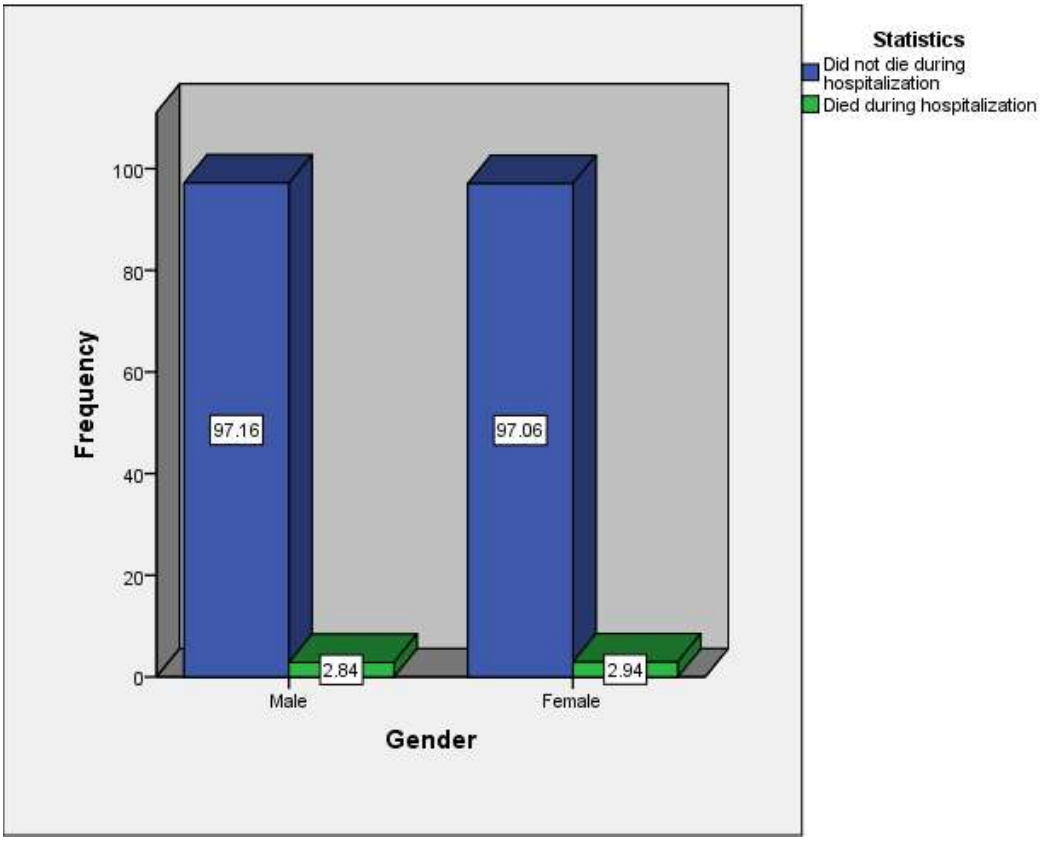


Figure 20 Mortality and gender of Down's syndrome patients

4.4.6 Mortality and race

There is a significant association found between the race and mortality of Down's syndrome patients. The White race showed highest incidence of mortality by 3.23%, followed by Other (2.96%) and Native American (2.93%) as shown in Figure 21.

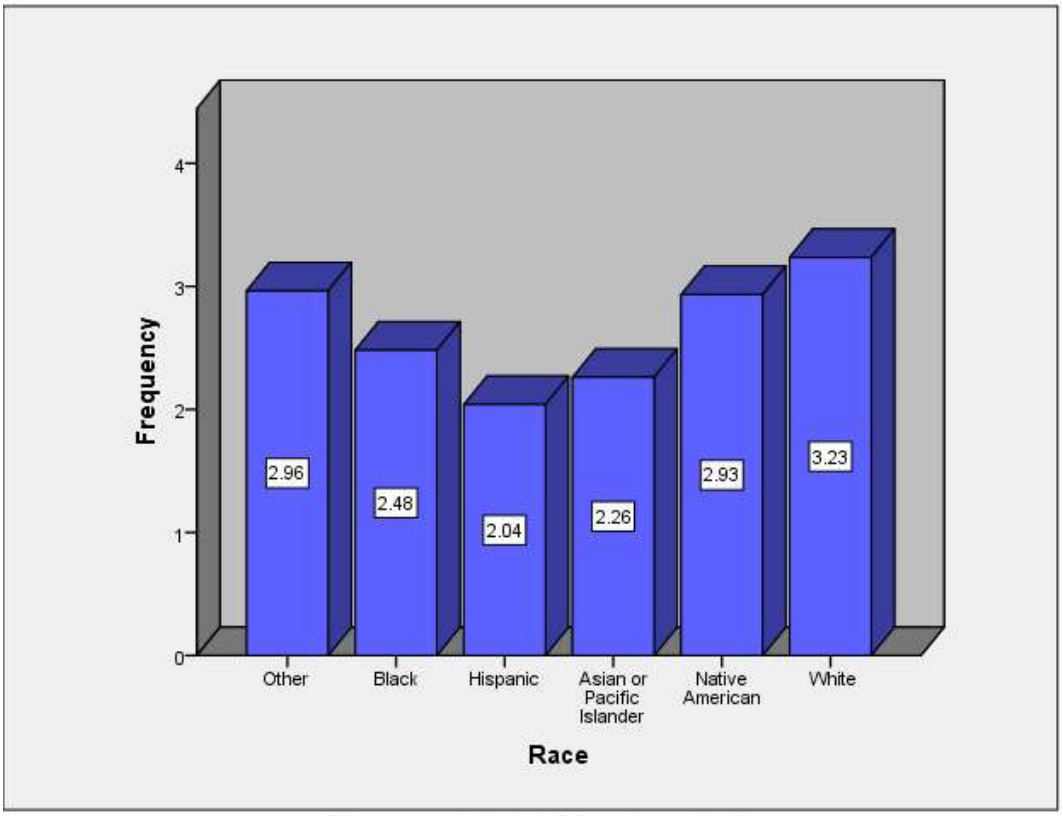


Figure 21 Mortality and race of Down's syndrome patients

4.4.7 Mortality and insurance

There is an association between the mortality of Down's syndrome patients and the type of insurance. Patients with private insurance (Including HMO), had the highest incidence of mortality by 4.81%, followed by Medicare (3.41%), and No charges (2.8%) as shown in Figure 22.

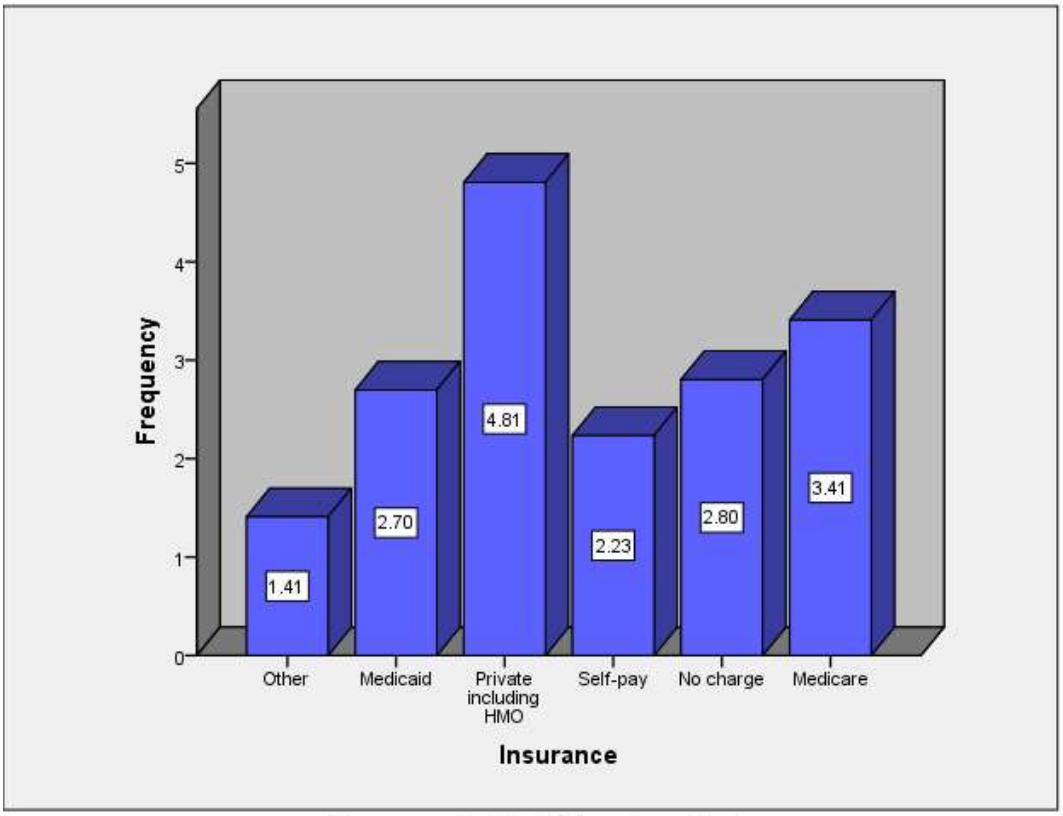


Figure 22 Mortality and insurance of Down's syndrome patients

4.4.8 Household income

There is no significant association found between the household income and mortality of Down's syndrome patients. However, there is a higher incidence of mortality observed with the individuals in the 0-25th percentile, as shown in Figure 23.

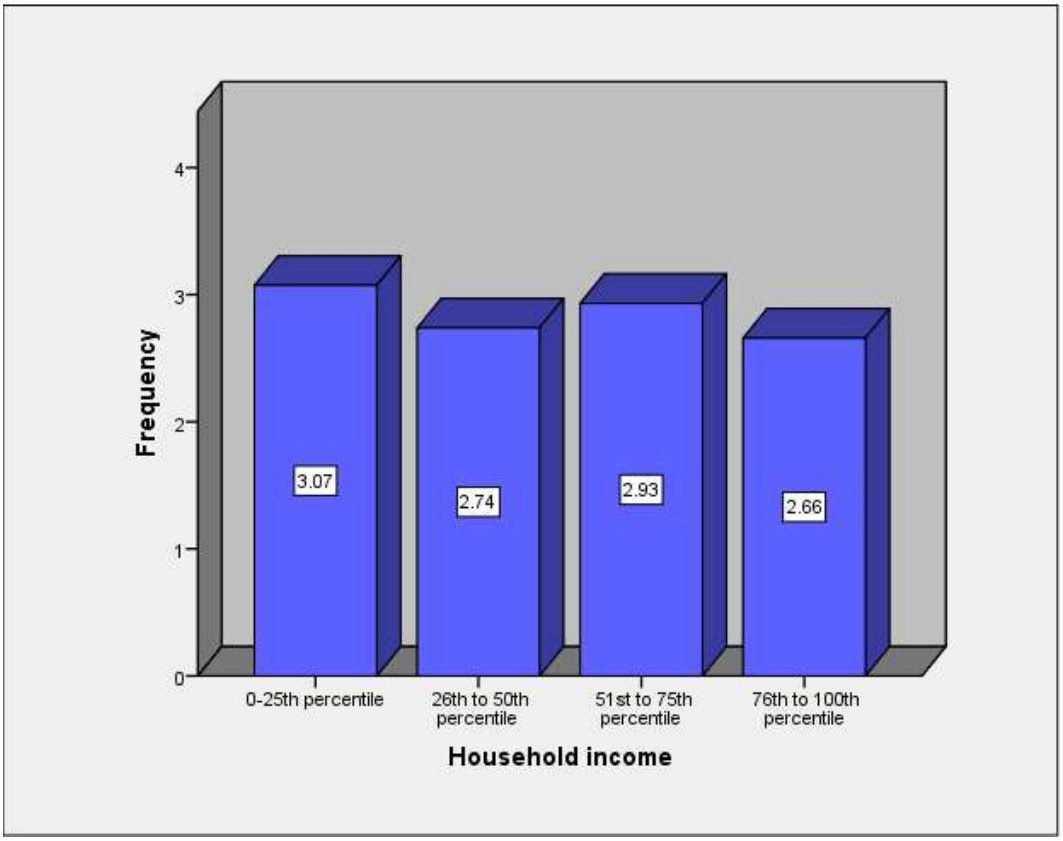


Figure 23 Household income and mortality of Down's syndrome patients

4.5 Association between Down's syndrome and aging diseases (or related)

Parkinson's (and related) is the only disease significantly associated with problems related to Down's syndrome. However, no significant association was found with Alzheimer's disease.

4.5.1 Down's atlantoaxial instability and Parkinson's disease (Hypothesis 4)

There is a significant association found between the existence of Parkinson's disease (or related) and the atlantoaxial instability of Down's syndrome. The incidence of patients with Down's syndrome instability with the occurrence of Parkinson's disease showed a higher incidence than those without (12.77% vs. 7.96%), as shown in Figure 24.

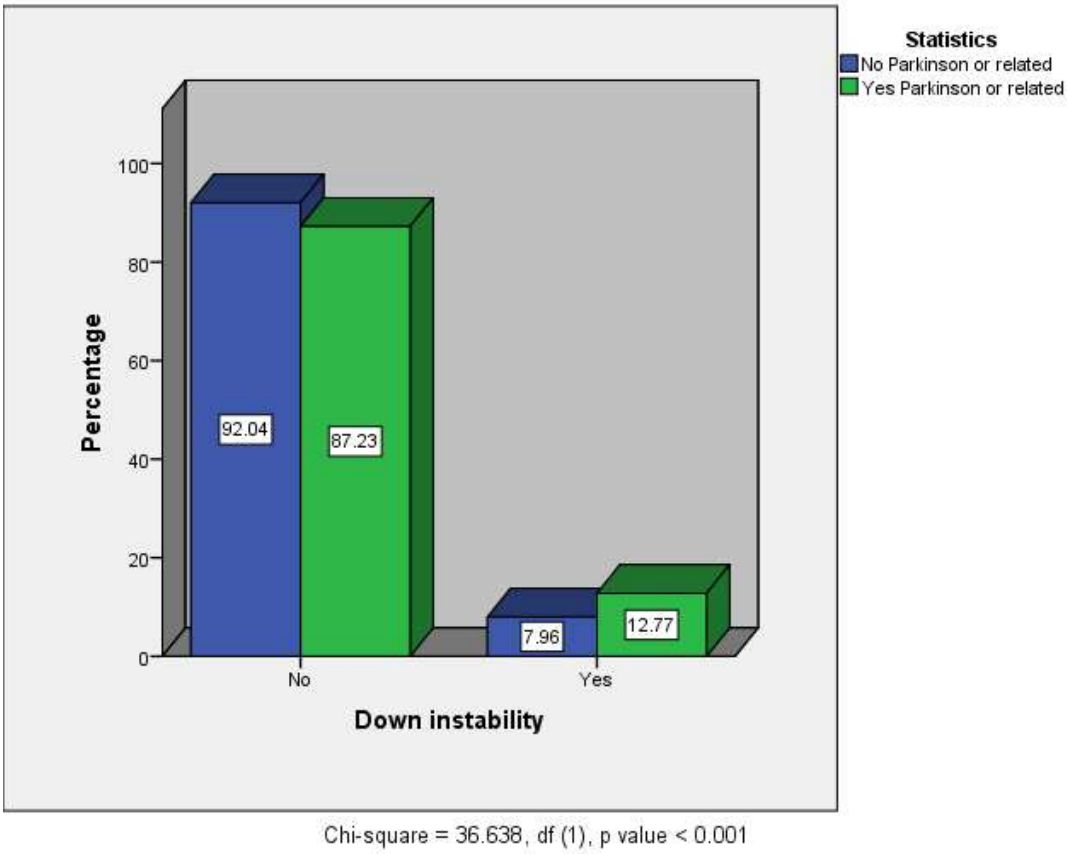


Figure 24 Parkinson's disease and Down's syndrome atlantoaxial instability

4.5.2 Down's atlantoaxial instability and Parkinson's disease gait disturbance

There is a significant association found between the existence of gait disturbance induced by Parkinson's disease and the atlantoaxial instability of Down's syndrome. The incidence of patients with Down's instability with the occurrence of gait disturbance of Parkinson's disease was higher than those without (21.47% vs. 7.98%), as shown in Figure 25.

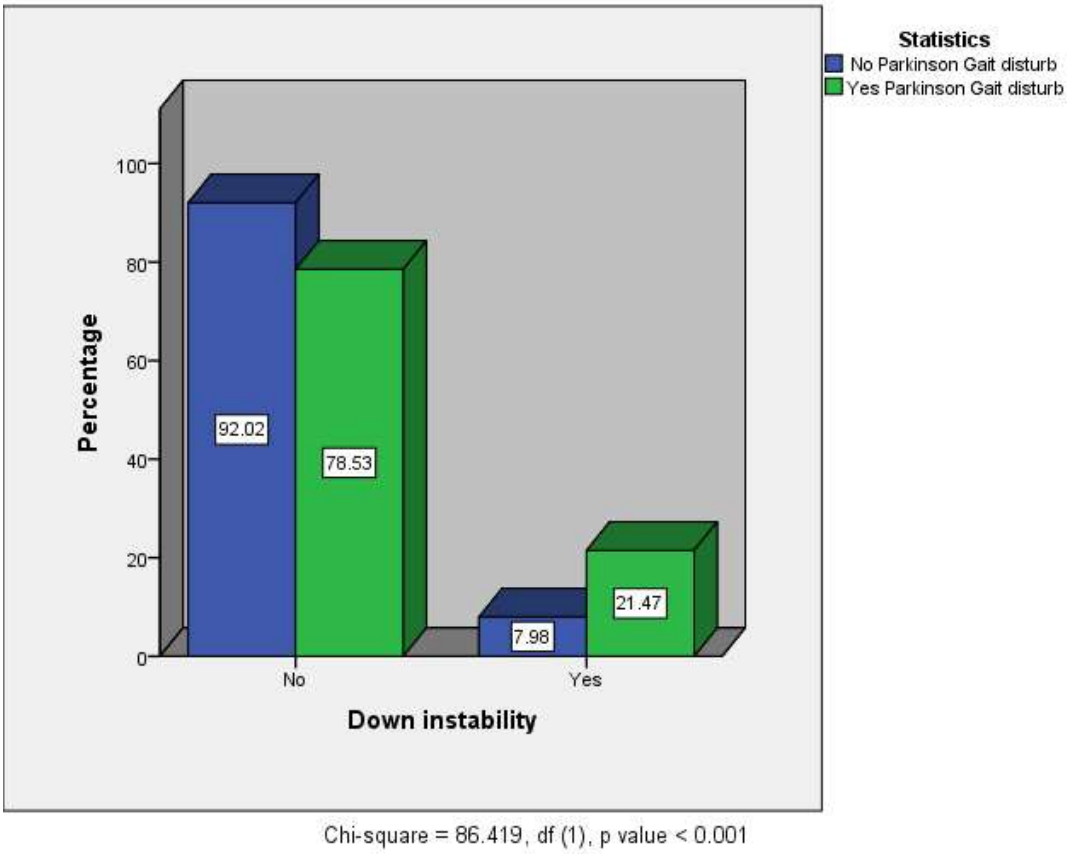


Figure 25 Gait disturbance of Parkinson's disease and Down's atlantoaxial instability

4.6 Predictors of study outcomes

4.6.1 Predictors and differences in length of hospital stay of Down's syndrome patients with and without aging diseases

a) Down's syndrome only (Hypothesis 5)

Multiple linear regression (dummy method) is used to find out the predictors of the length of hospital stay for Down's syndrome patients. Assumptions must be ensued to approve the results of the regression model. The assumptions are as follows:

Assumption 1, dependent variables should be continuous: Length of hospital stay is continuous. This assumption is accepted.

Assumption 2, two or more independent variables (numerical, ordinal, or categorical): Comorbidities, age categories, gender, race, type of insurance and household income are categorical while the number of procedures and number of chronic diseases are numerical. All groups were recategorized to be appropriate for the dummy method of analysis. This assumption is accepted.

Assumption 3, independence of observations or independence of residuals: The value of Durbin-Watson for length of stay should range from between 1 and 3, or near to 2 as an ideal result. The value of Durbin-Watson for length of stay is 1.868 for Down's syndrome. This assumption is accepted.

Assumption 4, linear relationship between the dependent and independent variable(s): Significant relationships between the dependent and independent variables. This assumption is accepted.

Assumption 5, data must show homoscedasticity: Results showed that the dots along the scatter plot are homogeneous and with the same distance around the linear fit line, as shown in Figure below. This assumption is accepted.

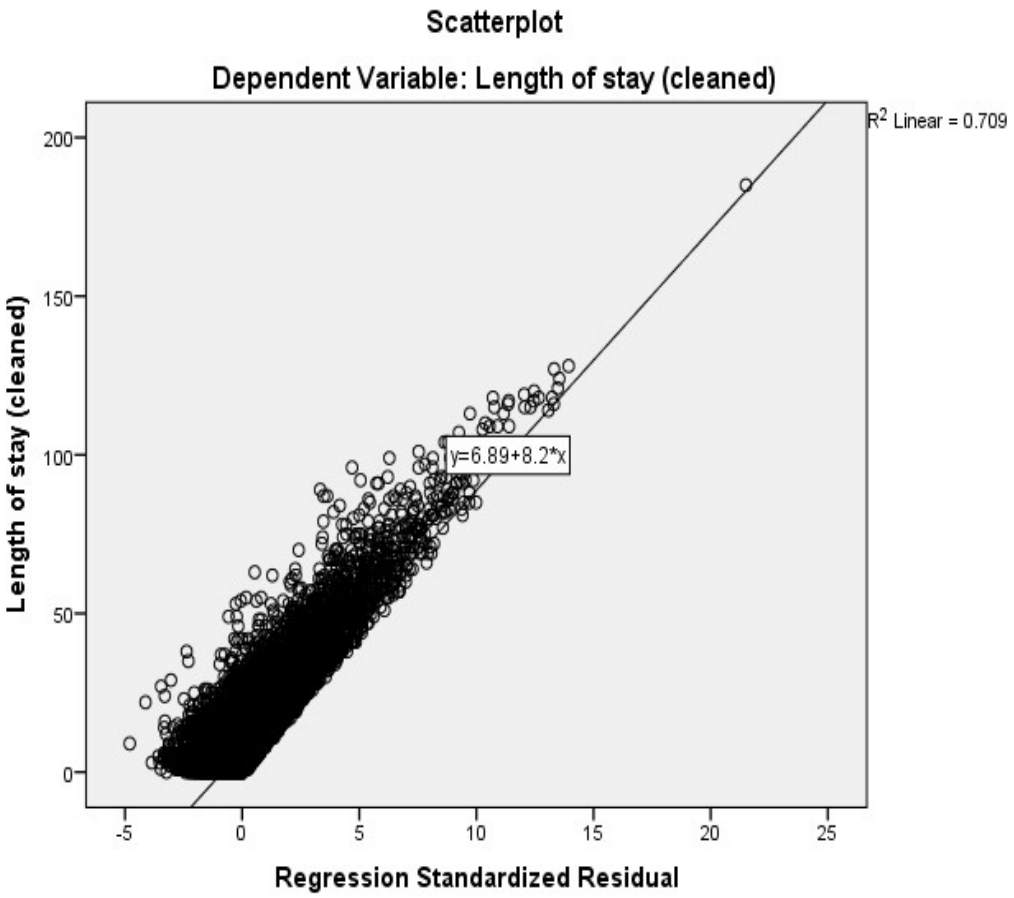


Figure 26 Homoscedasticity of length of hospital stay for Down's syndrome patients

Assumption 6, data must not show multicollinearity: Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 for an ideal result. All results of variables are less than 2. This assumption is accepted.

Assumption 7, no significant outliers: The cut point for the outliers while using Cook's distance is (4/n), which is equal to 0.000073. There were 224 cases considered as outliers. These cases were excluded in the regression model.

Assumption 8, the residuals must be normally distributed: The residuals are normally distributed, as shown in the figure above.

After accepting all assumptions for the length of stay, the final models for the predictors of Down's syndrome patients are shown in Table 14;

Congestive heart failure is the predictor with the highest effects on length of hospital stay for Down's syndrome patients with 3.145 days, followed by weight loss (2.438 days), fluid and electrolyte disorders (1.976 days), number of procedures (1.813 days), coagulopathy (1.735 days) and drug abuse (1.526 days). The factors more closely related to a reduction of length of hospital stay were ages 31-40 years (-1.300 days), ages 61-70 years (-1.189 days), and ages 41-50 years (-1.101 days), as shown in Table 15.

The length of hospital stay of Down's syndrome = 3.330 +.809 (Hispanic) + .522 (Asian or Pacific Islander) - 1.300 (Ages 31-40) – 1.101 (Ages 41-50) – .854 (Ages 51-60) - 1.189 (Ages 61-70) -1.076 (Self pay) -.253 (Income 51st-75th percentile) -.427 (Income 76th-100th percentile) + 1.813 (Number of procedures) + 1.023 (Deficiency anemias) + 3.145 (Congestive heart failure) + 1.735 (Coagulopathy) + 1.526 (Drug abuse) + .339 (Hypothyroidism) + 1.976 (Fluid and electrolyte disorders) + .797 (Other neurological disorders) + .666 (Paralysis) + .554 (Psychoses) + 1.040 (Pulmonary circulation disorders) + 2.438 (Weight loss).

Table 15 Predictors of length of hospital stay of Down's syndrome patients

	B	SE	Beta	t	Sig.	95% CI		Tolerance	VIF
						Lower Bound	Upper Bound		
(Constant)	3.330	.093		35.748	.000	3.148	3.513		
Female	-.058	.071	-.003	-.816	.414	-.196	.081	.988	1.012
Black	.057	.127	.002	.446	.656	-.193	.306	.938	1.066
Hispanic	.809	.099	.031	8.153	.000	.614	1.003	.900	1.111
Asian or Pacific Islander	.522	.251	.008	2.080	.038	.030	1.013	.982	1.018
Native American	.216	.439	.002	.491	.623	-.645	1.076	.991	1.009
Ages 31-40	**-1.300**	**.147**	**-.034**	**-8.850**	**.000**	**-1.588**	**-1.012**	**.892**	**1.121**
Ages 41-50	**-1.101**	**.119**	**-.037**	**-9.223**	**.000**	**-1.336**	**-.867**	**.800**	**1.250**
Ages 51-60	-.854	.115	-.031	-7.412	.000	-1.080	-.628	.743	1.345

Ages 61-70	**-1.189**	**.161**	**-.029**	**-7.376**	**.000**	**-1.505**	**-.873**	**.838**	**1.194**
Other insurance	-.987	.576	-.006	-1.714	.086	-2.115	.141	.997	1.003
Medicaid	-.283	.227	-.005	-1.246	.213	-.727	.162	.988	1.012
Private including HMO	-.196	.272	-.003	-.721	.471	-.729	.337	.994	1.006
Self-pay	-1.076	.315	-.012	-3.412	.001	-1.693	-.458	.992	1.008
No charge	-1.329	.809	-.006	-1.643	.100	-2.914	.257	.998	1.002
Income 26th-50th percentile	-.101	.095	-.004	-1.057	.291	-.288	.086	.717	1.395
Income 51st-75th_percentile	-.253	.097	-.011	-2.606	.009	-.442	-.063	.712	1.404
Income 76th-100th_percentile	-.427	.102	-.018	-4.177	.000	-.627	-.227	.721	1.387
Number of procedures	**1.813**	**.014**	**.489**	**131.543**	**.000**	**1.786**	**1.840**	**.937**	**1.068**
Acquired immune deficiency	1.021	2.474	.001	.413	.680	-3.829	5.871	.997	1.003
Alcohol abuse	-.531	.572	-.003	-.928	.353	-1.654	.591	.927	1.079
Deficiency anemias	1.023	.126	.031	8.139	.000	.777	1.269	.884	1.131
Rheumatoid arthritis	-.535	.375	-.005	-1.426	.154	-1.271	.200	.992	1.008
Chronic blood loss anemia	-1.571	.491	-.012	-3.196	.071	-2.534	-.607	.995	1.005
Congestive heart failure	**3.145**	**.154**	**.076**	**20.367**	**.000**	**2.842**	**3.448**	**.934**	**1.071**
Chronic pulmonary disease	-.322	.111	-.011	-2.898	.074	-.540	-.104	.974	1.027
Coagulopathy	**1.735**	**.175**	**.037**	**9.905**	**.000**	**1.392**	**2.079**	**.951**	**1.052**
Depression	-.376	.180	-.008	-2.091	.057	-.729	-.024	.948	1.055
Diabetes, uncomplicated	.047	.149	.001	.312	.755	-.246	.339	.887	1.128
Diabetes with chronic complications	.132	.379	.001	.348	.727	-.611	.876	.957	1.045
Drug abuse	**1.526**	**.430**	**.013**	**3.548**	**.000**	**.683**	**2.369**	**.933**	**1.072**
Hypertension	-1.203	.123	-.039	-9.780	.098	-1.444	-.962	.818	1.222
Hypothyroidism	.339	.090	.015	3.762	.000	.162	.516	.871	1.148
Liver disease	-.200	.315	-.002	-.634	.526	-.817	.418	.978	1.022
Lymphoma	-.896	1.019	-.003	-.879	.379	-2.893	1.102	.996	1.004

Fluid and electrolyte disorders	**1.976**	**.091**	**.082**	**21.695**	**.000**	**1.797**	**2.154**	**.915**	**1.093**
Metastatic cancer	-1.091	.688	-.006	-1.587	.113	-2.439	.257	.995	1.005
Other neurological disorders	.797	.117	.026	6.808	.000	.568	1.026	.890	1.124
Obesity	-.119	.149	-.003	-.802	.423	-.411	.172	.924	1.083
Paralysis	.666	.237	.010	2.805	.005	.200	1.131	.974	1.027
Peripheral vascular disorders	-.908	.362	-.009	-2.510	.082	-1.616	-.199	.981	1.020
Psychoses	.554	.246	.008	2.250	.024	.071	1.037	.977	1.024
Pulmonary circulation disorders	1.040	.190	.020	5.485	.000	.668	1.412	.966	1.036
Renal failure	-.605	.195	-.012	-3.105	.062	-.986	-.223	.898	1.114
Solid tumor without metastasis	-.422	.637	-.002	-.663	.508	-1.671	.827	.994	1.006
Peptic ulcer	-.560	2.594	-.001	-.216	.829	-5.644	4.525	.998	1.002
Valvular disease	.001	.169	.000	.006	.995	-.330	.332	.972	1.028
Weight loss	**2.438**	**.198**	**.046**	**12.289**	**.000**	**2.049**	**2.827**	**.937**	**1.067**

* Multiple linear regression: R = 0.540 (adjust R^2 = .291), df (47), p <0.001. Reference: White, male, age ≤30 years, Medicare, 0-25th percentile income, and no comorbidities.

b) Down's syndrome and aging diseases (Hypothesis 6 and 7)

Multiple linear regression (dummy method) is used to find out the predictors of length of hospital stay for Down's syndrome patients with aging diseases. Assumptions must be proceeded to approve the results of the regression model. These assumptions are as follows:

Assumption 1, dependent variables should be continuous: Length of hospital stay is continuous. This assumption is accepted.

Assumption 2, two or more independent variables (numerical, ordinal, or categorical): Comorbidities, age categories, gender, race, type of insurance and

household income are categorical while the number of procedures and number of chronic diseases are numerical. All groups were recategorized to be appropriate for the dummy method of analysis. This assumption is accepted.

Assumption 3, independence of observations or independence of residuals: The value of Durbin-Watson for length of stay should range between 1 and 3, or near to 2 as an ideal result. The value of Durbin-Watson for length of stay is 1.866 and 1.831for Down's syndrome with Parkinson's and Alzheimer's diseases respectively. This assumption is accepted.

Assumption 4, linear relationship between the dependent and independent variable(s): Significant relationships between dependent and independent variables. This assumption is accepted.

Assumption 5, data must show homoscedasticity: Results showed that the dots along the scatter plot are homogeneous and with the same distance around the linear fit line, as shown in the figures below. This assumption is accepted.

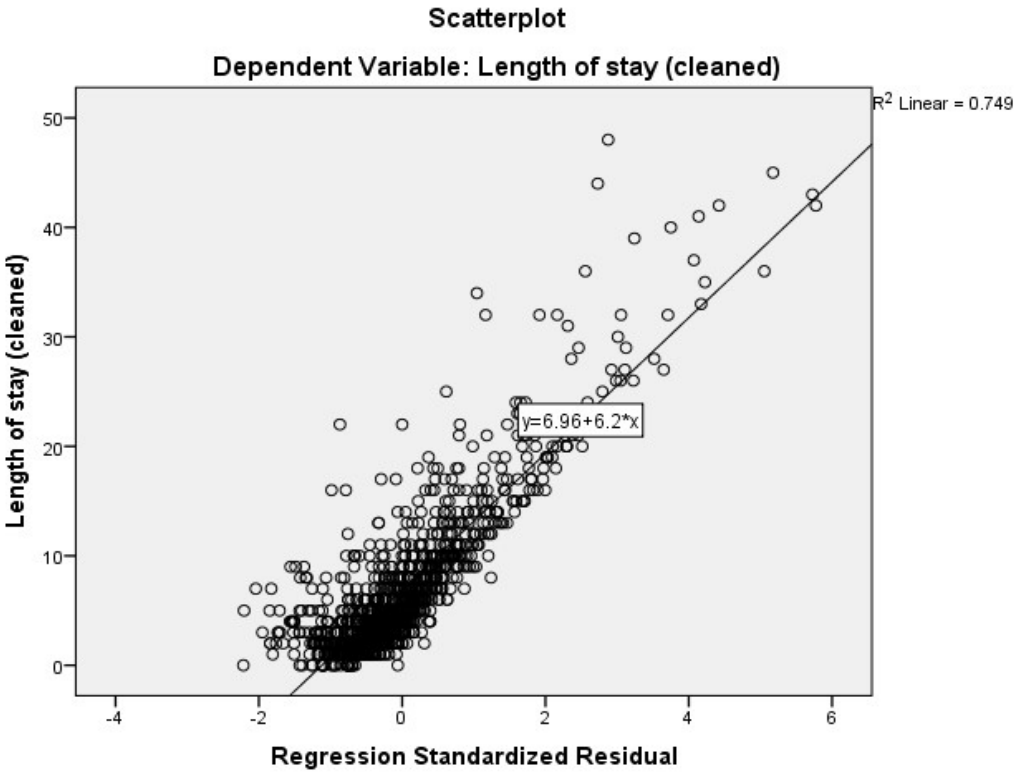


Figure 27 Homoscedasticity of length of hospital stay for Down's syndrome patients with Parkinson's disease

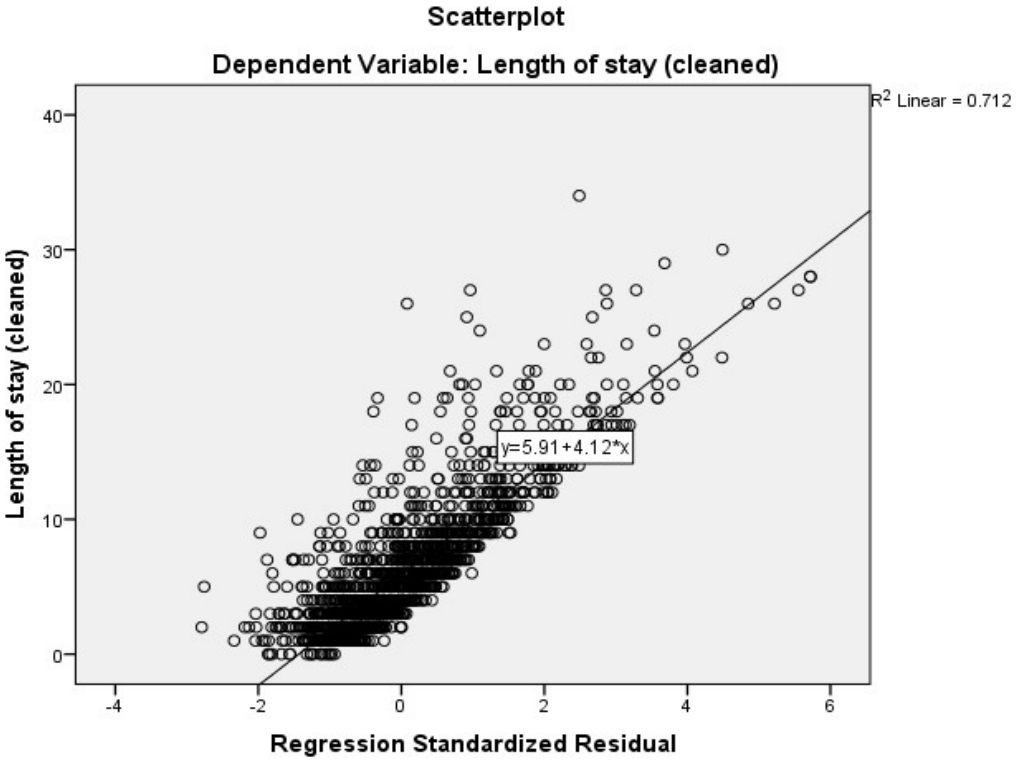


Figure 28 Homoscedasticity of length of hospital stay for Down's syndrome patients with Alzheimer's disease

Assumption 6, data must not show multicollinearity: Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as an ideal result. All results of variables are less than 2. This assumption is accepted.

Assumption 7, no significant outliers: The cut point for the outliers while using Cook's distance is (4/n), which equals to 0.003 and 0.002 for Parkinson's and Alzheimer's diseases respectively. There were 49 and 92 cases considered as outliers for Parkinson's and Alzheimer's diseases respectively. These cases were excluded in regression model.

Assumption 8, the residuals must be normally distributed: The residuals are normally distributed, as shown in the Figures above.

After accepting all assumptions for the length of stay, the final models for the predictors for Down's syndrome patients with aging diseases are shown in Table 16.

Drug abuse is the predictor with the highest effects on length of hospital stay for Down's syndrome patients with Parkinson's disease with 12.730 days, followed by congestive heart failure (2.181 days), Hispanic race (1.747 days) and number of procedures (1.506 days). The Self-pay type of insurance, is the only significant factor that reduced the length of hospital stay by 3.707 days, as shown in Table 16.

The length of hospital stays for Down's syndrome with Parkinson's disease = 3.983 + 1.747 (Hispanic) - 3.707 (Self-pay) + 1.506 (Number of procedures) + 2.181 (congestive heart failure) + 12.730 (Drug abuse).

Weight loss is the predictor with the highest effect on length of hospital stay for Down's syndrome patients with Alzheimer's disease by 1.973 days, followed by number of chronic conditions (1.267 days), deficiency anemia (0.879 days), congestive heart failure (0.872 days), lymphoma (0.738 days) and ages 41-50 years (0.513 days). No

charge, the type of insurance, showed the highest factor related to a reduction for length of stay for Down's syndrome patients with Alzheimer's disease by 0.743 days, followed by income 51st-75th percentile (-0.676 days) and income 26th-50th percentile (-0.662 days).

The length of hospital stay for Down's syndrome with Alzheimer's disease = 3.475 + .513 (Ages 41-50) -.743 (No charge) -.662 (Income 26th-50th percentile) -.676 (Income 51st-75th percentile) + 1.267 (Number of chronic conditions) + .879 (Deficiency anemias) + .872 (Congestive heart failure) + .738 (Lymphoma) + 1.973 (Weight loss).

In a comparison between the predictors of length of stay for Down's syndrome patients with Parkinson's and Alzheimer's diseases, drug abuse and weight loss are the main risk factors for patients with Parkinson's and Alzheimer's diseases respectively. Down's syndrome patients with Alzheimer's disease had more risk factors when compared to those individuals with Parkinson's disease. But the hospital stays induced by the factors of Parkinson's disease had a higher length of stay than Alzheimer's disease.

The risk factor interaction showed the highest impact on the length of hospital stay for Down's syndrome with aging diseases (Hypothesis 7). Number of procedures * Drug abuse and CHF* weight loss showed the highest length of stay for Down's syndrome patients with Parkinson's and Alzheimer's diseases by 4.009 and 5.672 days respectively, as shown in Table 17.

Table 16 Predictors of hospital of length stay of Down's syndrome patients with aging diseases

Predictors	Parkinson's disease*									Alzheimer's disease†								
	B	SE	Beta	T	*Sig.	95% CI		Tolerance	VIF	B	SE	Beta	t	†Sig.	95% CI		Tolerance	VIF
						Lower Bound	Upper Bound								Lower Bound	Upper Bound		
(Constant)	3.983	.510		7.813	.000	2.983	4.983			3.475	.488		7.116	.000	2.517	4.433		
Female	.683	.377	.048	1.815	.070	-.056	1.422	.961	1.041	.087	.193	.009	.452	.652	-.291	.465	.958	1.044
Other races										-.032	.513	-.001	-.062	.951	-1.037	.974	.707	1.414
Black	.308	.716	.012	.430	.667	-1.097	1.713	.923	1.084	.879	.563	.034	1.562	.118	-.225	1.984	.793	1.261
Hispanic	**1.747**	**.599**	**.081**	**2.915**	**.004**	**.571**	**2.923**	**.887**	**1.127**	-.353	1.249	-.006	-.282	.778	-2.802	2.096	.912	1.097
Asian Pacific Islander	.252	1.656	.004	.152	.879	-2.998	3.501	.947	1.056	-.880	2.085	-.008	-.422	.673	-4.968	3.209	.977	1.023
Native American	.214	2.374	.002	.090	.928	-4.444	4.872	.980	1.020	-.858	.906	-.019	-.947	.344	-2.635	.920	.949	1.054
Ages 31-40	-.442	1.028	-.012	-.430	.667	-2.459	1.575	.879	1.137	.224	.301	.017	.744	.457	-.367	.815	.714	1.401
Ages 41-50	.391	.636	.019	.615	.539	-.857	1.639	.741	1.349	**.513**	**.223**	**.053**	**2.300**	**.022**	**.076**	**.950**	**.717**	**1.395**
Ages 51-60	.422	.561	.025	.753	.452	-.679	1.523	.597	1.674	-.032	.513	-.001	-.062	.951	-1.037	.974	.707	1.414
Ages 61-70	-1.381	.739	-.058	-1.868	.062	-2.831	.070	.691	1.448	.879	.563	.034	1.562	.118	-.225	1.984	.793	1.261
Medicaid	-.889	1.649	-.014	-.539	.590	-4.125	2.346	.955	1.047	.875	.916	.019	.956	.339	-.921	2.672	.973	1.028
Private including HMO	-.588	1.836	-.008	-.320	.749	-4.190	3.015	.960	1.041	.131	.399	.007	.328	.743	-.651	.913	.955	1.047
Self-pay	**-3.707**	**1.825**	**-.054**	**-2.031**	**.043**	**-7.289**	**-.125**	**.972**	**1.029**	-2.429	1.700	-.028	-1.429	.153	-5.763	.906	.981	1.020
No charge	-1.757	4.470	-.010	-.393	.694	-10.527	7.013	.964	1.037	**-.743**	**.280**	**-.066**	**-2.658**	**.008**	**-1.292**	**-.195**	**.621**	**1.610**
Income 26th-50th percentile	.038	.517	.002	.073	.942	-.977	1.053	.684	1.463	**-.662**	**.278**	**-.059**	**-2.382**	**.017**	**-1.206**	**-.117**	**.612**	**1.633**
Income 51st-75th percentile	-.182	.519	-.011	-.350	.726	-1.200	.837	.686	1.459	**-.676**	**.274**	**-.063**	**-2.472**	**.014**	**-1.213**	**-.140**	**.597**	**1.676**
Income 75th-100th percentile	.387	.526	.023	.735	.462	-.646	1.419	.674	1.484	.050	.053	.025	.945	.345	-.054	.153	.560	1.785
Number of chronic conditions										**1.267**	**.057**	**.454**	**22.055**	**.000**	**1.154**	**1.380**	**.902**	**1.109**
Number of procedures	**1.506**	**.092**	**.456**	**16.446**	**.000**	**1.327**	**1.686**	**.880**	**1.137**	.875	.916	.019	.956	.339	-.921	2.672	.973	1.028
Alcohol abuse	-3.545	3.708	-.026	-.956	.339	-10.821	3.730	.935	1.070									
Deficiency anemias	.325	.618	.015	.526	.599	-.888	1.538	.867	1.154	**.879**	**.274**	**.065**	**3.204**	**.001**	**.341**	**1.418**	**.920**	**1.087**
Rheumatoid arthritis	1.402	2.397	.016	.585	.559	-3.301	6.106	.962	1.040	.517	.911	.011	.568	.570	-1.269	2.304	.940	1.064
Chronic blood loss anemia	1.718	3.636	.012	.472	.637	-5.416	8.853	.972	1.029	.580	1.575	.007	.368	.713	-2.509	3.669	.980	1.021

Congestive heart failure	**2.181**	**.885**	**.066**	**2.463**	**.014**	**.444**	**3.918**	**.937**	**1.068**	**.872**	**.391**	**.045**	**2.230**	**.026**	**.105**	**1.639**	**.922**	**1.085**
Chronic pulmonary disease	.055	.677	.002	.082	.935	-1.273	1.384	.927	1.079	-.043	.347	-.003	-.123	.902	-.722	.637	.916	1.092
Coagulopathy	-.437	.926	-.013	-.473	.637	-2.253	1.378	.939	1.066	.146	.522	.006	.280	.779	-.878	1.170	.948	1.055
Depression	-.851	.702	-.033	-1.211	.226	-2.229	.528	.903	1.108	-.373	.309	-.025	-1.208	.227	-.979	.233	.920	1.087
DM, uncomplicated	-.336	.808	-.012	-.417	.677	-1.921	1.248	.862	1.160	-.487	.417	-.024	-1.169	.243	-1.304	.330	.904	1.106
DM with chronic complications	-2.323	1.775	-.036	-1.309	.191	-5.805	1.160	.883	1.133	-1.633	1.856	-.017	-.880	.379	-5.273	2.007	.987	1.013
Drug abuse	**12.730**	**3.622**	**.092**	**3.514**	**.000**	**5.622**	**19.837**	**.979**	**1.021**	-.238	.302	-.016	-.789	.430	-.830	.354	.874	1.144
Hypertension	-.753	.556	-.039	-1.354	.176	-1.845	.338	.811	1.233	.028	.208	.003	.135	.893	-.380	.436	.823	1.215
Hypothyroidism	.326	.446	.021	.731	.465	-.549	1.201	.817	1.223	-.158	.895	-.003	-.177	.860	-1.913	1.597	.973	1.028
Liver disease	-1.703	1.850	-.025	-.920	.358	-5.332	1.927	.946	1.057	-1.748	4.150	-.008	-.421	.674	-9.888	6.392	.985	1.016
Lymphoma										**.738**	**.210**	**.071**	**3.511**	**.000**	**.326**	**1.150**	**.925**	**1.081**
Fluid and electrolyte disorders	.069	.485	.004	.141	.888	-.883	1.020	.815	1.228	-.238	.302	-.016	-.789	.430	-.830	.354	.874	1.144
Other neurological disorders	.646	.463	.041	1.397	.163	-.261	1.554	.783	1.277	.047	.234	.004	.202	.840	-.411	.505	.915	1.092
Obesity	.243	.806	.008	.301	.763	-1.338	1.824	.866	1.154	.062	.447	.003	.138	.891	-.816	.939	.920	1.087
Paralysis	1.223	1.048	.032	1.167	.243	-.833	3.279	.930	1.076	.474	.644	.015	.736	.462	-.789	1.738	.950	1.053
Peripheral vascular disease	-1.377	1.474	-.026	-.934	.351	-4.270	1.516	.900	1.111	-.514	.655	-.016	-.785	.433	-1.799	.771	.919	1.088
Psychoses	.342	.957	.010	.357	.721	-1.537	2.220	.912	1.096	-.025	.447	-.001	-.057	.955	-.902	.852	.939	1.064
Pulmonary circulation disorders	.530	.922	.015	.575	.565	-1.279	2.339	.946	1.057									
Renal failure	.840	.980	.024	.857	.392	-1.083	2.763	.870	1.149	-.118	.440	-.005	-.268	.788	-.980	.744	.925	1.081
Solid tumor without metastasis	-3.636	4.451	-.022	-.817	.414	-12.370	5.098	.972	1.029	4.930	2.944	.033	1.674	.094	-.845	10.704	.979	1.022
Valvular disease	-.399	.802	-.013	-.498	.619	-1.972	1.174	.948	1.054	-.300	.361	-.017	-.830	.406	-1.007	.408	.909	1.100
Weight loss	.848	.962	.024	.881	.378	-1.040	2.735	.886	1.129	**1.973**	**.362**	**.112**	**5.455**	**.000**	**1.263**	**2.682**	**.910**	**1.099**

* Multiple linear regression: R = 0.501 (adjust R^2 = .223), df (42), p <0.001. Reference: White, male, age ≥70 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.536 (adjust R^2 = .272), df (40), p <0.001. Reference: White, male, age ≥70 years, Medicare, 0-25th percentile income, and no comorbidities.

Table 17 Risk factor interactions of hospital length stay for Down's syndrome patients with aging diseases

Aging diseases	Interaction of risk factors	B	SE	Beta	t	Sig.	95% CI	
							Lower Bound	Upper Bound
Parkinson's disease	(Constant)	7.417	.303		24.467	.000	6.822	8.012
	Drug abuse * Hispanic	-11.569	11.490	-.031	-1.007	.314	-34.112	10.974
	CHF* Hispanic	6.634	3.628	.053	1.828	.068	-.484	13.753
	Number of procedures*Hispanic	**2.349**	**.304**	**.226**	**7.725**	**.000**	**1.753**	**2.946**
	Number of procedures*CHF	**1.200**	**.511**	**.070**	**2.347**	**.019**	**.197**	**2.203**
	Number of procedures* Drug abuse	**4.009**	**.812**	**.150**	**4.936**	**.000**	**2.416**	**5.603**
Alzheimer's disease	(Constant)	6.046	.177		34.201	.000	5.700	6.393
	Age41to50* No of chronic conditions	-.027	.073	-.009	-.377	.707	-.170	.115
	Age41to50 * Anemia	2.343	1.262	.043	1.857	.063	-.131	4.817
	Age41to50_CHF	1.100	1.960	.013	.561	.575	-2.743	4.942
	Age41to50* weight loss	-.629	1.504	-.010	-.418	.676	-3.578	2.319
	No of chronic conditions * Anemia	**.183**	**.065**	**.069**	**2.828**	**.005**	**.056**	**.310**
	No of chronic conditions * CHF	**.210**	**.085**	**.062**	**2.466**	**.014**	**.043**	**.377**
	No of chronic conditions * lymphoma	-.506	.872	-.023	-.580	.562	-2.215	1.204
	No of chronic conditions*weight loss	**.497**	**.086**	**.149**	**5.760**	**.000**	**.328**	**.666**
	Anemia * CHF	-1.093	1.639	-.016	-.667	.505	-4.308	2.121
	Anemia * Lymphoma	11.829	12.594	.035	.939	.348	-12.867	36.526
	Anemia * Weight loss	.883	1.264	.018	.699	.485	-1.596	3.362
	CHF * Weight loss	**5.672**	**2.108**	**.062**	**2.691**	**.007**	**1.539**	**9.806**
	Weight loss * Lymphoma	10.005	8.729	.030	1.146	.252	-7.113	27.124

4.6.2 Predictors and Differences in total charges for Down's syndrome patients with and without aging diseases.

a) Down's syndrome only (Hypothesis 8)

Multiple linear regression (dummy method) is used to find out the predictors of total charges for Down's syndrome patients. Assumptions must be proceeded to approve the results of the regression model. These assumptions are as follows:

Assumption 1, dependent variables should be continuous: Total charges are continuous. This assumption is accepted.

Assumption 2, two or more independent variables (numerical, ordinal, or categorical): Comorbidities, age categories, gender, race, type of insurance and household income are categorical, while number of procedures and number of chronic diseases are numerical. All groups were recategorized to be appropriate for the dummy method of analysis. This assumption is accepted.

Assumption 3, independence of observations or independence of residuals: The value of Durbin-Watson for total charges should range between 1 and 3, or near to 2 as an ideal result. The value of Durbin-Watson for total charges is 1.745 for Down's syndrome. This assumption is accepted.

Assumption 4, linear relationship between the dependent and independent variable(s): Significant relationships between dependent and independent variables. This assumption is accepted.

Assumption 5, data must show homoscedasticity: Results showed that the dots along the scatter plot are homogeneous and with the same distance around the linear fit line, as shown in the Figure below. This assumption is accepted.

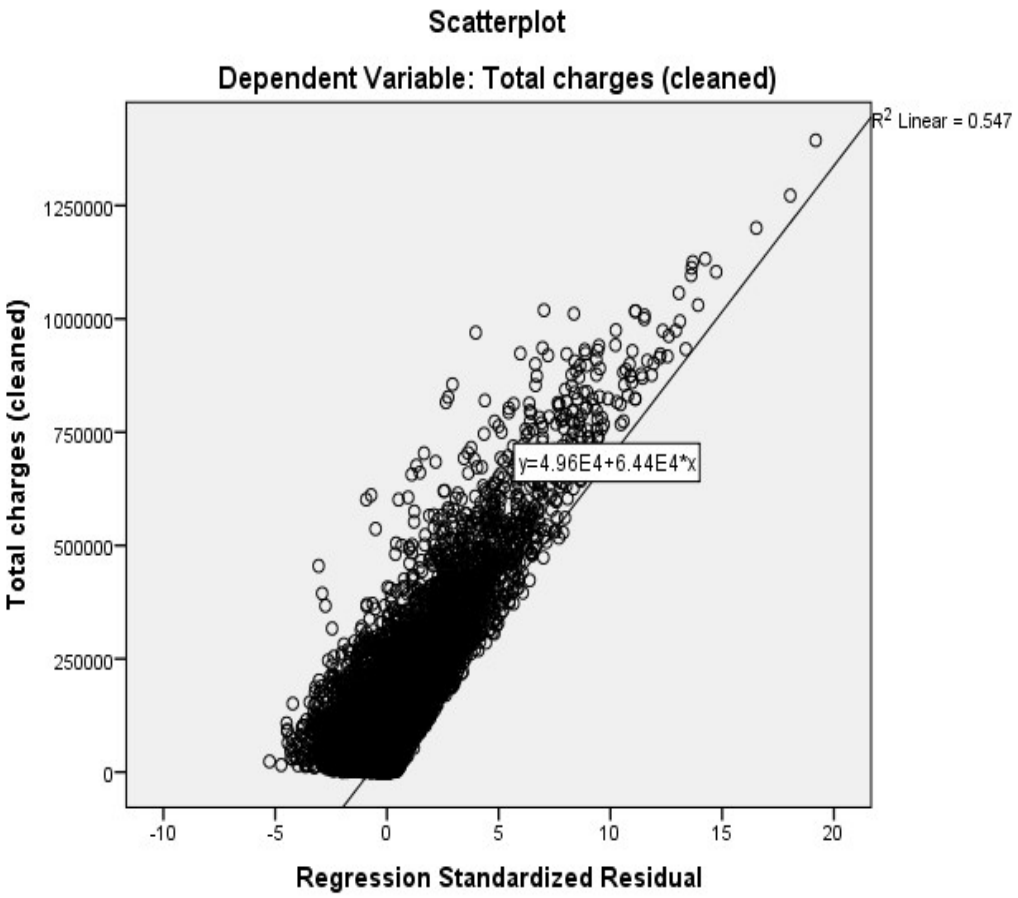


Figure 29 Homoscedasticity of total charges for Down's syndrome patients

Assumption 6, data must not show multicollinearity: Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as an ideal result. All results of variables are less than 2. This assumption is accepted.

Assumption 7, no significant outliers: The cut point for the outliers while using Cook's distance is (4/n), which equals to 0.000074. There were 232 cases considered as outliers. These cases were excluded in regression model.

Assumption 8, the residuals must be normally distributed: The residuals are normally distributed, as shown in the Figure above.

After accepting all assumptions for the total charges, the final models for the predictors of Down's syndrome patients are shown in Table 18.

The number of procedures is the predictor with the highest effect on total charges for Down's syndrome patients with $21471.895, followed by coagulopathy ($19247.127), congestive heart failure ($17482.777), fluid and electrolyte disorders ($16488.703), Hispanic ($15013.476), pulmonary circulation disorders ($12673.123), Asian or Pacific Islander ($12245.345) and drug abuse ($10121.430). The factors that are related to a reduction of total charges are other insurance ($-15645.39), self-pay ($-15610.43) and Medicaid ($-12795.92), as shown in Table 18.

The total charges of Down's syndrome = 4522.268 + 15013.476 (Hispanic) + 12245.345 (Asian or Pacific Islander) - 8271.817 (Age 31-40) - 8174.057 (Age 41-50) - 7145.478(Age 51-60) -8512.088 (Age 61-70) - 15645.39 (Other insurance) - 12795.92 (Medicaid) - 9705.478 (Private including HMO) - 15610.43 (Self-pay) + 1959.703 (Income 26th-50th percentile) + 2911.347 (Income 51st-75th percentile) + 2571.263 (Income 76th-100th percentile) + 21471.895 (Number of procedures) + 5295.531 (Deficiency anemias) + 17482.777 (Congestive heart failure) + 19247.127 (Coagulopathy) + 10121.430 (Drug abuse) + 2841.320 (Hypothyroidism) + 16488.703 (Fluid and electrolyte disorders) + 4516.825 (Other neurological disorders) + 5089.269 (Paralysis) + 4674.987 (Psychoses) + 12673.123 (Pulmonary circulation disorders) + 6017.204 (Weight loss).

Table 18 Predictors of total charges for Down's syndrome patients

	B	SE	Beta	t	Sig.	95% CI		Tolerance	VIF
						Lower Bound	Upper Bound		
(Constant)	4522.268	737.072		6.135	.000	3077.602	5966.934		
Female	67.578	560.813	.000	.121	.904	-1031.619	1166.775	.988	1.012
Black	195.812	1009.192	.001	.194	.846	-1782.211	2173.835	.938	1.066
Hispanic	15013.476	790.972	.064	18.981	.000	13463.165	16563.786	.901	1.110
Asian or Pacific Islander	12245.345	2043.227	.019	5.993	.000	8240.604	16250.085	.984	1.016
Native American	3063.453	3436.199	.003	.892	.373	-3671.523	9798.429	.991	1.009
Ages 31-40	-8271.817	1162.209	-.024	-7.117	.000	-10549.76	-5993.879	.891	1.122
Ages 41-50	-8174.057	943.654	-.031	-8.662	.000	-10023.63	-6324.487	.798	1.253
Ages 51-60	-7145.478	911.371	-.029	-7.840	.000	-8931.773	-5359.183	.742	1.348
Ages 61-70	-8512.088	1276.968	-.023	-6.666	.000	-11014.96	-6009.221	.838	1.194
Other insurance	-15645.39	4525.439	-.011	-3.457	.001	-24515.29	-6775.498	.997	1.003
Medicaid	-12795.92	1781.601	-.023	-7.182	.000	-16287.87	-9303.967	.988	1.013
Private including HMO	-9705.478	2141.583	-.015	-4.532	.000	-13902.10	-5507.959	.994	1.006
Self-pay	-15610.43	2494.416	-.020	-6.258	.000	-20499.50	-10721.35	.992	1.008
No charge	-11259.23	6327.745	-.006	-1.779	.075	-23661.66	1143.198	.998	1.002
Income 26th-50th percentile	1959.703	754.185	.010	2.598	.009	481.495	3437.911	.719	1.391
Income 51st-75th percentile	2911.347	768.180	.014	3.790	.000	1405.709	4416.985	.715	1.398
Income 76th-100th percentile	2571.263	811.644	.012	3.168	.002	980.435	4162.091	.725	1.380
Number of procedures	21471.895	110.948	.637	193.531	.000	21254.436	21689.354	.941	1.063
Acquired immune deficiency	-3003.130	19461.594	.000	-.154	.877	-41148.00	35141.741	.996	1.004
Alcohol abuse	-1859.770	4522.280	-.001	-.411	.681	-10723.47	7003.933	.922	1.085
Deficiency anemias	5295.531	997.737	.018	5.308	.000	3339.959	7251.102	.884	1.132
Rheumatoid arthritis	-4392.263	2996.958	-.005	-1.466	.143	-10266.32	1481.797	.992	1.008
Chronic blood loss anemia	-20724.13	3904.468	-.017	-5.308	.085	-28376.92	-13071.34	.995	1.005
Congestive heart failure	17482.777	1223.974	.047	14.284	.000	15083.779	19881.776	.934	1.070
Chronic pulmonary disease	-337.704	883.279	-.001	-.382	.702	-2068.938	1393.529	.974	1.027
Coagulopathy	19247.127	1394.844	.045	13.799	.000	16513.221	21981.032	.953	1.049
Depression	-839.280	1418.510	-.002	-.592	.554	-3619.571	1941.011	.947	1.056
Diabetes, uncomplicated	726.246	1179.245	.002	.616	.538	-1585.083	3037.575	.886	1.129

Diabetes with chronic complications	-3865.164	3051.444	-.004	-1.267	.205	-9846.018	2115.689	.959	1.043
Drug abuse	10121.430	3436.756	.010	2.945	.003	3385.363	16857.498	.926	1.080
Hypertension	-4239.893	972.263	-.015	-4.361	.071	-6145.536	-2334.251	.819	1.220
Hypothyroidism	2841.320	713.642	.014	3.981	.000	1442.575	4240.064	.870	1.149
Liver disease	1263.637	2507.324	.002	.504	.614	-3650.738	6178.011	.979	1.022
Lymphoma	-2804.660	8408.194	-.001	-.334	.739	-19284.78	13675.463	.996	1.004
Fluid and electrolyte disorders	16488.703	721.623	.076	22.849	.000	15074.316	17903.089	.916	1.091
Metastatic cancer	-12122.14	5463.381	-.007	-2.219	.087	-22830.41	-1413.871	.996	1.004
Other neurological disorders	4516.825	925.515	.017	4.880	.000	2702.809	6330.842	.889	1.125
Obesity	-438.854	1184.507	-.001	-.370	.711	-2760.496	1882.788	.923	1.084
Paralysis	5089.269	1886.830	.009	2.697	.007	1391.067	8787.470	.974	1.027
Peripheral vascular disorders	642.607	2895.987	.001	.222	.824	-5033.550	6318.763	.981	1.019
Psychoses	4674.987	1949.031	.008	2.399	.016	854.872	8495.102	.977	1.023
Pulmonary circulation disorders	12673.123	1509.996	.027	8.393	.000	9713.520	15632.726	.967	1.034
Renal failure	-4387.479	1541.433	-.010	-2.846	.054	-7408.699	-1366.258	.897	1.114
Solid tumor without metastasis	-6163.248	5055.361	-.004	-1.219	.223	-16071.79	3745.297	.993	1.007
Peptic ulcer	7636.969	19434.327	.001	.393	.694	-30454.46	45728.396	.999	1.001
Valvular disease	-2299.394	1340.320	-.006	-1.716	.086	-4926.432	327.643	.973	1.028
Weight loss	6017.204	1577.357	.013	3.815	.000	2925.572	9108.836	.938	1.067

* Multiple linear regression: R = 0.673 (adjust R^2 = .452), df (47), p <0.001. Reference: White, male, age ≤30 years, Medicare, 0-25th percentile income and no comorbidities.

b) Down's syndrome and aging diseases (Hypotheses 9 and 10)

Multiple linear regression (dummy method) is used to find out the predictors of total charges for Down's syndrome patients with aging diseases. Assumptions must be proceeded to approve the results of the regression model. These assumptions are as follows:

Assumption 1, dependent variables should be continuous: Total charge is continuous. This assumption is accepted.

Assumption 2, two or more independent variables (numerical, ordinal, or categorical): Comorbidities, age categories, gender, race, type of insurance and household income are categorical, while number of procedures and number of chronic diseases are numerical. All groups were recategorized to be appropriate for the dummy method of analysis. This assumption is accepted.

Assumption 3, independence of observations or independence of residuals: The value of Durbin-Watson for total charges should range between 1 and 3, or near to 2 as an ideal result. The value of Durbin-Watson for total charges is 1.929 and 1.984 for Down's syndrome with Parkinson's and Alzheimer's diseases respectively. This assumption is accepted.

Assumption 4, linear relationship between the dependent and independent variable(s): Significant relationships between dependent and independent variables. This assumption is accepted.

Assumption 5, data must show homoscedasticity: Results showed that the dots along the scatter plot are homogeneous and with the same distance around the linear fit line, as shown in the Figures below. This assumption is accepted.

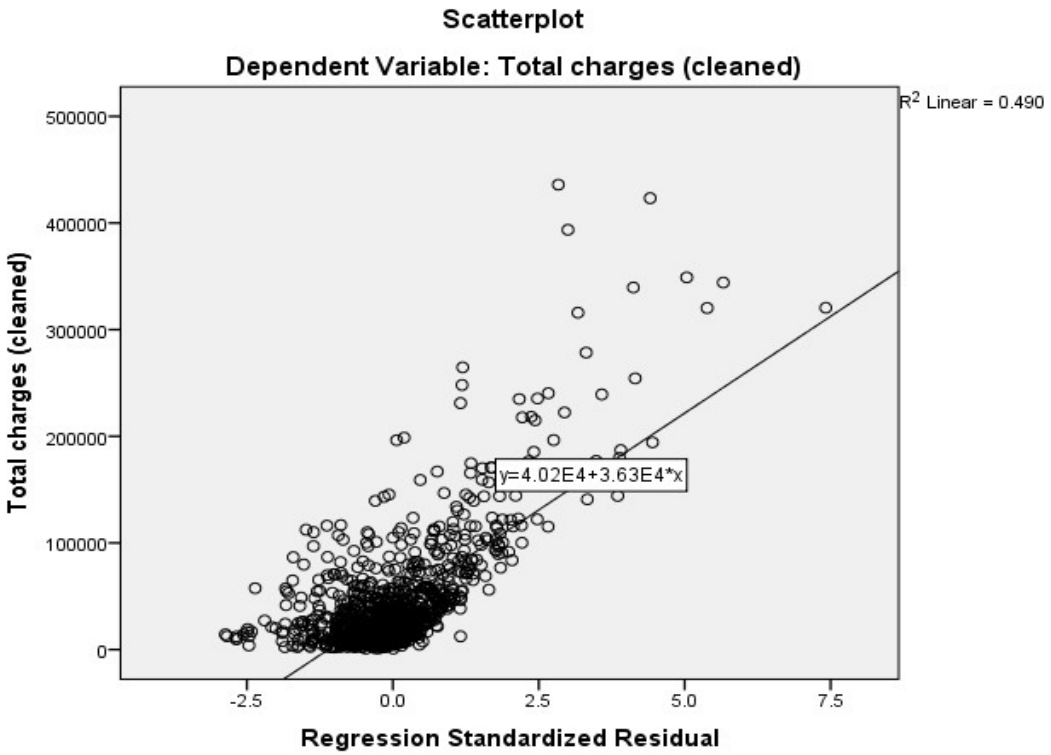


Figure 30 Homoscedasticity of total charges for Down's syndrome patients with Parkinson's disease

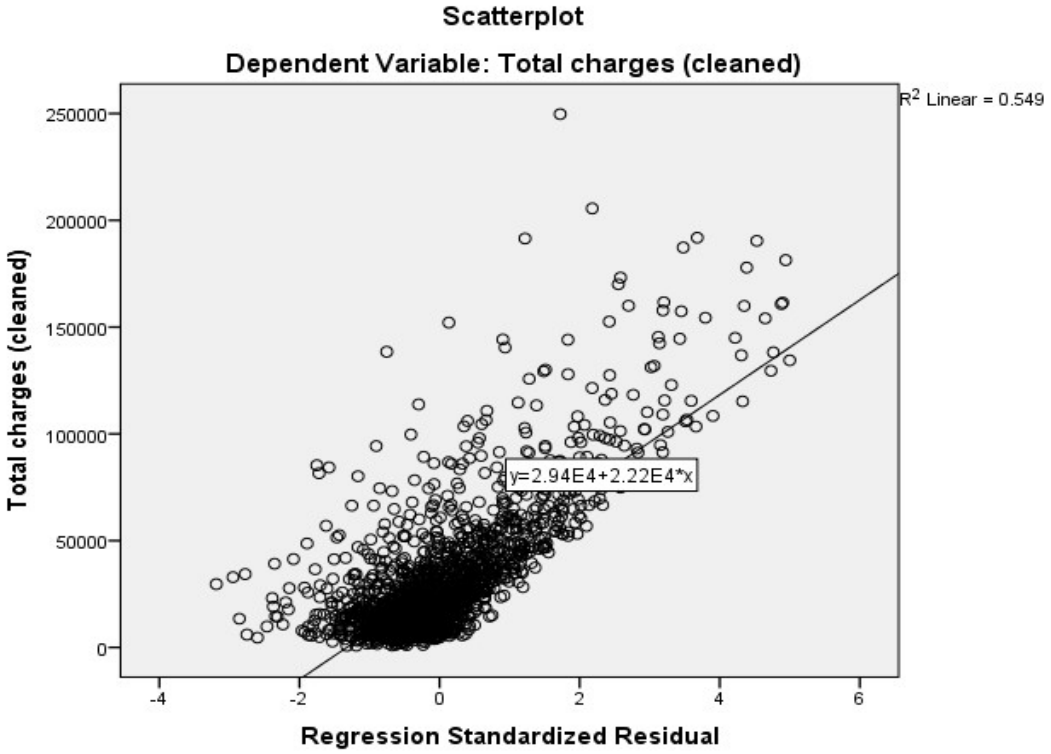


Figure 31 Homoscedasticity of total charges for Down's syndrome patients with Alzheimer's disease

Assumption 6, data must not show multicollinearity: Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as an ideal result. All results of the variables are less than 2. This assumption is accepted.

Assumption 7, no significant outliers: The cut point for the outliers while using Cook's distance is (4/n), which is equal to 0.003 and 0.002 for Parkinson's and Alzheimer's diseases respectively. There were 52 and 87 cases considered as outliers for Parkinson's and Alzheimer's diseases respectively. These cases were excluded in the regression model.

Assumption 8, the residuals must be normally distributed: The residuals are normally distributed, as shown in the figures above.

After accepting all assumptions for the total charges, the final models for the predictors of Down's syndrome patients with aging diseases are shown in Table 19.

Drug abuse is the predictor with the highest effect on total charges for Down's syndrome patients with Parkinson's disease with $34642.4, followed by Hispanic ($18932.98), number of procedures ($16229.73) and congestive heart failure ($13257.58). The Self-pay type of insurance showed the highest factor that reduced the total charges by $36128.6, followed by age 61-70 years ($-10796.6), as shown in Table 19.

The total charges of Down's syndrome with Parkinson's disease = 3234.539 + 7953.733 (Female) + 18932.98 (Hispanic) -10796.6 (Age 61-70) -36128.6 (Self-pay) + 7571.929 (Income 51st-75th percentile) +16229.73 (Number of procedures) + 13257.58 (Congestive heart failure) + 34642.4 (Drug abuse) + 5858.223 (Hypothyroidism) + 5969.67 (Fluid and electrolyte disorders) + 6921.995 (Other neurological disorders)

The number of procedures is the predictor with the highest effect on total charges for Down's syndrome patients with Alzheimer's disease by $10967.731, followed by

Hispanic ($10519.362), depression ($9951.371), fluid and electrolyte disorders ($5212.43),rheumatoid arthritis ($4923.043), income 75th-100th percentile ($ 4821.46), age 41-50 ($4778.165), age 51-60 ($4528.137), hypertension ($3799.883), other races ($3606.978), number of chronic conditions ($1048.655). Private insurance, including the type of HMO, showed the highest factor related to the total charges for Down's syndrome patients with Alzheimer's disease by $12873.779.

The total charges of Down's syndrome with Alzheimer's disease = 2205.289 + 3606.978 (Other races) + 10519.362 (Hispanic) + 4778.165 (Age 41-50) + 4528.137 (Ages 51-60) - 12873.779 (Private including HMO) + 4821.46 (Income 75th-100th percentile) + 1048.655 (Number of chronic conditions) + 10967.731 (Number of procedures) + 4923.043 (Rheumatoid arthritis) + 9951.371 (Depression) + 3799.883 (Hypertension) + 5212.43 (Fluid and electrolyte disorders).

In a comparison between the predictors of total charges for Down's syndrome patients with Parkinson's and Alzheimer's diseases, the areas of drug abuse and number of procedures were found to be the main risk factors. There were a greater number of risk factors for Down's syndrome patients with Alzheimer's disease when compared to those with Parkinson's disease. But there were higher total charges induced by the factors of Parkinson's disease than of Alzheimer's disease.

The risk factor interaction showed the highest impact in the area of total charges of Down's syndrome with aging diseases (Hypothesis 10). The number of procedures * Drug abuse and Hispanic* No procedures showed the highest total charges for Down's syndrome patients with Parkinson's and Alzheimer's diseases by $23509.810 and $16147.351 respectively, as shown in Table 20.

Table 19 Predictors of Hospital Total Charges of Down's Syndrome Patients with Aging Diseases

Predictors	Parkinson's disease*									Alzheimer's disease†								
	B	SE	Beta	t	*Sig.	95% CI		Tolerance	VIF	B	SE	Beta	t	†Sig.	95% CI		Tolerance	VIF
						Lower Bound	Upper Bound								Lower Bound	Upper Bound		
(Constant)	3234.539	3790.547		0.853	0.394	-4203.1	10672.2			2205.289	2638.531		0.836	0.403	-2969.5	7380.1		
Female	**7953.733**	**2225.547**	**0.078**	**3.574**	**0.000**	**3586.9**	**12320.6**	**0.96**	**1.042**	1480.012	1046.111	0.025	1.415	0.157	-571.7	3531.7	0.951	1.051
Other races	1076.933	3005.481	0.01	0.358	0.72	-4820.3	6974.2	0.548	1.825	**3606.978**	**1529.286**	**0.051**	**2.359**	**0.018**	**607.7**	**6606.3**	**0.627**	**1.594**
Black	6224.85	4792.421	0.033	1.299	0.194	-3178.6	15628.3	0.715	1.399	-125.267	2809.097	-0.001	-0.045	0.964	-5634.6	5384.1	0.715	1.399
Hispanic	**18932.984**	**8061.061**	**0.118**	**4.446**	**0.000**	**10578.0**	**27288.0**	**0.641**	**1.561**	**10519.362**	**3091.025**	**0.066**	**3.403**	**0.001**	**4457.1**	**16581.6**	**0.799**	**1.251**
Asian Pacific Islander	-1144.85	10676.08	-0.002	-0.107	0.915	-22093.0	19803.3	0.9	1.111	3604.527	6283.732	0.01	0.574	0.566	-8719.4	15928.5	0.9	1.112
Native American	6057.391	16603.79	0.008	0.365	0.715	-26521.8	38636.6	0.96	1.041	-11383.811	10078.95	-0.02	-1.129	0.259	-31151.1	8383.5	0.974	1.026
Ages 31-40	-2359.7	5941.181	-0.009	-0.397	0.691	-14017.2	9297.8	0.883	1.132	7055.843	5261.289	0.024	1.341	0.18	-3262.8	17374.5	0.948	1.055
Ages 41-50	1399.25	3711.284	0.009	0.377	0.706	-5882.9	8681.4	0.74	1.352	**4778.165**	**1633.666**	**0.06**	**2.925**	**0.003**	**1574.1**	**7982.2**	**0.708**	**1.413**
Ages 51-60	-2614.53	3314.534	-0.022	-0.789	0.43	-9118.2	3889.1	0.595	1.681	**4528.137**	**1210.303**	**0.076**	**3.741**	**0.000**	**2154.4**	**6901.8**	**0.713**	**1.403**
Ages 61-70	**-10796.6**	**4356.703**	**-0.063**	**-2.478**	**0.013**	**-19345.1**	**-2248.1**	**0.705**	**1.418**									
Other insurance	18936.23	36446.31	0.011	0.52	0.603	-52577.1	90449.5	0.993	1.007									
Medicaid	-14334.4	9065.263	-0.034	-1.581	0.114	-32121.9	3453.0	0.958	1.044	-5729.741	4384.126	-0.023	-1.307	0.191	-14328.1	2868.6	0.965	1.036
Private including HMO	-8937.14	10770.81	-0.018	-0.83	0.407	-30071.1	12196.8	0.957	1.045	**-12873.779**	**2145.858**	**-0.106**	**-5.999**	**0.000**	**-17082.3**	**-8665.2**	**0.954**	**1.049**
Self-pay	**-36128.6**	**11146.92**	**-0.07**	**-3.241**	**0.001**	**-58000.6**	**-14256.6**	**0.974**	**1.027**	-15809.111	9178.061	-0.03	-1.722	0.085	-33809.5	2191.3	0.98	1.021
No charge	-2216.572	6175.71	-0.002	-0.085	0.933	-53577.4	49144.2	0.964	1.038									
Income 26th-50th percentile	2104.299	3040.045	0.018	0.692	0.489	-3860.7	8069.3	0.686	1.459	131.424	1500.864	0.002	0.088	0.93	-2812.1	3075.0	0.627	1.595
Income 51st-75th percentile	**7571.929**	**3069.354**	**0.063**	**2.467**	**0.014**	**1549.4**	**13594.5**	**0.69**	**1.45**	1882.911	1501.889	0.028	1.254	0.21	-1062.7	4828.5	0.614	1.63
Income 75th-100th percentile	5432.614	3116.481	0.045	1.743	0.082	-682.4	11547.6	0.68	1.471	**4821.46**	**1480.754**	**0.072**	**3.256**	**0.001**	**1917.3**	**7725.6**	**0.604**	**1.657**
Number of chronic conditions										**1048.655**	**286.265**	**0.085**	**3.663**	**0.000**	**487.2**	**1610.1**	**0.556**	**1.799**
Number of procedures	**16229.73**	**545.229**	**0.671**	**29.767**	**0.000**	**15159.9**	**17299.6**	**0.888**	**1.126**	**10967.731**	**341.471**	**0.581**	**32.119**	**0.000**	**10298.0**	**11637.4**	**0.905**	**1.105**
Alcohol abuse	-30341.92	1779.82	-0.031	-1.393	0.164	-73077.3	12393.5	0.929	1.077									
Deficiency anemias	5232.623	3680.42	0.032	1.422	0.155	-1988.9	12454.2	0.882	1.134	9157.889	15817.026	0.01	0.579	0.563	-21863.2	40178.9	0.988	1.013
Rheumatoid arthritis	24701.71	13136.86	0.041	1.880	0.06	-1074.8	50478.3	0.961	1.04	**4923.043**	**1480.37**	**0.06**	**3.326**	**0.001**	**2019.7**	**7826.4**	**0.909**	**1.100**

Chronic blood loss anemia	-10656.12	1303.61	-0.011	-0.500	0.617	-52457.1	31144.9	0.971	1.03	-5364.818	4429.281	-0.021	-1.211	0.226	-14051.7	3322.1	0.945	1.058
Congestive heart failure	**13257.58**	**5298.508**	**0.055**	**2.502**	**0.012**	**2861.1**	**23654.1**	**0.946**	**1.057**	-6358.831	11204.044	-0.01	-0.568	0.57	-28332.7	15615.0	0.985	1.015
Chronic pulmonary disease	3616.183	3970.455	0.02	0.911	0.363	-4174.5	11406.8	0.926	1.08	2154.531	2124.3	0.018	1.014	0.311	-2011.7	6320.8	0.916	1.091
Coagulopathy	9066.716	5853.371	0.034	1.549	0.122	-2418.5	20551.9	0.951	1.051	872.829	1909.819	0.008	0.457	0.648	-2872.8	4618.5	0.913	1.095
Depression	-5114.6	4108.498	-0.028	-1.245	0.213	-13176.1	2946.9	0.906	1.104	**9951.371**	**2844.509**	**0.062**	**3.498**	**0.000**	**4372.6**	**15530.1**	**0.944**	**1.059**
DM, uncomplicated	-151.277	4747.762	-0.001	-0.032	0.975	-9467.1	9164.6	0.856	1.168	-1855.904	1672.485	-0.02	-1.11	0.267	-5136.1	1424.2	0.929	1.076
DM with chronic complications	7190.518	11554.27	0.014	0.622	0.534	-15480.8	29861.8	0.906	1.103	-1267.845	2282.16	-0.01	-0.556	0.579	-5743.7	3208.0	0.907	1.103
Drug abuse	**34642.4**	**15088.05**	**0.05**	**2.296**	**0.022**	**5037.3**	**64247.5**	**0.97**	**1.031**									
Hypertension	1494.59	3286.735	0.011	0.455	0.649	-4954.5	7943.7	0.814	1.229	**3799.883**	**1640.259**	**0.042**	**2.317**	**0.021**	**582.9**	**7016.8**	**0.881**	**1.134**
Hypothyroidism	**5858.223**	**2610.361**	**0.053**	**2.244**	**0.025**	**736.3**	**10980.2**	**0.82**	**1.22**	-1693.235	1125.292	-0.029	-1.505	0.133	-3900.2	513.7	0.822	1.217
Liver disease	-2758.71	10841.34	-0.006	-0.254	0.799	-24031.1	18513.7	0.945	1.059	-3248.453	4948.265	-0.011	-0.656	0.512	-12953.2	6456.3	0.971	1.03
Fluid and electrolyte disorders	**5969.67**	**2869.501**	**0.048**	**2.08**	**0.038**	**339.3**	**11600.1**	**0.832**	**1.202**	**5212.43**	**1142.797**	**0.082**	**4.561**	**0.000**	**2971.1**	**7453.7**	**0.92**	**1.087**
Metastatic cancer										-20606.735	15788.416	-0.023	-1.305	0.192	-51571.7	10358.2	0.991	1.009
Other neurological disorders	**6921.995**	**2732.255**	**0.061**	**2.533**	**0.011**	**1560.9**	**12283.1**	**0.779**	**1.284**	858.079	1263.905	0.012	0.679	0.497	-1620.7	3336.9	0.904	1.106
Obesity	6501.185	4742.732	0.031	1.371	0.171	-2804.8	15807.2	0.869	1.15	977.509	2399.885	0.007	0.407	0.684	-3729.3	5684.3	0.922	1.084
Paralysis	3045.426	6072.199	0.011	0.502	0.616	-8869.2	14960.0	0.927	1.079	-1434.248	3547.584	-0.007	-0.404	0.686	-8391.9	5523.4	0.955	1.047
Peripheral vascular disease	-4300.89	8646.216	-0.011	-0.497	0.619	-21266.1	12664.3	0.897	1.114	-4662.752	3561.998	-0.023	-1.309	0.191	-11648.7	2323.2	0.926	1.08
Psychoses	-3371.03	5575.532	-0.014	-0.605	0.546	-14311.1	7569.0	0.905	1.106	-3359.56	2427.688	-0.025	-1.384	0.167	-8120.8	1401.7	0.937	1.067
Pulmonary circulation disorders	-3929.68	5487.515	-0.016	-0.716	0.474	-14697.0	6837.7	0.952	1.05	3626.629	3095.369	0.021	1.172	0.241	-2444.1	9697.4	0.948	1.055
Renal failure	-9371.28	5884.068	-0.036	-1.593	0.112	-20916.7	2174.2	0.881	1.135	49.313	2436.469	-0.043	0.02	0.984	-4729.2	4827.8	0.931	1.074
Solid tumor without metastasis	2232.801	36545.04	0.001	0.061	0.951	-69474.2	73939.8	0.988	1.012	4945.011	12980.407	0.007	0.381	0.703	-20512.7	30402.8	0.978	1.022
Valvular disease	-87.719	4666.264	0.001	-0.019	0.985	-9243.7	9068.2	0.947	1.056	-4636.735	1955.978	-0.043	-2.371	0.098	-8472.9	-800.6	0.917	1.09
Weight loss	3398.696	5657.444	0.013	0.601	0.548	-7702.1	14499.5	0.896	1.116	3486.017	1960.711	0.032	1.778	0.076	-359.4	7331.4	0.918	1.089

* Multiple linear regression: R = 0.714 (adjust R^2 = .490), df (44), p <0.001. Reference: White, male, age ≥70 years, Medicare, 0-25th percentile income and no comorbidities.

† Multiple linear regression: R = 0.671 (adjust R^2 = .438), df (42), p <0.001. Reference: White, male, age ≥70 years, Medicare, 0-25th percentile income and no comorbidities.

Table 20 Risk Factor Interactions of Total Charges of Down's Syndrome Patients with Aging Diseases

Risk factor interactions	B	SE	Beta	t	Sig.	95% CI	
						Lower Bound	Upper Bound
Parkinson's disease							
(Constant)	31221.296	2695.098		11.584	.000	25933.4	36509.2
Female* Hispanic	-17152.957	11020.518	-.042	-1.556	.120	-38775.6	4469.7
Female*Income51st-75th	1563.685	8471.196	.005	.185	.854	-15057.1	18184.4
Female* No. procedures	**15959.422**	**1435.920**	**.327**	**11.114**	**.000**	**13142.1**	**18776.7**
Female*CHF	-20382.850	18757.888	-.034	-1.087	.277	-57186.4	16420.7
Female* Drug abuse	-102070.454	72142.656	-.056	-1.415	.157	-243616.7	39475.8
Female*Hypothyroidism	-10701.939	7897.822	-.040	-1.355	.176	-26197.7	4793.8
Female*Electrolyte and fluid disorders	-13786.496	9366.206	-.044	-1.472	.141	-32163.3	4590.3
Female* other neurological disorders	-3235.196	8792.106	-.011	-.368	.713	-20485.6	14015.2
Hispanic* Income51st to 75th	6561.963	13688.515	.013	.479	.632	-20295.3	33419.3
Hispanic* No. procedures	**18492.693**	**2708.039**	**.210**	**6.829**	**.000**	**13179.4**	**23806.0**
Hispanic* CHF	39710.190	30921.135	.035	1.284	.199	-20958.1	100378.5
Hispanic* Drug abuse	-48309.312	89606.164	-.015	-.539	.590	-224119.5	127500.9
Hispanic*Hypothyroidism	-21069.430	23210.742	-.027	-.908	.364	-66609.7	24470.8
Hispanic* Electrolyte and fluid disorders	26960.410	20927.091	.039	1.288	.198	-14099.2	68020.0
Hispanic* other neurological disorders	-7752.734	20260.161	-.010	-.383	.702	-47503.8	31998.4
Income51st to 75th* No. procedures	**7387.564**	**1893.833**	**.119**	**3.901**	**.000**	**3671.8**	**11103.3**
Income51st to 75th *CHF	-217.279	22362.554	.000	-.010	.992	-44093.3	43658.8
Income51st to 75th* Drug abuse	45667.127	56358.234	.032	.810	.418	-64909.6	156243.8
Income51st to 75th* Hypothyroidism	-12065.891	10831.531	-.033	-1.114	.266	-33317.7	9185.9
Income51st to 75th*Electrolyte and fluid disorders	3570.183	12970.982	.008	.275	.783	-21879.3	29019.7
Income51st to 75th * other neurological disorders	-14330.867	12071.810	-.035	-1.187	.235	-38016.2	9354.4
No. procedures*CHF	**8585.309**	**4164.355**	**.059**	**2.062**	**.039**	**414.7**	**16755.9**
No. procedures * Drug abuse	**23509.810**	**8039.931**	**.104**	**2.924**	**.004**	**7735.2**	**39284.4**
No. procedures* Hypothyroidism	**12154.181**	**2231.867**	**.154**	**5.446**	**.000**	**7775.2**	**16533.2**
No. procedures* Electrolyte and fluid disorders	**4834.154**	**1794.086**	**.088**	**2.694**	**.007**	**1314.1**	**8354.2**
No. procedures* other neurological disorders	841.984	2212.397	.011	.381	.704	-3498.8	5182.8
CHF* other neurological disorders	4250.470	20105.409	.006	.211	.833	-35197.0	43697.9
Drug abuse * Hypothyroidism	-8793.436	44518.136	-.006	-.198	.843	-96139.5	78552.6
Drug abuse * Electrolyte and fluid disorders	-34094.053	73545.104	-.015	-.464	.643	-178391.9	110203.8
Drug abuse * other neurological disorders	19288.679	76229.479	.011	.253	.800	-130276.0	168853.4
Hypothyroidism* Electrolyte and fluid disorders	5916.389	9586.594	.018	.617	.537	-12892.8	24725.6
Hypothyroidism * other neurological disorders	-6539.422	8167.067	-.024	-.801	.423	-22563.5	9484.6
Alzheimer's disease							
(Constant)	19443.507	1798.592		10.810	.000	15916.1	22970.9
Other races* Age 41to50	-5076.057	4448.148	-.036	-1.141	.254	-13799.7	3647.6
Other races* Age 51to60	-3189.218	3235.650	-.034	-.986	.324	-9534.9	3156.5
Other races*Income 76th-100th	3555.251	4396.621	.032	.809	.419	-5067.3	12177.8

Other races*No chronic condit.	-32.166	394.561	-.002	-.082	.935	-806.0	741.6
Other races* No procedures	**4350.301**	**1001.434**	**.157**	**4.344**	**.000**	**2386.3**	**6314.3**
Other races* Arthritis	22564.458	18410.858	.051	1.226	.220	-13542.7	58671.6
Other races*Depress	887.492	5814.328	.005	.153	.879	-10515.5	12290.5
Other races*HT	1552.309	5603.596	.010	.277	.782	-9437.4	12542.0
Other races* Fluid/Elect disorder	-115.309	4002.631	-.001	-.029	.977	-7965.2	7734.6
Hispanic* Age 41-50	-2961.124	17592.186	-.003	-.168	.866	-37462.7	31540.4
Hispanic* Age 51-60	-2354.776	8984.944	-.007	-.262	.793	-19975.9	15266.4
Hispanic*76th-100th	10783.732	9649.279	.027	1.118	.264	-8140.3	29707.8
Hispanic* No. chronic condit.	1035.849	1185.124	.029	.874	.382	-1288.4	3360.1
Hispanic* No procedures	**16147.351**	**2922.619**	**.131**	**5.525**	**.000**	**10415.5**	**21879.2**
Hispanic*Depress	-16258.329	16628.170	-.019	-.978	.328	-48869.3	16352.6
Hispanic*HT	1627.632	12167.368	.003	.134	.894	-22234.9	25490.1
Hispanic* Fluid/Elect disorder	-22251.402	10410.730	-.050	-2.137	.033	-42668.8	-1834.0
Ages 41-50* Income 76th-100th	4832.493	5573.285	.021	.867	.386	-6097.8	15762.7
Ages 41-50* No chronic condit.	135.890	655.002	.007	.207	.836	-1148.7	1420.5
Ages 41-50* No procedures	**5601.309**	**1385.760**	**.104**	**4.042**	**.000**	**2883.6**	**8319.0**
Ages 41-50* Arthritis	-15964.079	41700.176	-.008	-.383	.702	-97745.9	65817.8
Ages 41-50*Depress	8337.434	7809.849	.026	1.068	.286	-6979.1	23654.0
Ages 41-50*HT	-7456.695	8591.094	-.018	-.868	.386	-24305.4	9392.0
Ages 41-50* Fluid/Elect disorder	-3001.243	5521.679	-.012	-.544	.587	-13830.3	7827.8
Ages 51-60* Income 76th_100th	-1269.171	4049.724	-.010	-.313	.754	-9211.4	6673.1
Ages 51-60* No chronic condit.	658.870	458.899	.051	1.436	.151	-241.1	1558.9
Ages 51-60* No procedures	**3989.616**	**1033.116**	**.121**	**3.862**	**.000**	**1963.5**	**6015.8**
Ages 51-60* Arthritis	15236.061	17941.424	.019	.849	.396	-19950.4	50422.5
Ages 51-60*Depress	4017.634	5907.300	.019	.680	.497	-7567.7	15603.0
Ages 51-60*HT	-2461.301	5190.262	-.012	-.474	.635	-12640.4	7717.8
Ages 51-60* Fluid/Elect disorder	-5040.789	3592.717	-.041	-1.403	.161	-12086.8	2005.2
Income 76th-100th* No chronic condit.	-782.464	624.023	-.053	-1.254	.210	-2006.3	441.4
Income 76th-100th*No procedures	**3762.988**	**983.827**	**.097**	**3.825**	**.000**	**1833.5**	**5692.5**
Income 76th-100th* Arthritis	5090.584	20647.143	.006	.247	.805	-35402.3	45583.5
Income 76th-100th*Depress	92.739	6306.020	.000	.015	.988	-12274.5	12460.0
Income 76th-100th*HT	6973.829	5941.728	.027	1.174	.241	-4679.0	18626.7
Income 76th-100th* Fluid/Elect disorder	-1718.695	4120.513	-.010	-.417	.677	-9799.8	6362.4
No chronic condit*No procedures	**468.091**	**127.395**	**.155**	**3.674**	**.000**	**218.2**	**717.9**
No chronic condit* Arthritis	-1997.095	2495.188	-.043	-.800	.424	-6890.6	2896.4
No chronic condit. *Depress	-268.254	750.286	-.014	-.358	.721	-1739.7	1203.2
No chronic condit. *HT	-608.359	664.356	-.037	-.916	.360	-1911.3	694.6
No chronic condit. * Fluid/Elect disorder	**1434.876**	**552.965**	**.107**	**2.595**	**.010**	**350.4**	**2519.3**
No procedures*Arthritis	-3306.540	6907.903	-.012	-.479	.632	-16854.2	10241.2
No procedures *Depress	**-7492.742**	**1818.326**	**-.089**	**-4.121**	**.000**	**-11058.8**	**-3926.7**
No procedures *HT	**4975.105**	**1466.666**	**.084**	**3.392**	**.001**	**2098.7**	**7851.5**
No procedures * Fluid/Elect disorder	**4142.453**	**980.395**	**.123**	**4.225**	**.000**	**2219.7**	**6065.2**
Arthritis*Depress	-8818.769	24068.174	-.009	-.366	.714	-56021.0	38383.4
Arthritis *HT	8816.141	19273.406	.011	.457	.647	-28982.6	46614.9
Arthritis * Fluid/Elect disorder	-11610.133	16187.070	-.018	-.717	.473	-43356.0	20135.7
Depress*HT	4437.659	8659.896	.011	.512	.608	-12546.0	21421.3
Depress* Fluid/Elect disorder	-1285.782	5884.343	-.005	-.219	.827	-12826.1	10254.5
HT* Fluid/Elect disorder	-7807.242	5638.979	-.034	-1.385	.166	-18866.3	3251.9

4.6.3 Predictors for mortality of Down's syndrome patients with and without aging diseases

a) Down's syndrome only (Hypothesis 11)

Multinomial logistic regression is the appropriate statistical test used to determine the predictors of mortality for Down's syndrome patients. Six assumptions were tested to approve the results of the logistic regression model.

Assumption 1: The dependent variable must be nominal. The mortality is nominal. This assumption is accepted.

Assumption 2: The independent variables are continuous, ordinal or nominal; Comorbidities, age categories, gender, race, type of insurance and household income are categorical, while the number of procedures and number of chronic diseases are numerical. This assumption is accepted.

Assumption 3: Independence of observation. All subjects of dependent variables were different. This assumption is accepted.

Assumption 4: Ten patients were considered as outliers for predicting the mortality of Down's syndrome patients and those were excluded in the model. This assumption is accepted.

The number of procedures showed the highest incidence of mortality for Down's syndrome patients (χ^2 = 60.852, df (1), p value < 0.001), followed by fluid and electrolyte disorders (χ^2= 24.952, df (1), p value < 0.001), age categories (χ^2= 21.626, df (6), p value = 0.001), pulmonary circulation disorders (χ^2= 5.040, df (1), p value = 0.025), and diabetes mellitus (uncomplicated) (χ^2= 4.963, df (1), p value = 0.026).

Age is considered as a significant predictor for mortality of Down's syndrome patients, where those aged older than 71 years showed the highest increment in the incidence of mortality by 450.9% (OR = 5.509), followed by patients aged 61-70 years (410.7%, OR = 5.107), patients aged 51-60 years (252.1%, OR= 3.521), patients aged 41-50 years

(133.1%, OR = 2.331), and patients aged 31-40 years (218.9%, OR = 3.189) than those aged equal and younger than 30 years. The number of procedures increased the incidence of mortality for Down's syndrome patients by 23.5% (OR = 1.235). Private (HMO) patients got a higher incidence of mortality than Medicare by 127.8% (OR = 2.278). Patients with fluid/electrolyte disorders and pulmonary circulation disorders had a higher incidence of mortality by 204.2% (OR=3.042) and 159.4% (OR = 2.594) than those without, respectively. See Table 21 below.

Table 21 Predictors of mortality for Down's syndrome patients

Predictors		B	SE	Wald	Df	Sig.	Exp(B)	95% CI for Exp(B)	
								Lower	Upper
Intercept		-5.646	.545	107.269	1	.000			
No. of chronic dis.		.020	.060	.114	1	.736	1.020	.907	1.148
No. of procedures		**.211**	**.027**	**62.527**	**1**	**.000**	**1.235**	**1.172**	**1.301**
Gender	Male	-.165	.218	.567	1	.451	.848	.553	1.302
	Female (ref.)	0	.	.	0	.	.	.	.
Age (years)	**31-40**	**1.160**	**.464**	**6.256**	**1**	**.012**	**3.189**	**1.285**	**7.911**
	41-50	**.846**	**.386**	**4.799**	**1**	**.028**	**2.331**	**1.093**	**4.972**
	51-60	**1.259**	**.356**	**12.517**	**1**	**.000**	**3.521**	**1.753**	**7.070**
	61-70	**1.631**	**.424**	**14.788**	**1**	**.000**	**5.107**	**2.225**	**11.726**
	71-80	**1.706**	**.723**	**5.566**	**1**	**.018**	**5.509**	**1.335**	**22.733**
	≤30(ref.)	0	.	.	0	.	.	.	.
Race	Others	-.621	.764	.662	1	.416	.537	.120	2.400
	Black	-.067	.369	.033	1	.856	.935	.454	1.927
	Hispanic	.315	.448	.494	1	.482	1.370	.569	3.297
	Asian/Pacific Islander	-.236	1.090	.047	1	.829	.790	.093	6.689
	Native American	.091	.827	.012	1	.912	1.095	.217	5.541
	White (ref.)	0	.	.	0	.	.	.	.
Household income	Income 0-25th	.064	.345	.034	1	.853	1.066	.543	2.094
	Income 26th-50th	.040	.351	.013	1	.908	1.041	.523	2.071
	Income 51st-75th	-.069	.385	.032	1	.858	.933	.438	1.986
	Income75th-100th (Ref,)	0	.	.	0	.	.	.	.
Type of insurance	Others	-.378	.928	.166	1	.684	.685	.111	4.224
	Medicaid	.291	.307	.898	1	.343	1.337	.733	2.440
	Private (HMO)	**.824**	**.312**	**6.971**	**1**	**.008**	**2.278**	**1.236**	**4.199**
	Self-pay	-.053	.427	.015	1	.901	.948	.411	2.188
	No charge	.737	.788	.874	1	.350	2.089	.446	9.783
	Medicare (ref.)	0	.	.	0	.	.	.	.
Deficiency anemias	Yes	.199	.284	.494	1	.482	1.221	.700	2.129
	No (ref.)	0	.	.	0	.	.	.	.
Arthritis	Yes	.715	.797	.804	1	.370	2.044	.429	9.744
	No (ref.)	0	.	.	0	.	.	.	.
CHF	Yes	.234	.351	.444	1	.505	1.263	.635	2.511

	No (ref.)	0	.	.	0	.	.	.	.
Chronic	Yes	-.733	.437	2.812	1	.094	.481	.204	1.132
pulmonary disease	No (ref.)	0	.	.	0	.	.	.	.
Coagulopathy	Yes	.304	.376	.652	1	.419	1.355	.648	2.832
	No (ref.)	0	.	.	0	.	.	.	.
Depression	Yes	-.611	.554	1.216	1	.270	.543	.183	1.608
	No (ref.)	0	.	.	0	.	.	.	.
DM uncomplicated	Yes	-1.114	.566	3.874	1	.050	.328	.108	.995
	No (ref.)	0	.	.	0	.	.	.	.
DM complicated	Yes	-.591	1.083	.298	1	.585	.554	.066	4.627
	No (ref.)	0	.	.	0	.	.	.	.
Drug abuse	Yes	-.084	1.202	.005	1	.944	.919	.087	9.698
	No (ref.)	0	.	.	0	.	.	.	.
Hypertension	Yes	-.607	.369	2.706	1	.100	.545	.264	1.123
	No (ref.)	0	.	.	0	.	.	.	.
Hypothyroidism	Yes	.245	.269	.826	1	.363	1.277	.753	2.166
	No (ref.)	0	.	.	0	.	.	.	.
Liver disease	Yes	-.702	1.078	.424	1	.515	.496	.060	4.097
	No (ref.)	0	.	.	0	.	.	.	.
Lymphoma	Yes	2.193	1.455	2.272	1	.132	8.964	.518	155.241
	No (ref.)	0	.	.	0	.	.	.	.
Fluid and	**Yes**	**1.112**	**.222**	**25.146**	**1**	**.000**	**3.042**	**1.969**	**4.699**
electrolyte disorder	**No (ref.)**	**0**	**.**	**.**	**0**	**.**	**.**	**.**	**.**
Metastasis	Yes	.193	1.464	.017	1	.895	1.213	.069	21.369
	No (ref.)	0	.	.	0	.	.	.	.
Other neurological	Yes	.439	.291	2.271	1	.132	1.551	.876	2.744
disorder	No (ref.)	0	.	.	0	.	.	.	.
Obesity	Yes	-.369	.520	.504	1	.478	.691	.249	1.917
	No (ref.)	0	.	.	0	.	.	.	.
Paralysis	Yes	.312	.532	.344	1	.557	1.366	.481	3.878
	No (ref.)	0	.	.	0	.	.	.	.
Peripheral vascular	Yes	.245	.829	.088	1	.767	1.278	.252	6.490
disorder	No (ref.)	0	.	.	0	.	.	.	.
Psychosis	Yes	.513	.575	.795	1	.373	1.670	.541	5.158
	No (ref.)	0	.	.	0	.	.	.	.
Pulmonary	**Yes**	**.953**	**.398**	**5.740**	**1**	**.017**	**2.594**	**1.189**	**5.658**
circulation disorder	**No (ref.)**	**0**	**.**	**.**	**0**	**.**	**.**	**.**	**.**
Renal failure	Yes	.552	.422	1.715	1	.190	1.737	.760	3.971
	No (ref.)	0	.	.	0	.	.	.	.
Valvular disease	Yes	-.457	.521	.770	1	.380	.633	.228	1.758
	No (ref.)	0	.	.	0	.	.	.	.
Weight loss	Yes	.601	.344	3.045	1	.081	1.823	.929	3.580
	No (ref.)	0	.	.	0	.	.	.	.

Multinomial logistic regression. Model of fitting: $\chi^2 = 196.994$, df(45) $p < 0.001$. The reference category is: did not die during hospitalization

b) Down's syndrome and aging diseases (Hypotheses 12)

The filtering method of variables was implemented to determine the factors that are involved in the final model of logistic regression. This is due to the small number of mortality incidences in relation to both aging diseases and the number of variables. The chi-square test was used to determine the significance of the variables with mortality for each aging disease.

Table 22 Chi-square of variables that influence the mortality of Down's syndrome with aging diseases

Variables	X^2	*df*	*p value*
Parkinson's disease			
Age	12.683	6	0.048
Coagulopathy	4.970	1	0.026
DM complicated	5.517	1	0.019
Fluid and electrolyte disorders	16.115	1	<0.001
Neurological disorder	7.245	1	0.007
Pulmonary circulation disorders	13.367	1	0.011
Weight loss	12.724	1	0.012
Alzheimer's disease			
Age	4.560	6	0.033
Chronic pulmonary disorder	7.974	1	0.006
Hypothyroidism	4.454	1	0.021
Neurological disorders	22.881	1	<0.001
Pulmonary circulation disorders	6.605	1	0.017

Chi-square

Multinomial logistic regression is the appropriate statistical test used to determine the predictors of mortality for Down's syndrome patients with aging diseases. All assumptions of this test are approved.

The variables that showed a high incidence of mortality for Down's syndrome patients with Parkinson's disease are the number of procedures (χ^2 = 72.967, df (1), p value =0.010) and patients aged 51-60 years (χ^2= 70.913, df (1), p value = 0.031).

Chronic pulmonary disorders and the number of procedures is the only significant risk factors of mortality for Down's syndrome patients with Parkinson's disease, as shown in Table 22. The incidence of mortality observed was 636.9% (OR = 7.369) and 38.1% (OR = 1.381) for chronic pulmonary disorder and number of procedures, respectively.

The variables showed the highest incidence of mortality for Down's syndrome patients with Alzheimer's disease with number of procedures (χ^2 = 28.182, df (1), p value <0.001, followed by neurological disorders (χ^2 = 17.801, df (1), p value <0.001), and chronic pulmonary disorders (χ^2= 4.069, df (1), p value = 0.044).

The number of procedures increased the incidence of mortality for Down's syndrome patients with Alzheimer's disease by 24% (OR = 1.240). Chronic pulmonary disease, neurological disorders and pulmonary circulation disorders increased the mortality for Down's syndrome patients with Alzheimer's by 82.5% (OR = 1.825), 278.9% (OR = 3.789) and 138.5% (OR = 2.385) respectively, as shown in Table 23.

A comparison done on the incidence of mortality for Down's syndrome patients showed the risk factor with the highest incidence of mortality was observed with pulmonary circulation disorder and neurological disorders for Parkinson's and Alzheimer's diseases respectively. However, the mortality with the impact of severity of risk factors showed a higher incidence with Parkinson's disease than with Alzheimer's.

Table 23 Predictors of Mortality for Down's syndrome patients with aging diseases

Predictors			B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B) Lower Bound	95% CI for Exp(B) Upper Bound
Parkinson's disease*										
Intercept			-6.192	2.846	4.734	1	.030			
No. chronic conditions			.028	.138	.042	1	.838	1.029	.785	1.347
No. procedures			**.323**	**.118**	**7.413**	**1**	**.006**	**1.381**	**1.095**	**1.742**
Age (years)	51-60	No	-2.248	1.246	3.257	1	.071	.106	.009	1.214
		Yes	0	.	.	0	.	.	.	.
	61-70	No	-1.123	1.603	.490	1	.484	.325	.014	7.536
		Yes	0	.	.	0	.	.	.	.
	71-80	No	.494	1.769	.078	1	.780	1.639	.051	52.586
		Yes	0	.	.	0	.	.	.	.
Coagulation		Yes	1.333	.929	2.060	1	.151	3.791	.614	23.397
		No	0	.	.	0	.	.	.	.
DM complication		Yes	1.152	1.613	.510	1	.475	3.163	.134	74.630
		No	0	.	.	0	.	.	.	.
Fluid and electrolyte disorders		Yes	1.387	.898	2.384	1	.123	4.002	.688	23.273
		No	0	.	.	0	.	.	.	.
Neurological disorders		Yes	1.439	1.020	1.989	1	.158	4.214	.571	31.121
		No	0	.	.	0	.	.	.	.
Pulmonary circulation disorders		**Yes**	**1.997**	**.970**	**4.243**	**1**	**.039**	**7.369**	**1.102**	**49.297**
		No	**0**	**.**	**.**	**0**	**.**	**.**	.	.
Weight loss		Yes	.737	.880	.700	1	.403	2.089	.372	11.734
		No	0	.	.	0	.	.	.	.
Alzheimer's disease†										
Intercept			-2.909	.464	39.296	1	.000			
No. chronic conditions			-.148	.046	10.509	1	.051	.862	.788	.943
No. procedures			**.215**	**.038**	**31.941**	**1**	**.000**	**1.240**	**1.151**	**1.336**
Age (years)	61-70	No	-.310	.210	2.175	1	.140	.733	.486	1.107
		Yes	0	.	.	0	.	.	.	.
Chronic pulmonary diseases		**Yes**	**.602**	**.293**	**4.223**	**1**	**.040**	**1.825**	**1.028**	**3.239**
		No	0	.	.	0	.	.	.	.
Hypothyroidism		Yes	-.480	.207	5.387	1	.070	.619	.413	.928
		No	0	.	.	0	.	.	.	.
Neurological disorders		**Yes**	**1.332**	**.375**	**12.646**	**1**	**.000**	**3.789**	**1.818**	**7.896**
		No	**0**	**.**	**.**	**0**	**.**	**.**	**.**	**.**
Pulmonary circulation disorders		**Yes**	**.869**	**.398**	**4.774**	**1**	**.029**	**2.385**	**1.094**	**5.202**
		No	0	.	.	0	.	.	.	.

*Multinomial logistic regression. Model of fitting: χ^2 = 1520.348, df(11) p <0.001. The reference category is: did not die during hospitalization

†Multinomial logistic regression. Model of fitting: χ^2 = 556.860, df(7) p <0.001. The reference category is: did not die during hospitalization

CHAPTER V

DISCUSSION AND LIMITATIONS

5.1 Discussion

5.1.1 Introduction

This study is conducted to highlight the main outcomes related to patients with Down's syndrome admitted to hospitals in the United States between the years 2007-2012. The main objectives of this study were to point out the impact of the patients' sociodemographic characteristics, diseases and other medical conditions on their hospital total charges, length of hospital stay, and mortality induced by Down's syndrome. Moreover, this study revealed the relationships and negative coexistence of other aging diseases, Alzheimer's and Parkinson's diseases, on these patients' outcomes. This study is believed as the first among others, especially regarding the comparisons in the study outcomes, between the two aging diseases of Down's patients in United States. This study is considered as a significant novelty for science. Also, this chapter emphasized the need for the revision in the plans of therapy to reduce the cost and enhance the services. It minimized the incidence of mortality which in turn will enhance the patients' quality of life and the burden on the governmental services.

5.1.2 Patients' sociodemographic characteristics and medical information

The data was obtained with permission from the NIS database and involved 58438 patients who were diagnosed with Down's syndrome between the years 2007-2012. The highest incidence of patients admitted to the hospitals are those aged 30 years and younger (55.2%), White race (53.8%), Males (53.9%), Medicare insurance (36.7%) and in the 0-

25th household income (27.5%). Hypothyroidism is the comorbidity with the highest incidence by 23.5%, followed by fluid and electrolyte disorders (20.9%), other neurological disorders (14.2%), hypertension and chronic pulmonary diseases (11.3%, each), while the lowest incidences of comorbidities were observed in peptic ulcer (0.02%), followed by acquired immune deficiency syndrome (0.03%), lymphoma (0.1%), metastatic cancer and solid tumor without metastasis (0.3%, each).

5.1.3 Mortality rate

The incidence of mortality for patients with Down's syndrome was 2.9% of total patients, as shown in Figure 8. The different results were collected from previous studies which stated the incidence of mortality for patients with Down's syndrome. This incidence is lower than the incidence of mortality reported by Day et al. with 4.05%, which is the incidence of death for Down's syndrome in the state of California between the years 1988-1999 (Day et al., 2005). Also, the results of the present study showed a lower incidence than reported by Glasson et al. (12%) for Australian patients for the past 60 years. This study was focused on the mortality of the disease in children (Emma J. Glasson, Jacques, Wong, Bourke, & Leonard, 2016). Another study conducted by the Glasson group in Australia found the incidence of mortality ranged between 23%-40% (Bittles et al., 2007), based on the age group

The results of the present study is slightly higher due to the incidence of mortality reported by Hithersay et al (2.32%) for Down's syndrome patients in the United Kingdom (Hithersay et al., 2019). This differences in the incidence of mortality is dependent upon the type of study, age of patients, concurrent diseases and the variation of genetics.

5.1.4 Hospital Stay

The median length of hospital stay for patients with Down's syndrome was 4 days (Table 11). This result is like the findings reported by the American study done by Fitzgerald et al (3.8 days) and Stagliano et al (4 days). This statistic is slightly higher than the 3 days reported by Chenbhanich et al but it is lower than the Taiwanese study (22.26 days) of Hung et al and the Singaporean study (6 days) of Ting et al. (Chenbhanich et al., 2019; Fitzgerald, Leonard, Pikora, Bourke, & Hammond, 2013; Stagliano, Nylund, Eide, & Eberly, 2015; Ting, Chan, Wong, Testoni, & Lee, 2016). The difference in length of hospital stay was related to the quality of service, type of concurrent disease, age, country and genetics.

5.1.5 Total charges

The median total charges of inpatients with Down's syndrome in the present study was $20,823. This value was close to the total charges reported in the American study of Shoffstall et al. ($21,842) (Shoffstall et al., 2016), but lower than the results of the Australian study of Geelhoed et al $2,159. (Geelhoed, Bebbington, Bower, Deshpande, & Leonard, 2011). The total cost is much lower than another American study conducted by Derrington et al., ($40,075) because they involved the children at birth and post birth (Derrington et al., 2013), while the present study involved all ages.

5.1.6 Down's syndrome and aging diseases

The number of patients with Down's syndrome had a higher rate of hospital admissions with Alzheimer's than with Parkinson's disease. Figure 10 depicted the percentages of hospital admissions based on the years and type of aging disease. There is a higher percentage of patients with Down's syndrome and Alzheimer's disease than with Parkinson's disease (3.7%-4.4% vs. 1.4%-2.8%). Wiseman et al., discussed the genetic relationships between Down's syndrome and Alzheimer's disease. They found the incidence of Alzheimer's disease in patients with Down's syndrome was dependent on age; <5% for <40 years, 5-15% for 40-49 years, and >30% for 50-59 years (Wiseman et al., 2015). Hestnes et al., reported the incidence of Parkinson's disease for patients with Down's syndrome was also depended on age; 1.8% for 50-59 years and 10.7% for 60-69 years (Hestnes, Daniel, Lees, & Brun, 1997). The differences in the incidences of the present results and literature is that they depended on all ages. Most patients in this study are of an age younger than 30 years old.

5.1.7 Demographics and aging diseases

The females of Down's syndrome patients with Alzheimer's disease had a significantly higher prevalence in the present study than their matched males (4.2% vs. 3.8%) (Figure 7). This is because the females are more prone to changes in their pathological and phenotypes expressions than males (Raghavan et al., 1994). However, no previous study has stated the higher prevalence of Down's syndrome with the coexistence of Parkinson's disease, when compared to females.

No previous study has determined the relationship between the type of insurance for patients with Down's syndrome based on aging diseases. The present study has stated that the private HMO had a higher incidence (13.9%) of Down's syndrome patients with

Alzheimer's disease than the other groups (Figure 12). However, this may be attributed to the higher incidence of Alzheimer's disease in patients with Down's syndrome. There has not been any previous study that stated the association between the household income and aging diseases. However, the present study showed a higher incidence of Alzheimer's disease in patients with Down's syndrome who had higher incomes than those with lower incomes when compared to the results of Parkinson's disease (Figure 14).

Down's syndrome patients of the White race had a significantly higher prevalence rate of Alzheimer's disease than other races (5.6%, Figure 13). This is because of the neurodegeneration and other pathological changes. De la Monte et al., investigated the association between the prevalence of aging diseases in Down's syndrome. They noticed the significant association between White race patients and genetic changes which can promote neurological diseases (De La Monte, Hutchins, & Moore, 1989). Moreover, they found a significant association of Alzheimer's disease with the White race, but it did not significantly impact the Black and Asian races. This supported the findings of the present study.

Age is considered as the main cause of Alzheimer's and Parkinson's diseases. This belief is reported by several previous studies (Hestnes et al., 1997; Wiseman et al., 2015). The present study showed a higher incidence of Alzheimer's disease with age than Parkinson's disease. This may be attributed to the higher number of patients and the significant association between Alzheimer's disease and Down's syndrome. However, the patients who were aged older than 80 years had similar results related to the incidences between the aging diseases (Figure 15).

5.1.8 Mortality and aging diseases

The first and second hypothesis regarding the association between the mortality of Down's syndrome based on the type of aging disease was achieved and 'Rejected the null hypothesis'. There was a significant association found between the mortality and Alzheimer's disease in Down's syndrome patients. The incidence of mortality for patients with Down's syndrome and the coexistence of Alzheimer's disease was more than 70% (Figure 16), i.e. the survival rate of patients with Alzheimer's was smaller compared to the mortality rate (3.9% vs. 9.1%). Dementia showed a high incidence of mortality with 13.49% (Figure 17). The literature revealed that dementia in Alzheimer's disease is considered as one of the major causes of mortality. The incidence of mortality reported in the present study was similar to the mortality (70%) reported by Hithersay et al. (Hithersay et al., 2019). However, the present result is higher than the 40% mortality rate reported by Sinai et al., because their study was implemented based on the database of a disability center which included both in and outpatients (Sinai et al., 2017).

5.1.9 Mortality and complications of aging diseases

Hypothesis three is about the association between cardiac malformation and mortality for patients with Down's syndrome. The null hypothesis was rejected, and a significant association was found between the incidence of death and cardiac malformation of Down's syndrome patients. The present study showed a rate of 7.78% as shown in Figure 18. This percentage is higher than the results of Evans et al. with 1.9% (Evans et al., 2014) but it is lower than the 15% of de Rubens Figueroa et al. (de Rubens Figueroa, del Pozzo Magaña, Pablos Hach, Calderón Jiménez, & Castrejón Urbina, 2003) and 16.3% of the

Fuad Abbag study (Abbag, 2006). The wide range of mortality is due to the cardiac malformation that was attributed to the age, race and genetic variations.

The results of the present study showed a significant association between the Down's syndrome complications and Parkinson's disease, where a higher incidence was observed for Down's atlantoaxial instability by 12.77% (Figure 24). Moreover, there was a significant association found between the gait disturbance of Parkinson's disease and Down's atlantoaxial instability by 21.47% (Figure 25). West et al reported the association between the complications of Down's syndrome and Parkinson's disease They attributed the relationship to the neurological disorders such as secondary dystonia which aggravate and worsen the neurodegeneration of the diseases (West, Gray, & Standaert, 2013). Unfortunately, there was no research study obtained that highlighted the association between Parkinson's disease and the complications of Down's syndrome.

5.2 Risk factors of the study outcomes

Multiple linear regression is used to determine the risk factors of length of hospital stay and total charges for Down's syndrome cases and Down's syndrome patients with aging diseases. The multinomial logistic regression is used to determine the risk factors of mortality in Down's syndrome patients. The risk factors with the highest incidences will be discussed in this section. There will also be a comparison of the findings of previous studies.

5.2.1 Length of hospital stay

Congestive heart failure showed the highest risk factor of length of hospital stay for patients with Down's syndrome (Table 15). This is because most patients with Down's syndrome had a problem in their upper respiratory tract which induces the abnormality of growth and other respiratory disorders. This leads to congestive heart failure (Fudge et

al., 2010). Sandeep Chauhan & Ungerleider et al, believed that the main reason of congestive heart failure for patients with Down's syndrome is the atrioventricular septal defect considered to be a cause of premature death and hypertension. These problems required surgical operations on the heart and respiratory tract to overcome the amount of complications related to Down's syndrome. The medical issues in turn consumed a high rate of medical services and expenses (Chauhan S., 2006; Ungerleider et al., 1997).

Previous studies have emphasized the association between Down's syndrome and weight loss (Guffroy et al., 2019; Prasher, Metseagharun, & Haque, 2004). Fudge et al., showed that weight loss is significantly influenced by atrial, ventricular and atrioventricular septal defects. This issue requires several surgical interventions and clinical services at the hospital which prolongs the length of stay (Fudge et al., 2010). This may be attributed to the growth and respiratory defects for patients with Down's syndrome. An increase in the number of surgical operations will escalate the hospital length of stay. These procedures often lead to other medical considerations causing the need for surgery. An example is the loss of fluid and electrolyte balance which contributes to the growth problems mentioned ealier in this section. Fluid and electrolyte disorders are also asscoiated with the number of surgeries in patients with Down's syndrome (Chauhan S., 2006; Ungerleider et al., 1997).

The present study showed the impact of drug abuse, as a main risk factor, on the overall health evaluation for patients diagnosed with Down's syndrome. Prasher et al., discussed the association between Down's syndrome and the probability of drug abuse. They attributed the medical needs of patients with Down's syndrome to the pschotherapy and Parkinson's medications. Drug abuse is known to induce several health problems due to the continual misuse of psychotherapeautic medications. This also aggrevates the need for medical services which in turn prolongs the period of therapy (Vee P Prasher &

Routhu, 2011). This opinion supports the findings of the present study related to patients with Down's syndrome. Age is considered to be a moderate factor of risk that influences the length of hospital stay. Elderly patients with Down's syndrome had a higher length of stay compared to younger patients (Bittles et al., 2007).

Drug abuse is the comorbidity with the highest impact on length of hospital stay for Down's syndrome patients with Parkinson's disease. Prasher et al., stated there are strong pathological relationships between Parkinson's disease and Down's syndrome. Approximately 20% of patients with Down's syndrome developed Parkinson's disease (Vee P Prasher & Routhu, 2011). Drug abuse was related to certain medications for Parkinson's disease administered to patients. The medications affected the normal activities and processes of the individuals. Medications such as Haloperidol induced the condition of catalepsy and Reserpine provoked the patient sedation. The medications aggravated and worsened the complications of the patients with Down's syndrome requiring additonal healthcare services, a longer therapy period and an extended hospital stay. Congestive heart failure and the number of procedures, as discussed previously, are significant risk factors of the length of hospital stay. This is due to the consequences of cardiosurgical interventions for patients with Down's syndrome (Chauhan S., 2006; Ungerleider et al., 1997).

Weight loss is the risk factor with the highest impact on the length of hospital stay for Down's patients with Alzheimer's disease. This belief is in agreement with the opinion reported by Prasher et al. The view is that there are several factors influencing the relationship between Alzheimer's disease, Down's syndrome and the impact on weight loss. The correlation leads to an increase in the length of hospital stay according to therapy plans (Prasher et al., 2004). Chronic conditions are the second highest risk factor affecting the length of stay for Down's syndrome patients with Alzheimer's disease. The

Down's Syndrome Association (2019) highlighted the difficulties exhibited for Down's syndrome patients with Alzheimer's disease and a chronic condition. Learning disabilities, cognitive difficulty and dementia are the most common chronic conditions accompanying the Down's syndrome and Alzheimer's disease patient. Alzheimer's disease also induces other chronic conditions such as depression, epilepsy, infections, sensory impairments, life changes, menopause, thyroid dysfunction and insomnia. The conditions also increase the incidence of side effects as a result of medications (Down's Syndrome Association, 2019). These chronic conditions elevate the expenses and length of hospital stay for patients with Down's syndrome and Alzheimer's disease. Several chronic disorders were noted in patients with Down's syndrome and Alzheimer's diseases. The chronic disorders are as follows: cardiovascular diseases, immunosupression, coagulation problems, diabetes, arithritis, ulcers and anemia. The patients also acquired bad habits such as smoking and consumption of alcohol (Brodaty & Donkin, 2009). Bayen et al., revealed in their study the high levels of risks in the comorbidities for patients with Down's syndrome and Alzheimer's disease. Some of the comorbidities are anemia, weight loss, and tumors (Bayen et al., 2018). Previous studies have indicated an association between the incidence of cancer in Down's syndrome patients with Alzheimer's disease (Goldacre et al., 2004; Hill et al., 2003; Ram & Chinen, 2011). Age plays a role in the prevalence and progression of diseases and comorbdidities which is discussed earlier in this chapter. An increase in comorbidities may boost the need for medical services and a longer length of hospital stay. This is supported in the results of the present study, as shown in Table 15. No previous studies have shown the interaction of risk factors and their impact on the length of hospital stay for patients with Down's syndrome and aging diseases. This topic is considered unique to the present study.

5.2.2 Total charges

Total charges is another outcome for the patients with Down's syndrome due to the negative psychological and finanicial impact on the patients and family's quality of life. It is also a burden to health services and governmental support. The number of procedures is considered as the highest rated risk factor related to the total charges for patients of Down's syndrome in the present study. This is because medical and surgical interventions consume a high level of total charges. Down's syndrome patients are subjected to several therapy plans including surgical operations and other auxillary services. Coagulation is considered as one of the most significant risk factors of total charges for patients with Down's syndrome in the present study. Martínez-Valverde et al., found that coagulopathy is a comorbid condition in at least eight percent of patients with Down's syndrome. This condition elevates the total expenses for families and medical services for the government (Martínez-Valverde et al., 2019), This information supports the results of the present study.

Congestive heart failure and fluid with electrolyte imbalance is considered a serious health problem impacting Down's syndrome patients. It requires surgical interventions to enhance the health status of patients (Chauhan S., 2006; Fudge et al., 2010; Ungerleider et al., 1997). This opinion is in line with the findings of the present study where congestive heart failure and fluid with electrolyte disorders are the risk factors that induced the highest total charges. Race plays a role in the type and amount of medical services provided to patients with Down's syndrome (Bayen et al., 2018). The present study showed the Hispanic and Asian/Pacific Islander race for Down's syndrome patients had higher total charges than other races. Patients with pulmonary circulation disorders required surgical operations to reduce the respiratory dysfunction induced by Down's syndrome, as discussed earlier in this chapter. All services and surgical interventions

incurred higher financial expenses for Down's syndrome patients. Finally, drug abuse also increased the total charges of hospital services (Table 18), which is discussed earlier in this chapter.

Drug abuse revealed the risk factor with the highest effect on total charges for Down's syndrome patients with Parkinson's disease. This is discussed by Prasher & Routhu, who believed that the medications for Parkinson's and pschotherapy were considered as the main cause of drug abuse. This in turn required additional medical attention for the consequences of this comorbidity (Vee P Prasher & Routhu, 2011). These amenities usually required additional expenses for medical services and the administration of medications. Sayegh et al., highlighted the common health problems faced by Hispanic patients compared to the other races. These common problems were agitation, disinhibition, irritability, anxiety, depression, delusions, hallucinations, apathy, sleep, appetite abnormalities and other psychotic disorders. Moreover, they stated there were high total charges paid for their medical services, especially those individuals with dementia (Sayegh & Knight, 2014). These observations supported the results of the present study where the Hispanic Down's syndrome patients with Parkinson's disease obtained higher total charges than the other races. The patients with Down's syndrome and Parkinson's disease exhibited a significant association to cardiovascular disorders. Several studies have shown the associations between cardiovascular and aging diseases but they have not highlighted the cost of services provided to Down's syndrome patients (Bayen et al., 2018; Chauhan S., 2006; Mayeux, 2003). Chenbhanich et al investigated the significant impact of Down's syndrome and congestive heart failure on the total costs paid for medical services, but they focused on the dementia of Alzheimer's disease patients only (Chenbhanich et al., 2019). Therefore, the present study explored the relationship with Parkinson's disease and the impact on the progression of congestive

heart failure. Congestive heart failure and other cardiovascular diseases, as discussed previously, required that a greater number of surgical and health services be provided to patients with Down's syndrome. This outcome influenced the total charges of the present patients.

The number of procedures contained risk factors with the highest impact on the total charges for the medical services provided to patients with Down's syndrome and Alzheimer's disease. Martínez-Valverde et al., discussed the variations of total expenditures for patients with Down's syndrome (Martínez-Valverde et al., 2019), but they focused on children rather than individuals with an aging disease. Another study showed that Down's syndrome patients who were diagnosed with late stage Alzheimer's disease were more likely to experience cardiac bypass sugeries and related heart diseases (such as hypertension and dyslipidemia). These disorders contributed to declining cognitive ablity and changes in cerbrospinal fluid (Palotás et al., 2010). Therefore, the present study revealed the association related to elderly patients. However, the number of procedures still influenced the total charges of Down's syndrome with Alzheimer's disease because of the medical services provided to these patients. The Hispanic race patients with Down's syndrome and Alzheimer's disease had higher total charges than other races. This perception is reported by a previous study (Sayegh & Knight, 2014), because they found that patients of the Hispanic race consumed a higher percentage of their money for their medical services. Moreover, they found that depression is a significant comoribidity of Down's syndrome patients with Alzheimer's disease and they also were subjected to higher charges for their medical services. One of the risk factors of Down's syndrome, fluid and electrolyte disorders, are associated to a higher number of surgeries for patients with the disease. Saghazadeh et al. found a diffeciency of electrolytes and minerals in patients with Down's syndrome due to an abnormal

metabolism. This is also seen in patients with dementia induced by Alzheimer's disease (Saghazadeh, Mahmoudi, Ashkezari, Rezaie, & Rezaei, 2017). A previous study discussed the histopathological relationship between rheumatoid arthritis and Down's syndrome. Rheumatoid arthritis is more prevalent in the elderly. The disease has an onset that starts at childhood in Down's syndrome patients and causes an increase in health services and medical interventions (Roizen & Patterson, 2003). The impact of age and the relationship with total charges was discussed previously in this chapter. Finally, the number of chronic conditions influenced the total charges of Down's syndrome with Alzheimer's disease patients (Down's Syndrome Association, 2019). Unfortunately, few studies have ascertained the direct impact of comorbidities for Down's syndrome patients with an aging disease and their impact on total charges. This is considered the novelty of the present study.

5.2.3 Mortality

The number of procedures is the risk factor with the incidence of mortality for patients with Down's syndrome in the present study. The number of procedures is in relationship to the number of complications patients had with a coexistence disorder. An example is cardio and urogenital surgeries which increased the risk or mortality of Down's syndrome patients. This was previously explored for both children and adults who were Down's syndrome patients (Cua et al., 2017; Henderson et al., 2007). Fluid and electrolyte imbalance showed a significant relationship to mortality especially to patients with Down's syndrome.

These results were also confirmed by the opinion and findings of a previous study (Saghazadeh et al., 2017). Numerous studies have found an association between the mortality of Down's syndrome and age (Bittles et al., 2007; Kucik, Shin, Siffel, Marengo,

& Correa, 2013; Kathryn K Ostermaier, 2018; Yang et al., 2002). However, Zhu et al. found the association between the ages and reason for the mortality. The findings were that the individuals aged younger than twenty years and older than twenty years were impacted by mortality because of congenital heart defects and respiratory/circulatory diseases, respectively (Zhu et al., 2013). These opinions were supported by the results of the present study related to age and pulmonary diseases. Hill et al, reported the high incidence found between diabetes mellitus type-I and mortality for Down's syndrome patients (Hill et al., 2003). Saghazadeh et al, believed that diabetes is another comorbidity for patients with Down's syndrome due to an abnormal metabolism (Saghazadeh et al., 2017). The present study showed a high incidence of mortality for all ages of the patients.

The number of procedures showed a higher significant association to the rate of mortality for patients with Down's syndrome with both aging diseases (Parkinson's and Alzheimer's diseases). They showed a similarity to the risk factors, but the severity was higher with Parkinson's disease than with Alzheimer's disease. Age was the second risk factor of mortality for patients with Down's syndrome and Parkinson's disease. Patients with Down's syndrome and Parkinson's disease were more prone to have mortality due to age (Hestnes et al., 1997). This finding supported the results of the present study. Alzheimer's disease increased the rate of mortality for Down's syndrome patients due to the neurological, respiratory, growth and other complications. These disorders aggravated the health problems and caused urgent surgical interventional needs that increased the percentage of deaths (West et al., 2013). Although Alzheimer's disease is investigated more in the previous studies with Down's syndrome patients, the severity of risk factors is higher with Parkinson's disease in terms of mortality, as shown in Table 22. Therefore, it should be a requirement to have the medical professional provide attention to Down's syndrome patients with Parkinson's disease.

5.3 Study limitation

Several limitations involved in the present study include the type of database utilized for the analysis. This data is from a secondary database and was obtained from the National Inpatient Sample. Some of the information presented did not have a detailed and full investigation of the objectives. The missing data required in this type of study includes the laboratory data, patients' medical history, pharmacological therapy and signs and symptoms. Other missing information is believed to have had significant essential requirements to complete the prediction of disorders such as the onset of diseases, number and dates of readmissions, duration of therapy, type of therapy and doses.

The last limitation is the inadequate literature regarding the association of comorbidities and risk factors with the main findings for Down's syndrome patients with aging diseases. This requires an indirect justification such as the existence of comorbidities that elevate the needs for health services and increase the total charges, length of stay and mortality rate. Finally, the karyotypes of Down's syndrome were not involved in the investigation of the present study.

CHAPTER VI

CONCLUSION AND FUTURE RESEARCH

6.1 Study Summary

This study highlighted the significant risk factors for the hospitalization outcomes related to patients with Down's syndrome in hospitals in the United States between the years 2007-2012. These outcomes affected either the patients, hospitals or governmental and institutional levels. The patient levels were influenced by their quality of life and the issue of mortality. The hospital level is associated to the type and quality of healthcare services provided to their patients. The governmental level has a correlation to the insurance and payments provided for the medical services. The bridge among these levels are the risk factors and outcomes. The length of hospital stay, total charges and mortality are considered as the dependent variables. The patients' medical information and socio-demographic characteristics are the independent variables. The socio-demographic characteristics included the gender, age, race, type of insurance and income levels. The patients' medical information included the number of procedures, chronic conditions, comorbidities and type of aging disease. There were 58438 Down's syndrome patients admitted to the hospital. There were 1198 and 2352 patients who were diagnosed with Parkinson's and Alzheimer's diseases respectively. Multiple linear regression (dummy method) and multinomial logistic regression were used to determine the risk factors to achieve the objectives of the present study.

Descriptive analysis was used to measure the incidence of the variables of the study. The highest incidences were observed in those aged younger than thirty years, of the White race, Males, with Medicare insurance and in the 0-25th household income percentile. The highest five incidences of comorbidities were observed in hypothyroidism, fluid and

electrolyte disorders, neurological disorders, hypertension and chronic pulmonary disease. There was a higher increase in the number of hospital admissions for patients with Down's syndrome and Alzheimer's disease than of Parkinson's disease during this time period. The socio-demographic characteristics are significantly associated to the type of aging disease for patients with Down's syndrome. Alzheimer's-Down's patients had a significantly higher incidence of mortality than Parkinson's-Down's patients. But, the severity of risk factors had a higher influence on the individuals with Parkinson's disease than Alzheimer's disease. Moreover, the area of mortality was influenced with complications from aging diseases such as the cardiac malformation of Down's syndrome and the gait disturbance of Parkinson's disease.

For the length of hospital stay, the risk factors of all patients with Down's syndrome were as follows: congestive heart failure, weight loss, fluid and electrolyte disorders, number of procedures, coagulopathy, age and drug abuse. For those patients with Parkinson's disease, the risk factors related to the length of stay were drug abuse, congestive heart failure, Hispanic race and the number of procedures. For the patients with Alzheimer's disease, the risk factors for the length of stay were as follows: weight loss, number of chronic conditions, deficiency anemia, congestive heart failure, lymphoma and age. For the total charges, the risk factors for all patients with Down's syndrome were the number of procedures, coagulopathy, congestive heart failure, fluid and electrolyte disorders, Hispanic race, pulmonary circulation disorders, Asian or Pacific Islander and drug abuse. For the patients with Parkinson's disease, the risk factors for total charges were drug abuse, Hispanic, number of procedures and congestive heart failure. For the patients with Alzheimer's disease, the risk factors for total charges were the number of procedures, Hispanic race, depression, fluid and electrolyte disorders, rheumatoid arthritis, income, age, hypertension, other races and the number of chronic conditions. For the mortality of

Down's syndrome patients, the risk factors were the number of procedures, fluid and electrolyte disorders, age, pulmonary circulation disorders and diabetes mellitus. For the patients with Parkinson's disease, the risk factors related to mortality were the number of procedures and age. For the patients with Alzheimer's disease, the risk factors were the number of procedures, chronic pulmonary, neurological and pulmonary circulation disorders.

Differences were noticed in the incidences and risk factors of the study findings between the aging diseases for patients with Down's syndrome, where there is a higher mortality rate obtained in the individuals with Alzheimer's disease, but a higher impact of risk factors observed with individuals diagnosed with Parkinson's disease. Therefore, it requires serious attention for healthcare professionals and research scholars to manage and control the preventable risk factors. There is a need to update the guidelines of therapy plans for Down's syndrome patients diagnosed with an aging disease. If there is an adverse impact on the patients' quality of life, it will be considered as a burden to the health services in this country.

6.2 Future research

Clinical trials and investigational studies are needed to determine the risk factors based on laboratory and screening measurements. This will help to determine the association of the effect of aging diseases on the mortality rate, length of stay and total charges. Genetic studies should be implemented to compare the outcomes for patients with Down's syndrome, Parkinson's and Alzheimer's diseases to the impact and severity of their risk factors. Educational and interventional studies are recommended for healthcare professionals. This will ensure they have the latest updated knowledge required to

improve their relationship of working with patients diagnosed with Down's syndrome and the specific types of aging diseases.

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