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"IS THERE AN ASSOCIATION BETWEEN CHILDHOOD IMMUNIZATIONS & CHILDHOOD ASTHMA?"

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Is There an Association Between Childhood Immunizations and Childhood Asthma?

by

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of

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BACKGROUND: Today childhood asthma is one of the most common childhood diseases in the developed world. There exists a great breadth of research on asthma – the possible causes, possible triggers, and treatments. However, there was a lack of epidemiological research on whether or not childhood immunizations can affect childhood asthma. Immunological theory has established that pertussis stimulates the production of IgE, which is predominantly associated with the Th2 arm of the immune system. Enhanced Th2 activity and elevated levels of IgE are associated with atopy and asthma. Different immunizations and different components of immunizations are thought to elicit different immune responses which can subsequently increase or decrease asthma rates.

OBJECTIVES: The objectives of this research study were to determine if the following childhood immunizations were associated with childhood asthma rates – Diphtheria / whole-cell Pertussis / Tetanus (DPT) vaccine, Diphtheria / acellular Pertussis / Tetanus (DaPT) vaccine, Diphtheria / Tetanus (DT) vaccine; Measles / Mumps / Rubella (MMR); and BCG. Adherence to the Canadian Immunization Schedule in terms of timing and number of doses were of particular interest.

METHODS: This is a retrospective birth cohort study of all children who were born in Manitoba in 1995 and remained in Manitoba until age 7. SAS was used to compile and analyze administrative data such as hospital, medical and prescription records which were linked to MIMS data (Manitoba Immunization Monitoring System). Logistic Regressions were performed to obtain adjusted Odds Ratios.

RESULTS: The following findings were both of particular interest and statistical significance. Children who had all four of their first DPT immunizations delayed were less likely to develop Asthma when compared to children who had received all of their first four DPT immunizations on time. Children who had their fist two DPT immunizations delayed were less likely to develop Asthma than children who had their first and / or second DPT immunizations on time. Children who did not receive one or more DT immunizations were less likely to develop Asthma than children who had received a DT and DPT combination. Children who had received three different DPT combination vaccines (DT / DPT /DaPT) were less likely than children who received DT and DPT to develop Asthma. Children who had a DPT/DaPT immunization status of either "Complete" (5 doses), "incomplete" (1-5 doses) or "Over" (6+ doses) were more likely to have experienced Wheezing than children who had never been immunized with DPT/DaPT. Children who had been immunized with 1 to 5 doses of DPT and 2 doses of DaPT were more likely to have had Wheezing than children who had never been immunized with DPT/DaPT. Children who had been immunized with 1 to 3 doses of DPT and 1 dose of DaPT were more likely to have had Wheezing than children who had never been immunized with DPT/DaPT. Children who had received one or more doses of BCG were more likely to have had Wheezing than children who had not been immunized with BCG.

CONCLUSION: This data suggests that the timing or age at which children receive their DPT doses can affect the Asthma rate – a delay decreases the Asthma rate. The number of doses or DPT/DaPT administered seems to affect the Wheezing rates. As DPT is no longer used in Canada these findings are not of direct relevance to the Canadian Immunization Schedule but rather serves as an excellent base for future research on DaPT. The fact that many other countries around the world still use DPT makes this research relevant and of interest. Findings presented in this project may influence changes in immunization policy.

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INTRODUCTION & LITERATURE REVIEW:

This thesis project is one component of a larger New Emerging Team (NET) research study called the SAGE (Study of Asthma and Genetics) by Dr. Anita Kozyrskyj and Dr. Allen Becker. The population of interest for SAGE was a 1995 birth cohort of Manitoba children. This set a perfect opportunity to perform further analyses on this data, such as linking the children's immunization records to their health and prescription records with an outcome of asthma being the main variable of interest. When each part of the study is combined there will be data analyses on the genetics, environmental allergens, history of antibiotic use, birth weight, parental history of asthma among others. Together the different parts of this study will provide one of the most in depth and varied childhood asthma studies to date.

The idea to investigate the possible association between childhood immunizations and childhood asthma, stemmed from a fairly recent immunological research on the Th1 and Th2 pathways. For the purpose of this study the main childhood vaccinations of interest were Diphtheria / Pertussis / Tetanus (DPT) combination vaccines, DaPT with an acellular Pertussis component, DT without Pertussis, Measles / Mumps / Rubella (MMR) combination, and BCG vaccine for Tuberculosis.

LITERATURE REVIEW:

Asthma is a respiratory disorder that is typically characterized by chronic airway inflammation and airway hyper-reactivity which at times can involve reversible airway obstruction.[1] Childhood asthma has become an increasingly common chronic disease of developed countries around the world. In Canada, for almost the past two decades the prevalence of childhood asthma has steadily increased. In the late 1970's the estimated prevalence for children under the age of 15 was 2.5% and by 1995 it was estimated to be around 11.2% or 672,000 children. Asthma rates vary by region, with the highest rates in Atlantic Canada and Quebec and the lowest rates found in British Columbia. The prevalence of asthma not only varies across the country but also within provinces – which is also true in Manitoba.[2]

In Canada, asthma is one of the top five reasons for hospital admission among children.[3] In 1997 asthma was listed as the primary diagnosis for 12% of all admissions for children age 0 - 4 and 10% for children age 5-14.[4] In 1990 the direct cost of asthma was estimated at $504 million and the indirect cost at $648 million.[5] This cost has undoubtedly risen every year since. However, the economic cost is not the only consideration when assessing the magnitude of this chronic disease. Data from the National Population Health Survey Asthma Supplement, Stats Canada reported that in 1997, 28% of children who had been diagnosed with asthma age 2-19 had missed 1-5 days of school in the past year due to their condition and 16% of children in the same age group were reported to have missed 6+ days.[6] Other things to consider would be the restriction in daily activity or physical limitations due to asthma, depending on the severity of the illness, the psychological impact and stress caused by a chronic disease, as well as the possible side effects of the drugs required to control asthma.

There exist several theories as to why asthma has become so prevalent in developed countries. One such theory is the "Hygiene Hypothesis" which was expanded from the initial work of D.P.Strachan who first coined the term in 1989. With the advent of modern medicine and the development of its main arsenals for fighting disease (i.e. antibiotics and vaccines) in turn came the reduced incidence of childhood infectious diseases. The theory holds that with these new tools combined with the higher standards of living (improved sanitation, hygiene and antibacterial soaps etc.) came newfound living environments for growing children in which their exposure to endotoxins and parasites were reduced and if or when infection did occur, it was now conquerable. The Hygiene Hypothesis states that our immune systems have not been able to adapt quickly enough to these changes and thus have made it much easier for them to slip into unbalanced states where autoimmunities such as allergies and asthma can arise.[7] Although the benefits of antibiotics and vaccines are widely known there is a mounting desire to find out what is not known about them in terms of the short and long-term immunological effects.

From an immunological and molecular cell biology perspective the Hygiene Hypothesis is much more complex and difficult to explain. The proceeding simplified explanation will serve as a context for the information that will follow. Antigens are the foreign bodies that are recognized by macrophages and dendritic cells, which stem from myeloid progenitor cells, which originate from pluripotent hematopoietic cells of the bone marrow. The macrophages and dendritic cells are considered to be "professional" antigen presenting cells (APC), as one of their main purposes are to guard the immune system from foreign invaders. The APC then elicits the help of the T-helper cells, which once activated can directly activate B-cells. T-cells respond to cytokines which can be interferons (INF), interleukins (ILs), or tumor necrosis factor (TNFs). These cytokines are highly active chemical messengers which stimulate T-cells to grow, divide, differentiate or move. There are two groups of T-helper cells (TH-1 and TH-2) which are associated with different cytokines. TH1 is associated with INF-y and IL-2 where as TH2 is

associated with Il-4, Il-5, IL-9 and IL-13 (TABLE 1).[8] Asthma patients have been found to have significantly higher levels of IL-13 present when compared to non-asthmatics and in experiments with IL-13 deficient mice researchers have found that the mice do not generate goblet cells. Goblet cells are responsible for mucus production, which in asthmatics is overproduced. Mucus plugs which block airways can be found in fatal cases.[9]

TABLE 1: The Major Functions of Several Cytokines Associated with the TH1 and TH2 Pathways.

Cytokine	*Major Function*
TH1	
IFN-*y*	Activates Natural Killer Cells (NK), Induces MHC expression in APCs
IL-2	Stimulates T and B cell proliferation
TH2	
IL-4	Induces the isotope switching of B cells to synthesis of IgE, Stimulates T lymphocytes into TH2
IL-5	Controls eosinophils (differentiation, recruitment, activation, and survival
IL-13	Shares many of the activities of IL-4 but does not effect the T lymphocytes

(modified from Holgate & Busse, 1998)

The activated B-cells then proliferate and differentiate into plasma cells that can synthesize antibodies that can bind to antigens, neutralize and target them for destruction by phagocytes. The immune system can produce many different types of antibodies with different functions. Antibodies are globular proteins called immunoglobulins (Igs) which are categorized into five different classes IgA, IgD, IgE, IgG, and IgM. The TH2 class is associated with IgE production which in turn binds with high affinity to mast cells which then trigger histamines, causing inflammation which can then cause atopic[1] disorders such as allergies and asthma.[10]

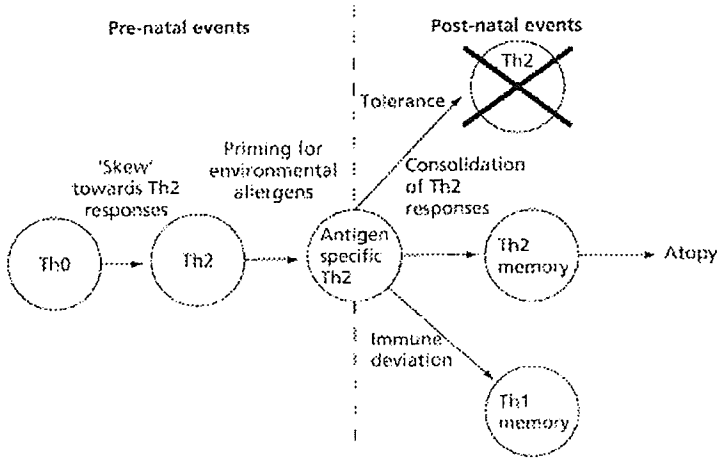
[1] Atopic disorders / Atopy: is defined as the excessive production of specific IgE in response to exposure to common environmental and other allergens which results in inflammation (Lowe *et.al.* 2003).

In the pre-natal period the fetus's immune system is weighted towards the TH2 pathway. Normally, after birth the infant's immune system matures and balances out between the TH1 and TH2 responses. This maturation process occurs as the infant is exposed to antigens from microbial agents (Fig.1). However, there is the theory that if the infant does not acquire sufficient natural immunity then the imbalance concentrated on the TH2 side can result in the inflammatory responses as stated above. Antibiotics and vaccines can alter the function of the immune system and may propagate TH2 and associated responses. Vaccinations may promote allergies and associated disorders by either reducing the ability of the immune system to naturally fight off infections which would strengthen the TH1 mechanisms or by further stimulating the TH2 responses. The latter could be stimulated by either an adjuvant[2] of the vaccine or by the antigen itself. [11]

At the same time many people are aware of the benefits of vaccines and that in populations where there are not high rates of immunization, infectious diseases are more likely to occur. In a study, which will be discussed in greater detail in the literature section of this proposal, there was a group of children who had very low rates of being vaccinated with MMR. As a result 61% of the children had at some point in their lives been infected with measles. From "wild" infections there exists the possibility of future sequela or even death. These risks have to be weighed in relation to the risk of adverse events associated with immunizations. It is possibly that asthma is an example of this risk.[12]

[2] Adjuvant: enhances the rate and quantity of antibodies produced.

FIGURE 1: The "Skewed" Pre-natal Immune System and the Possible Events the Occur Post-natal Period.



(Johnston S & Holgate S, 2002)

The Hygiene Hypothesis has been supported by studies looking at children who have anthroposophic lifestyles. In the early 20th century Rudolf Steiner founded the school of anthroposophy. His ideology and theology has been applied to agriculture, architecture, education, and medicine. Today there are many "Steiner Schools", mainly in Europe, where children are raised in an anthroposophic environment. Children's diets are composed of mainly organic foods that are locally produced. There are also very high rates of breast-feeding among their infants. This group has provided an interesting comparison group to mainstream society because their children have very low rates of immunizations and antibiotic use.

A cross-sectional study by Alm J. Swartz J, *et.al.* of 295 children from two Steiner schools and 380 children from two neighboring schools analyzed the differences in: the incidence of infection, use of antibiotics, vaccination rates, and other social and environmental variables (such as, diet and rates of breast-feeding). The researchers found that on average only 52% of the Steiner children had used antibiotics compared to 90% of control school children. They also found that only 18% of the Steiner school children had been immunized against measles, mumps, and rubella (MMR) whereas 93% of the control school children had been immunized with MMR.

As a result, 61% of the Steiner children had had measles. The children from the Steiner schools who were not immunized with the MMR vaccine were less likely to develop atopy when compared to children who had received the vaccine, an OR of 0.67 with a 95%CL of (0.46 to 0.99). Overall the Steiner children had lower rates of atopic disorders, with an average asthma rate of 5.8% compared to the control group's average of 17%. In conclusion, they found that there was an inverse relationship between the number of anthroposophic lifestyle "features" and the risk of atopy.[13]

In 2001, researchers at The John Hopkins University School of Medicine performed a study involving peripheral blood lymphocyted (PBLs) and the MMR vaccine. They concluded that the viral vaccine has the ability to induce IgE class switching. The researchers then performed the same study with individual vaccines of measles, mumps, and rubella. From this they determined that the rubella vaccine was the most potent inducer of IgE class switching. As was discussed before IgE antibodies are associated with allergic disorders.[14] Another study on allergic reactions to the MMR vaccination found that vaccine had the ability to exacerbate asthma symptoms in those who were previously diagnosed as being asthmatic.[15]

The Whole cell Pertussis vaccine:

In a British retrospective cohort study of 1, 934 people born between 1975 and 1984, researchers reviewed public health and physician practice records and then made temporal records of all immunizations, diagnoses of asthma, hay fever, eczema, maternal atopy and others. Using logistic regression analysis the researchers identified three statistically significant predictors of atopic disease: maternal atopy, immunization with whole cells pertussis and receiving oral antibiotics within the first two years of life. The odds ratios of subsequent atopy in individuals who: had mothers with atopy was 1.97 with a 95%CL of 1.46 to 2.66); were exposed to the pertussis immunization alone was 1.76 with a 95%CL of (1.39 to 2.23); those who had received antibiotics was 2.07 with a 95%CL of (1.64 to 2.6). The rate for those who were

exposed to all three independent variables was 67%. The authors warn, however, that these results may be influenced by unknown confounders, or the effects of reverse causation.[16]

Pertussis vaccines are made with chemically detoxified pertussis toxin. Pertussis toxin is often used in lab experiments to enhance IgE production in lab animals. A study which was published in 1998 by Nilsson L, Gruber C. *et.al.* reported that the initial IgE levels were higher in children who received the acellular version of the Pertussis vaccine when compared to children who had received the whole cell version. They hypothesized that this short-term elevation in IgE levels could have been due to adjuvants or other components in the acellular vaccines.[17] Elevated levels of IgE against pertussis toxin have been found in children who had a local adverse reaction to a acellular Pertussis vaccine. It has also been found that children who are atopic or have a family history of atopy will also present higher levels of IgE to pertussis toxin after a pertussis vaccine.[18]

The Acellular Pertussis vaccine:

The acellular pertussis vaccine was developed because of the overall high rates of adverse reactions recorded to the whole-cell vaccine. Today Health Canada advises for the acellular version in the combination vaccine DTaP as opposed to the DTP vaccine. The newer DTaP combination vaccine has been found to be less problematic, with lower incidence of adverse events.[19,20] In general the combination of DTaP has been less reactogenic in causing the known side effects of this vaccine. However, in 2000 a US study reported that children and adolescents who had been routinely vaccinated with DTP or plain Tetanus had an increased risk for allergies / respiratory problems and were twice as likely to develop asthma.[21] Another study on Tetanus and Diphtheria found that there was a significant increase in the IgE immune response associated with atopic disorders after the children involved in the study received Td vaccines.[22]

The differences between the Whole cell and acellular Pertussis vaccine:

DPT:

1. Contains the heat-killed pertussis whole-cell vaccine (wP)
2. Very reactogenic
3. Both local and systemic (local swelling, high-fever etc.)
4. Rare but very serious adverse events → neurological (seizures, encephalopathy)

(Geier D, Geier M. *Brain & Development,* 2004)[23]

DaPT:

1. Contains acellular pertussis (aP) which is composed purified bacterial protein → 1 to 5 components → derived from virulence factors
2. Filamentous hemagglutinin (FHA)
3. Fimbriae (FIM)
4. Pertactin (PRN)
5. Toxins: pertussis toxin, adenlate cyclase-hemolysin, tracheal cytotoxin

(Guiso N. *ASM News,* 2005)[24]

Additional components of vaccines:

The chemical preservatives and adjuvants used to manufacture vaccines have also been in question. Thimerosal, used as preservative, is an ethylmercury derivative that has been of concern as mercury is a known neurotoxin. Thimerosal is currently used in over 30 US-licensed and marketed vaccines. Infants who are of low relative body weight are more susceptible to the effects of cumulative thimerosal exposure as no dose adjustments are made based on weight. The levels which they are exposed to may exceed the toxic level.[25] Thimerosal has also been associated with exacerbating atopic eczema in sensitive infants. Although it is commonly used, many new thimerosal-free vaccines are about to be launched onto the market in the USA.[26] The childhood immunizations analyzed in this project did not contain thimerosal.

Aluminum salts (Al_3PO_4 and $Al(OH)_3$) are common adjuvants used in vaccines. $Al(OH)_3$ in particular is known to enhance IgG and IgE production and is also known to increase bronchial hyper-reactivity.[27,28] A study of workers in the primary aluminum industry found aminoethyl ethanolamine to be the causative agent in occupational asthma. A substantial proportion of workers in this industry develop what is commonly referred to as "pot room asthma". It has also been found that some workers who are exposed to potassium aluminum tetrafluoride, which is used in aluminum soldering, present clinical asthma or bronchial hyper-responsiveness.[29] In 1978 a Bulgarian study on tetanus toxoid combined with either aluminum phosphate or calcium phosphate was published in the journal *Allergy*. The researchers determined that when the tetanus vaccine was combined with aluminum phosphates it had the ability to stimulate a high frequency of specific IgE in laboratory animals. However, the same immune response was not triggered by the tetanus vaccine with calcium phosphate.[30]

Another component of general suspicion has been egg protein. As many vaccines are prepared from chick or duck fibroblast tissue of embryonated eggs, residual proteins do exist and for those with allergies to eggs it has been found to be a significant problem.[31] Gelatin is used as a vaccine stabilizer and is derived from porcine and bovine sources. It has been found to be a contributing factor in cases where people have had anaphylactic reactions after receiving immunizations containing gelatin.[32] Other components to consider are formaldehyde (a preservative) and neomycin (an antibiotic), especially in individuals with known sensitivities to these components (TABLE 2).

TABLE 2: Common Childhood Vaccines and Typical Constituents

Vaccine	Aluminum compounds	Mercury compounds	Antibiotics	Human gelatin	Yeast formaldehyde	Egg albumin	Derived
Diphtheria	+	(+)	–	–	+	–	–
Tetanus	+	(+)	–	–	+	–	–
Pertussis	+	(+)	(+)	–	+	–	–
Polio (IPV)	–	–	+	–	–	–	–
Polio (Sabin)	–	–	+	+	–	–	–
Measles	–	–	+	+	–	+	–
Mumps	–	–	+	+	–	+	–
Rubella	–	–	+	(+)	–	+	–
Hib	(+)	(+)	–	–	–	–	–
Hepatitis B	+	(+)	–	–	(+)	–	+
Hepatitis A	+	–	+	–	+	–	–
Influenza	–	+	+	–	+	–	–
Tick-borne disease	–	–	+	(+)	+	(+)	–
BCG	–	–	–	+	–	–	–
Pneumococci	–	(+)	(+)	–	–	–	–
Meningococci	–	(+)	–	–	–	–	–
Varicella	–	–	(+)	–	–	+	–
Yellow fever	–	–	–	+	–	–	–

+, common; (+), some; –, uncommon.
BCG, bacille Calmette–Guérin; Hib, *Haemophilus influenzae* type b; IPV, inactivated polio vaccine.

(Gruber *et.al.* 2001)

More recently there have been many studies published concerning the possibility that the bacille Calmette-Guerin vaccine (BCG) may offer some protection against asthma and other allergic diseases. Tuberculosis (TB) skews the immune system towards the TH1 mechanisms by significantly suppressing the TH2 mechanisms. Some studies indicate that when comparing different countries the TB rates are inversely proportionate to the asthma rates. It was with this observation that experiments began on the "protective" abilities of the BCG vaccine.[33]

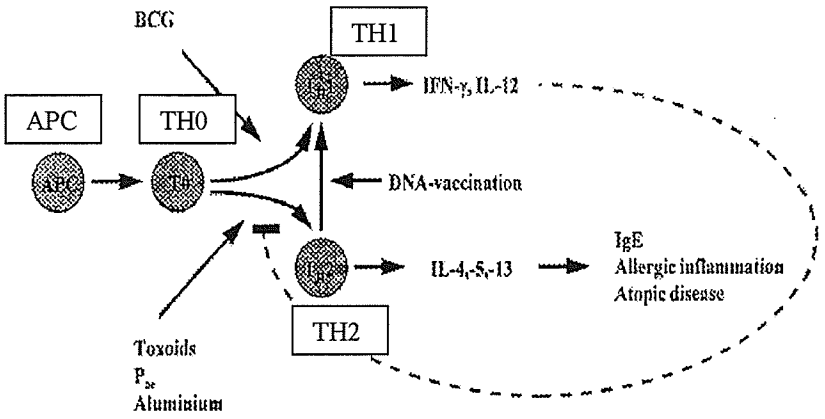


FIGURE 2: Early Childhood Immunizations: Influence on development of atopy and allergic reactions.

The potential interference of vaccines with the natural course of atopic diseases.

Pac, pertussis acellular vaccine

The arrow and solid line = promoting effect.

The broken line = inhibitory effect.

(modified from Gruber *et.al.* 2001)

A review of studies on this effect indicates that BCG infection in rats significantly inhibits the TH2 immune response and asthmatic reactions and there is also evidence that the BCG vaccine does prevent atopy and airway hyper-reactivity in mice. However, other studies argue that there is no conclusive evidence that this is the case in humans. [34,35,36]

In a Korean study published in 2002 which included 43 participants with moderate to severe asthma the researchers vaccinated 21 of the participants in a double blind fashion with BCG and the 22 other participants with a placebo. Over the course of the study they reported that they observed improved lung function and a reduction in the amount of medication required among those who had been vaccinated with BCG. They also observed a suppression in the TH2-type immune response.[37]

A recent study published in the *Journal of Asthma* enrolled six children with confirmed cases of asthma (according to criteria of the American Thoracic Society) into a study where they collected peripheral blood mononuclear cells (PBMC) from the children before and after they were vaccinated with BCG. Researchers found that the children had a significant decline in the IgE production after the BCG vaccine when compared to the 5 non-atopic control group after testing the PBMC IgE levels in vitro with allergen stimulants. This is the first study that has demonstrated this kind of response in vitro of PBMC taken from atopic children who had received in vivo exposure to BCG (immunization). As a result this study supports the hypothesis that BCG immunizations can downregulate IgE production in atopic children.[38]

As this type of research is truly in the early stages there are very few absolutes and many questions remain. In reality the TH1 and TH2 balance is undoubtedly even more complex than previously thought. The suggestion and attempts to treat asthma with BCG vaccination are premature in nature. There is probably not only one single exposure to an antigen or vaccine that could result in long-lasting induction of the TH1 immune pathways. Rather it is most likely naturally acquired through the continuous exposure to a variety of microbial antigens.[39]

It is also possible that the atopic and like responses (asthma) are the result of a general immune dysfunction in which both the humoral and cellular immunity are at work – but where the TH2 mechanisms are more obvious. If this is the case then stimulating the TH1 response could result in the exacerbation of symptoms.[40] It has been suggested that if the sole mechanism at play for atopy/allergy/asthma was the TH1/TH2 balance then there should be a decrease in the number of TH1 prone autoimmune diseases such as type 1 diabetes mellitus and inflammatory bowel disease at the same time the TH2 prone diseases are increasing.[41]

Mechanisms by which infections and vaccinations affect the human immune system are not completely understood. Vaccinations have been the cornerstone of modern medicine and as a result the incidence of many infectious diseases have been drastically reduced. However, they are given on the premise that the risk of the disease is greater than the risks associated with the

vaccine itself. As more questions are asked, the extent to which this assumption holds true will be challenged. Through more complete research, statements like these can be made with greater assurance.

TABLE 3: Summary of References

Vaccine	IgE / Atopy Increase	/ Asthma decrease	possible assoc.*	no assoc.**	Source	Limitations & Sources of Bias in Epidemiological Studies
MMR	X				Alm J, Swartz J. *et.al.*	selection bias
	X				Imani F, Kehoe K.	
			X		Patja A, Makinen-Kiljunen S. *et.al.*	
Measles			X		Farooqi S, Hopkin J	observational and reverse causation
Pertussis	X (wP)***				Farooqi S, Hopkin J	observational and reverse causation
	X (wP, aP****)				Nilsson L, Gruber C. et.al.	
DTP			X		Hurwitz E, Morgenstern H.	temporality and recall bias
Td	X				Dannemann A, VanRee R. *et.al.*	
Tetanus			X		Hurwitz E, Morgenstern H.	temporality and recall bias
BCG		X			Choi I, Koh Y.	
		X			Barlan I, Tukenmez F. *et.al.*	
				X	Koh Y, Choi I, Kim W	
				X	Shirtcliffe P, Easthope S. *et.al.*	small sample size
				X	Alm J, Lilja G. *et.al.*	recall bias
				X	Renz H, Herz U	
				X	Krishna M, Salvi S.	
Adjuvant						
Thimerosal			X		Patrizi A, Rizzoli L. *et.al.*	
Aluminum	X				Gupta R.	
	X				Vassilev T.	
	X				Vandenplas O, Delwiche J. *et.al.*	

*Possible association between the vaccine and outcome (elevated IgE / atopy / asthma)
**No association the vaccine and outcome (elevated IgE / atopy / asthma)
*** whole-cell Pertussis
**** acellular Pertussis

This research study will not analyze the possible association between the Hib and Polio vaccine and asthma. The literature review did not find existing articles which discussed the Hib vaccine and the onset of asthma, nor were there articles on Polio and asthma. For this reason the decision was made to focus on the childhood immunizations which had the strongest literature to support a possible association with asthma.

Manitoba Childhood Immunization data:

The rate of immunizations in Manitoba children is comparable to other provinces. A report from the Public Health Agency of Canada presented results of a 2002 study which indicated that 74.3% to 76.8% of Canadian children (2 years of age) had been immunized with 4 doses of Diphtheria, Pertussis and Tetanus.[42] According to a report from the Manitoba Immunization Monitoring System (MIMS) in 1995, 71.6% of 24 month olds had received 4 or more DPT/DT immunizations and 16.8% had received at least 3. However, at the same age only 50.5% of Treaty status children had received 4 or more DPT/DT immunizations.

The average percentage of children age 24 months who had received 3 or more OPV/IPV was 76.7% and 13.7% had received at least 2. Again Treaty status children had lower rates at 54.5% for 3 or more OPV/IPV. In 1995, 65.7% of the same age group of all Manitoba children had received 4 or more Hib immunizations. The average percentage of two-year olds who had fully up to date immunization records (4+ DPT/DT, 3+ OPV/IPV, and 1+ MMR) in 1995 was 68.9%.[43] These factors are important to consider for the objectives of this study and its design.

TABLE 4: Vaccines of Interest & Manitoba's Routine Immunization Schedule for Infants and Children

Age at Immunization	*Vaccines*	
	DPT/ DaPTP	*MMR*
2 months	*x*	
4 months	*x*	
6 months	*x*	
12 months		*x*
18 months	*x*	
5 years	*x**	*x***

*not required if fourth dose was given after fourth birthday.[44]
** The second dose of MMR should be given sometime between 4 and 6 years after birth.

MIMS reported the following levels of immunizations in 1995: 81.5% of 18 - month-olds had received 1 or more MMR immunization and this varied only slightly by region.[45] However, Treaty status infants had noticeably lower rates of MMR immunizations at 72.31%.

FIGURE 3: Percentage of 18 month olds given 1+ MMR vaccines by Manitoba Health Region in 1995.

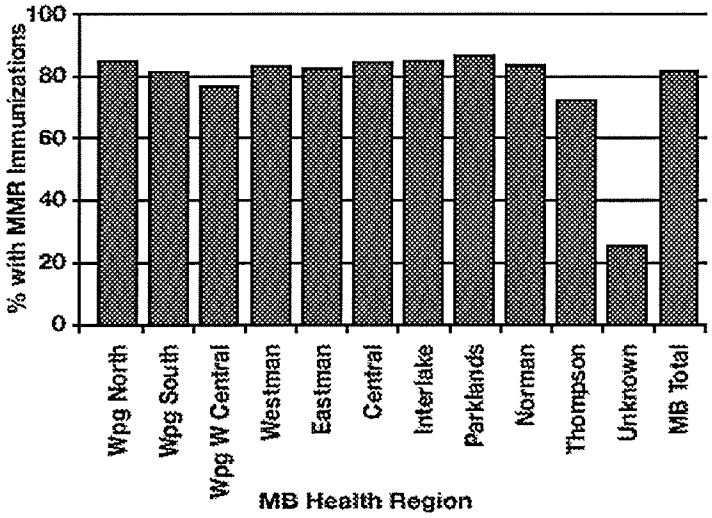
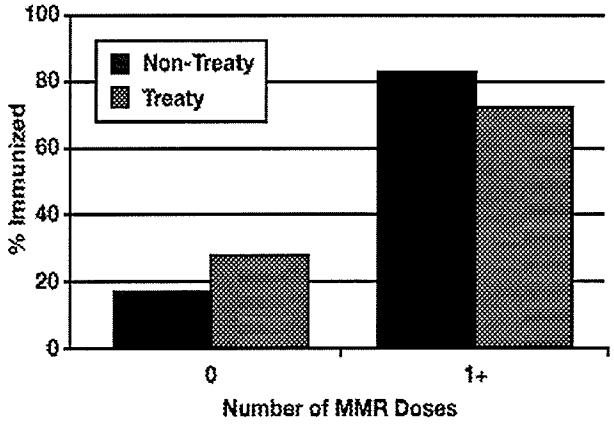
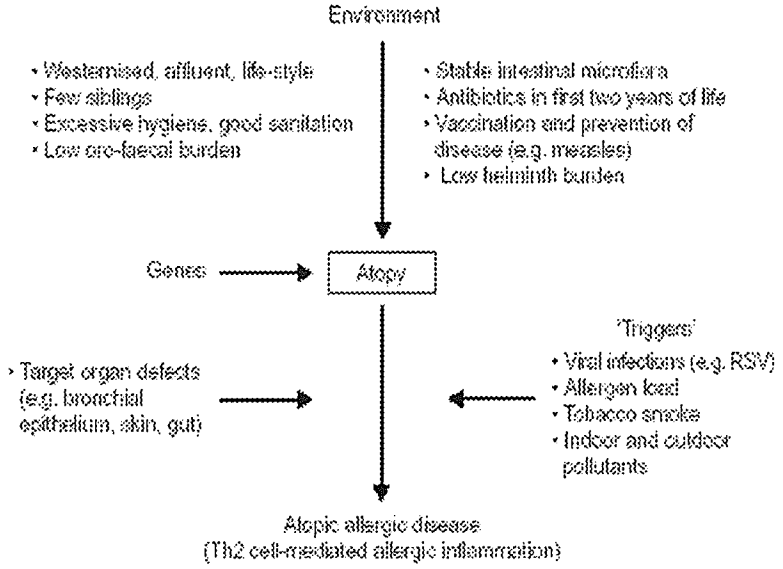


FIGURE 4: The Percentage of Treaty Status 18 month olds given 1+ MMR vaccine in 1995.



There are other factors to consider when assessing the development of asthma. It has been well established that there is often a temporal association between lower respiratory tract infections and the development of asthma.[46,47,48,49] Currently some argue that viral infections cause asthma while others believe that they trigger asthma by aggravating or exacerbating underlying imbalances.[50]

FIGURE 5: The possible influences on the development of asthma.



(Kay A, 2003)[51]

The cause of asthma, like any other disease, is multifactorial. Research suggests that some infants have a genetic predisposition to developing the disease and that as they grow their immune systems are influenced by many factors. The use of vaccinations and antibiotics may more easily trigger atopic disorders in susceptible individuals, who then may become more sensitive to their living environments whereby previously innocuous agents i.e. cat dander may now exacerbate symptoms.

There are other well documented triggers of asthma which some would also argue as having a causal association with asthma; however, they will not be directly accounted for in this study. One of these is tobacco smoke. One Canadian study reported that in 1996-97 there were 1.6 million Canadian children under the age of 12 who were exposed to tobacco smoke on a regular basis in their homes. This same study indicated that 33% of children live with a daily smoker and that 85% of these children are regularly exposed to environmental tobacco smoke (ETS).[52] Children who are exposed to tobacco smoke in their homes on a regular basis are more

likely to experience persistent or chronic asthma.[53,54] Another possible cause which has been extensively researched is house dust mite allergens and their ability to trigger and exacerbate asthma.[55]

Variables that were controlled for in this study:

As with any study there was the potential for confounding and this was taken in to consideration. One such confounder was Environmental exposure, especially for children who were exposed to tobacco smoke in their homes on a regular basis. Although an environmental assessment of those is this cohort was outside the scope of this study a proxy measure can be used. In this case socioeconomic status was used as it has been associated with tobacco smoke and other kinds of house allergens. The decision to use these independent variables was based on previous literature, which detailed their association with asthma.

Recently there has been research investigating the potential of antibiotics as a contributing factor for causing asthma.[56,57] Antibiotics as a potential confounder was accounted for in the logistic regression model used in the analyses of the data. Another influence on asthma which was partially controlled for is a genetic predisposition or susceptibility to developing asthma by accounting for whether there was a maternal history of asthma.[58]

Another potential confounder which was accounted for is that parents who have children with up to date immunizations are also likely to bring their children to their physicians more frequently. This would then lead to a higher likelihood of their children being diagnosed with asthma should it exist. It is also important to recognize that children who are consistently seen by the same physician are more likely to be diagnosed with asthma and have up to date immunizations due to the consistency of care.

Another potential confounder that was also taken into consideration was the fact that most if not all BCG vaccines in Manitoba are given to Aboriginal children in rural and northern communities.

CHAPTER 2: DEVELOPING THE THESIS

RESEARCH QUESTIONS & HYPOTHESIS:

1 – Is there an association between immunization status and incidence of asthma?

My research hypothesis is that children who have complete immunization records have a higher incidence of asthma than children who have never received an immunization or who have incomplete immunizations.

2 – Is there a difference in the incidence of asthma in children who have completed their immunizations according to the set schedule and in those who their immunizations are complete but have been delayed for one reason or another?

My research hypothesis is that children who had delayed immunizations will have a lower incidence of asthma.

3 – Is there a difference in the incidence of asthma among children who have been immunized with DPT (Diphtheria, whole cell pertussis, tetanus) as opposed to DaPTP (Diphtheria, acellular pertussis, tetanus, polio) or dT (diphtheria and tetanus) or aP (acellular pertussis)?

My research hypothesis is that the combination vaccines containing pertussis as well the acellular pertussis vaccine will be associated with an increase in the incidence of asthma compared to dT.

4 – Is there a difference in the rates of asthma between those who have been immunized with MMR and those who have not?

My research hypothesis is that the incidence of asthma will be higher among individuals who have been immunized with MMR than among those who have not been immunized with MMR.

5 – Is there a difference in the incidence of asthma between those who have been immunized with the BCG vaccine and those who have not?

My research hypothesis is that the incidence of asthma will be lower among individuals who have been immunized with BCG than among those who have not been immunized with BCG.

Although the primary objective is to analyze the outcome of asthma, the secondary objective is to asses the outcome of wheezing. The same research questions and hypothesis apply for wheezing.

RATIONALE FOR THE RESEARCH:

There is currently a debate about the possible association between immunizations and asthma. This type of research is relatively new, and little research has been performed on childhood immunizations and childhood asthma. As a result there exist limitations with many of the current published research studies which renders this particular study at somewhat of a disadvantage when it comes to referring to supporting evidence. However, the strengths of this study lie in its design and its ability to utilize health databases within Manitoba to answer several timely and very important questions. Childhood asthma is responsible for a large portion of hospital visits among children and costs Canadians hundreds of millions of dollars every year in both direct and indirect costs. Childhood asthma places a large burden of illness on society and without research to gain increased knowledge of this disease, treatment of this disease and eventually prevention of this disease will continue to be in the forefront of threats to children's health in North America and throughout the world.

CHAPTER 3: THEORY AND STRUCTURE

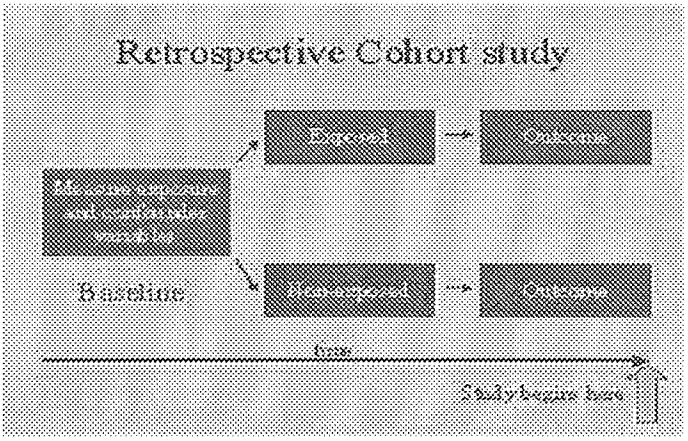
Part I – METHODS

Part II – COMPLETENESS & ACCURACY OF THE DATA

STUDY DESIGN & STUDY POPULATION:

This study was a retrospective cohort design, also known as a historical prospective study. This type of study begins at the current time and looks backward at the data and organizes it in the sequence in which the various events occurred (FIGURE 6).

FIGURE 6: A Visual model of the Retrospective Cohort Design[59]



The benefits of using a retrospective cohort design are: (1) The data already exist and researchers do not have to wait years for certain outcomes to occur, (2) The sequence of events can be determined (if the outcome came before or after the exposure(s) in question), and (3) researchers also have the opportunity to observe additional data / trends when sequencing the data that may have otherwise been overlooked.

The cohort for this study consists of all 13, 980 children who were born in Manitoba in 1995 and confirmed to still live in Manitoba in 2002. All children born in Manitoba receive a Personal Health Identification Number (PHIN) at the time of their birth. The children's PHINs can be used to link their medical histories to their vaccination records in the Manitoba Immunization Monitoring System (MIMS) program. One main benefit of a birth cohort is that

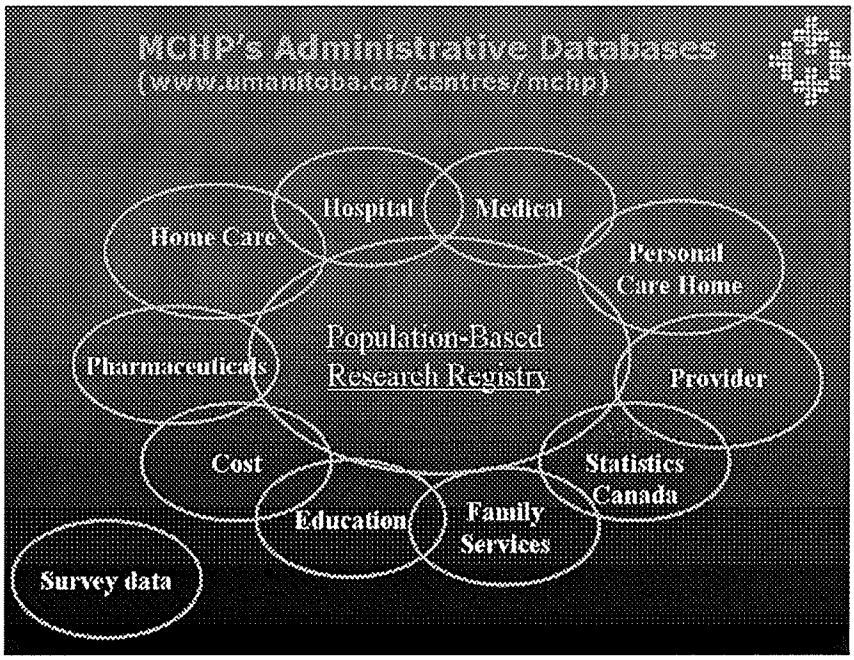
the individuals begin the study at the same place in their lives and the same point in time. Thus, their previous exposures become a non issue. The study links data from 1995 to 2002 therefore there is approximately 7 to 8 years of data for each child in the cohort. As 80% of all asthmatic children are diagnosed by the time they reach 6 years of age, this study design allows for sufficient time (7 to 8 years) to detect most of the eventual asthma outcomes in this cohort.[60]

The limitations of this study design are the following: Cohort designs do not allow for the manipulation or allocation of "exposure" to a certain event or drug; in this case the exposure is an immunization. Therefore the number of individuals who are and who are not exposed to certain immunization can vary greatly. This may result in two groups (based on exposure) where the exposed group makes up the majority or a very large percentage of the cohort. The consequence of this may result in difficulties in the analysis of the data. Another limitation of a cohort design is that people's environments can not be directly controlled for i.e. exposure to tobacco smoke. Thus, known potential confounders can only be controlled for indirectly during statistical analyses. There may also be unknown confounders (certain unknown exposure) which can also not be controlled for i.e. exposure to marijuana smoke.

DATA SOURCES:

The Manitoba Centre for Health Policy's Population Health Research Data Repository was used as the main source of data for this research study.

FIGURE A:



Note: This figure is missing MIMS data in an additional sub-circle.

The Manitoba Centre for Health Policy's (MCHP) Health Repository contains health records for all Manitoban residents. Manitoba Health anonymize the health records by scrambling the personal health identification numbers (PHIN) of each Manitoban resident in their database prior to sending the information to the MCHP Health Repository. As Manitoba has a universal health care system, Manitoba Health can record almost every medical claim, from both physicians and hospitals.

DRUG (DPIN) DATA:

The Drug Programs Information Network (DPIN) is a computer network within Manitoba that connects all retail pharmacies to a central database. Prescription information of patients / clients is transmitted by pharmacies to the network. The network is a real-time network that can calculate if and how much payment is required by the patient for eligible drug benefits. The network can then directly reimburse the pharmacy for the eligible drug costs. Payment is administered by the network for the following programs / carriers: Pharmacare (Health), Personal

Care Home Services (Health), Palliative Care Drug Access (Health), and Employment and Income Assistance (Family Services and Housing). Although not all prescriptions qualify for payment through one of the programs listed above (approximately 15%), most of these prescriptions are captured by the DPIN network through monitoring for drug/drug interactions and patient counseling.[61]

Each Manitoba resident has a drug history profile where their past and present prescription history is saved. The Drug Utilization Review (DUR) reviews all new claims entered into the DPIN system and checks for possible interactions or duplications.[62] This allows for the identification of children who have been prescribed medications used to treat and control the symptoms of asthma.

MIMS DATA:

The Manitoba Immunizations Monitoring System (MIMS) is a computerized registry of all Manitoba children and their immunization records. These records are also contained within the MCHP registry. The MIMS system was created to monitor the immunization status of children to ensure that the immunization levels would be high enough to avoid outbreaks of vaccine preventable diseases. This system also allows for the monitoring of adverse reactions related to vaccines. The system has been fully operational since January 1, 1989 but does have incomplete records of children that date back to 1980.

MIMS data is collected from: 1. direct physician billing claims 2. the manual entry of immunization record forms completed by public health nurses and 3. hospital departments for immunizations that are not billed by physicians. Immunization tariff codes from the billing claims are entered into the children's records. MIMS monitors each record at set intervals (1 year, 2 year and 6 years of age) to identify which children are behind in their immunization schedule. When this is detected a letter reminding the child's health care provider of their missed immunization(s) is mailed out. When children turn five and a half years of age their parents or legal guardians receive a notification letter of all the immunizations which the child should have

received and then states the one(s) which were either missed or MIMS has no record of the child receiving.[63]

MEDICAL & DEMOGRAPHIC DATA:

Physician and hospital claims billed to Manitoba Health were used to determine the asthma diagnosis. International Classification of Disease, 9th revision (ICD-9-CM) code specific to asthma (493) was submitted and kept on record. The population registry from Manitoba was also used to determine basic demographic information of the 1995 cohort.

Census data was also used to help compile the variables in this dataset. The MCHP created a Census Dictionary and took definitions, terms, and mathematical expressions from the 1996 and 2001 Statistics Canada Electronic Dictionary. An example of the type of information of interest for this project is Winnipeg Postal Codes to devise the various communities within Winnipeg.

The Child Health Income Quintile scale is an ecological measure that is based on dissemination areas. It was used for demographic data as well as statistical analyses and for proxy measures of living and environmental exposure such as tobacco smoke and dust mites. The scale divides the population into 5 income groups so that 20% of the population falls into each group. Urban areas are considered to be Winnipeg and Brandon while all other areas are rural. The quintiles use data from the 1996 Census to determine enumeration area (EA) level and average household income values. This information is also linked to the 1996 Manitoba population from the Manitoba population registry.[64]

INSTRUMENTATION:

SAS was the main program used to compile and analyze the data. Excel was also used to produce tables, figures, and graphs.

ETHICAL CONSIDERATIONS:

All data are in the form of computerized files derived from Manitoba Health master files. Each data record is identified by a scrambled PHIN. The data files do not contain identifiable

personal information such as name and address for individual users of health care or physicians. The analysis was conducted under the secure computing environment of the Manitoba Centre for Health Policy (MCHP). Strict security measures are in place to protect the data files (firewall, multiple passwords, encryption of information when transmitted). Destruction and/or storage of the study data was in accordance with MCHP's policies. In the published form, no data was reported with cell size <5 to ensure that identification of health care users or physicians was not possible

This study received ethics approval from both the University of Manitoba Ethics committee and Manitoba Health's Health Information Privacy Committee prior to the commencement of this research. This research project was also operating under the umbrella of a larger project on antibiotics and asthma performed by Dr. Anita Kozyrskyj and Dr. Allan Becker, both of which are a part of The New Emerging Team for asthma, a CIHR initiative.

ASTHMA & WHEEZING:

Children were considered to have asthma if they presented with a medical or hospital visit for asthma (diagnostic code of 493), or a prescription for asthma in 2002. Children were considered to have wheezing if they presented with a medical or hospital visit for asthma (diagnostic code of 493), or a prescription for asthma between 1995 to 2001 but not did not present in 2002. If children presented for the first time with asthma-like symptoms in 2002 they then fell into both the asthma definition and the wheezing definition (first presentation of symptoms).

IMPLEMENTATION of MEASURMENTS & PROGRAMS:

Due to the number of objectives, the size of the cohort and the complexity of the questions the data analysis was an evolving process that took on several variations of the same approach until the final results were obtained.

The DaPT vaccine was authorized for use in Manitoba and began to replace DPT in November of 1997. This was a major event to consider when setting up the approach for analyses

data from the 1995 birth cohort. The following is a list of the variations in the vaccines used in Manitoba from 1995 to 1997.

TABLE 5: Different Combination of Vaccines Given in Manitoba[65]

- **Combinations for 1995**
- DPT alone
- Polio alone
- Hib alone
- DPT + Polio
- DPT + Hib
- Polio + Hib
- DPT + Polio + Hib
- **Combinations for 1996**
- DPT alone
- Polio alone
- Hib alone
- DPT + Polio
- DPT + Hib
- Polio + Hib
- DPT + Polio + Hib
- DaPTP
- DaPTP + Hib
- Acellular Pertussis
- **Combinations for 1997**
- DPT alone
- Polio alone
- Hib alone
- DPT + Polio
- DPT + Hib
- Polio + Hib
- DPT + Polio + Hib
- DaPTP
- DaPTP + Hib
- Acellular Pertussis
- DaPTPHib
- ***After 1997***
- Acellular Pertussis
- DaPTPHib

Each vaccine used in Manitoba is assigned a tariff code, which is used to keep records of an individual's immunization history in the Manitoba Immunization Monitoring System (MIMS). To organize these various vaccines into groups of interest each tariff in the 1995 cohort database

was recorded and labeled. Once completed, the vaccines were grouped by type and labeled again for the analysis.

TABLE 6: Tariff Groupings

COMBINATION OF VACCINES	TARIFF CODES	SAS Name
Containing whole cell Pertussis		compdi
DPT	8601	
	8602	
	8603	
	8609	
DPT / HiB	8781	
	8782	
	8783	
	8789	
DPT / IPV	8798	
DPTP(IPV)	8921	
	8922	
	8923	
	8929	
Combination vaccines containing acellular P		compdap
DaPTP/HiB	8802	
	8804	
	8806	
	8807	
	8904	
DaPTP(IPV)	8924	
Vaccine of strictly aP		
aP	8720 aP alone	
Combination vaccines of Tetanus / Dpitheria or Polio		compdt
TdP single inactivated polio	8805	
DT	8641	
	8642	
	8643	
	8649	
dT	8651	
	8652	
	8653	
	8659	
Single vaccines of Tetanus		compt
Tetanus	8701	
	8702	
	8703	
	8709	
Single vaccines of Diptheria		compdip
Diptheria	8711	
	8712	
	8713	
	8719	

From this point, code was written to develop a SAS program that could produce different vaccine counts at various points in time. Counts for each month after birth until approximately 7.5 years of age were established and recorded. Demographic data was analyzed and mapped out for geographical presentation of the data.

CREATING VARIABLES FOR SAS PROGRAMS:

As SAS was the main tool used to form and analyze the database the following explains the purpose of several of the main SAS programs. There are two programs in Appendix B which were used to extract the children who had Wheezing and Asthma. After this was completed further analyses was possible. It was important to develop permanent variables for the various vaccines to include to the database to help simplify analyses. Program 2 demonstrates how variables were created for DPT and DaPT at different periods in time. Program 6 demonstrates how the number of new Asthma cases per month was determined. These variables (Jan1995 Feb1995 etc.) could then be used in other programs.

Programs 8 and 9 show how the (asthma3m1sbfa = **asthma** determined at **3 m**onths after birth were the child had **1** vaccine **b**efore he developed **a**sthma) type variables were created. Two existing variables of asthma and immunization were combined to create a new variable. The exact date of the X immunization was then determined. From there the children who fell into the new variable (asthma3m1) were further tested to see if their asthma date (first incidence) came before or after their immunization date. Then the variable of (asthma3m1sbfa) could be given a value of 1 or 0.

There were many instances where it was important to determine which event came first. For example, Program 10 determines how many children were immunized with DT before they received a DPT vaccine. This program could then be altered to fit the question of how many children were immunized with DaPT before DPT or how many children were immunized with MMR before DPT.

The logistic regression model was chosen because it was the most appropriate method to analyze the data. The goal of the research questions was to test the outcome variables of Asthma / Wheezing in a binary manner (Yes or No) and the logistic regression was able to do this. There were relatively few children in this cohort who were not immunized and as a result there was low power. By focusing on the adjusted odds ratios the magnitude of effect (vaccines) could be established and the 95%CL indicated the effect size and whether or not it was statistically significant.

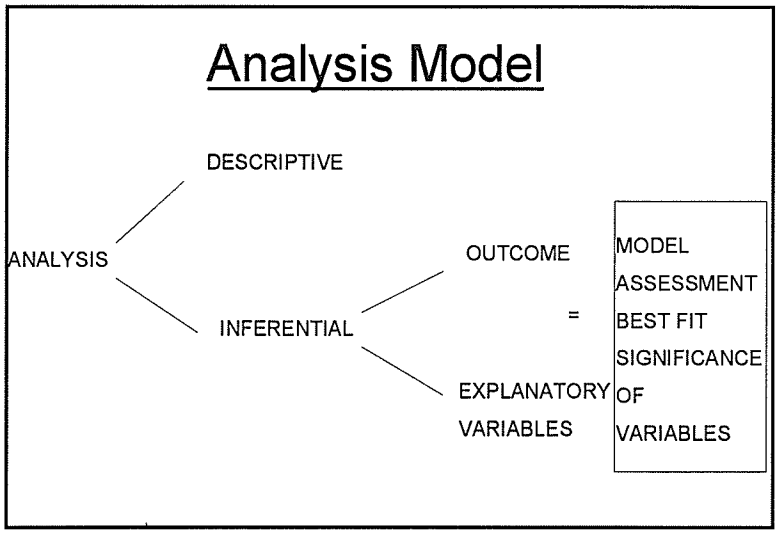
Independent variables could be included into the logistic regression model as either categorical or continuous variables. This model assumed that there was a linear association between the log of the odds ratios and each independent variable in the model.

Program 11 demonstrates how the variables were categorized and entered into the Logistic Model. By simply changing the outcome variable from Asthma to Wheeze (Wheezing) the two different groups were tested. The vaccine type was easily changed by adding the new independent variable to the model and removing the old one.

METHODS BEHIND EACH OBJECTIVE:

By using the programs discussed as well as many others, all of the objectives were met. The approach or methods to answer Objective one *"Is there an association between immunization status and incidence of asthma?"* was to begin by looking at the big picture: children who had had no DPT or DaPT immunizations, those who were incomplete in their DPT and DaPT immunizations, those who were complete, those who had more than required by the Canadian Immunization Schedule. Chi-square and unadjusted Odds Ratios were computed. Logistic regression analysis was undertaken.

FIGURE 7: THE ANALYSIS MODEL



To further analyze the data, immunization status was assessed by Regional Health Authority. Then the frequency with which children in the various immunization categories visited or consulted physicians was also assessed. The variations within Winnipeg communities were also assessed. Another point which was investigated was how many children within each of the Winnipeg communities come from low income homes and whether that affected immunization or Asthma rates.

This objective focused on DPT and DaPT vaccines only because of the other vaccines of concern MMR and BCG almost all the children had received at least 1 MMR vaccine and very few (relatively) received a BCG vaccine. It was important to assess DPT and DaPT alone because it was required to have multiple doses over a specific time period. This approach made the analyses possible and its findings more specific.

The research question 2 *"Is there a difference in the incidence of asthma in children who have completed their immunizations according to the set schedule and in those who their immunizations are complete but have been delayed for one reason or another?"* began by presenting all of the various (on schedule and delayed) immunization combinations possible in this cohort. Then next step was the statistical analyses, followed by further categorization of children who belonged to specific groups such as, those who had their first DPT vaccination delayed, then those children who had their second DPT vaccine delayed. For question 2 MMR was analyzed by itself and presented in the chapter on MMR.

The third research question looked at whether there was a difference in the incidence of asthma in children who were immunized with DPT / DaPT / DT and aP. The approach for this chapter was to analyze the differences in the number of children who received DT the number of doses of DT and DT in combination with DPT and DaPT. As the majority of children who received a DT vaccine also had had a DPT or DaPT or all, it was important to thoroughly investigate these various combinations. Isolated vaccines were also analyzed; however, the number of children who had only received DaPT versus DPT was relatively few.

The approach for research objective 4 for MMR was very similar to the approach for the other types of vaccines. The statistical and demographic analyses were once again performed. Research objective 5 turned out to be somewhat disappointing as the data necessary to perform an in depth analysis was not accessible due to ethical guidelines i.e. the data on first nations children within the province. However, a basic analysis of some interest could still be performed.

CHAPTER 3:

Part II: THE COMPLETENESS & ACCURACY OF THE DATA SOURCE

Overall the childhood asthma / immunization database was very complete and highly accurate as the data was mainly from Manitoba Health. As Manitoba Health is the only provider of health insurance the majority of Manitobans will receive medical care that will be billed to Manitoba Health, with the exception of First Nations people who live on reserves. The ability of the data to answer or account for all of the objectives outlined in the thesis proposal was limited when it came to information concerning the ethnic status of the individuals who received a BCG immunization. Logical reasoning suggests that these children were most likely First Nations children; however, this could not be confirmed due to ethical restrictions or guidelines concerning use of data involving First Nations people for research.

The immunization data (MIMS) and the medical data on First Nations children throughout Manitoba may also be inaccurate. The fact that Health Canada's First Nation Inuit Health Branch is responsible for children living on First Nations communities means that the provincial health data for these children may not be complete. As a result a lack or gaps in data may significantly contribute to the lower immunization and asthma rates amongst several of the northern and rural communities within Manitoba.

Another limitation of this database was using low income as a proxy measure for smoking. Unfortunately the real exposure to tobacco smoke could not be measured or accounted for directly by a variable in this database. Living in a low income household is associated with an increased likelihood of being exposed to tobacco smoke.

CHAPTER 4: STATISTICAL ANALYSES & DESIGN

As previously mentioned the Logistic Regression model was chosen based on the study design and the research questions posed. The outcome variables of interest were Asthma and Wheezing, whereby the variables were binary i.e. Yes or No. The base model included both dichotomous and categorical independent variables (gender, maternal history of asthma, income, region, antibiotic use in the first year of life, the number of medical consults in the first 7 years of life). These variables were chosen based on previous literature and their known association with asthma and wheezing.

The exact model was chosen based on model fit statistics, the association of predicted probabilities and observed responses, 95% confidence limits, and Asymptotic Tests (ASE). The Hosmer and Lemeshow was also used and is another "Goodness of Fit Test". This is a goodness of fit test that divides the data into approximately ten groups of the same size where the observations are sorted in increasing order of their estimated probability of having an event outcome. The Pearson chi-square statistic summarizes the differences between the observed and expected number of observations. The Pearson chi-square statistic is compared to a chi-square distribution. Large Hosmer and Lemeshow Chi-square values and small p-values indicate a lack of fit of the model.

However, before the final model was chosen the issue of collinearity had to be ruled out. Collinearity occurs when variables are so highly correlated that it becomes very difficult to establish reliable estimates of their individual regression coefficients and the degree to which they are predictors of the model. When variables are perfectly collinear the R2 value is 1.[66] For this model "Medical Consults" and "Antibiotic use" were tested for collinearity. As they did not demonstrate collinearity they were both included into the model.

NOTE: The following page describes some of the statistical measures used to choose the final model

Model Fit Statistics:

Akaike Information Criterion (AIC): is an adjustment to the -2LOG L score and is based on the number of explanatory variables in the model and the number of observations used. AIC is a goodness-of-fit measure whereby a lower value indicates a superior model, which can then be compared to other models.

Schwartz Criterion (SC): is also an adjustment to -2LOG L based on the number of explanatory variables in the model and the number of observations used. SC is a goodness-of-fit measure whereby a lower value indicates a superior model, which can then be compared to other models.

Likelihood Ratio: has a chi-square distribution under the null hypothesis that all regression coefficients of the model are zero. This prints out the chi-square value, the degrees of freedom, and the *p*-value statistic whereby less than .05 is significant.

Score: This has an asymptotic chi-square distribution under the null hypothesis and the procedure prints out the chi-square value, the degrees of freedom and the p-value.

Wald Chi-Square: is obtained by dividing the parameter estimate by its standard error.

Association of Predicted Probabilities and Observed Responses:

Measures of ordinal association asses weather Y increases with X. Using the Proc Freq procedure with SAS this is defined by Somer's D, gamma, Tau-a and c. Thus, larger values indicate a closer or better association.

Gamma: only includes concordant and discordant pairs and ignores tied pairs. It is also only appropriate when both variables lie on an ordinal scale.

Stuart's Tau-*b*: Is also only appropriate when both variables lie on an ordinal scale (-1 =< Tc =< +1).

Somers'D: Here X is viewed as the independent variable and Y is viewed as the dependent variable. These classify pairs of observations as **concordant** or **discordant**. If the pair with the

larger X value also has a larger Y value the pair is **concordant.** If the pair with the larger X value has a smaller Y value the pair is **discordant**.

Confidence limits:

For the confidence limits *a* is automatically set to 0.05 as to produce the 95% confidence limits.

Asymptotic Tests (ASE):

The ASE is the asymptotic standard error of the estimate

THE FINAL LOGISTIC REGRSSION MODEL:

The final model used the same independent variables; however, they were organized or categorized into a different order to better represent the distribution of the cohort within each section.

The Medical consults were categorized as follows:

```
if 0 <=consults<= 35 then
md= '1';
else if 36 <=consults<= 49 then
md = '2';
else if 50 <=consults<= 66 then
md = '3';
else if 67 <=consults<= 151 then
md = '4';
else if 152 <=consults<= 459 then
md = '5';
run;
```

Region or area of residence was categorized the same as before. If the children who lived in Winnipeg or Brandon are considered Urban and all other areas are considered Rural.

Prescriptions (Rx) were categorized as follows:

Children who had 0 prescriptions were Rx group 1
Children who had between 1 to 3 prescriptions were Rx group2
Children who had between 4 to 11 prescriptions were Rx group3
Children who had between 12 to 40 prescriptions were Rx group4

Gender was also numbered the same as before – males were Gender = 1 and females were Gender = 0.

Maternal History of Asthma was coded as – children with a history of maternal asthma (Mom hx = 1) and children with no history of maternal asthma (Mom hx = 0).

Income was grouped into to groups Low income = 1 (if the children's Child Health Income Quintile was either R1 or U1) otherwise the children belonged to Low income = 0.

The different independent variables were put into a Logistic Regression with either dependent variable of (Asthma or Wheeze).

```
proc logistic data= children order=data;
class Rx md;
model Asthma=Rx md Urban gender hx lowincome;
run;
```

The different types of vaccines and groupings were tested by adding them to the SAS code above.

CHAPTER 5: Operational Definitions & Main Variables of Interest

Operational Definitions:

The main "outcome" of interest was asthma and the DPIN database allowed for the assessment of prescription records pertaining to asthma such as, inhaled beta – agonists (salbutamol, fenoterol) and a maintenance drug such as, an inhaled corticosteroids (beclomethasone, budesonide, fluticasone) or an oral corticosteroid was used to draw possible correlations. The ICD-9 code of 493 for asthma was also used to identify cases from medical and hospital data.

Independent variables were included into the database as either categorical or continuous variables. Gender was included as a binary variable where male = 1 and female = 0. Age was defined as the number of days or months after birth. This varied with the research questions and what information was necessary to answer the research questions. The number of antibiotic prescriptions each child had in their first year of life was originally included as a continuous variable and was then modified in to a categorical variable for the sake of analysis. The same method was used to create the "medical consults" variables (the number of physician claims per child from birth until ~ 7 years of age). Maternal history of asthma was included into the database as a binary variable of yes or no, based on her medical and prescription history.

Each vaccine type was grouped together based on their components and tariff codes were used to isolate them from the children's immunization histories. The exact method varied per research objective; however, the underlying principle remained the same.

TABLE 7: Summary of Measures

Measures	Operational definition	Data sources
CHILD		
Independent		
Age and gender		MHSIP registry
Vaccination history	All routine childhood immunizations and BCG	MIMS
Antibiotics	antibiotics prescribed in the 1st year of life	DPIN
Child's utilization history	number of physician visits	Physician claims
Parent history of asthma	have been diagnosed and treated for asthma	DPIN, Physician & Hospital claims
Dependent		
Asthma	have been diagnosed and treated for asthma	DPIN, Physician & Hospital claims
GEOGRAPHIC		
Independent		
Income quintiles	proxy measure for household environmental exposure	Census data

MAIN VARAIABLES OF INTEREST:

This project uses two asthma definitions as the dependent variables of interest. The following are the definitions:

Abbreviated Definition:

Asthma at age 7: children with health care visits or prescriptions for asthma in 2002 – includes children meeting this definition in any year (1995 to 2001) from time of birth or presenting for the first time in 2002.

Ever wheeze (Wheezing): children with health care visits or prescriptions for asthma in any year from 1995 to 2002 – includes children meeting this definition in any year from 1995 to 2001, but not in 2002. This category is called ever wheeze because the asthma definition was not validated under the age of 7 years.

Note: Children who presented with symptoms for the first time in 2002 were included in both definitions (Asthma and Wheezing).

Complete Definition:

A child is defined as having asthma if the criteria for the diagnosis-based OR the prescription-based definitions are met. The diagnosis-based definition is at least one hospitalization (primary diagnosis) or physician visit over one year for asthma (ICD-9-CM=493: Asthma). The prescription-based definition is at least one prescription over one year for an asthma drug: bronchodilators (BR_INH, BR_ORL, BL_INH), inhaled corticosteroids (ST_INH), non-steroidal anti-inflammatory drugs/ leukotriene receptor antagonists (PR_INH, PR_ORL), identified by generic or trade name. Oral corticosteroids (ST_ORL) are excluded from the prescription-based definition.

Asthma has been defined as children who had asthma sometime between 1995 -2001 and again in 2002 or for the first time in 2002. Wheezing has been defined as children who had asthma between the years of 1995 to 2002 only. Wheezing includes children with Asthma (Ashtma02). View FIGURE 14 for help with this definition.

Independent variables used in statistical analyses:

Medical Consults (MD):

The physician visits counted were limited to those which have a prefix which was equal to '7' (which are 'calls, special tests'). Medical Consults also included any hospitalization for the child (from birth to 7 years old).

The medical consults variable used in the SAS programs was defined as follows:

(0 to 35 medical consults) = MD 1

(36 to 49 medical consults) = MD 2

(50 to 66 medical consults) = MD 3

(67 to 151 medical consults) = MD 4

(152 to 459 medical consults) = MD 5

These categories were chosen based on the distribution of 25%, 50%, 75% and higher. This way each category was more evenly weighted (in terms of n / size). The group of (0 to 35 medical

consults) was used as the reference category because it is more likely that children would have fewer medical consults than many (152 to 459 medical consults) by 7 years of age.

Region:

From Child Health Income Quintiles (U1, U2, U3, U4, U5) = Urban

All other fall into Rural

Antibiotic Prescriptions in the First Year of Life (Rx):

The antibiotic prescriptions were a count of all the antibiotic prescriptions dispensed to the child during their first year of life. The prescriptions were selected from the database based on the generic name of the drug on the prescription.

The prescription variable used in the SAS programs was defined as follows:

0 prescriptions = Rx 1

1 to 3 prescriptions = Rx 2

4 to 11 prescriptions = Rx 3

12 to 40 prescriptions = Rx 4

As with the medical consults, the prescriptions were grouped based on the distribution of the number of children with X prescriptions (25%, 50%, 75% and higher). The first group of 0 prescriptions was used as the reference category because children are more likely to have had no antibiotic prescriptions in their first year of life then 12 to 40 prescriptions.

Gender:

Male = gender 1

Female = gender 0

Maternal History of Asthma (Mom hx):

Maternal Asthma was determined over the 2001/02 fiscal year (the DPIN prescriptions, hospitalizations, and physician visits that occurred in 2001/02 only).

Asthma was defined if the criteria for either the diagnosis-based OR the prescription-based definitions were met.

The diagnosis-based definition was:

1. At least one hospitalization (primary diagnosis) or physician visit over one year for asthma (ICD-9-CM=493: Asthma) or…
2. At least one hospitalization (primary diagnosis) or physician visit over one year for asthma-like diagnoses, (ICD-9-CM=464: Acute laryngitis and tracheitis, 466: Acute bronchitis and bronchiolitis, 490: Bronchitis, not specified as acute or chronic, 491: Chronic bronchitis) in conjunction with at least one prescription for an asthma drug: bronchodilators (BR_INH, BR_ORL, BL_INH), corticosteroids (ST_INH, ST_ORL), non-steroidal anti-inflammatory drugs/ leukotriene receptor antagonists (PR_INH, PR_ORL), identified by generic or trade name.

   The prescription-based definition is at least one prescription over one year for an asthma drug: bronchodilators (BR_INH, BR_ORL, BL_INH), corticosteroids (ST_INH), non-steroidal anti-inflammatory drugs/ leukotriene receptor antagonists (PR_INH, PR_ORL), identified by generic or trade name. Oral corticosteroids (ST_ORL) are excluded from the prescription-based definition.

The maternal history of asthma variable used in the SAS programs is defined as follows:

A maternal history of asthma = Mom hx 1

No maternal history of asthma = Mom hx 0

Family Income (lowincome):

Children from low-income family homes are indicated by grouping R1 and U1 from the Child Health Income Quintile Scale so that (lowincome = 1) and all else is (lowincome = 0, indicating children are not from low-income households

CHAPTER 6: DESCRIPTIVE DATA & DATA ANALYSIS

PART I: REGIONAL DISTRIBUTION OF ASTHMA & WHEEZING

TABLE 8: The Asthma distribution across the Regional Health Authorities of Manitoba

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
Asthma02													
No	1172	447	612	810	330	402	998	27	453	379	305	6444	12379
Yes	110	47	68	97	24	44	47	2	48	16	28	1038	1569
Rate	8.58	9.51	10	10.69	6.78	9.87	4.5	6.9	9.58	4.05	8.41	13.87	11.25*
Overall**	7.01	3	4.33	6.18	1.53	2.8	3	0.13	3.06	1.02	1.78	66.16	100

Note: Asthma02 = Asthma

The distribution of Asthma varies considerably across the province. Winnipeg has the highest rate of Asthma at 11.25% and Marquette with the lowest at 4.05%. It is commonly thought that children who reside in urban environments have higher asthma rates than children who live in rural homes. Although this is true statistically on the larger scale, on a smaller scale there are variations in this theory as Brandon, which is considered urban, has an Asthma rate of 9.58% and Parkland and the Interlake have Asthma rates of 9.87% and 10.69%. Because this study itself does not have primary environmental data, it is difficult to conclude at this stage what may be the cause of this variation.

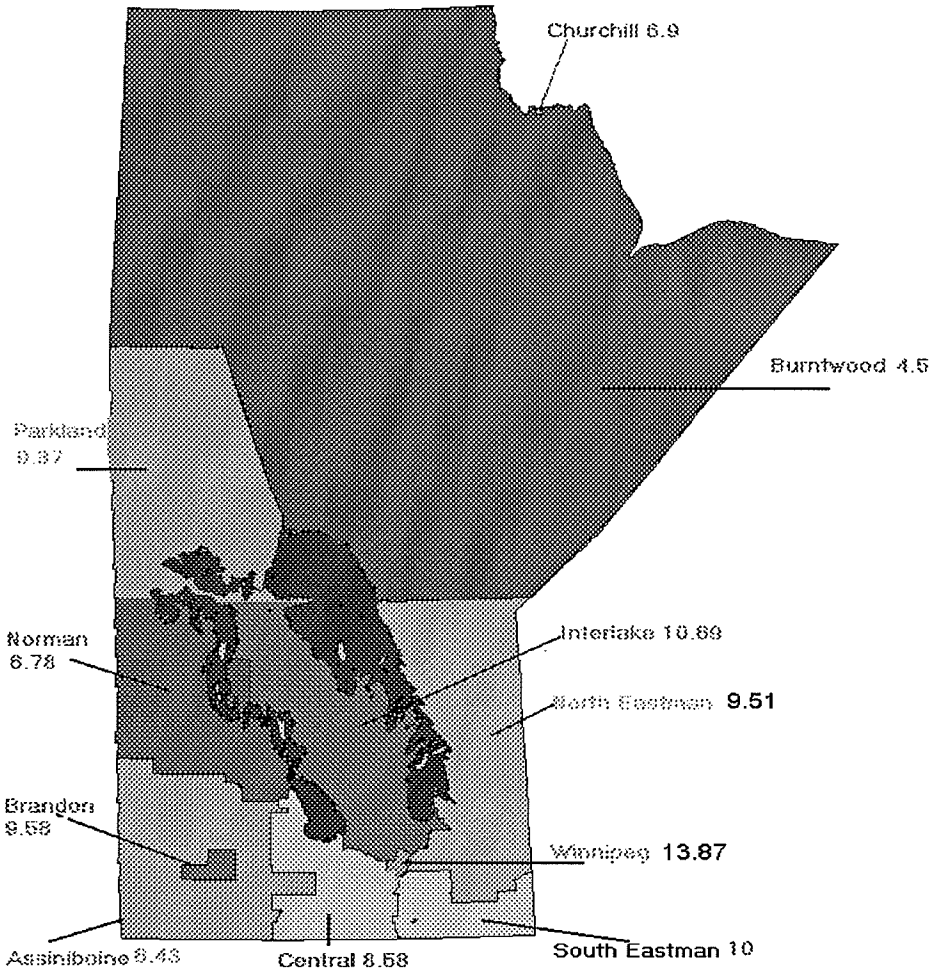
TABLE 9: The Wheezing distribution across the Regional Health Authorities of Manitoba

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
Asthma95													
No	861	281	449	493	215	261	716	16	302	261	219	3976	8050
Yes	421	213	231	414	139	185	329	13	199	134	114	3506	5898
Rate	32.84	43.12	33.97	45.64	39.27	41.48	31.48	44.83	39.72	33.92	34.23	46.86	42.29*
Overall**	7.14	3.61	3.92	7.02	2.36	3.14	5.58	0.22	3.37	2.27	1.93	59.44	100

Note: Asthma95 = Wheezing

The Wheezing rates are high across the province but there are still variations from one RHA to another. Winnipeg has the highest rate at 46.86%, the Interlake has the second highest rate at

FIGURE 8: The Asthma Rate Distribution by Regional Health Authority



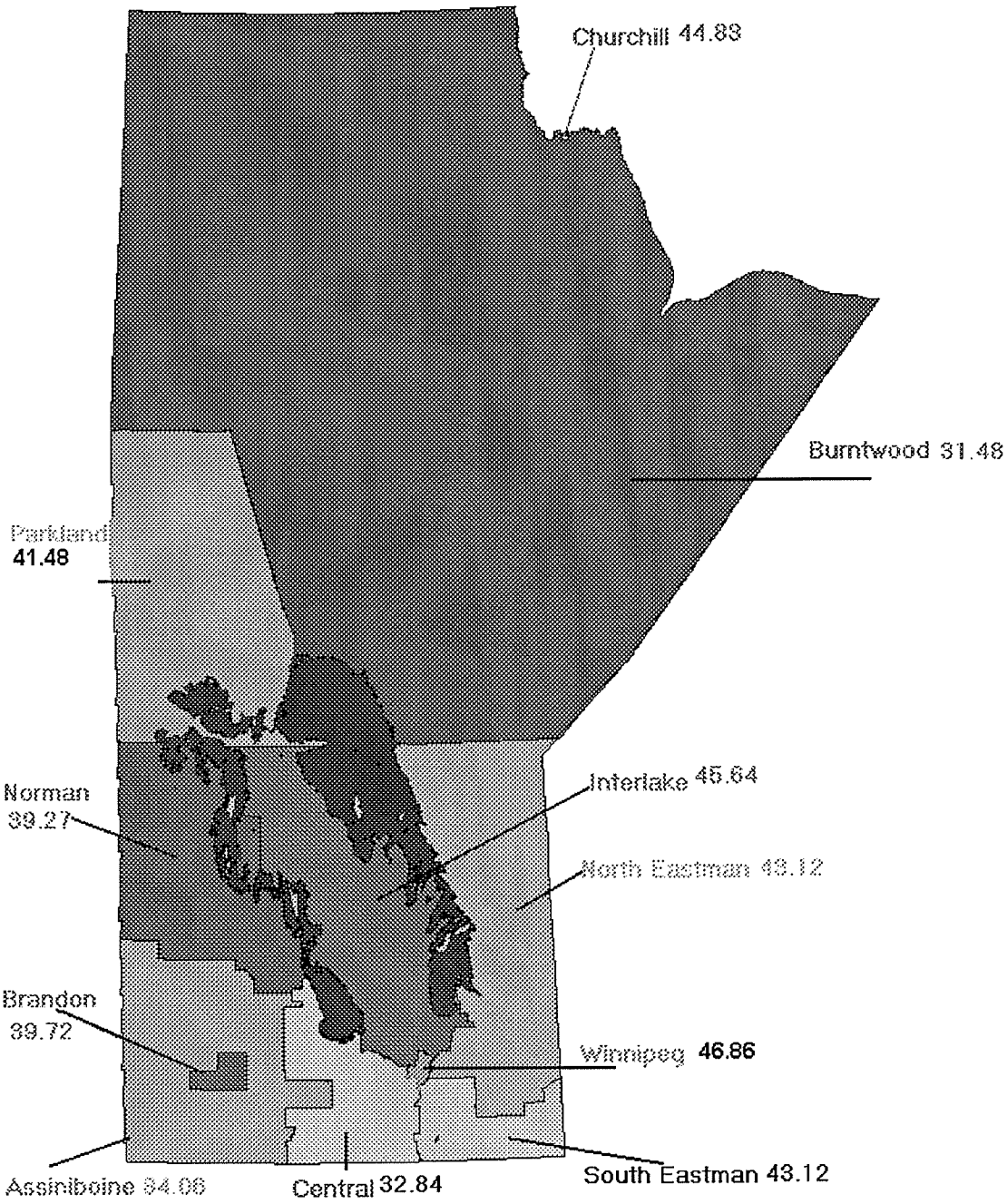
Note: RHA's Marquette and South Westman were combined to form Assiniboine.

Winnipeg has the highest Asthma rate at 13.87% and the former Marquette RHA with the lowest rate at 4.05%. It is typical to observe increased asthma rates in urban regions and therefore the higher Asthma rate in Winnipeg is expected; however, Brandon is also considered to be an urban center and its rate is much lower at 9.58%. Both Winnipeg and Brandon are combined to form the urban variable, which then has an Asthma rate of 13.6%. Winnipeg has a much larger N than Brandon and thus has a greater influence on the overall rate. Alone Brandon does not demonstrate what would be expected of an urban region with respect to the Asthma rate.

The following FIGURE indicates the Wheezing rates are much higher overall than the Asthma rates. Burntwood has a Wheezing rate of 31.48% compared to the provincial average of 42.29%. This indicates that 31.48% of the children who were born in 1995 and who live in Burntwood were at some point diagnosed to have asthma-like symptoms. The Burntwood Wheezing rate is the lowest in the province but only by about 2%. This indicates that when compared to other rural regions like Marquette, South Eastman and Central – Burntwood has very similar Wheezing rates, suggesting that Burntwood's access to health care professionals is similar to other rural regions.

Winnipeg has the highest Wheezing rate (46.86%) compared to the provincial average of 42.29% and the other RHA's on an individual basis. The Interlake again came in second with a Wheezing rate of 45.64%, also above the provincial average. Brandon
did not have the lowest Wheezing rate but it was not in the high end as would be expected of an urban region.

FIGURE 9: The Wheezing Rate Distribution by Regional Health Authority



The variability that was seen across the province with Asthma is also seen with Wheezing, although overall Wheezing has much higher rates.

TABLE 10: Asthma rates in Urban vs. Rural regions

REGION			
	Asthma		
	No	Yes	Total
Rural	5512	485	5997
	91.91%	8.09%	42.99%
Urban	6869	1084	7953
	86.37%	13.63%	57.01%
Total	12381	1569	13950
	88.75%	11.25%	100%

When Asthma data was grouped between Rural and Urban there is a relatively large difference in rates. Rural has an Asthma rate of 8.09% and Urban has an Asthma rate of 13.63% (a difference of 5.54%). A Chi-square test of this data confirms that there is a significant difference between the Asthma rate in the two regions – a Chi-square value of 105.2212 with 1 degree of freedom with a probability of <.0001. This result is to be expected as this is what current and past literature of the difference in asthma rates by region also indicates.

TABLE 11: Wheezing rates in Urban vs. Rural regions

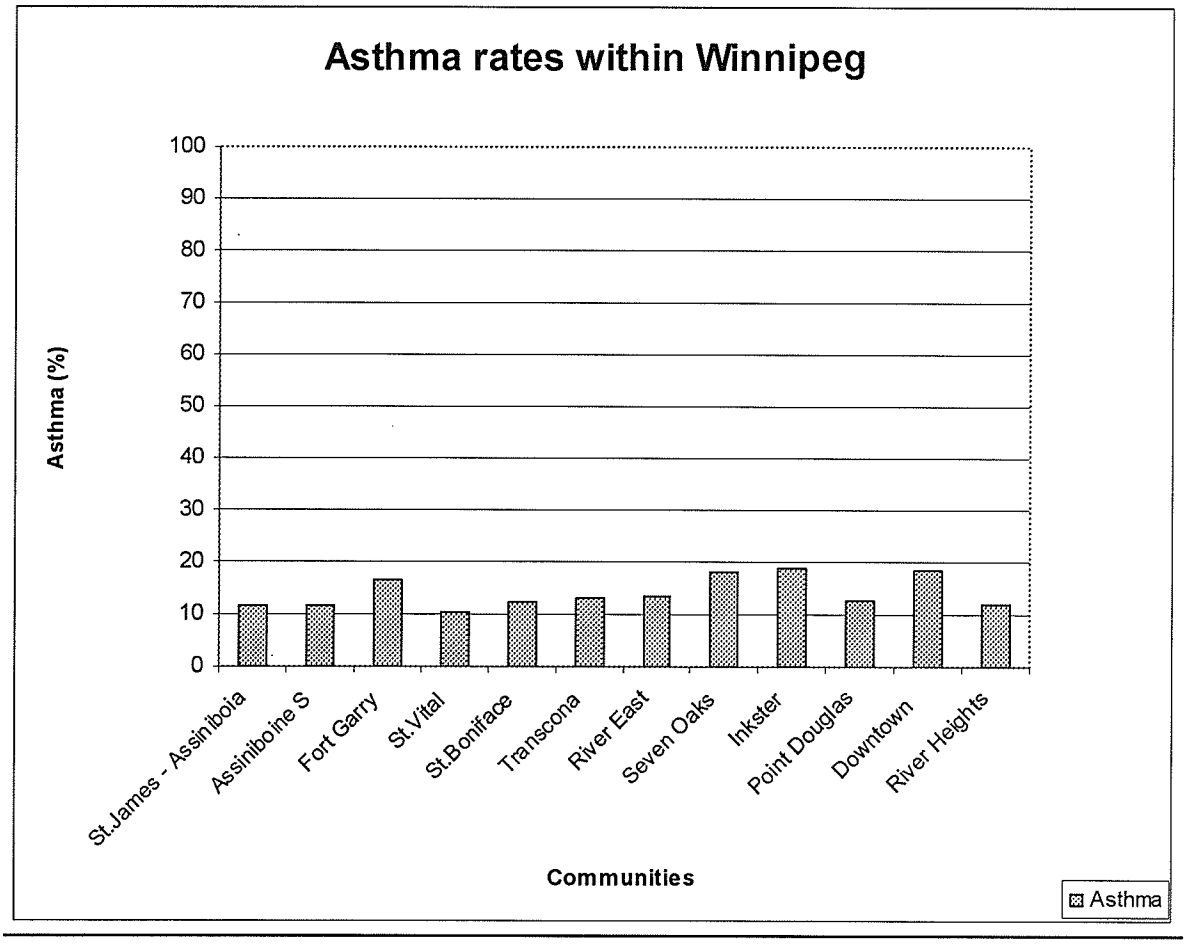
REGION			
	Wheezing		
	No	Yes	Total
Rural	3791	2206	5997
	63.21%	36.79%	42.99%
Urban	4261	3692	7953
	53.58%	46.42%	57.01%
Total	8052	5898	13950
	57.72%	42.28%	100%

The difference in the Wheezing rate is even more obvious than it was for Asthma. Rural has a Wheezing rate of 36.79% and Urban has a Wheezing rate of 46.42% (a difference of 9.63%). A Chi-square test of this data confirms that there is a significant difference between the Wheezing

rate in the two regions – a Chi-square value of 130.1293 with 1 degree of freedom with a probability of <.0001.

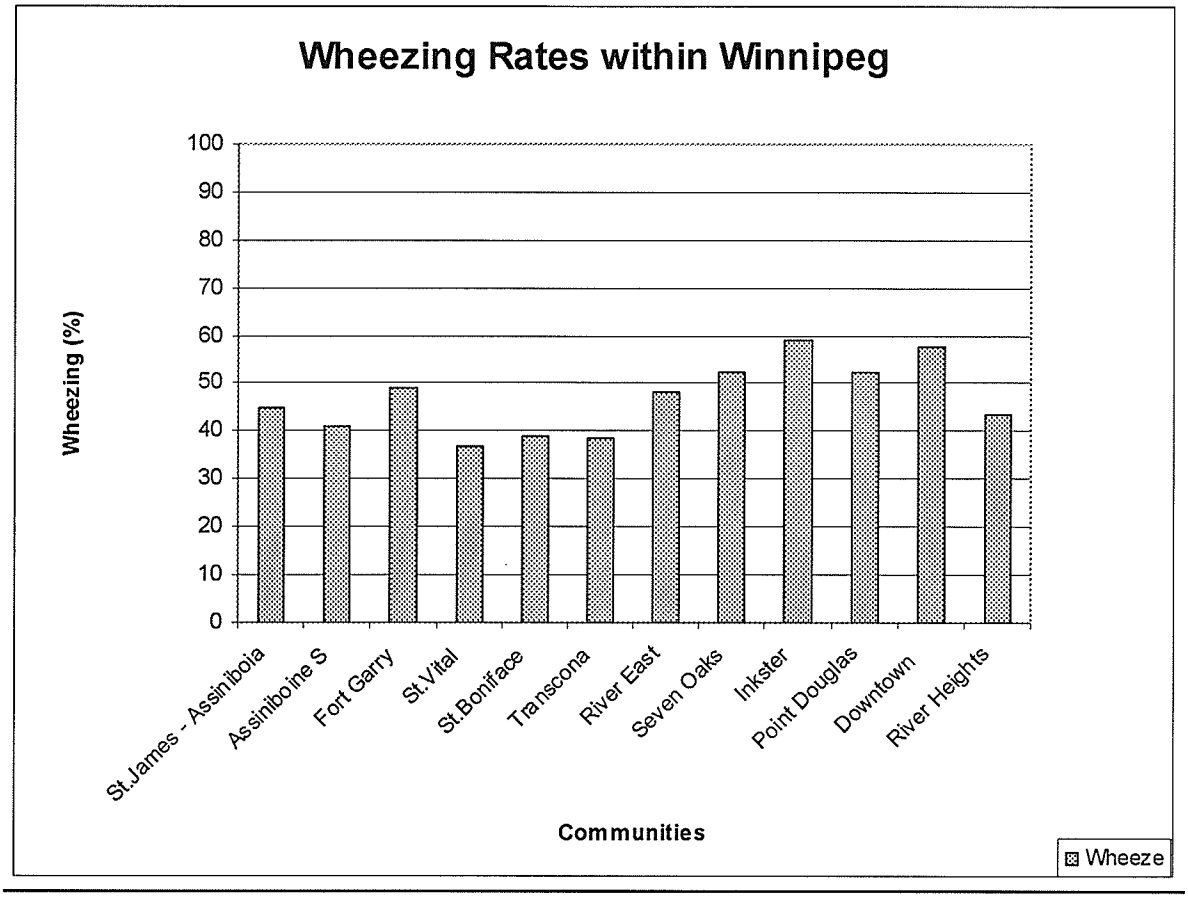
Although there is a difference in the number of children who reside in Urban and Rural areas of Manitoba, with a little over 14% more children in Urban settings, there are still significantly more children with Asthma and Wheezing in Urban areas than would be expected in Rural areas if there were no difference in geography and asthma.

FIGURE 10:



The Asthma rates within Winnipeg vary from a high of just under 20% in Seven Oaks, Inkster and Downtown to a low of around 10% in St.Vital.

FIGURE 11:



Wheezing rates vary across Winnipeg with very high rates found in Inkster and Downtown to lower rates in St.Vital and St.Boniface.

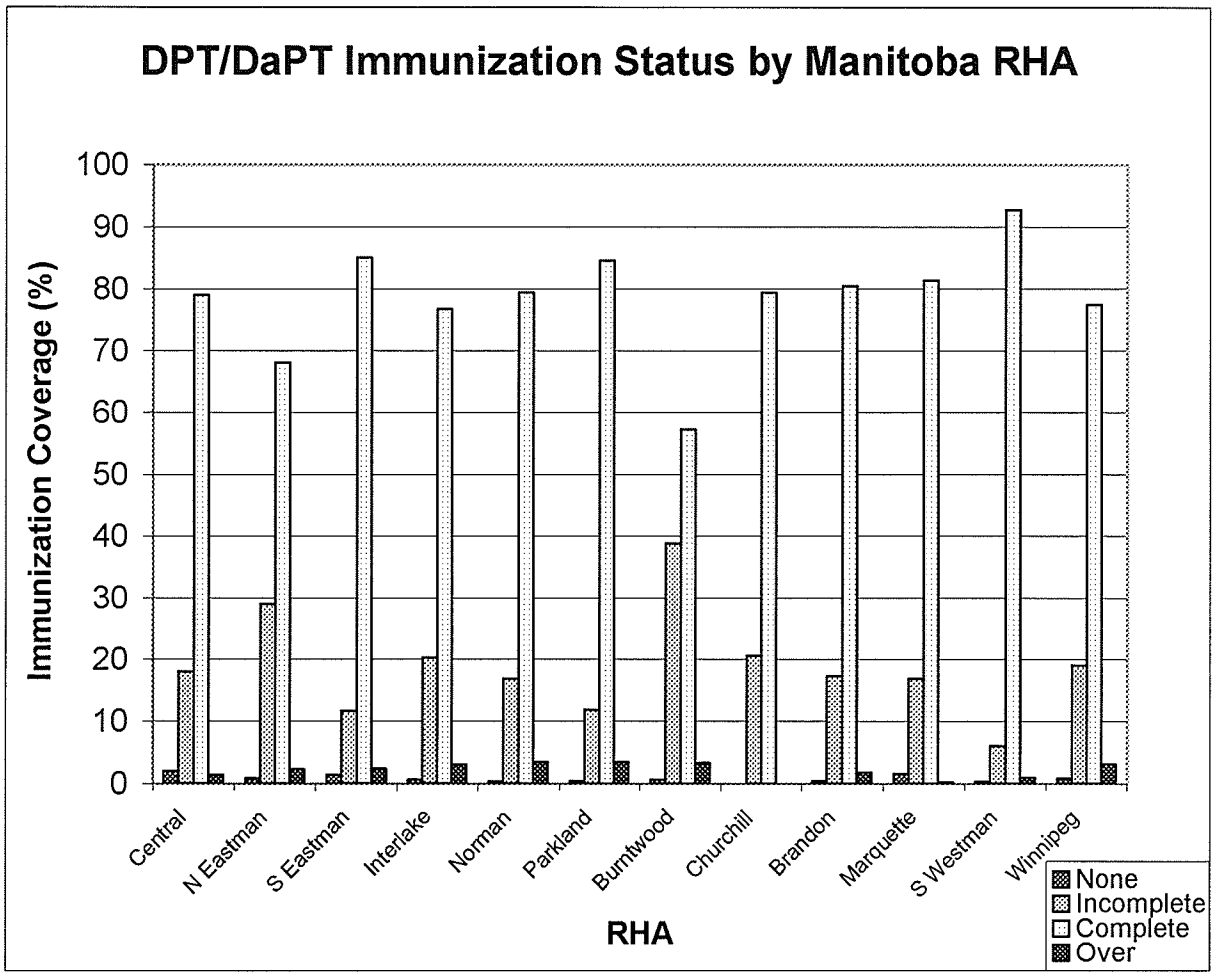
Although there are variations across the province, the two FIGUREs above demonstrate the variation in both Asthma and Wheezing within the Winnipeg.

Note: The exact values for Asthma and Wheezing Rates within Winnipeg can be found in Appendix III.

PART II: THE REGIONAL DISTRIBUTION OF IMMUNIZATIONS

Tables with the exact values can be found in Appendix III.

FIGURE 12:



Note: Immunization categories are as follows: None = 0, Incomplete = 1 to 4 doses, Complete = 5 doses, Over = 6 + doses.

South Westman has Complete DPT immunization status of over 90% while Burntwood has an Incomplete DPT immunization status of close to 40%. North Eastman takes second place for Incomplete DPT immunizations with a rate of close to 30%. The other RHA's have 20% or lower for incomplete DPT immunizations.

FIGURE 13:

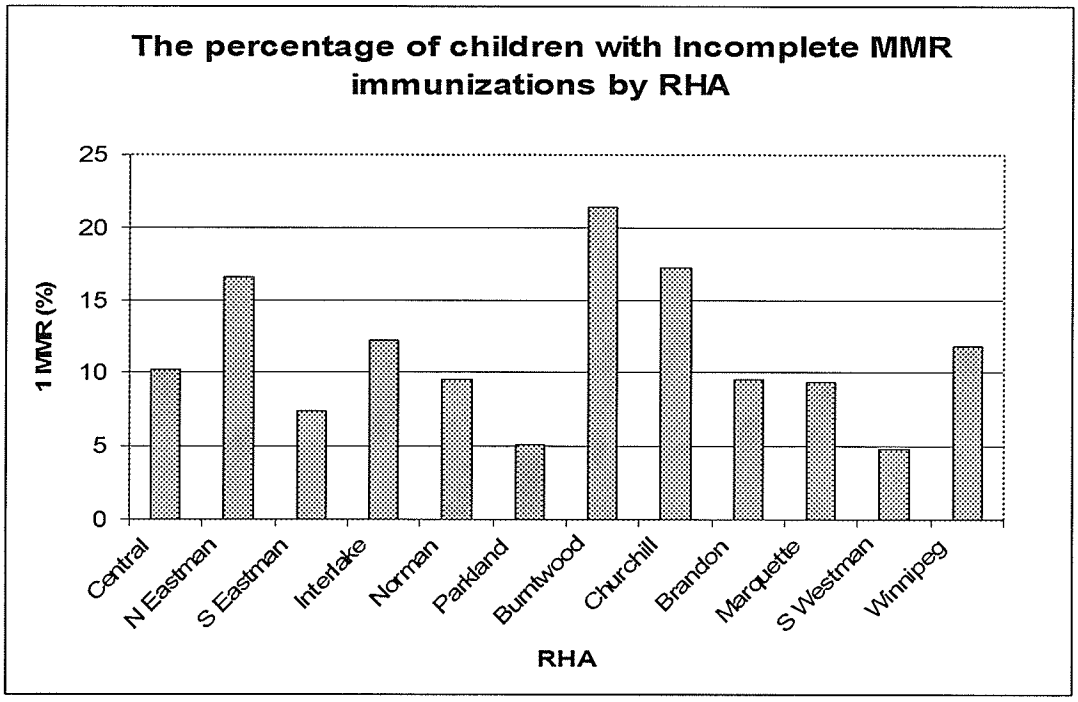


FIGURE 14:

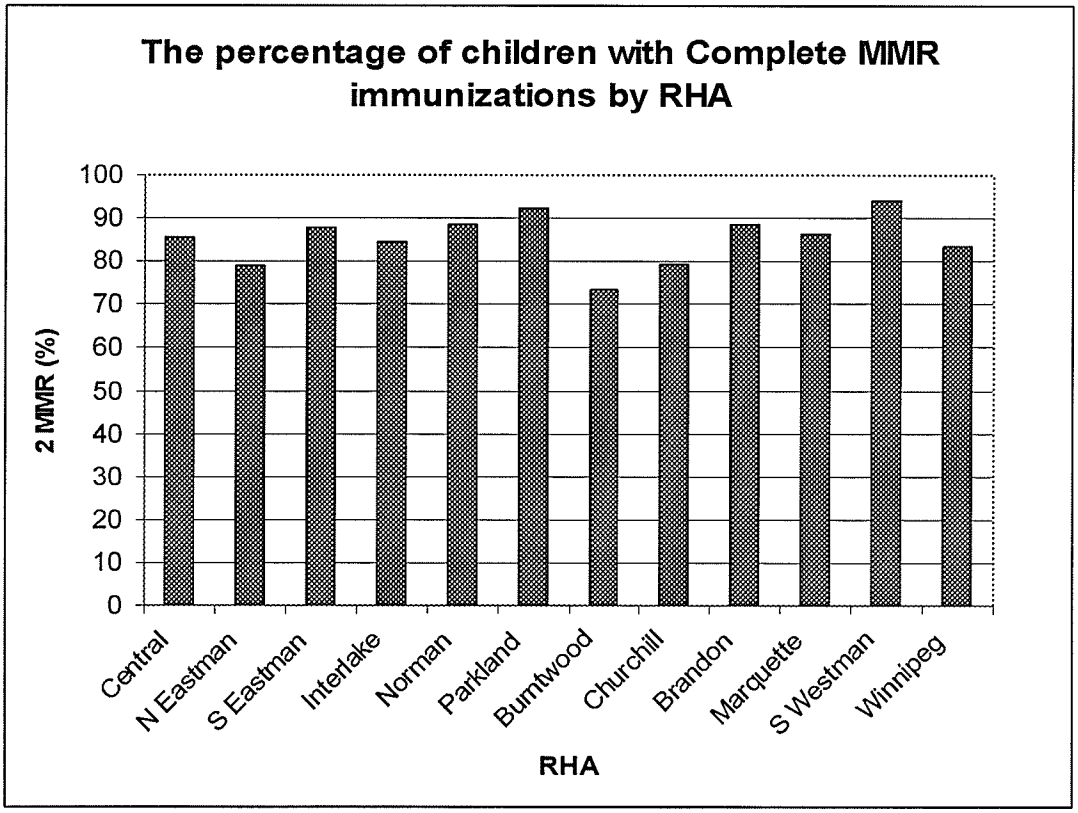


FIGURE 15:

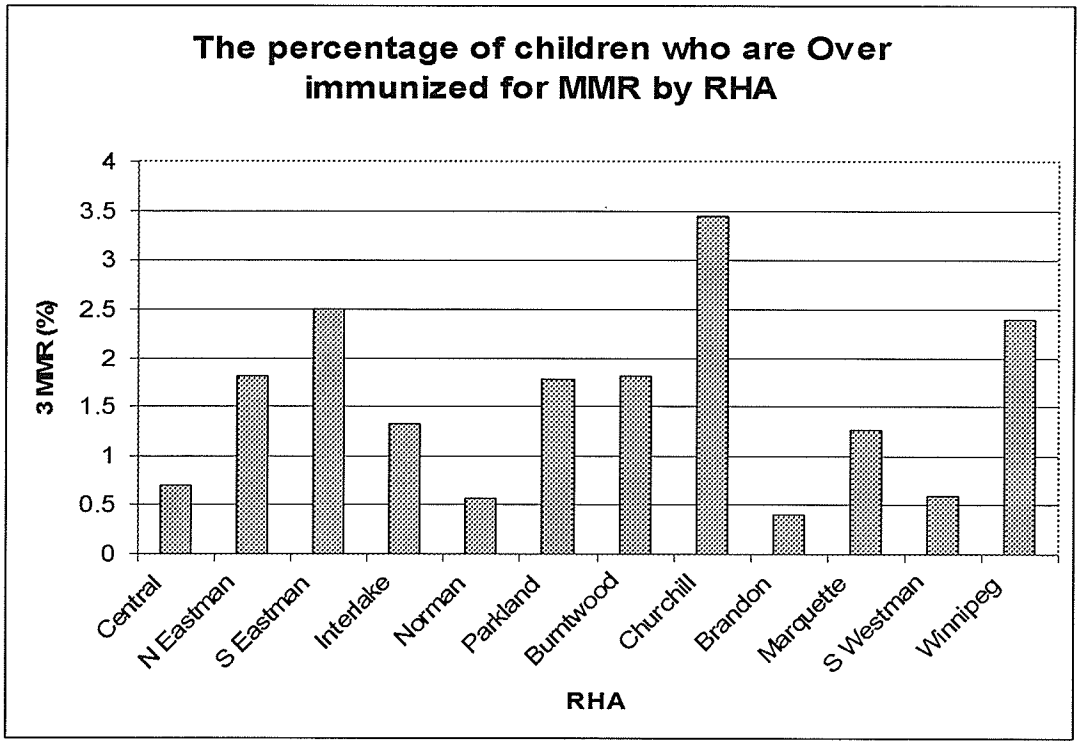
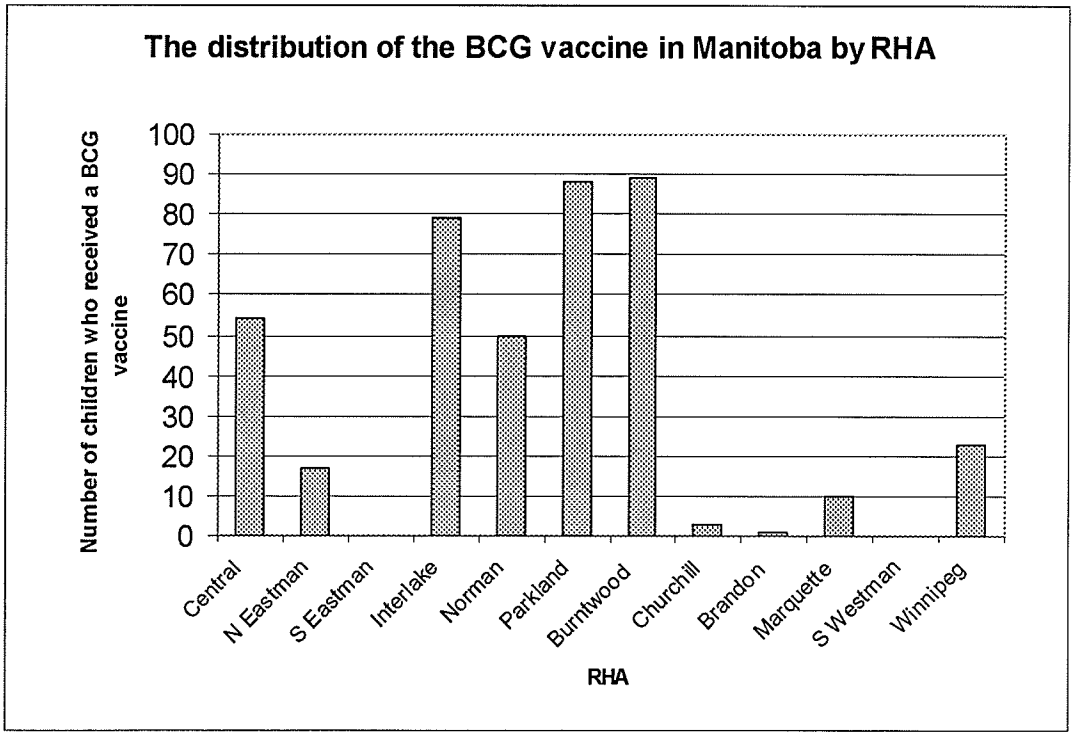


FIGURE 16:



WINNIPEG IMMUNIZATION RATES BY WINNIPEG COMMUNITIES

FIGURE 17:

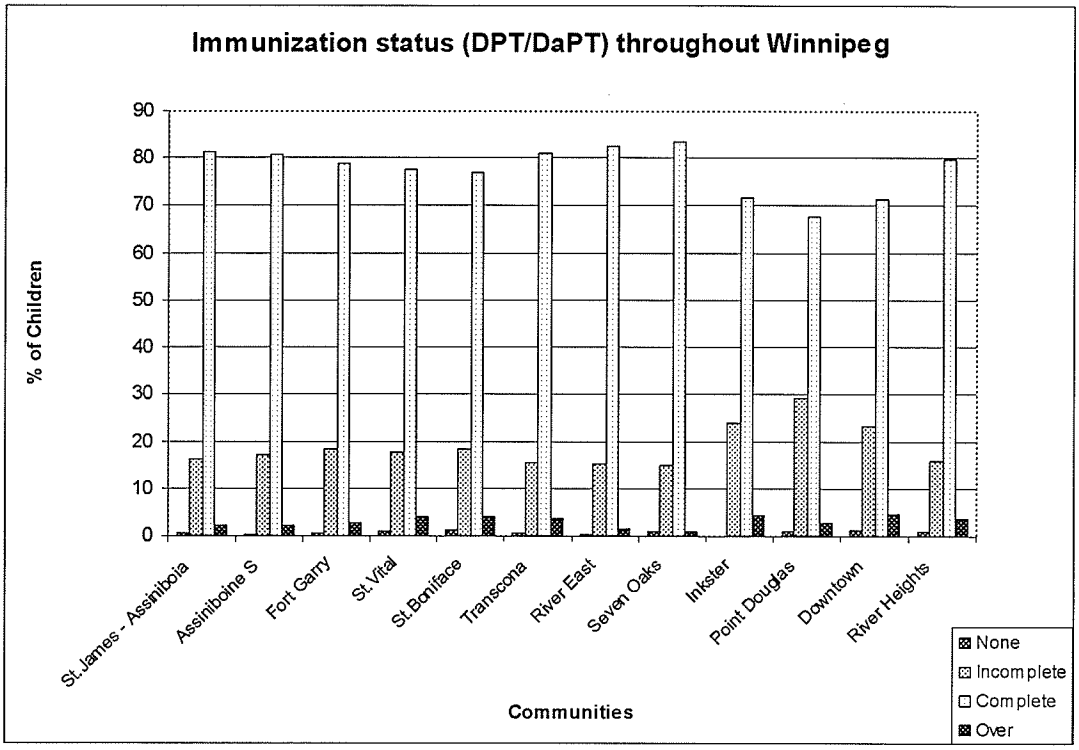
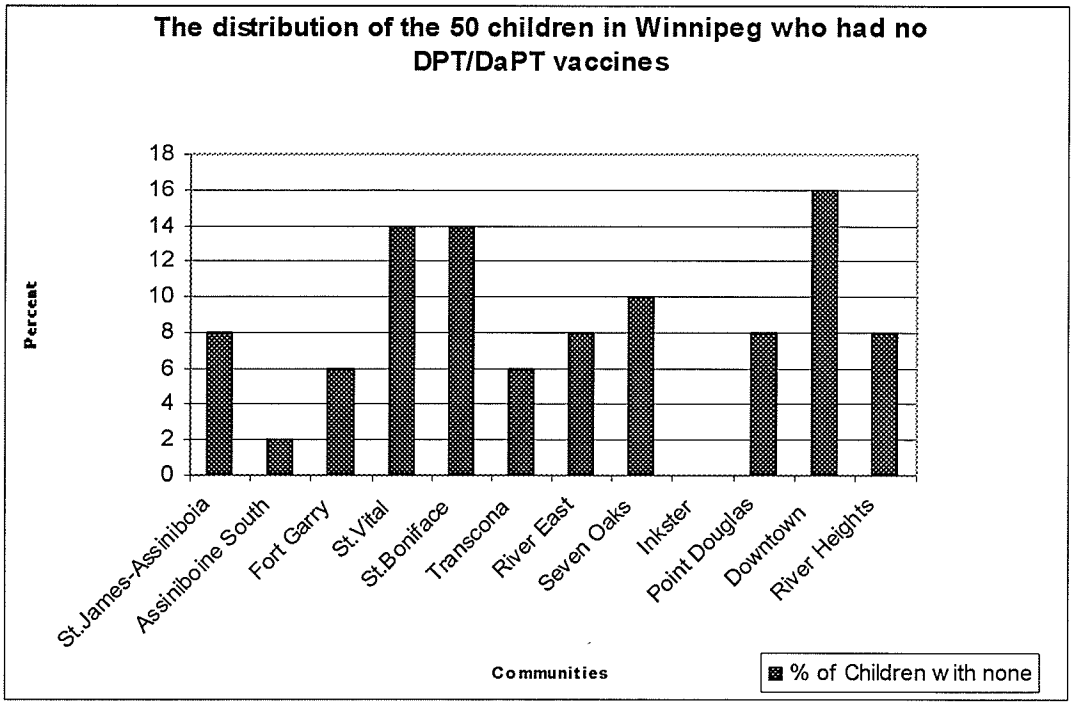
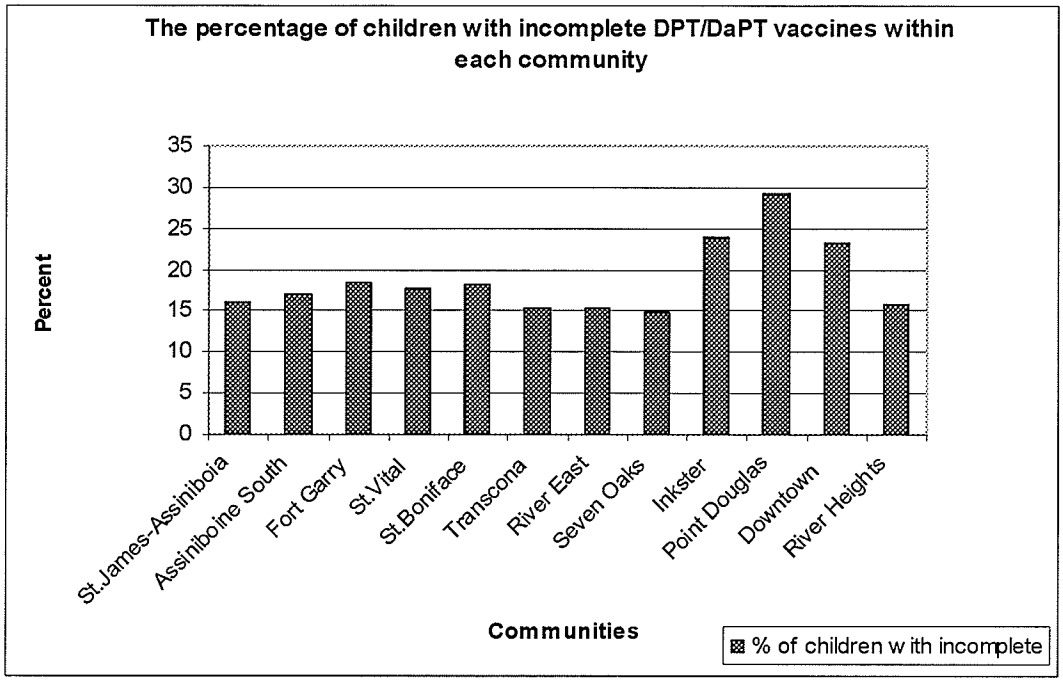


FIGURE 18:



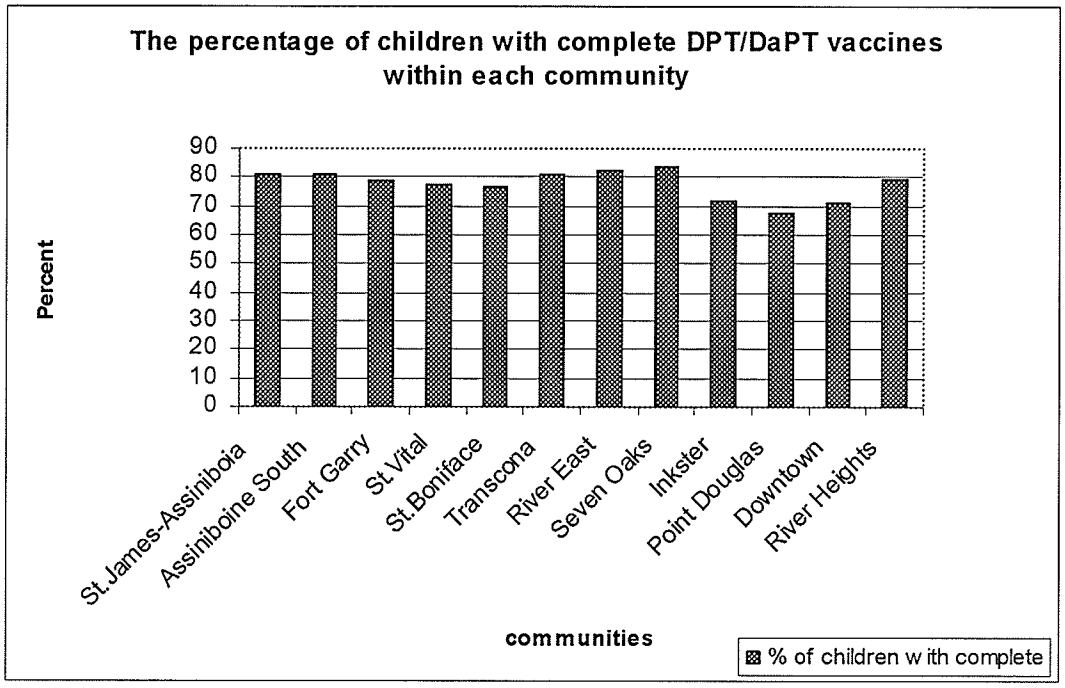
Although there is a higher number of children in the downtown than any other community who have had no DPT/DaPT vaccines, there is also a relatively high number of these children living in St Vital and St. Boniface.

FIGURE 19:



The number or percentage of children within each community who have incomplete DPT/DaPT immunizations peaks with Inkster, Point Douglas, and Downtown. There is also a slight increase in the percentages among Fort Garry, St. Vital and St. Boniface.

FIGURE 20:



This last FIGURE is almost the reverse of the previous FIGURE.

FIGURE 21:

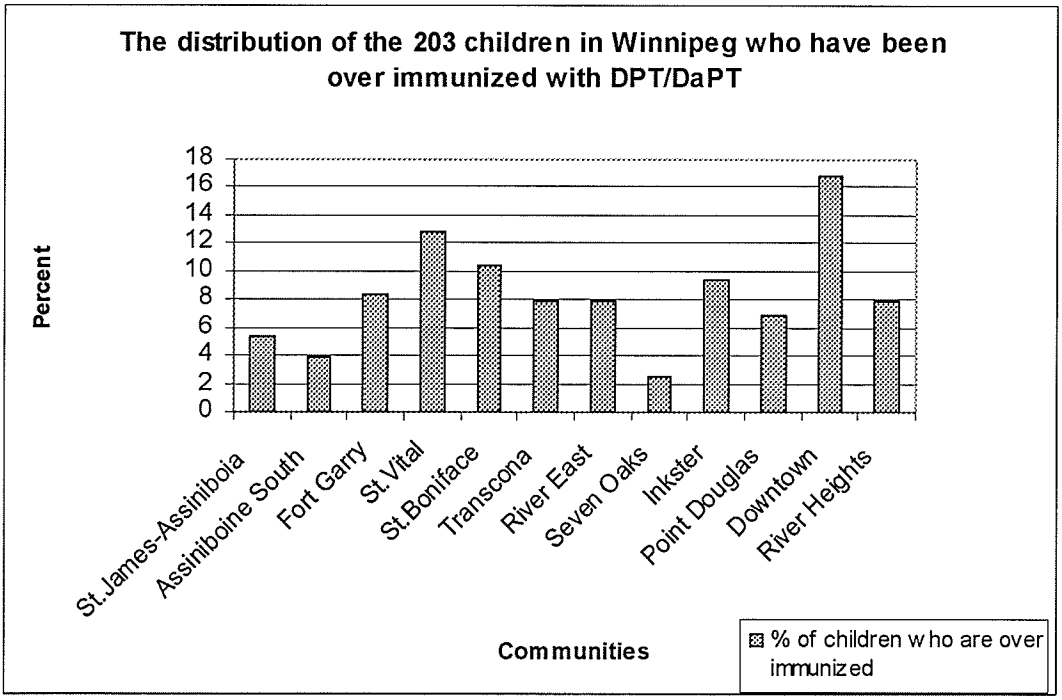


FIGURE 22:

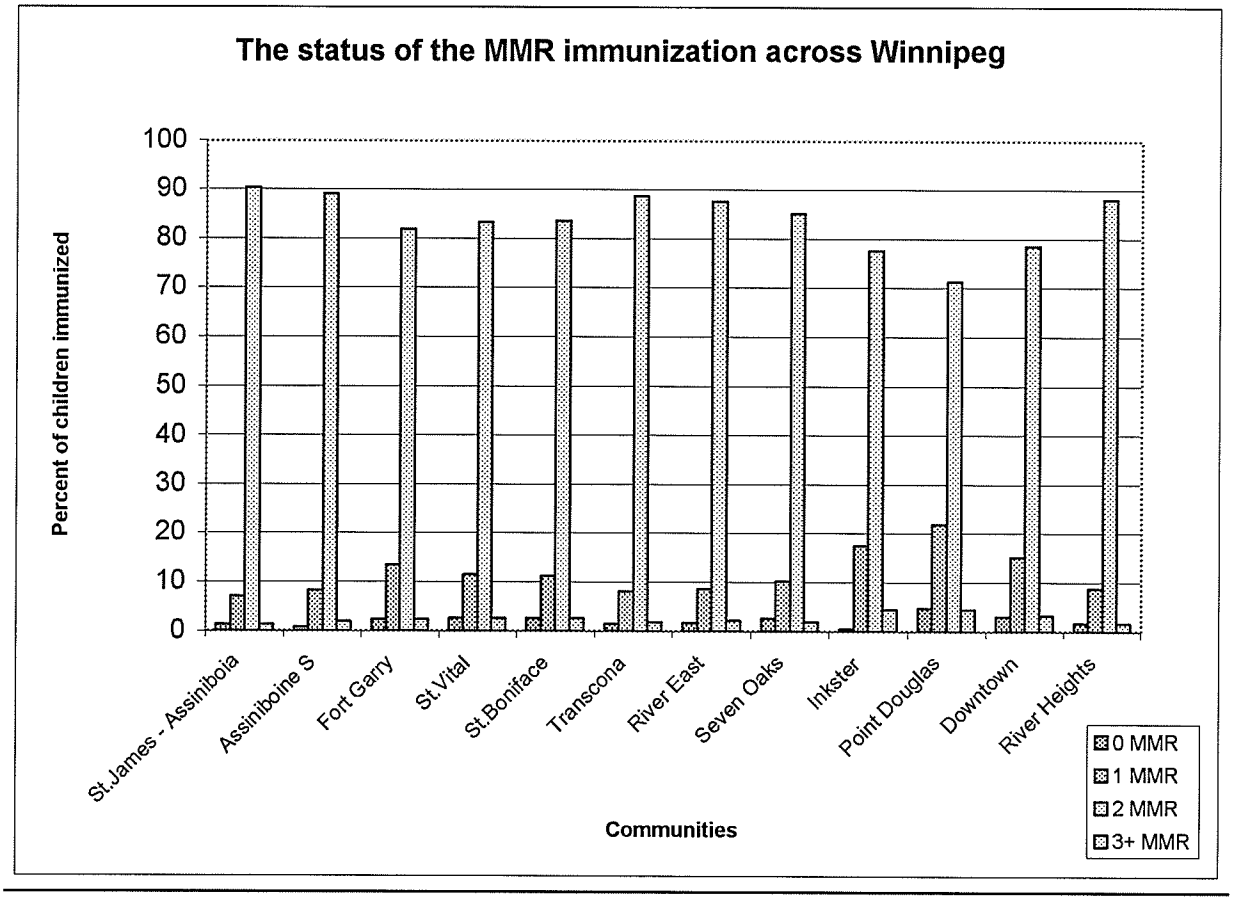
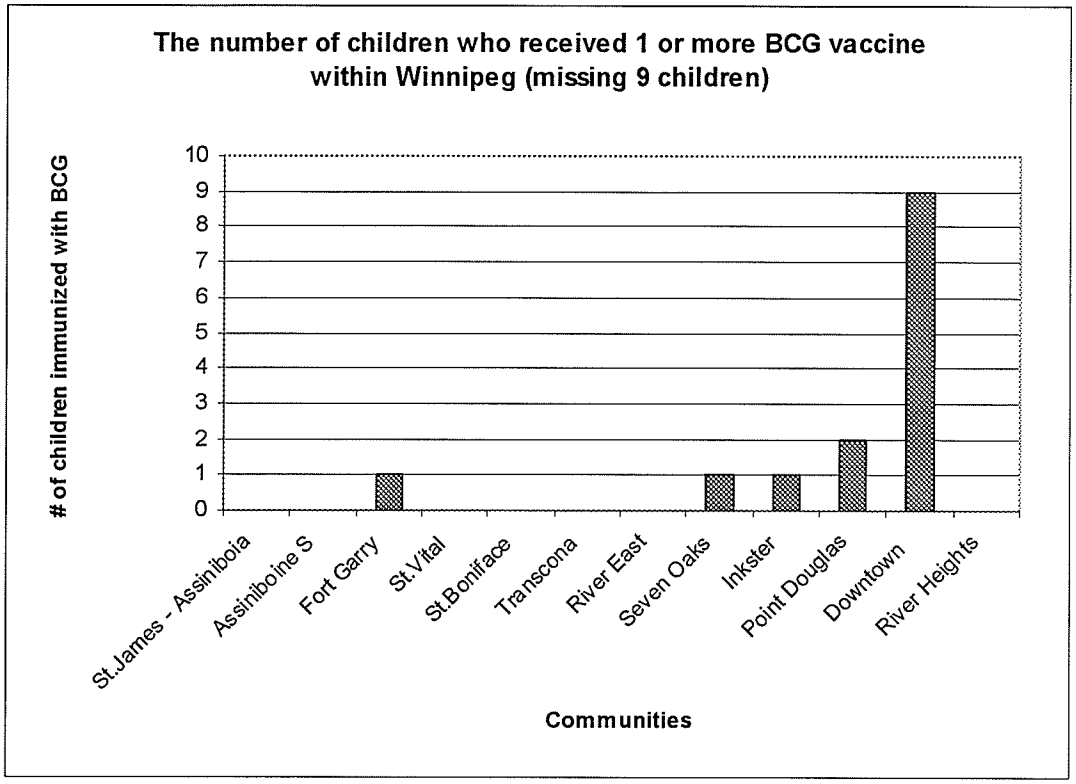

The status of the MMR immunization across Winnipeg
Percent of children immunized
100
90
80
70
60
50
40
30
20
10
0
St.James - Assiniboia
Assiniboine S
Fort Garry
St.Vital
St.Boniface
Transcona
River East
Seven Oaks
Inkster
Point Douglas
Downtown
River Heights
Communities
0 MMR
1 MMR
2 MMR
3+ MMR

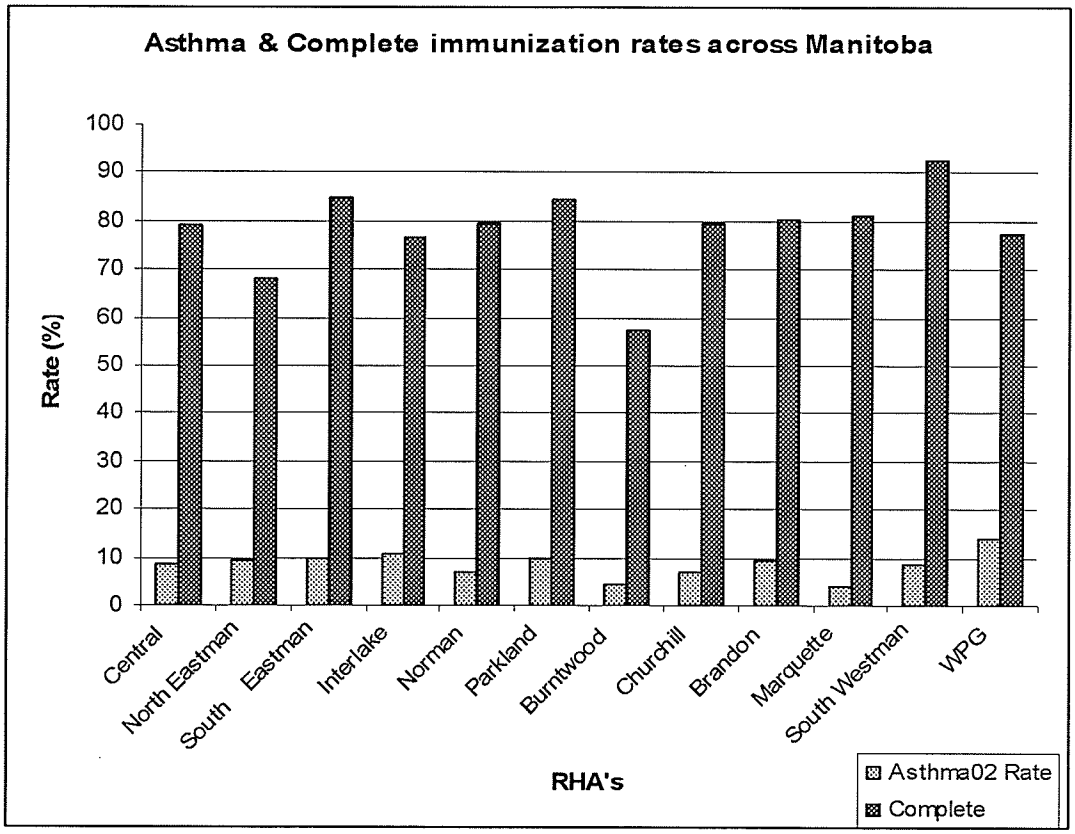
FIGURE 23:



PART III: REGIONAL DISTRIBUTION OF BOTH ASTHMA / WHEEZING & IMMUNIZATIONS

The following figures are of DPT and DaPT immunizations across Manitoba. An individual is Complete for their DPT/DaPT immunizations after they have received 5 doses; Over immunized with DPT/DaPT is anything over 5 doses; Incomplete is considered between 1 to 4 doses.

FIGURE 24:



The results are very similar across the province; however, Winnipeg does have the highest Asthma rate and South Westman has the highest DPT Complete immunization rate.

FIGURE 25:

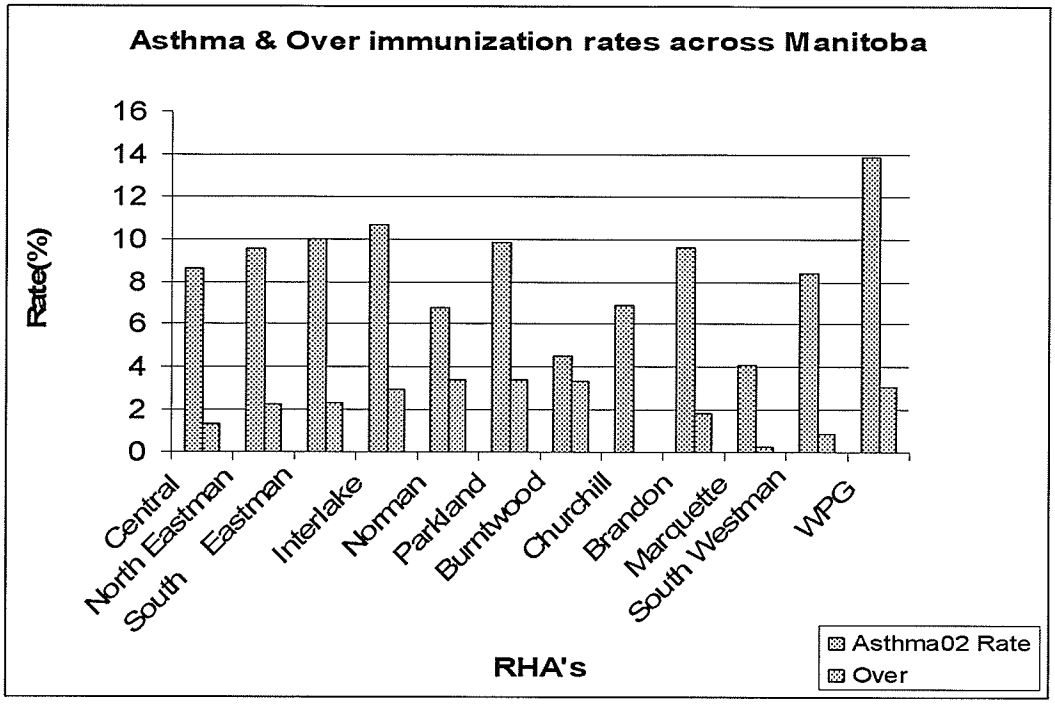


FIGURE 26:

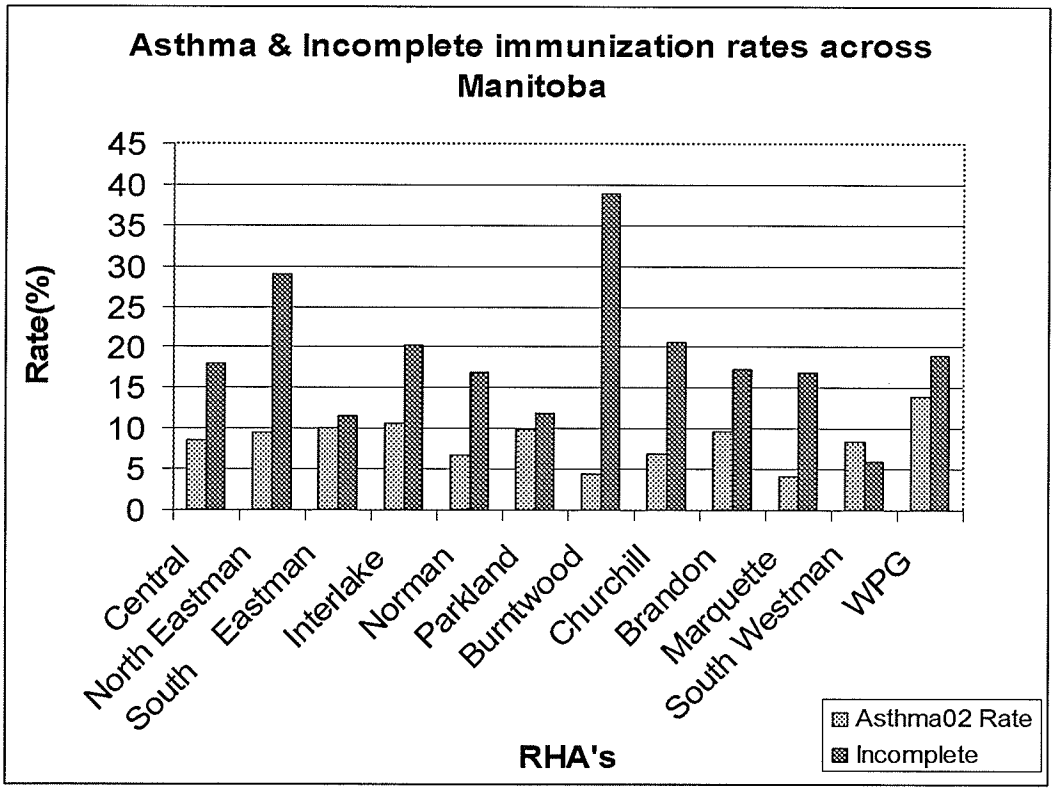


FIGURE 27:

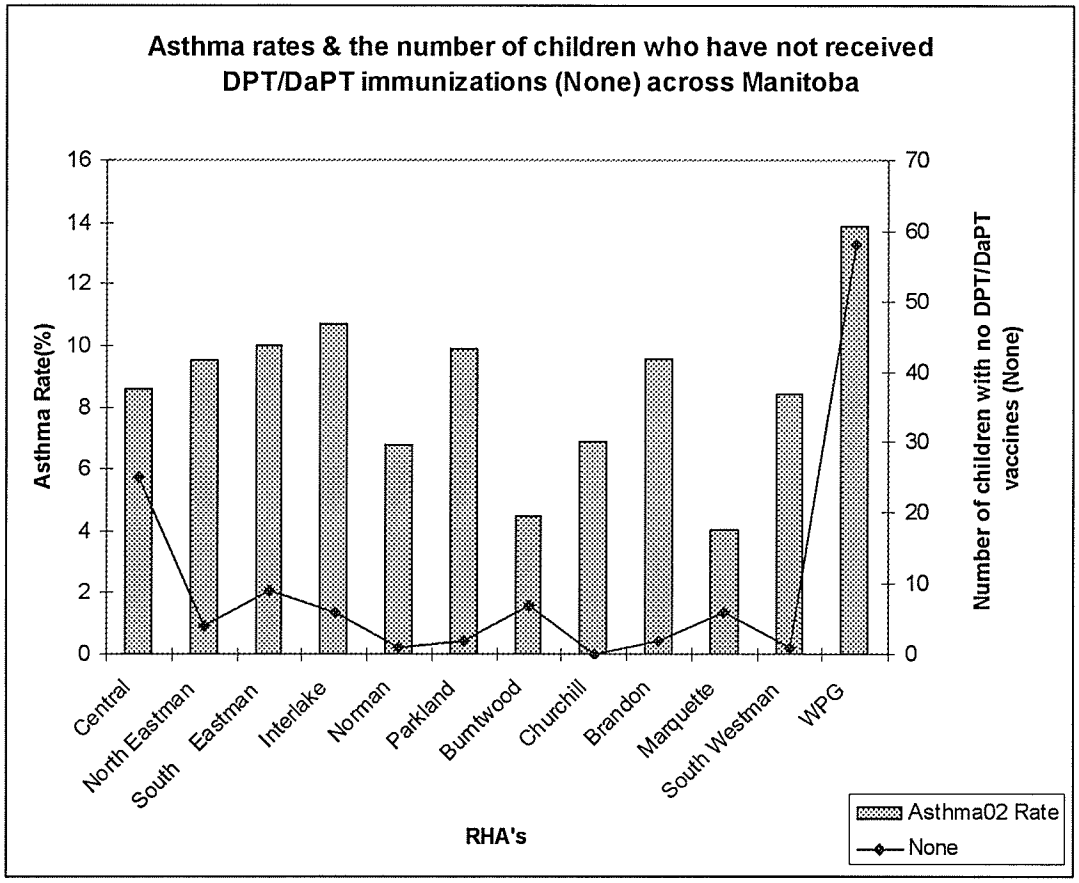

Asthma rates & the number of children who have not received DPT/DaPT immunizations (None) across Manitoba
Asthma Rate(%)
Number of children with no DPT/DaPT vaccines (None)
0
2
4
6
8
10
12
14
16
0
10
20
30
40
50
60
70
Central
North Eastman
South Eastman
Interlake
Norman
Parkland
Burntwood
Churchill
Brandon
Marquette
South Westman
WPG
RHA's
Asthma02 Rate
None

FIGURE 28:

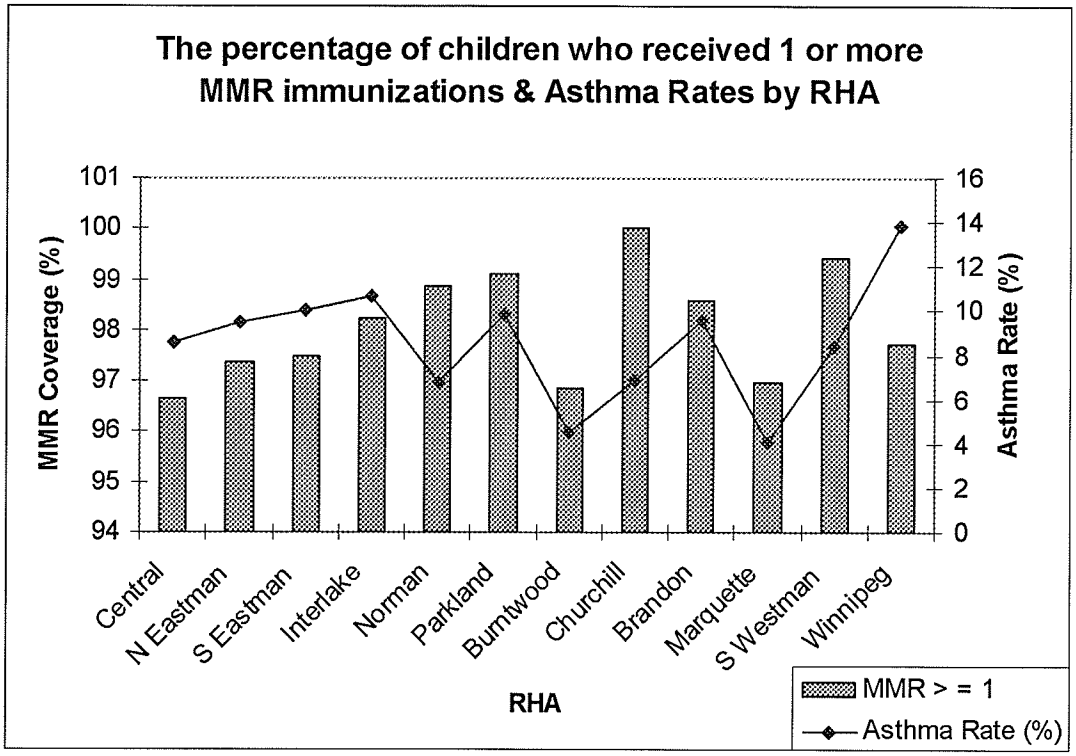
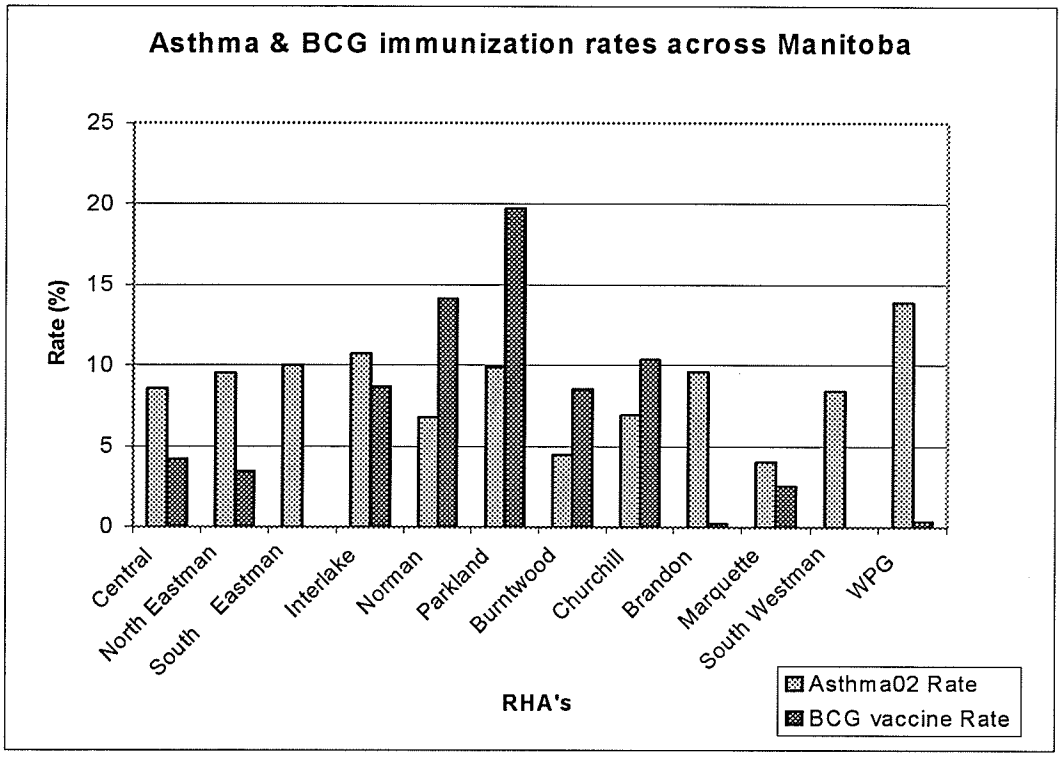


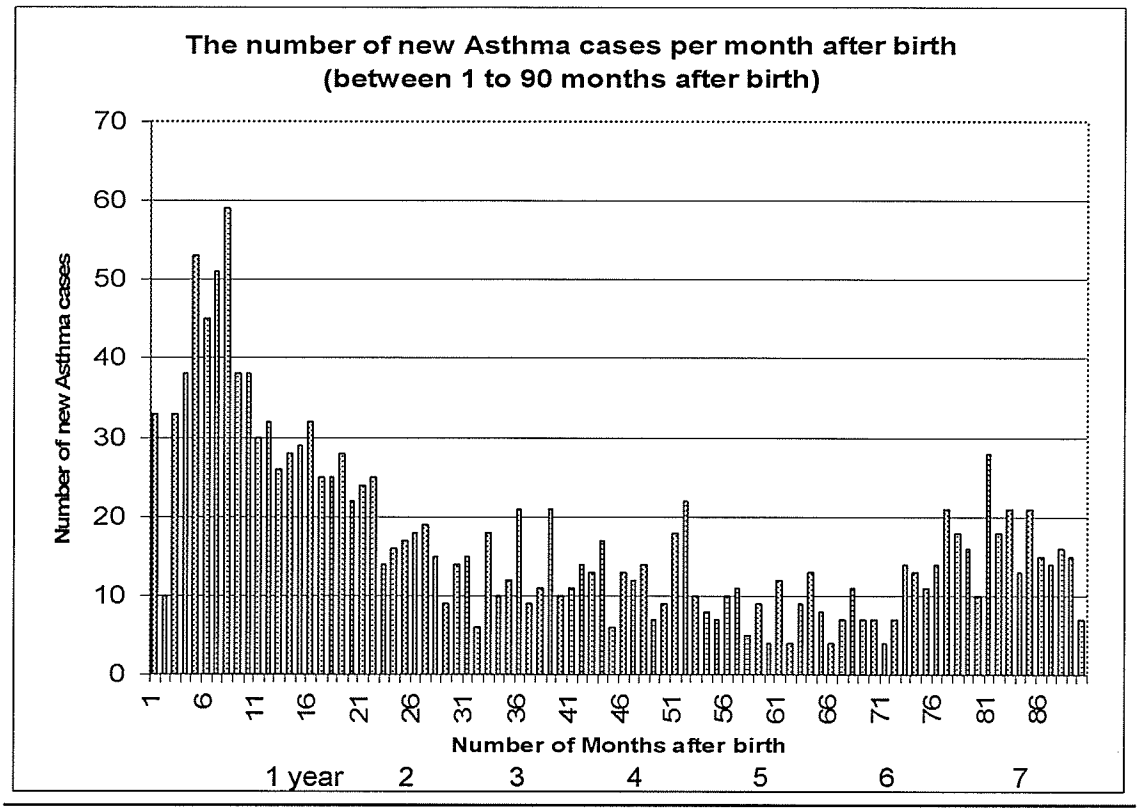
FIGURE 29:



Hypotheses suggest that there may be an inverse association between % of children immunized with BCG and % of children afflicted with Asthma. However, this hypothesis is not observed across all RHAs. Although, Norman, Parkland, Burntwood, and Churchill present this inverse pattern.

PART IV: TEMPORAL PATTERNS OF IMMUNIZATION & ASTHMA

FIGURE 30:



The monthly Asthma incidence peaks at 8 months after birth, with new Asthma 59 cases. After 8 months of age the monthly incidence drops dramatically and after two years of age or 24 months after birth the monthly incidence mostly remains under 20 new Asthma cases per month. The monthly Asthma incidence decreases after 28 months and fluctuates between 4 to 15 new Asthma cases per month (on average with the exception of a few months where the incidence is slightly above 20 new Asthma cases). Then around 73 months after birth the monthly Asthma incidence begins to rise and for the most part fluctuates between 14 to a new peak at 81 months after birth of 28 new cases. This second peak begins to occur because in 2002 all children who present for the first time are included in both the Asthma and Wheezing definitions.

FIGURE 31:

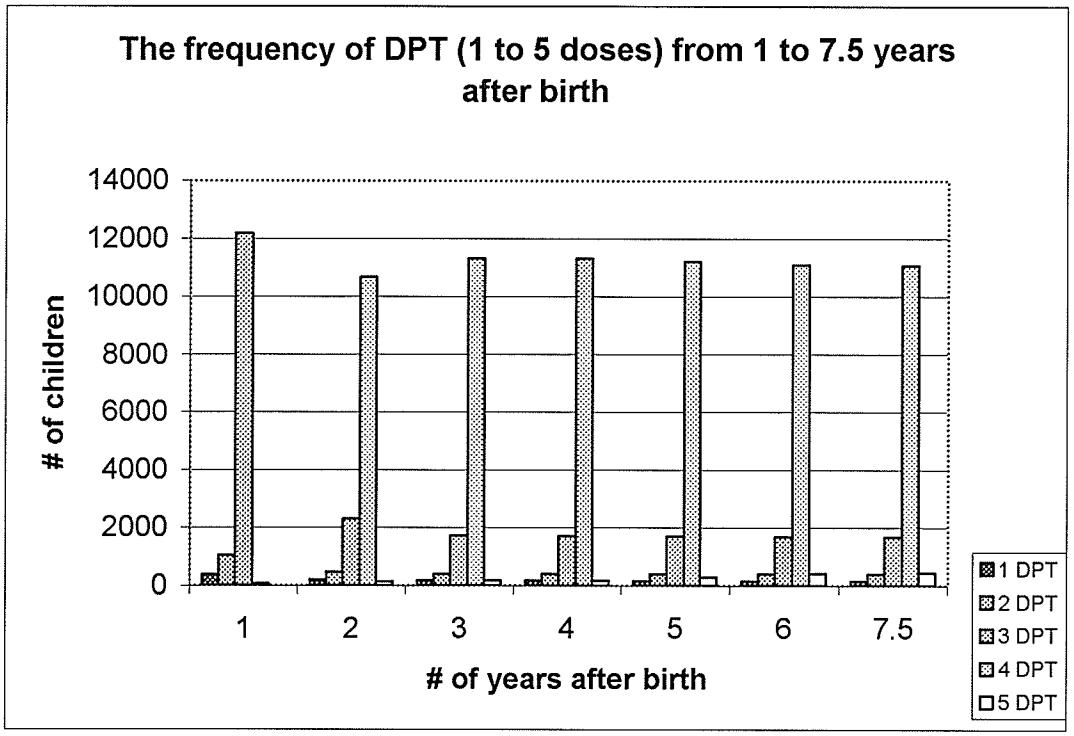
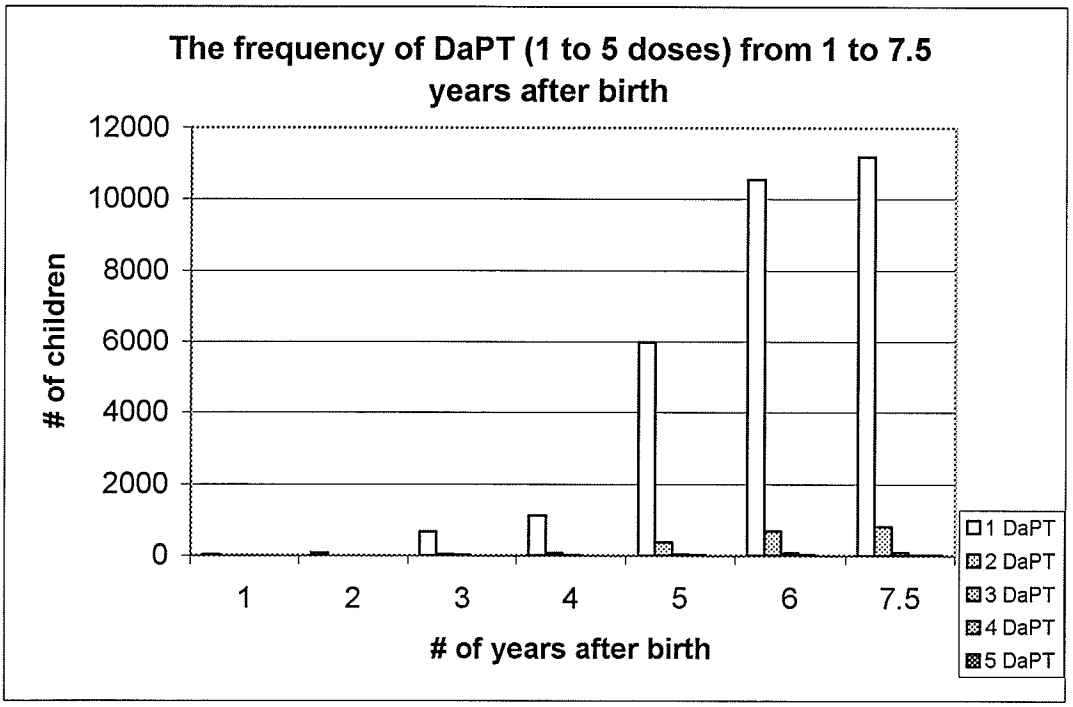


FIGURE 32:



By 6 years of age the majority of children in the cohort have received 1 dose of DaPT

The two figures above demonstrate the frequency of DPT (1 to 5 doses) by year and DaPT (1 to 5 doses) by year. It can be seen that when the frequencies for DPT became relatively stable after 3 years of age, the frequencies for DaPT increase. This is because most children in the cohort received 4 doses of DPT and 1 dose of DaPT. The Canadian Immunization schedule recommends an immunization schedule of DPT and DaPT at 2, 4, 6 and 18 months and again once sometime between 4 to 6 years. Although this is the recommended schedule the figures above demonstrate that many children are delayed in the immunization schedule. The temporal sequence of the monthly incidence of Asthma and the real temporal sequence of immunizations are very similar.

FIGURE 33:

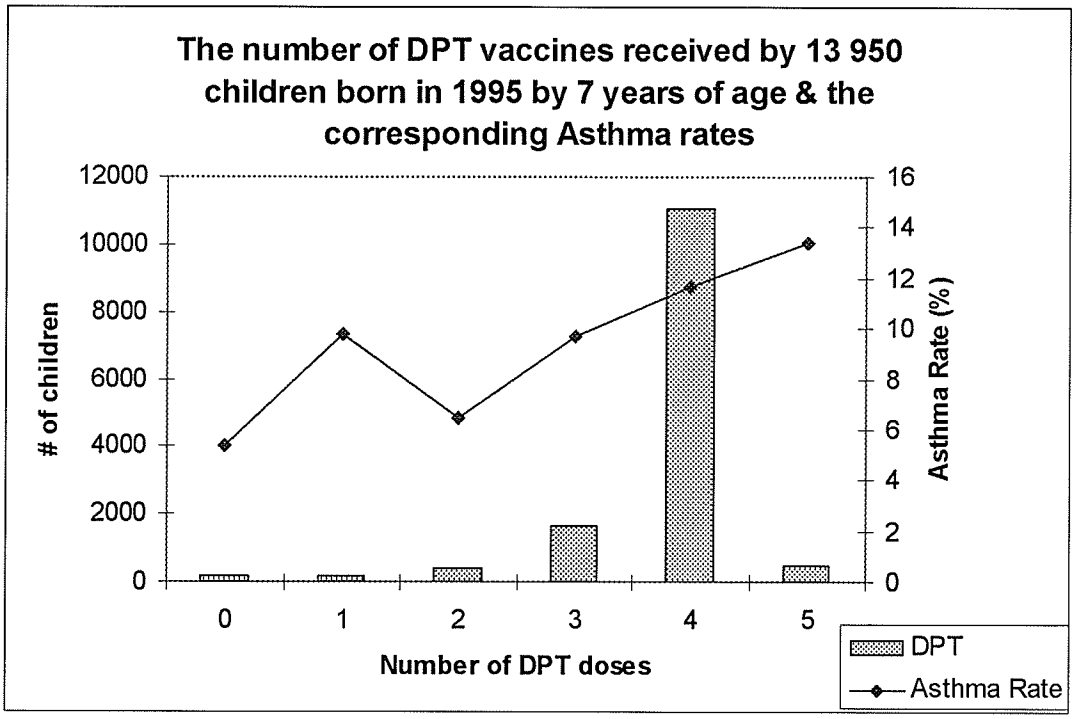
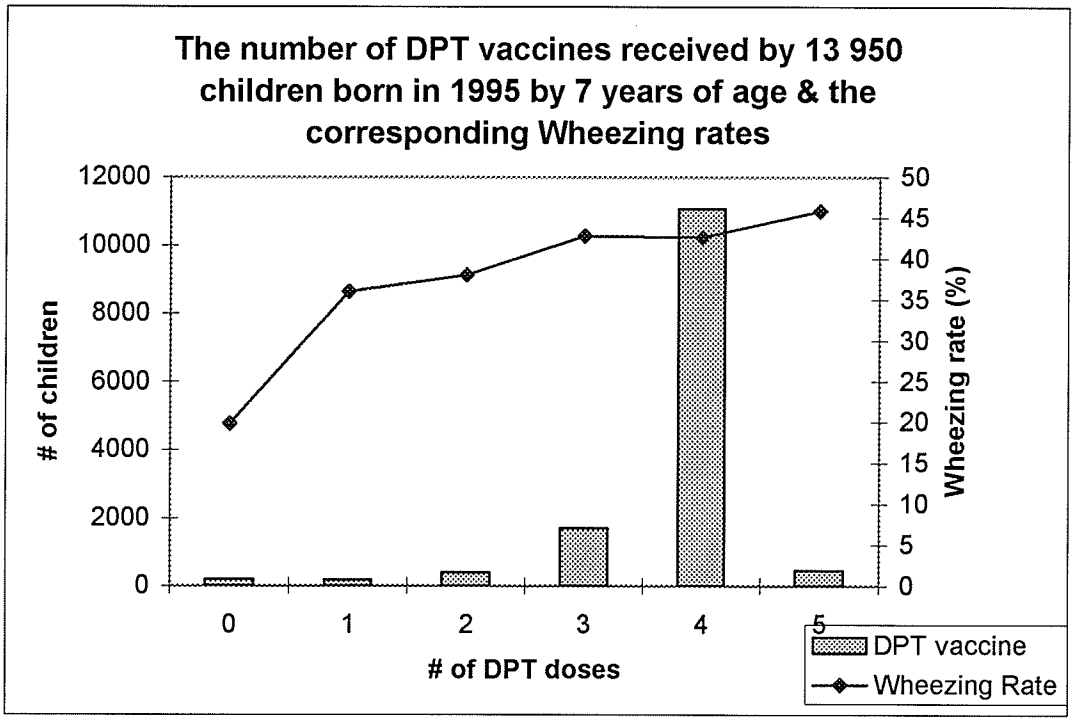
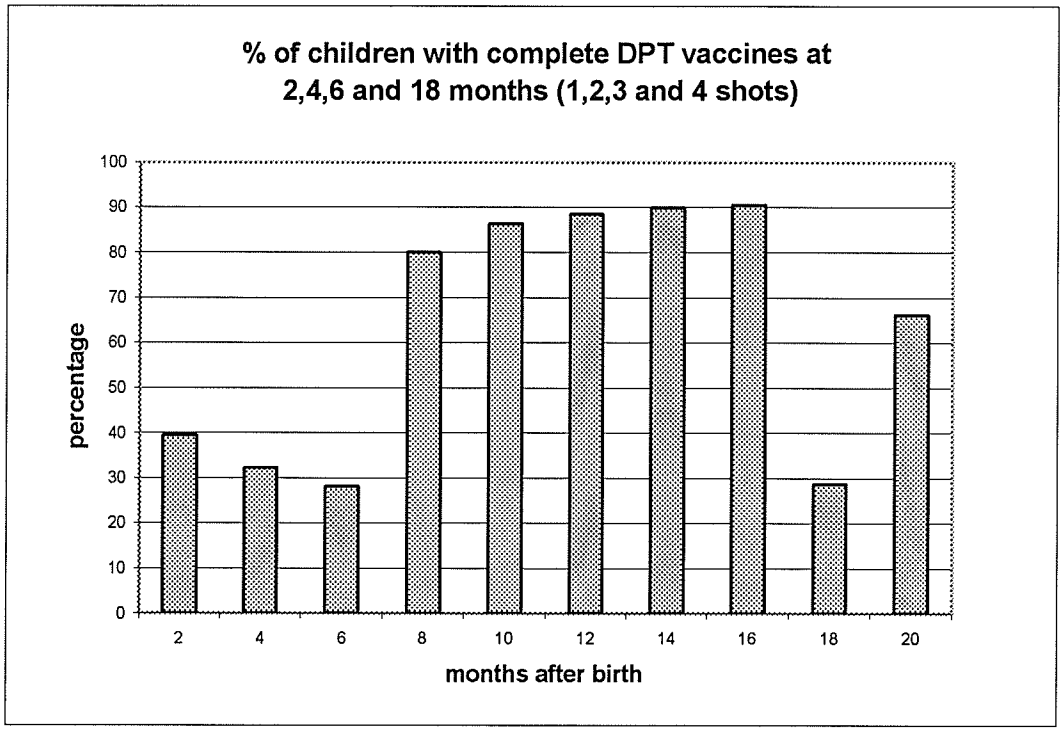


FIGURE 34:



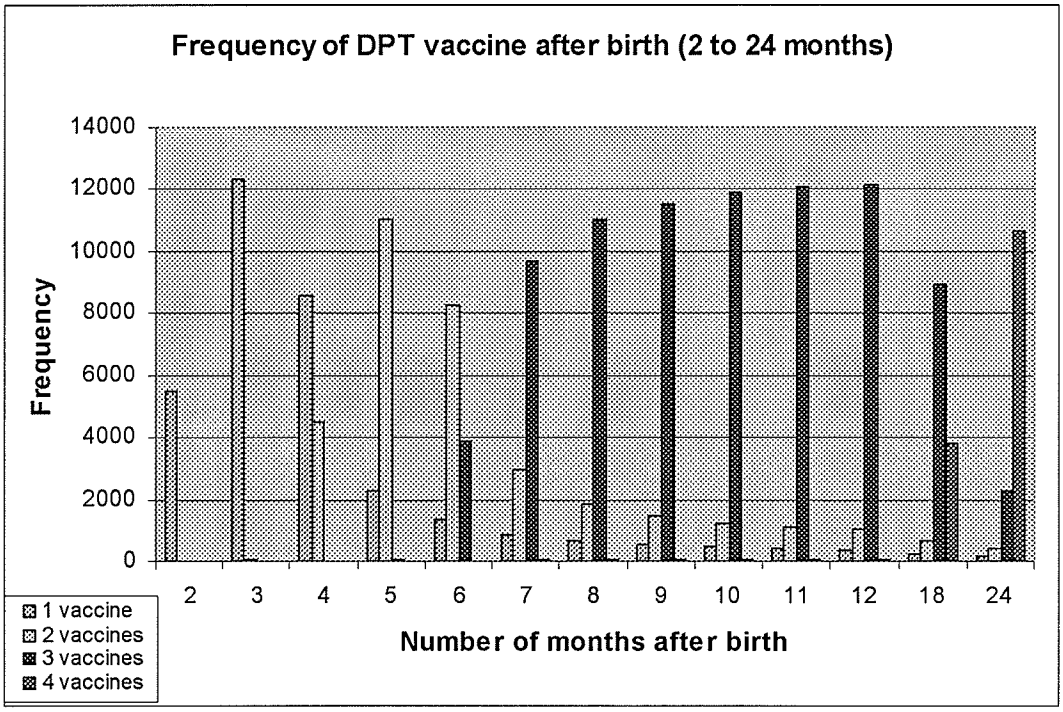
The Wheezing rate increases with the number of DPT vaccines increases. Although this alone is not enough to determine an association, it does suggest a temporal pattern. This may be accounted for by age; as a child ages they receive more vaccines and as a child ages they are more likely to develop asthma symptoms. This pattern will be elaborated on further in this document.

FIGURE 35: The percentage of children who follow the Manitoban immunization schedule



Typically, children in Manitoba were supposed to be vaccinated at 2, 4, 6 and 18months of age. The red bars in the FIGURE above indicate the months after birth when an immunization should take place according to the provincial schedule. The blue bars indicate the number of children who were vaccinated but whose vaccinations were delayed. This figure indicates that for many children there is quite a lag period between the actual time that they are vaccinated and the time when they were supposed to be vaccinated.

FIGURE 36: The frequency of DPT vaccination (1 to 4) during the scheduled immunization period after birth



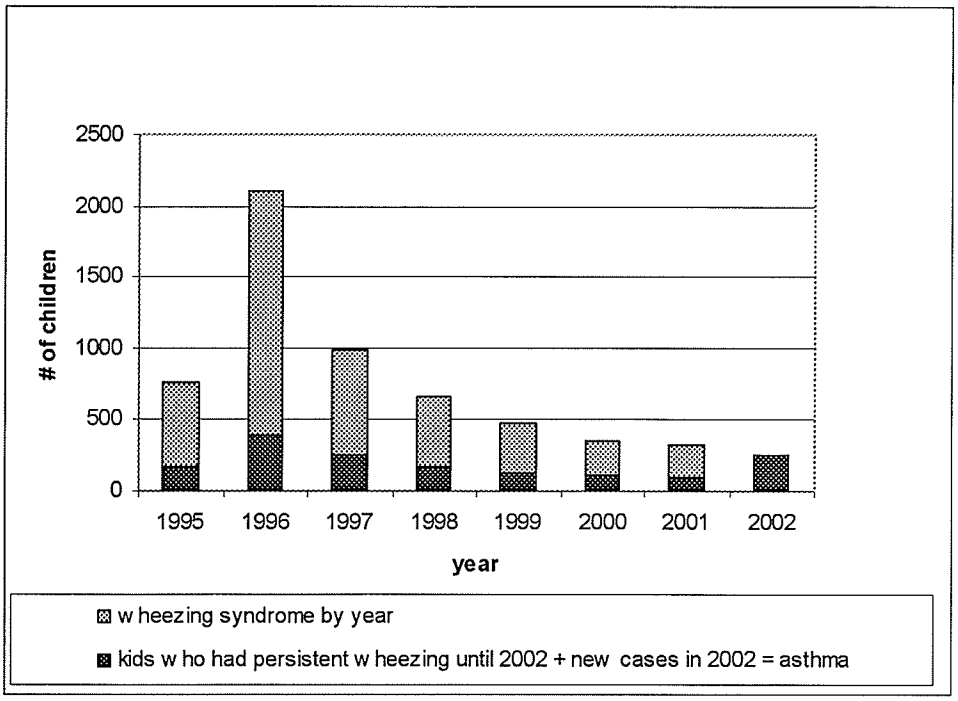
This FIGURE is helpful to visualize the immunization trend with this cohort, or the time over which DPT vaccination was completed. There is definitely not a clear delineation between the scheduled months for vaccination (2, 4, 6 and 18 months after birth) and the actual time of vaccination. This is to be expected because although Health Canada and Manitoba Health print a recommended schedule for immunization, it is just that – a recommendation.

TABLE 12: The number of new Asthma Cases per year (N=1569)

Year	# of new Asthma cases
1995	167
1996	399
1997	250
1998	162
1999	128
2000	118
2001	98
2002	247

The number of children who developed Asthma by year from 1995 to 2002 follows what would be expected; however, there is a surge in 2002. This can be accounted for by the two different definitions of Wheezing and Asthma. The light blue portion of the columns are the children who presented with asthma symptoms between the years1995 to 2001 but did not present with asthma symptoms in 2002 = Wheezing. The dark blue portion of the columns represent children who presented with asthma symptoms between the years of 1995 to 2001 and again in 2002, or for the first time in 2002.

FIGURE 37: The number of children with Wheezing & Asthma by year



It is interesting that over a 7 year period there were 1569 children who developed Asthma, but in 1996 over 2000 children developed Wheezing. Aside from a technical definition, these Wheezing children still experienced asthma like symptoms and placed a huge burden of illness on society at that time.

PART V: THE INDEPENDENT VARIABLES ASSOCIATED WITH ASTHMA & WHEEZING

TABLE 13: The source of Asthma diagnosis

METHOD OF INITIAL ASTHMA02 DIAGNOSIS					
Description			Category	Frequency	(%)
Prescription	Hospital	MD consult			
Rx = 0	hsp = 0	MD = 1	d001	208	13.26
Rx = 0	hsp = 1	MD = 1	d011	3	0.19
Rx = 1	hsp = 0	MD = 0	d100	638	40.66
Rx = 1	hsp = 0	MD = 1	d101	640	40.79
Rx = 1	hsp = 1	MD = 0	d110	5	0.32
Rx = 1	hsp = 1	MD = 1	d111	75	4.78
Total				1569	100

Note: The first row is categorized as d001 because the value for Rx is 0, the value for hsp is 0, and the value for MD consult is 1.

A SAS program extracted and merged the hospital, medical, and prescription data for the 1995 birth cohort. From these data the children who had hospital, medical, or prescription histories of being treated for asthma were extracted. If a child saw his physician and was diagnosed as having asthma and the physician wrote the diagnosis code as asthma (493) and the child's parent then filled a prescription for asthma medication, then that child would fall into the d101 category and be included as 1 of the 640 children in that group.

TABLE 14: The Frequency Distribution of Medical Consults (MD)

Medical Consults		
MD	Frequency	Percent
1	3573	25.61
2	3635	26.06
3	3259	23.36
4	3348	24
5	135	0.97
Total	13950	100

The distribution of medical consults was divided into 5 categories based on percentiles of (25%, 50%, 75%, 99% and over 99%). Therefore there is an even distribution of children in each

category. The MD group number (1 to 5) increases as the frequency of office visits increases, as was seen on the previous page.

TABLE 15: The Distribution of Children Among Urban and Rural Regions

Region		
Urban	Frequency	Percent
0	5997	42.99
1	7953	57.01
Total	13950	100

The Urban / Rural split between regions of residence indicates that more individuals live in urban centers.

TABLE 16: The Distribution of Antibiotic Prescriptions Among Children (Rx)

Antibiotic Prescriptions		
Rx	Frequency	Percent
1	4685	33.58
2	6531	46.82
3	2628	18.84
4	106	0.76
Total	13950	100

As with the medical consults groupings, the number of antibiotic prescriptions which a child received in their first year of life was also split into groups by percentiles. However, here the distribution results were skewed

TABLE 17: Summary of Independent variables and Asthma

	Asthma (n)	Asthma (%)	No Asthma (n)	No Asthma (%)	Total (%)
Medical Consults		Column		Column	
0 to 35	110	7.01	3463	27.97	
36 to 49	258	16.44	3377	27.28	
50 to 66	411	26.2	2848	23	
67 to 151	736	46.91	2612	21.1	
152 to 459	54	3.44	81	0.65	
Total	**1569**	**100**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**
Antibiotic Rx's					
None	401	25.56	4284	34.6	
1 to 3	752	47.93	5779	46.68	
4 to 11	398	25.37	2230	18.01	
12 to 40	18	1.15	88	0.71	
Total	**1569**	**100.01**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**
Region					
Rural	485	30.91	5512	44.52	
Urban	1084	69.09	6869	55.48	
Total	**1569**	**100**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**
Income					
Average - high	1152	73.42	9318	75.26	
Low	417	26.58	3063	24.74	
Total	**1569**	**100**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**
Gender					
Male	939	59.85	6219	50.23	
Female	630	40.15	6162	49.77	
Total	**1569**	**100**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**
Maternal History					
No	1409	89.8	11777	95.12	
Yes	160	10.19	604	4.88	
Total	**1569**	**100**	**12381**	**100**	
Total (%)	**11.25**		**88.75**		**100**

Children with Asthma were more likely to have had more medical consults / physician visits (46.91% had between 67 to 151 medical consults compared to 21.1% of the children who did not have Asthma); they were slightly more likely to have received between 1 to 3 prescriptions for antibiotics within their first year of life (47.93% vs. 46.68%); children with Asthma were also more likely to live in an Urban center than children with no asthma (69.09% vs. 55.48%); children with Asthma were slightly more likely to live in low income households when compared to children without Asthma (26.58% vs. 24.74%); children with Asthma were more likely to be male than female (59.85% vs. 40.15%); and finally children with Asthma were more likely to have mothers with a positive history of asthma when compared to children without asthma (10.19% vs. 4.88%).

TABLE 18: Summary of Independent variables and Wheezing

	Wheeze (n)	Wheeze (%)	No Wheeze (n)	No Wheeze (%)	Total (%)
Medical Consults		Column		Column	
0 to 35	695	11.78	2878	35.74	
36 to 49	1319	22.36	2316	28.76	
50 to 66	1580	26.79	1679	20.85	
67 to 151	2197	37.25	1151	14.29	
152 to 459	107	1.81	28	0.35	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**
Antibiotic Rx's					
None	1380	23.4	3305	41.05	
1 to 3	2859	48.47	3672	45.6	
4 to 11	1587	26.91	1041	12.93	
12 to 40	72	1.22	34	0.42	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**
Region					
Rural	2206	37.4	3791	47.08	
Urban	3692	62.6	4261	52.92	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**
Income					
Average - high	4242	71.92	6228	77.35	
Low	1656	28.08	1824	22.65	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**
Gender					
Male	3357	56.92	3744	46.49	
Female	2541	43.08	4308	53.5	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**
Maternal History					
No	5426	91.99	7760	96.37	
Yes	472	8.01	292	3.63	
Total	**5898**	**100**	**8052**	**100**	
Total (%)	**42.28**		**57.72**		**100**

Children with a positive history of Wheezing were more likely to have had more medical consults / physician visits than children who did not experience Wheezing (37.25% of the Wheezing children had between 67 to 151 medical consults, while only 14.29% who did not experience Wheezing had between 67 to 151 medical consults or higher); they were slightly more likely to have received between 1 to 3 prescriptions for antibiotics within their first year of life (48.47% vs. 45.6%) but almost twice as likely to have received between 4 to 11 antibiotic prescriptions when compared to children without Wheezing (26.91% vs. 12.93%); children with Wheezing were also more likely to live in an Urban center than children with no history of wheeze (62.6% vs. 52.92%); children with Wheezing were more likely to live in low income households when compared to children without Wheezing (28.08% vs. 22.65%); children with a history of Wheeze were more likely to be male than female (56.92% vs. 46.49%); and finally children with Wheezing were more likely to have mothers with a positive history of asthma when compared to children without Wheezing (8.01% vs. 3.63%).

TABLE 19: SUMMARY TABLE OF DPT/DaPT IMMUNIZATION STATUS & INDEPENDENT VARIABLES

Immunization Status	None (n=121)	Incomplete (n=276)	Complete (n=10723)	Over (n=378)
Medical Consults				
0 - 35	52.89	34.37	23.26	19.13
36 - 49	19.83	22.67	27.1	22.9
50 - 66	11.57	19.56	24.45	24.06
67 - 151	14.88	22.38	24.29	31.01
152 - 459	0.83	1.01	0.9	2.9
Total Percent	100	100	100	100
Antibiotic Prescriptions				
0 Rx	60.33	34.99	33.09	28.41
1 - 3 Rx	30.58	44.51	47.57	47.54
4 - 11 Rx	8.26	19.67	18.6	23.19
12 - 40 Rx	0.83	0.83	0.74	0.87
Total Percent	100	100	100	100
Region				
Urban	49.59	54.51	57.53	63.43
Rural	50.41	45.49	42.47	36.52
Total Percent	100	100	100	100
Gender				
Male	45.45	52.26	50.55	52.75
Female	54.55	47.74	49.45	47.25
Total Percent	100	100	100	100
Maternal History of Asthma				
Yes	5.79	6.37	5.22	6.09
No	94.21	93.63	94.78	93.91
Total Percent	100	100	100	100
Income				
Low	22.31	35.42	22.1	30.43
Average / High	77.69	64.58	77.9	69.57
Total Percent	100	100	100	100

Children who never received any DPT or DaPT immunizations were more likely than the children in the other groups (Incomplete, Complete and Over) to have had between 0 to 35 medical consults / physician visits; these children were less likely than children in any other immunization group to have had 0 antibiotic prescriptions in their first year of life; children in the "None" groups were also more likely than all of the other children to live in a rural region. Interestingly, children in the "None" group were more likely to be female; whereas, every other group (Incomplete, Complete and Over) were more likely to be male; all of the groups had very similar percentages of mothers with a history of asthma (between 5.22% to 6.37%); children in the "None" and the "Complete" immunization group were more likely than the children in the "Incomplete" and the "Over" immunization group to be from average to high income homes.

CHAPTER 7: THE FORMATION OF THE LOGISITC REGRESSION MODEL – THE RESULT OF VARIOUS STATISTICAL MEASURES

The following information is a detailed account of the step by step process and information required to pick the "best fit" model for the Logistic Regression.

Logistic Regression Model:

The number of antibiotic prescriptions are divided into four groups whereby group #1 (6 – 30), group #2 (4 – 5), group #3 (2 – 3), and group #4 (0 – 1).

Region is a dichotomous variable whereby Urban is 1 and Rural and Unknown is 0.

The number of medical consults are divided into nine groups whereby group #1 (181 – 459), group #2 (161 – 180), group #3 (141 – 160), group #4 (101 – 140), group #5 (81 – 100), group #6 (61 – 80), group #7 (41 – 60), group #8 (21 – 40), group #9 (0 – 20).

Gender is classified where male is 1 and female is 0.

If there is a maternal history of asthma it is classified as 1 where as no history of asthma is 0.

Different Combinations of Logistic Regression Models:

1. The logistic regression model including prescriptions, urban, gender and maternal history of asthma (hx):

	Intercept only	Intercept and Covariates
AIC	10274.763	10032.727
SC	10282.309	10018.727
-2 Log L	10272.763	10018.727

Percent concordant 57.8
Percent discordant 34.0
Percent tied 8.3
Somer's D 0.238
Gamma 0.260
Tau-a 0.050
C 0.619

2. The logistic regression model including medical consults, urban, gender, and maternal history of asthma (hx):

	Intercept only	Intercept and Covariates
AIC	10274.763	9211.133
SC	10282.309	9301.678
-2 Log L	10272.763	9187.133

Percent concordant 70.7
Percent discordant 23.4
Percent tied 5.9
Somer's D 0.473
Gamma 0.502
Tau-a 0.100
C 0.736

3. The logistic regression model including prescriptions, medical consults, urban, gender, and maternal history of asthma (hx).

	Intercept only	Intercept and Covariates
AIC	10274.763	9186.025
SC	10282.309	9299.206
-2 Log L	10272.763	9156.025

Percent concordant 73.0
Percent discordant 25.0
Percent tied 2.0
Somer's D 0.481
Gamma 0.490
Tau-a 0.102
C 0.740

4. Here the logistic regression model includes prescriptions as a dichotomous value where none or one prescription = 1 and over 1 prescription = 0.

The number of medical consults is also a dichotomous value where less or equal to 45 medical visits = 1 and over 45 medical visits = 0.

This model also includes urban, gender and maternal history of asthma.

	Intercept only	Intercept and Covariates
AIC	10274.763	9484.036
SC	10282.309	9529.309
-2 Log L	10272.763	9472.036

Percent concordant 66.1
Percent discordant 26.6
Percent tied 7.2
Somer's D 0.395
Gamma 0.426
Tau-a 0.084
C 0.697

5. This logistic regression model includes prescription as a dichotomous value where none or one prescription = 1 and over 1 prescription = 0. It also includes urban, gender and maternal history of asthma (hx).

	Intercept only	Intercept and Covariates
AIC	10274.763	10048.969
SC	10282.309	10086.695
-2 Log L	10272.763	10038.969

Percent concordant 53.2
Percent discordant 30.7
Percent tied 16.1
Somer's D 0.225
Gamma 0.268
Tau-a 0.048
C 0.613

6. This logistic regression model includes medical consults (less or equal to 45 = 1 else = 0), urban, gender, and maternal history of asthma (hx).

	Intercept only	Intercept and Covariates
AIC	10274.763	9482.828
SC	10282.309	9520.554
-2 Log L	10272.763	9472.828

Percent concordant 62.9
Percent discordant 23.7
Percent tied 13.4
Somer's D 0.392
Gamma 0.453
Tau-a 0.083
C 0.696

7. This logistic regression model includes:
The number of antibiotic prescriptions are divided into four groups whereby group #1 (6 – 30), group #2 (4 – 5), group #3 (2 – 3), and group #4 (0 – 1).

Region is a dichotomous variable whereby Urban is 1 and Rural and Unknown is 0.

The number of medical consults are divided into nine groups whereby group #1 (181 – 459), group #2 (161 – 180), group #3 (141 – 160), group #4 (101 – 140), group #5 (81 – 100), group #6 (61 – 80), group #7 (41 – 60), group #8 (21 – 40), group #9 (0 – 20).

Gender is classified where male is 1 and female is 0.

If there is a maternal history of asthma it is classified as 1 where as no history of asthma is 0.

As well as income R1 and U1 equals income = 1 (low income) else = 0.

	Intercept only	Intercept and Covariates
AIC	10274.763	9188.006
SC	10282.309	9308.732
-2 Log L	10272.763	9156.006

Percent concordant 73.2
Percent discordant 25.2
Percent tied 1.6
Somer's D 0.480
Gamma 0.488
Tau-a 0.102
C 0.740

Summary of logistic regressions:

Of the different logistic regression models, the third and seventh models demonstrate the best fit to the model. Out of all the different models number 3 and 7 had the lowest values for the intercept and covariate AIC and SC. The percent concordant was 73.0 for model #3 and 73.2 for model #7. Also, the values for Somer's D, Gamma, and Tau-a were the highest for model 3 and 7 which also indicates that relative to the other models that these two models are the best fit.

The Hosmer and Lemeshow "Goodness of Fit Test":

This is a goodness of fit test that divides the data into approximately ten groups of the same size where the observations are sorted in increasing order of their estimated probability of having an event outcome. The Pearson chi-square statistic summarizes the differences between the observed and expected number of observations. The Pearson chi-square statistic is compared to a chi-square distribution. Large Hosmer and Lemeshow Chi-square values and small p-values indicate a lack of fit of the model.

The Hosmer and Lemeshow Goodness-of-Fit Test for the variables of antibiotic use and medical consults.

Chi-square	DF	Pr >ChiSq
0.0110	2	0.9945

*This indicates that antibiotic use and medical consults are a good fit for the model.

The Hosmer and Lemeshow Goodness-of-Fit Test for the variables of maternal history of asthma and medical consults.

Chi-square	DF	Pr > ChiSq
2.1056	1	0.1468

*This indicates that maternal history of asthma and medical consults indicate a lack of fit of the model.

The Hosmer and Lemeshow Goodness-of-Fit Test for the variables of maternal history of asthma and antibiotic use.

Chi-square	DF	Pr > ChiSq
0.0259	1	0.8722

*This indicates that maternal history of asthma and antibiotic use are a good fit for the model.

The Hosmer and Lemeshow Goodness-of-Fit Test for the variables of maternal history of asthma, gender, antibiotic use, medical consults, and urban.

Chi-square	DF	Pr > ChiSq
3.7236	8	0.8812

*This indicates that maternal history of asthma, gender, antibiotic use, medical consults, and urban are a good fit for the model.

Chi-Square:

Is a non-parametric test of statistical significance for bivariate analysis. The null hypothesis is that there is no difference between the two groups being tested. The data is significant when the Chi-square value is larger than the critical value with df = (r – 1)(c – 1).[67]

The Chi-square value for prescription of antibiotics and medical consults with 24 df has a Chi-square value of 2956.9949 with a probability of < .0001. Which is therefore significant and the null hypothesis can be rejected.

Tests of Collinearity:

Collinearity occurs when variables are so highly correlated that it becomes very difficult to establish reliable estimates of their individual regression coefficients and the degree to which they are predictors of the model. When variables are perfectly collinear the R2 value is 1.[68]

Testing for collinearity between medical consults and prescriptions for antibiotics:

Statistic	Value	ASE
Gamma	0.5067	0.0082
Kendall's Tau-b	0.3577	0.0063
Staurt's Tau-c	0.3271	0.0060
Somers'D C/R	0.3188	0.0057
Somers'D R/C	0.4012	0.0070
Pearson's Correlation	0.4301	0.0076
Spearman Correlation	0.4147	0.0072

These results do not indicate that medical consults and prescriptions for antibiotics demonstrate a problem with collinearity.

Testing for collinearity between urban and medical consults:

Statistic	Value	ASE
Gamma	- 0.3556	0.0116
Kendall's Tau-b	- 0.2220	0.0074
Staurt's Tau-c	- 0.2727	0.0091
Somers'D C/R	-0.2782	0.0093
Somers'D R/C	-0.1772	0.0059
Pearson's Correlation	-0.2217	0.0081
Spearman Correlation	-0.2465	0.0082

These results also do not indicate that urban and medical consults demonstrate a problem with collinearity.

Testing for collinearity between income and medical consults:

Statistic	Value	ASE
Gamma	-0.0369	0.0147
Kendall's Tau-b	-0.0202	0.0080
Staurt's Tau-c	-0.0217	0.0086
Somers'D C/R	-0.0289	0.0115
Somers'D R/C	-0.0141	0.0056
Pearson's Correlation	-0.0312	0.0091
Spearman Correlation	-0.0224	0.0089

These results also do not indicate that income and medical consults demonstrate a problem with collinearity.

Testing for collinearity between maternal history of asthma and medical consults:

Statistic	Value	ASE
Gamma	-0.3275	0.0232
Kendall's Tau-b	-0.0946	0.0072
Staurt's Tau-c	-0.0534	0.0043
Somers'D C/R	-0.2577	0.0192
Somers'D R/C	-0.0347	0.0028
Pearson's Correlation	-0.1092	0.0093
Spearman Correlation	-0.1050	0.0080

These results also do not indicate that maternal history of asthma and medical consults demonstrate a problem with collinearity.

NOTE: THIS PAGE BREIFLY OUTLINE THE DIFFERENCE BETWEEN THE RELATIVE RISK AND THE ODDS RATIO

Relative Risk (RR):

Relative Risk is the number of individuals who have the disease among the exposed divided by the number of individuals who have disease but who have not been exposed.

	D_1	D_0
E_1	a	b
E_0	c	d

N

$I_1 = a / a + b$

$I_0 = c / c + d$

$RR = I_1 / I_0$ If RR < 1 then the exposure is protective

Odds Ratio (OR):

Odds ratio is a cross product ratio that determines the probability of a rare event.

	D_1	D_0
E_1	a	b
E_0	c	d

N

$OR = a\ d / c\ b$ where (Exposed and diseased) * (Exposed and no disease) / (Not exposed and diseased) * (Not exposed and no disease)

The Risk Ratios and Odds Ratios :

The children with asthma and the mothers with a history of asthma.

Type of Study	Value	95%CI	
Odds Ratio	1.6941	1.3998	2.0502
Risk Ratio	1.0353	1.0199	1.0510

Thus, children who have asthma are more likely to have mothers with a history of asthma.

The children with asthma and the mothers with a history of allergy.

Type of Study	Value	95%CI	
Odds Ratio	1.3514	1.2162	1.5017
Risk Ratio	1.1108	1.0677	1.1557

Therefore children with asthma are more likely to have mothers with a history of allergies.

The children with asthma and gender where male = 1 and female = 0.

Type of Study	Value	95%CI	
Odds Ratio	1.4277	1.2876	1.5831
Risk Ratio	1.2132	1.1430	1.2877

Thus, children who have asthma are more likely to be male.

The children with asthma and income where lower income (R1 and U1) is inc = 1 and all other income groups are inc = 0.

Type of Study	Value	95%CI	
Odds Ratio	1.0794	0.9611	1.2123
Risk Ratio	1.0197	0.9893	1.0510

The 95%CL crossed 1.00, so there was no statistical difference between Rural and Urban.

The children with asthma and the number of medical consults where low is under 45 and high is over 45.

Type of Study	Value	95%CI	
Odds Ratio	5.3398	4.6257	6.1641
Risk Ratio	3.3504	2.9668	3.7836

Thus, children diagnosed with asthma are much more likely to have had over the median number of medical visits for this cohort.

The children with asthma and antibiotic use where low is under 1 prescription (ab = 0) and high is over 1 prescription (ab = 1).

Type of Study	Value	95%CI	
Odds Ratio	1.6086	1.4315	1.8077
Risk Ratio	1.3972	1.2813	1.5235

Therefore children with asthma are more likely to have had more than 1 prescription for antibiotics.

The children with asthma and those who have had 2 or more DPT type immunizations (combos including polio and Hib etc.)

Type of Study	Value	95%CI	
Odds Ratio	1.6627	1.1191	2.4703
Risk Ratio	1.6452	1.1148	2.4280

Thus, the children who have asthma are more likely to have had two or more DPT vaccines.

CHAPTER 8: THE ASSOCIATION BETWEEN IMMUNIZATION STATUS & THE ASTHMA RATES

The first objective was to determine the final DPT/DaPT immunization status for all of the children in the cohort and then statistical analysis was performed on the data. In Part II of this chapter the timing of Asthma onset relative to immunization status (the number of DPT doses) was determined.

Research Question One:

1 – Is there an association between immunization status and incidence of asthma?

My research hypothesis is that children who have complete immunization records have a higher incidence of asthma than children who have never received an immunization or who have incomplete immunizations.

TABLE 20: The final status of DPT and DaPT vaccination & Asthma & Wheezing

DPT and DaPT Status at 2790 Days			
Vaccine Status	Frequency	Asthma	Rate %
none	121	8	6.61
incomplete	2761	277	10.03
complete	10723	1236	11.53
over	345	48	13.91
Total	13950	1569	11.25

Note: *complete* is 5 immunizations, *incomplete* is between 1 to 4 immunizations and *over* more than 5 immunizations

The children in the "**Over**" group had an Asthma rate of 13.91% compared to 11.17% (the combined Asthma Rate of **None, Incomplete**, and **Complete**). The unadjusted Odds Ratio was 1.0203 with 95%CL of .98909 to 1.0612, which is also not statistically significant.

Only 121 children out of 13 950 did not receive any DPT or DaPT vaccines "**None**", this is 0.87% of the cohort. As the number of children in this group were so small, it is very difficult if not impossible to make fair comparisons to the other groups, mainly those in the "Complete" group. However, the unadjusted Odds Ratio was 0.9499 with a 95%CL of 0.9056 to 0.9964 was

significant. This indicates that children who are in the "None" group are less likely to have Asthma when compared to other children in the cohort.

The Chi-square test for trends indicated that there was a significant trend whereby children who received more vaccines (**None, Incomplete, Complete,** and **Over**) were more likely to have Asthma. The Chi-square test for trends value was 9.9801 with 3 df and a probability of 0.0187.

For the purpose of a logistic regression the four different groups in the table above were numbered as follows:

Number of doses	Group Name	SAS Group #
5	Complete	4
1 to 4	Incomplete	3
6+	Over	2
0	None	1

TABLE 21: The adjusted Odds Ratio of the Status groups and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.621	0.361	1.067
Rx	4 to 11	0.806	0.684	0.951
Rx	1 to 3	0.947	0.827	1.084
Rx	0 (reference)			
MD consults	152 to 459	19.294	12.783	29.121
MD	67 to 151	8.353	6.695	10.42
MD	50 to 66	4.139	3.306	5.182
MD	36 to 49	2.227	1.764	2.81
MD	0 to 35 (ref.)			
Region	U vs Rural	1.291	1.145	1.455
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.73	1.429	2.095
Income	Low vs High	1.021	0.901	1.157
DPT/DaPT	4	1.316	0.587	2.953
	3	1.279	0.607	2.694
	2	1.185	0.558	2.518
	1 (ref)			

For this model the "**None**" group was used as a reference group for the others (**Incomplete, Complete** and **Over**).

For the following adjusted Odds Ratios the DPT/DaPT groups were regrouped as follows:

Vaccine group	SAS group #	New SAS group #
Complete	4	2
Over	3	2
Incomplete	2	1
None	1	1

Here the "**Complete**" and "**Over**" groups were combined and the "**Incomplete**" and "**None**" groups were combined to form the new reference group. As the (n) of the original reference group "**None**" for Asthma only had 114 people it is very difficult to compare to other groups. By combining the "**None**" group to the "**Incomplete**" group the (n) is substantially increased.

TABLE 22: The adjusted Odds Ratios of Group#2 (None, Incomplete) and Group#1 (Complete, Over) and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.622	0.362	1.069
Rx	4 to 11	0.808	0.685	0.952
Rx	1 to 3	0.948	0.829	1.085
Rx	0 (reference)			
MD	152 to 459	19.327	12.809	29.162
MD	67 to 151	8.36	6.701	10.428
MD	50 to 66	4.142	3.309	5.186
MD	36 to 49	2.229	1.766	2.813
MD	0 to 35 (ref.)			
Region	U vs Rural	1.291	1.146	1.455
Gender	M vs F	1.418	1.27	1.584
Mom Hx	Yes vs No	1.73	1.428	2.095
Income	Low vs High	1.022	0.902	1.158
DPT/DaPT	2 vs 1	1.086	0.943	1.251

Note: For Region U = Urban / For Income low vs. high + average

Although the size of the reference group was increased, the result remained non-significant. The adjusted OR for Group 2 vs. 1 had the same outcome for Wheezing.

** Additional TABLEs on the demographics of immunization status can be found in Appendix III.

PART II: THE MONTH OF ASTHMA ONSET & NUMBER OF DPT IMMUNIZATIONS RECEIVED

In addition to a question of whether immunization status has an effect over the Asthma rate, there is also a question to the effect of – At what point in the immunization schedule or after how many vaccines are received does Asthma appear? The following table is a summary of specific data extracted from the database. It was possible to determine in what month of what year Asthma arose and how many DPT vaccines had been received prior to the initial onset of Asthma. Only DPT was investigated and presented to simplify the analysis. As DPT began to be phased out in 1997, the majority of the children in this cohort were primarily immunized with DPT and then with the newer version of DaPT (usually between 1 to 2 doses).

The following table and calculations serve as an example of how the following seven figures were compiled. The remaining tables and calculations for year 2 to 7 can be found in Appendix III.

TABLE 23: The number of DPT immunizations received between 2 to 12 months after birth (1st year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
2	DPT	6					6
3	DPT	29					29
4	DPT	22	6	1			29
5	DPT	13	36				49
6	DPT	5	31	4			40
7	DPT	2	12	34			48
8	DPT	4	6	46	1		57
9	DPT		3	35			38
10	DPT	2	2	34			38
11	DPT	2	4	23	1		30
12	DPT	2	1	29			32
Asthma Total		87	101	206	2		396
Asthma Total (%)		21.97	25.51	52.02	0.5		100
Immunization status at 12 M	(# of Children)	384	1047	12169	71	5	

The number of months that have passed since birth are under the (Months of Age) column. The vaccine of concern is the DPT vaccine. At each month after birth the number of DPT vaccines from 1 to 5 is examined and the number of children who have developed Asthma within the same month are indicated in the cells within the middle section of the TABLE. The program insured that the children developed Asthma after their last vaccine and not before. For example, at 4 months after birth of the children who were immunized with one DPT vaccine there were 29 children who went on to develop Asthma within the 4th month. There were 22 of these children who received their 1st DPT vaccine, 6 children who received their second vaccine, and 1 child who received his or her 3rd DPT vaccine. The last row indicates how many children belonged to each "DPT dose group". At the end of 12 months there were 384 children who had only received one dose of DPT, while there were 1047 children who had only received 2 doses etc..

SAMPLE CALCULATION:

Total number (Frequency) of X doses received:

5 children had received	1	2	3	4	5	doses of DPT
5 + 71= 76 children had received	1	2	3	4		doses of DPT
76 + 12 169 = 12 245	1	2	3			doses of DPT
12 245 + 1047 = 13 292	1	2				doses of DPT
13 292 + 384 = 13 676	1					dose of DPT

Doses	Frequency of X doses received	Total Asthma Cases per dose	Relative Asthma Rate
5	5	0	0
4	76	2	2.63%
3	12 169	206	1.68%
2	13 292	101	0.75%
1	13 676	87	0.64%

There were 13 676 children who received at least one dose of DPT and of these children there were 87 of them whose initial onset of Asthma developed after their first dose of DPT (Relative Asthma rate of 0.64%). The following figures demonstrate the changes in dose frequency and the Relative Asthma rate over time.

FIGURE 38: THE FREQUENCY # OF CHILDREN IMMUNIZED WITH 1 TO 5 DOSES OF DPT AND THE CORRESPONDING ASTHMA RATE IN THE FIRST 12 MONTHS OF LIFE

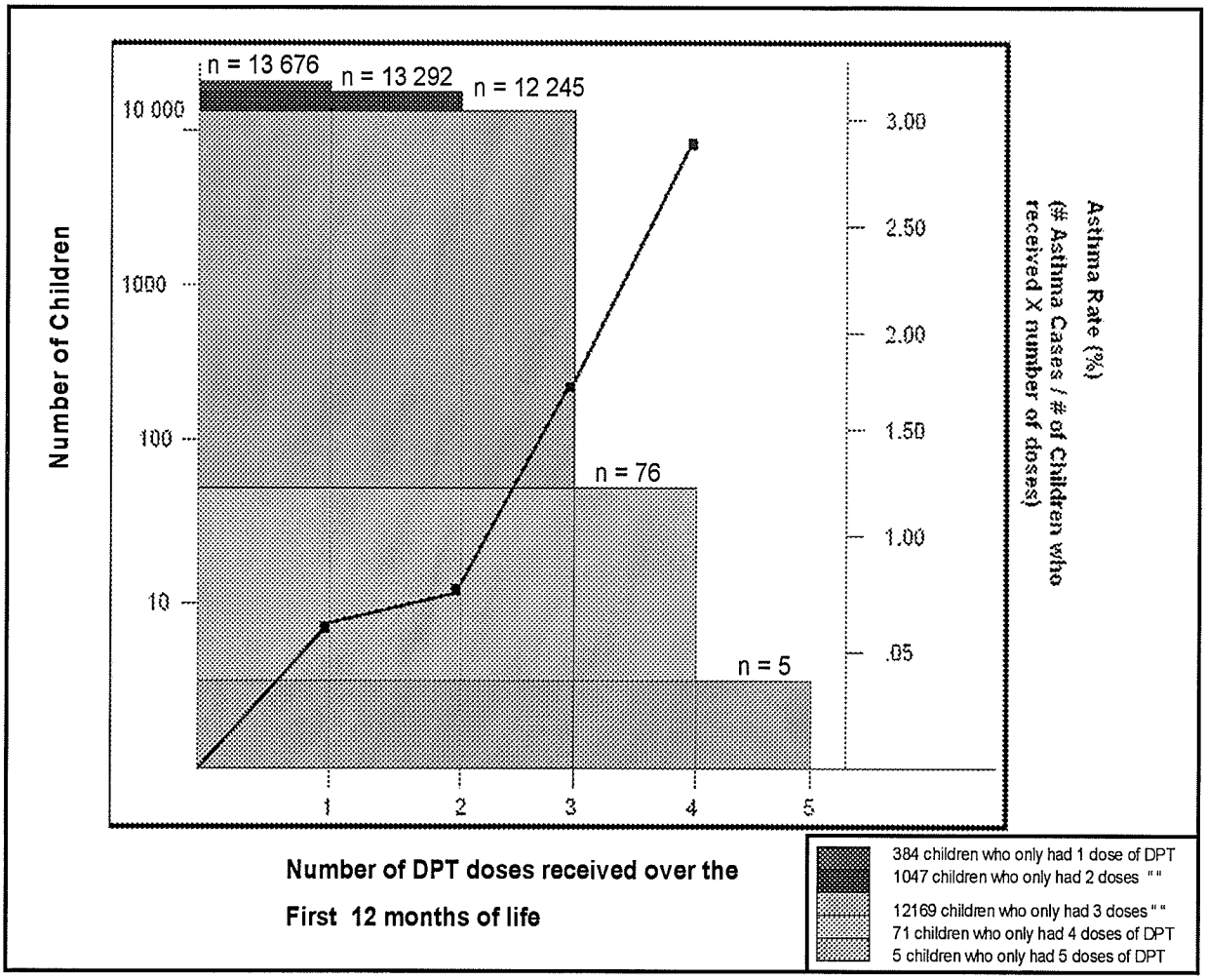
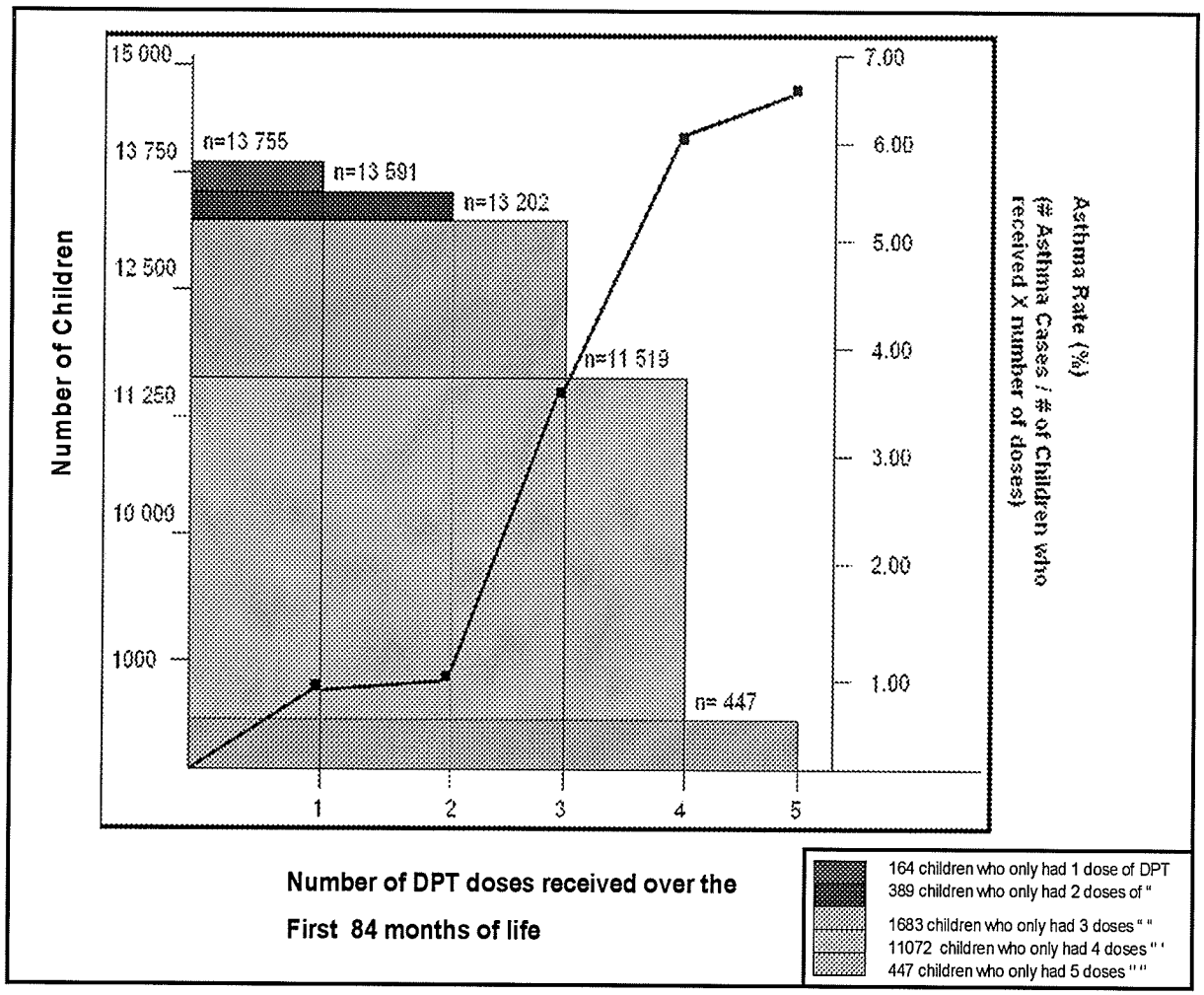


FIGURE 39: THE FREQUENCY # OF CHILDREN IMMUNIZED WITH 1 TO 5 DOSES OF DPT AND THE CORRESPONDING ASTHMA RATE IN THE FIRST 84 MONTHS OF LIFE



Note: The tables which include the exact number of new Asthma cases per month (1 to 7 years after birth) can be found in Appendix III.

Over time children in the cohort move towards completing their immunizations according to the childhood immunization schedule requirements. The number of children who receive a higher number of DPT doses increases. By 84 months after birth only 164 children have received only 1 dose of DPT while the majority of the children have received 4 doses (11 072 children). Although there are fluctuations over time in the asthma prevalence when distributed by number of DPT doses received at 84 months after birth, the asthma prevalence increases with the number of doses received. However, as age is a major confounder of this trend, conclusions can not be made from this data. The figure containing the incidence of Asthma can be found in Chapter 3.

Part III:

THE ASSOCIATION BETWEEN IMMUNIZATION STATUS & WHEEZING RATES

Research Question One – *Second Objective:*

1 – Is there an association between immunization status and incidence of wheezing?

My research hypothesis is that children who have complete immunization records have a higher incidence of wheezing than children who have never received an immunization or who have incomplete immunizations.

TABLE 24: The final status of DPT and DaPT vaccination & Wheezing

DPT and DaPT Status at 2790 Days			
Vaccine Status	Frequency	Wheeze	Rate%
none	121	27	22.31
incomplete	2761	1140	41.29
complete	10723	4560	42.53
over	345	171	49.57
Total	13950	5898	42.28

Note: *complete* is 5 immunizations, *incomplete* is between 1 to 4 immunizations and *over* more than 5 immunizations

The "**Over**" group had a Wheezing rate of 49.47% compared to 42.08% among the other children not in the "**Over**" group. The unadjusted Odds Ratio was 1.1463 with a 95%CL of 1.0984 to 1.6534, which is significant. The Wheezing rate of the "**None**" children was 22.31% (27/121) compared to 42.09% (5871/13829) of the other children. The unadjusted OR was 0.7407 with a 95%CL of 0.6726 to 0.8158, which is also significant. The Wheezing rate of the "**Over**" children was 49.57% (171/345) compared to 42.08% (5711/13572) of the other children. The unadjusted Odds Ratio was 1.1463 with a 95%CL of 1.0364 to 1.2678, which is also significant.

The Chi-square test for trends indicated that there was a significant trend whereby children who received more vaccines (**None, Incomplete, Complete,** and **Over**) were more likely to have Wheezing. The Chi-square test for trends value was 28.6434 with 3 df and a probability of <0.0001.

For the following TABLE the DPT/DaPT groups were regrouped as follows:

Number of doses	Group Name	SAS Group #
5	Complete	4
1 to 4	Incomplete	3
6+	Over	2
0	None	1

TABLE 25: The adjusted Odds Ratios of Group (None, Incomplete, Complete, Over) and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.675	1.091	2.572
Rx	4 to 11	1.803	1.611	2.018
Rx	1 to 3	1.398	1.283	1.522
Rx	0 (reference)			
MD	152 to 459	10.312	6.674	15.935
MD	67 to 151	5.969	5.29	6.735
MD	50 to 66	3.225	2.874	3.618
MD	36 to 49	2.15	1.923	2.404
MD	0 to 35 (ref.)			
Region	U vs Rural	1.106	1.023	1.194
Gender	M vs Female	1.443	1.342	1.552
Mom Hx	Yes vs No	1.824	1.536	2.119
Income	Low vs High	1.294	1.189	1.409
DPT/DaPT	4	1.926	1.159	3.203
	3	1.701	1.079	2.683
	2	1.74	1.097	2.758
	1 (ref.)			

Once the potential confounding variables were controlled for, all of the adjusted ORs were statistically significant. Each group of children (**Incomplete**, **Complete** and **Over**) were compared to the "**None**" group and in each case these children were more likely to have Wheezing than the children who had not been immunized with DPT or DaPT vaccines.

CHAPTER 9: DPT IMMUNIZATION DELAYED & ON TIME & ASTHMA

The Canadian immunization schedule for children indicates that Diphtheria, Pertussis, and Tetanus should be given at 2, 4, 6 and 18 months after birth and then again one time between 4 to 6 years. This chapter will look at adherence to the set immunization schedule and the Asthma rates associated with the different groups of children, which are based on immunization status, after which logistic Regression and other statistical tests are presented.

To reiterate the **Second Research Question** –

> *2 – Is there a difference in the incidence of asthma in children who have completed their immunizations according to the set schedule and in those whose immunizations are complete but have been delayed for one reason or another?*
>
> *My research hypothesis is that children who had delayed immunizations will have a lower incidence of asthma.*

For this objective the Asthma definition was used as the dependent outcome variable. DPT combinations (whole cell and acellular pertussis) were the main vaccines of interest. For this objective, the interest lies in which pattern of immunization is associated with a higher or lower rate of Asthma by assessing the Asthma rate at the end of the study period (7 years).

Below are the various combinations in which a vaccine could have been delayed as well as the incidence of asthma. The number of vaccines received are indicated in the far left column; the next two columns indicate whether the vaccines (1 to 4) were given on schedule or if they were delayed; the next column indicates the time in days when each dose should have been administered. The remaining cells indicate the frequency or the number of children who fell into this pattern of immunization, the number of children who had Asthma, and the Asthma rate. Below each Group is a "Note" about which vaccines were administered and how many and the end date (DPT5_2790 [5 doses of DPT were given by 2790 days after birth], DPT4DaPT1_2790, DaPT4_2790).

**The complete version of TABLE 47 (Groups 1 to 18 A and B) can be found in Appendix III.

TABLE 26: (Group C 1 to 18): The Children who have complete DPT (4 or 5 doses) vaccinations both on schedule and delayed (Abbreviated TABLE)

Group 1 C						
Onsched & Over			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		1005	145	14.43
1	X		62			
2	X		124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 2 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		941	139	14.77
1	X		62			
2	X		124			
3	X		186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 3 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		646	89	13.78
1	X		62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 4 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		1354	175	12.92
1	X		62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 5 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		362	44	12.15
1		X	62			
2	X		124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 6 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		271	31	11.44
1		X	62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						

Group 7	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		997	117	11.74
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 8	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		443	57	12.87
1	X		62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 9	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		342	38	11.11
1		X	62			
2	X		124			
3	X		186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 10	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		209	29	13.88
1	X		62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 11	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		348	35	10.06
1		X	62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 12	C		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		376	52	13.83
1	X		62			
2	X		124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						

Group 13 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		332	40	12.05
1		X	62			
2		X	124			
3	X		186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 14 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		3708	338	9.12
1		X	62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 15 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 16 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 17 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1		X	62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						
Group 18 C			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		181	24	13.26
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4 + DPT5_2790 = 5						

The 18 different groups have different frequencies and different Asthma rates. The two groups of interest are Group C #1 (had each of their first 4 DPT vaccines on schedule) and Group C # 14 (had each of their first 4 DPT vaccines delayed). The TABLE below of the adjusted Odds Ratios confirms this.

TABLE 27: Adjusted Odds Ratio of Group C (1 to 18) and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.646	0.375	1.111
Rx	4 to 11	0.821	0.696	0.969
Rx	1 to 3	0.952	0.832	1.09
Rx	0 (reference)			
MD	152 to 459	18.993	12.576	28.684
MD	67 to 151	8.124	6.503	10.149
MD	50 to 66	4.028	3.214	5.049
MD	36 to 49	2.182	1.728	2.756
MD	0 to 35 (ref.)			
Region	U vs Rural	1.249	1.106	1.41
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.718	1.418	2.081
Income	Low vs High	1.04	0.917	1.18
Group C	Other	0.798	0.63	1.012
	2	1.055	0.813	1.37
	3	1.005	0.748	1.35
	4	0.965	0.754	1.24
	5	0.862	0.594	1.251
	6	0.816	0.532	1.251
	7	0.883	0.674	1.158
	8	0.942	0.671	1.324
	9	0.779	0.527	1.152
	10	0.887	0.569	1.383
	11	0.742	0.496	1.111
	12	0.893	0.628	1.271
	13	0.847	0.575	1.248
	14	0.786	0.631	0.978
	18	0.893	0.552	1.445
	#1 (ref.)			

When each Group (Other, 2 to 18) was compared to Group C # 1 only Group C #14's OR was statistically significant. Where Group 1 (all 4 DPT vaccines on schedule) and Group 14 (all 4 DPT vaccines delayed).

PART II

Additional research questions for the timing of DPT immunization are –

Is there a difference in the incidence of asthma in children who did not receive their first DPT immunization by 62 days after birth and those who did, regardless of whether or not they received their other DPT doses on time?

Is there a difference in the incidence of asthma in children who did not receive their second DPT immunization by 124 days after birth and those who did, regardless of whether or not they received their other DPT doses on time?

Is there a difference in the incidence of asthma in children who did not receive their third DPT immunization by 186 days after birth and those who did, regardless of whether or not they received their other DPT doses on time?

Is there a difference in the incidence of asthma in children who did not receive their fourth DPT immunization by 558 days after birth and those who did, regardless of whether or not they received their other DPT doses on time?

Is there a difference in the incidence of asthma in children who did not receive their first and second DPT immunization by 62 and 124 days after birth and those who did, regardless of whether or not they received their other DPT doses on time?

Is there a difference in the incidence of asthma in children who did receive their first and second DPT immunization by 62 and 124 days after birth and those who did not, regardless of whether or not they received their other DPT doses on time?

TABLE 28: The number of children who had their DPT vaccines delayed & their Asthma Rates

Vaccines Delayed	Frequency	Asthma	Asthma Rate (%)
First	6541	667	10.19
Second	7495	811	10.82
Third	8053	887	11.01
Fourth	7671	854	11.13
First & Second	5489	550	10.02
Vaccines on time			
First & Second	2968	425	14.32

LOGISTIC REGRESSIONS & ADJUSTED ODDS RATIOS

TABLE 29: Adjusted Odds Ratio of Group C # 1 (All 4 DPT On Schedule) and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.629	0.366	1.08
Rx	4 to 11	0.812	0.688	0.957
Rx	1 to 3	0.953	0.833	1.09
Rx	0 (reference)			
MD	152 to 459	19.292	12.785	29.11
MD	67 to 151	8.377	6.717	10.447
MD	50 to 66	4.158	3.322	5.203
MD	36 to 49	2.238	1.774	2.823
MD	0 to 35 (ref.)			
Region	U vs Rural	1.284	1.139	1.447
Gender	M vs F	1.419	1.27	1.585
Mom Hx	Yes vs No	1.721	1.421	2.084
Income	Low vs High	1.018	0.899	1.153
Group C	#1 vs Other	1.007	0.997	1.017
	Other			

When Group C # 1 (First 4 doses of DPT received on schedule) was compared to all of the other children for the outcome of Asthma the adjusted Odds Ratio was not significant as the 95% CL crossed over 1.

TABLE 30: Adjusted Odds Ratio of Group 14 vs. Other and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.628	0.366	1.08
Rx	4 to 11	0.811	0.688	0.957
Rx	1 to 3	0.953	0.833	1.09
Rx	0 (reference)			
MD	152 to 459	19.257	12.762	29.058
MD	67 to 151	8.348	6.694	10.411
MD	50 to 66	0.14	3.308	5.181
MD	36 to 49	2.23	1.767	2.814
MD	0 to 35 (ref.)			
Region	U vs Rural	1.269	1.125	1.432
Gender	M vs F	1.415	1.267	1.581
Mom Hx	Yes vs No	1.719	1.419	2.081
Income	Low vs High	1.023	0.903	1.159
Group C	#14 vs Other	0.873	0.765	0.997
	Other			

The children who were in Group C #14 (first 4 DPT doses were delayed) were less likely than all of the other children to have Asthma.

TABLE 31: The adjusted Odds Ratio of the First DPT Delayed and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.64	0.372	1.102
Rx	4 to 11	0.816	0.692	0.962
Rx	1 to 3	0.951	0.831	1.088
Rx	0 (reference)			
MD	152 to 459	19.024	12.606	28.711
MD	67 to 151	5.16	6.535	10.189
MD	50 to 66	4.054	3.235	5.079
MD	36 to 49	2.195	1.738	2.771
MD	0 to 35 (ref.)			
Region	U vs Rural	1.259	1.116	1.42
Gender	M vs F	1.419	1.271	1.585
Mom Hx	Yes vs No	1.725	1.424	2.089
Income	Low vs High	1.036	0.914	1.175
1st DPT delayed	Other vs. 1st on time	0.815	0.686	0.967
	1st Delay vs 1st on t	0.827	0.734	0.931
	1st on time DPT (ref.)			

Note: Other includes children who did not receive at least 4 doses of DPT

The adjusted ORs indicate that children who did not have their first DPT on time and who either received 4 or more doses of DPT or did not were less likely to have Asthma than those who did have their first dose of DPT on time and who received at least 4 doses of DPT.

TABLE 32: The adjusted Odds Ratio of the First & Second DPT Delayed and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.634	0.368	1.091
Rx	4 to 11	0.814	0.69	0.96
Rx	1 to 3	0.95	0.83	1.087
Rx	0 (reference)			
MD	152 to 459	19.06	12.629	28.765
MD	67 to 151	8.181	6.552	10.216
MD	50 to 66	4.058	3.239	5.085
MD	36 to 49	2.194	1.738	2.771
MD	0 to 35 (ref.)			
Region	U vs Rural	1.261	1.118	1.423
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.732	1.43	2.098
Income	Low vs High	1.035	0.913	1.174
1st & 2nd DPT delayed	Other vs. 1st and/or 2nd DPT ontime	0.843	0.713	0.998
	1st & 2nd DPT delayed vs. 1st and/or 2nd ot	0.86	0.762	0.97
	1st and/or 2nd DPT ontime (reference)			

Note: children in the "Other" group did not receive at least 4 doses of DPT

The adjusted OR indicates that children who were delayed for their 1st and 2nd DPT vaccine were less likely to develop Asthma than children who either received one or both of their 1st and 2nd DPT vaccine on time. The adjusted OR for the "Other" group also indicated that the children within this group (1st and / or 2nd DPT delayed and a total of less than 4 doses of DPT) were also less likely to develop Asthma than the children who received their 1st and 2nd DPT on time and who received at least 4 doses of DPT.

TABLE 33: The adjusted Odds Ratio of the First & Second DPT On time and Asthma

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	0.639	0.371	1.1
Rx	4 to 11	0.818	0.694	0.965
Rx	1 to 3	0.95	0.83	1.087
Rx	0 (reference)			
MD	152 to 459	18.996	12.583	28.677
MD	67 to 151	8.129	6.51	10.151
MD	50 to 66	4.032	3.218	5.053
MD	36 to 49	2.182	1.728	2.755
MD	0 to 35 (ref.)			
Region	U vs Rural	1.251	1.108	1.413
Gender	M vs F	1.415	1.266	1.58
Mom Hx	Yes vs No	1.726	1.425	2.09
Income	Low vs High	1.041	0.918	1.18
1st & 2nd DPT Ontime	Other vs. 1st and/or 2nd DPT delayed	0.873	0.771	0.989
	1st and 2nd DPT ontime vs. " "	1.11	0.952	1.294
	1st and/or 2nd DPT delayed			

The adjusted the OR indicates that children who received both their 1st and 2nd DPT immunizations on time and who also received at least 4 doses of DPT were not more or less likely to develop Asthma than children who also received at least 4 doses of DPT and had their 1st and / or 2nd DPT vaccine delayed. The adjusted OR for the "Other" group (had their 1st and / or 2nd DPT on time but had less than 4 doses of DPT) were less likely than children who had at least 4 doses of DPT and who had their 1st and / or 2nd DPT delayed to develop Asthma.

PART III:

DPT IMMUNIZATION DELAYED & ON TIME & WHEEZING

Research Question Two – *Second Objective:*

2 – Is there a difference in the incidence of wheezing in children who have completed their immunizations according to the set schedule and in those who their immunizations are complete but have been delayed for one reason or another?

My research hypothesis is that children who had delayed immunizations will have a lower incidence of wheezing.

Note: Refer to Table for the order of Group C.

TABLE 34: Adjusted Odds Ratio of Group C (1 to 18) and Wheezing

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	1.679	1.093	2.579
Rx	4 to 11	1.802	1.609	2.017
Rx	1 to 3	1.4	1.285	1.525
Rx	0 (reference)			
MD	152 to 459	10.417	6.74	16.102
MD	67 to 151	6.054	5.358	6.84
MD	50 to 66	3.273	2.914	3.677
MD	36 to 49	2.169	1.939	2.427
MD	0 to 35 (ref.)			
Region	U vs Rural	1.109	1.026	1.2
Gender	M vs F	1.444	1.342	1.553
Mom Hx	Yes vs No	1.79	1.524	2.103
Income	Low vs High	1.293	1.188	1.408
Group C	Other	1.001	0.85	1.179
	2	0.973	0.804	1.177
	3	0.987	0.797	1.22
	4	1.011	0.848	1.206
	5	0.73	0.563	0.948
	6	0.792	0.591	1.063
	7	0.935	0.774	1.13
	8	0.846	0.665	1.077
	9	0.841	0.645	1.097
	10	0.769	0.557	1.061
	11	1.199	0.921	1.56
	12	0.901	0.698	1.162
	13	1.099	0.841	1.435
	14	0.928	0.796	1.081
	18	0.986	0.702	1.385
	#1 (ref.)			

The adjusted OR's for Wheezing indicated that the children in Group C # 5 (their first DPT vaccine was delayed) were less likely to develop Wheezing than children in Group C #1 (their first 4 DPT vaccines were on schedule).

PART IV: Additional research questions (the same questions as those on page 121, except for the outcome of wheezing).

TABLE 35: The number of children who had their DPT vaccines delayed & their Wheezing Rates

Vaccines Delayed	Frequency	Wheeze	Wheeze Rate (%)
First	6541	2686	41.06
Second	7495	3122	41.65
Third	8053	3403	42.26
Fourth	7671	3271	42.64
First & Second	5489	2233	40.68
Vaccines on time			
First & Second	2968	1354	45.62

LOGISTIC REGRESSIONS:

TABLE 36: Adjusted Odds Ratio of Group C # 1 (All 4 DPT On Schedule) and Wheezing

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	1.683	1.096	2.584
Rx	4 to 11	1.817	1.624	2.034
Rx	1 to 3	1.406	1.291	1.531
Rx	0 (reference)			
MD	152 to 459	10.343	6.695	15.979
MD	67 to 151	5.969	5.292	6.733
MD	50 to 66	3.227	2.877	3.62
MD	36 to 49	2.151	1.925	2.405
MD	0 to 35 (ref.)			
Region	U vs Rural	1.104	1.022	1.193
Gender	M vs F	1.445	1.344	1.554
Mom Hx	Yes vs No	1.801	1.533	2.115
Income	Low vs High	1.301	1.196	1.415
Group C	#1 vs Other	1.003	0.996	1.01
	Other			

The adjusted odds ratio for Wheezing was not statistically significant.

TABLE 37: Adjusted Odds Ratio of Group 14 vs. Other and Wheezing

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	1.681	1.095	2.581
Rx	4 to 11	1.817	1.624	2.034
Rx	1 to 3	1.406	1.291	1.531
Rx	0 (reference)			
MD	152 to 459	10.345	6.696	15.982
MD	67 to 151	5.965	5.288	6.728
MD	50 to 66	3.224	2.874	3.616
MD	36 to 49	2.15	1.923	2.403
MD	0 to 35 (ref.)			
Region	U vs Rural	1.101	1.018	1.19
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.8	1.532	2.114
Income	Low vs High	1.301	1.196	1.416
Group C	#14 vs Other	0.962	0.884	1.047
	Other			

There was no significant difference for wheezing.

TABLE 38: The adjusted Odds Ratio of the First DPT Delayed and Wheezing

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	1.673	1.09	2.569
Rx	4 to 11	1.811	1.618	2.027
Rx	1 to 3	1.406	1.291	1.531
Rx	0 (reference)			
MD	152 to 459	10.4	6.731	16.068
MD	67 to 151	6.013	5.324	6.79
MD	50 to 66	3.25	2.895	3.649
MD	36 to 49	2.165	1.935	2.421
MD	0 to 35 (ref.)			
Region	U vs Rural	1.105	1.023	1.195
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.796	1.529	2.109
Income	Low vs High	1.294	1.189	1.409
1st DPT delayed	Other vs. 1st DPT ontime	1.037	0.928	1.159
	1st DPT delayed vs. 1st DPT ot	0.963	0.888	1.044
	1st DPT on time (reference)			

There was no significant difference for wheezing.

TABLE 39: The adjusted Odds Ratio of the First & Second DPT Delayed and Wheezing

ODDS RATIO ESTIMATES				
Effect	Categories	Estimate	95% CL	
			Lower	Upper
Rx	12 to 40	1.669	1.087	2.562
Rx	4 to 11	1.81	1.617	2.026
Rx	1 to 3	1.405	1.29	1.53
Rx	0 (reference)			
MD	152 to 459	10.419	6.744	16.098
MD	67 to 151	6.026	5.337	6.804
MD	50 to 66	3.256	2.899	3.656
MD	36 to 49	2.167	1.937	2.424
MD	0 to 35 (ref.)			
Region	U vs Rural	1.107	1.024	1.197
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.797	1.53	2.111
Income	Low vs High	1.293	1.187	1.407
1st & 2nd DPT delayed	Other vs. 1st and/or 2nd DPT ontime	1.05	0.943	1.17
	1st & 2nd DPT delayed vs " "	0.98	0.904	1.063
	1st and/or 2nd DPT ontime (ref.)			

The adjusted OR for these groups and Wheezing were not statistically significant.

The adjusted ORs for the all of the other groups (Second DPT delayed, Third DPT delayed etc.) were also not statistically significant for both the Asthma and Wheezing outcome.

CHAPTER 10: VARIATIONS OF THE DPT VACCINE & THE ASTHMA RATES

This chapter explores the relationship between the different types of DPT vaccinations and the Asthma and Wheezing rates associated with the different groups of children, based on their immunization status.

Research Question Three:

3 – Is there a difference in the incidence of asthma among children who have been immunized with DPT (Diphtheria, whole cell pertussis, tetanus) as opposed to DaPTP (Diphtheria, acellular pertussis, tetanus, polio) or DT (diphtheria and tetanus) or aP (acellular pertussis)?

My research hypothesis is that the combination vaccines containing pertussis as well the acellular pertussis vaccine will be associated with an increase in the incidence of asthma compared to DT.

There were 421 children who received 1+ Diphtheria, Tetanus vaccines either alone or in combination. Nearly all of the children (381 / 388 or 98.19%) who received a DT vaccine also received the conventional DPT or DaPT combinations. Only 7 children had histories of receiving only the DT combinations without ever have receiving DPT or DaPT. There were 49 children who received a DT vaccine before they received a DPT vaccine. Only 5 of these children (10.2%) had Asthma. There were 133 children who received a DT vaccine before they received a DaPT vaccine, 17 of which had Asthma (12.78%). Of these two groups of children there were 26 who had a DT vaccine, either before a DPT or DaPT vaccine and 3 of the 26 had Asthma. There were only 4 children who received an aP immunization and because of this small number they were combined with the children who received a DaPT vaccine, for analyses.

TABLE 40: The Frequency of Diphtheria / Tetanus Vaccines & Asthma

The Vaccine Dose and Type and Asthma Rates at 90 months (2790 days)				
Dose	Type	Frequency	Asthma	Rate%
1 or more	DipT_2790	33	0	0
1	DT1_2790	310	47	15.16
2	DT2_2790	47	9	19.15
3	DT3_2790	19	4	21.05
4	DT4_2790	12	1	8.33
Overall Total		421	61	14.49

Note: Dip T was two separate vaccines received by the same individual, combined for the purpose of analyses. DT is a combined vaccine of Diphtheria and Tetanus. DT 1 to 4 indicates the number of doses which were received and 2790 is the number of days after birth (~ 7.5 years).

When the children who had 1 or more DT vaccines (388 children) are grouped together and compared to all other children who never received a DT type vaccine the Asthma rate becomes 16.01%. The unadjusted Odds Ratio (OR) for Asthma for the 310 children who received 1 DT vaccination was 1.0472 with a 95% Confidence Limit (C.L.) of 0.9987 to 1.0981, which is not significant. If the children are grouped to include 1 or more DT vaccines (388 children) then the unadjusted OR is 1.0576 with a 95% CL of 1.0116 to 1.1057, which is then significant.

TABLE 41: Logistic Regression of Asthma and DT (1 or more)

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.625	0.364	1.074
Rx	4 to 11	0.804	0.682	0.948
Rx	1 to 3	0.947	0.828	1.084
Rx	0 (reference)			
MD	152 to 459	19.366	12.836	29.219
MD	67 to 151	8.421	6.753	10.5
MD	50 to 66	4.188	3.347	5.24
MD	36 to 49	2.249	1.783	2.837
MD	0 to 35 (ref.)			
Region	U vs Rural	1.288	1.143	1.452
Gender	M vs F	1.416	1.268	1.582
Mom Hx	Yes vs No	1.725	1.425	2.089
Income	Low vs High	1.014	0.895	1.149
DT	1+ vs None	1.295	0.965	1.736

Note: here DT includes children who received 1 or more DT vaccination

The adjusted Odds Ratio for DT is 1.295 with a 95% CL of 0.965 to 1.736, which is not significant.

PART II: DT & DPT & DaPT VACCINE COMBINATIONS & ASTHMA RATES

Another approach for analyzing this data was to determine how Asthma may vary with the variations in DT and DPT and DaPT combinations. For this cohort this was more realistic and testable questions or objectives.

Did the children who received a combination (1 or more of each type of vaccine) of DT with DPT vaccines have a higher incidence of Asthma when compared to the children who had a combination of DT and DaPT?

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Asthma when compared to the children who had a combination of DT and DaPT and DPT?

TABLE 42: Part A – Two Vaccine Combinations of DT (1 to 4) and DPT (1 to 6)

Vaccine Combination	Frequency	Asthma
DT1_DPT1	2	0
DT1_DPT2	8	0
DT1_DPT3	29	6
DT1_DPT4	148	31
DT1_DPT5	2	0
DT1_DPT6	1	0
DT2_DPT1	1	0
DT2_DPT2	4	1
DT2_DPT3	15	3
DT2_DPT4	0	0
DT2_DPT5	0	0
DT2_DPT6	0	0
DT3_DPT1	4	1
DT3_DPT2	8	1
DT3_DPT3	1	0
DT3_DPT4	0	0
DT3_DPT5	0	0
DT3_DPT6	0	0
DT4_DPT1	3	0
DT4_DPT2	0	0
DT4_DPT3	0	0
DT4_DPT4	0	0
DT4_DPT5	0	0
DT4_DPT6	0	0
Total	**226**	**43**
Rate		**19.03%**

Note: this table presents the different combinations of vaccines. DT1_DPT1 (children who received 1 DT vaccine and 1 DPT vaccine over ~7.5 years). DT2_DPT (children who received 2 DT vaccines and 1 DPT vaccine over ~7.5 years).

TABLE 43: Part B – Two Vaccine Combinations of DT (1 to 4) and DaPT (1 to 6)

Vaccine Combination	Frequency	Asthma
DT1_DaPT1	0	0
DT1_DaPT2	1	0
DT1_DaPT3	1	0
DT1_DaPT4	0	0
DT1_DaPT5	0	0
DT1_DaPT6	0	0
DT2_DaPT1	1	1
DT2_DaPT2	0	0
DT2_DaPT3	0	0
DT2_DaPT4	0	0
DT2_DaPT5	0	0
DT2_DaPT6	0	0
DT3_DaPT1	0	0
DT3_DaPT2	0	0
DT3_DaPT3	0	0
DT3_DaPT4	0	0
DT3_DaPT5	0	0
DT3_DaPT6	0	0
DT4_DaPT1	5	1
DT4_DaPT2	0	0
DT4_DaPT3	1	0
DT4_DaPT4	0	0
DT4_DaPT5	1	0
DT4_DaPT6	0	0
Total	10	2

Note: here the groups are organized in the same manner as the table above except the DaPT vaccine is presented instead of DPT.

The first part of the new objective could also not be adequately tested due to the very small number of children who received DT and DaPT only (10 children). The TABLE above categorizes DT and DPT and makes it obvious that children who received DT and DPT vaccines only were more likely to have a higher incidence of Asthma (19.03%) when compared to the overall averages of 11.25% for Asthma.

TABLE 44: Three Vaccine Combinations of DT (1 to 4) / DPT (1 to 6) / DaPT (1 to 2)

Vaccine Combination	Frequency	Asthma
DT1_DPT1_DaPT1	3	0
DT1_DPT2_DaPT1	9	0
DT1_DPT3_DaPT1	57	6
DT1_DPT4_DaPT1	33	1
DT1_DPT5_DaPT1	0	0
DT1_DPT6_DaPT1	2	0
DT2_DPT1_DaPT1	2	1
DT2_DPT2_DaPT1	14	0
DT2_DPT3_DaPT1	5	1
DT2_DPT4_DaPT1	2	1
DT2_DPT5_DaPT1	0	0
DT2_DPT6_DaPT1	0	0
DT3_DPT1_DaPT1	4	2
DT3_DPT2_DaPT1	0	0
DT3_DPT3_DaPT1	0	0
DT3_DPT4_DaPT1	0	0
DT3_DPT5_DaPT1	0	0
DT3_DPT6_DaPT1	0	0
DT4_DPT1_DaPT1	1	0
DT4_DPT2_DaPT1	0	0
DT4_DPT3_DaPT1	0	0
DT4_DPT4_DaPT1	0	0
DT4_DPT5_DaPT1	0	0
DT4_DPT6_DaPT1	0	0
DT1_DPT1_DaPT2	4	2
DT1_DPT2_DaPT2	5	0
DT1_DPT3_DaPT2	2	1
DT1_DPT4_DaPT2	0	0
DT1_DPT5_DaPT2	0	0
DT1_DPT6_DaPT2	0	0
DT2_DPT1_DaPT2	0	0
DT2_DPT2_DaPT2	1	1
DT2_DPT3_DaPT2	0	0
DT2_DPT4_DaPT2	0	0
DT2_DPT5_DaPT2	1	0
DT2_DPT6_DaPT2	0	0
Total	145	16
Rate		11%

DT Combinations	Frequency	Asthma
Overal Total	381	61
Overal Rate		16.01%

Note: This Table is organized in the same manner as the two prior tables, except all three vaccines are presented in this table (DT / DPT / DaPT).

The children who received DT and DPT vaccines but in combination with DaPT vaccines (above Table) had a much lower Asthma rate than the children who received the DT and DPT combinations (11% compared to 19.03%).

TABLE 45: UNADJUSTED ODDS RATIOS

ASTHMA					
Vaccine Combinations	Test	Value	95% CL		Statistically
	ODDS RATIO		Lower	Upper	Significant
DT_DPT		1.0977	1.0301	1.1696	Yes
DT_DaPT		1.974	0.4188	9.3039	No
DT_DPT_DaPT		0.9976	0.9417	1.0568	No

When the children who received both DT and DPT vaccinations were combined into one group and compared to all other children, there was a significant difference. Children in this group are more likely to have Asthma when compared to other children in this cohort.

A logistic regression was also performed using the children who received DT_DPT combinations as the reference category and it was tested with children who received DT_DaPT combinations and DT_DPT_DaPT combinations as well as all other children who did not receive any DT vaccines. The groups were numbered as follows:

Groups	SAS Group #
Other	4
DT_DaPT	3
DT_DPT_DaPT	2
DT_DPT	1

TABLE 46: Logistic Regression of Asthma and DT_DPT / DT_DaPT / DT_DPT_DaPT

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.628	0.365	1.079
Rx	4 to 11	0.806	0.683	0.95
Rx	1 to 3	0.948	0.828	1.085
Rx	0 (reference)			
MD	152 to 459	19.393	12.842	29.286
MD	67 to 151	8.432	6.762	10.513
MD	50 to 66	4.182	3.343	5.233
MD	36 to 49	2.247	1.781	2.834
MD	0 to 35 (ref.)			
Region	U vs Rural	1.285	1.141	1.449
Gender	M vs F	1.418	1.269	1.584
Mom Hx	Yes vs No	1.726	1.425	2.09
Income	Low vs High	1.014	0.895	1.148
DT	4	0.602	0.423	0.856
	3	0.744	0.138	3.997
	2	0.485	0.256	0.919
	1 (ref.)			

Group 4 (children who did not receive a DT vaccine) were less likely to have asthma than children in the reference group (DT_DPT). Children who belonged to Group 2 (DT_DPT_DaPT) were also less likely to have Asthma when compared to Group 1.

PART III: COMPLETE vs. INCOMPLETE DPT/DaPT IMMUNIZATIONS & ASTHMA

Another important question is to asses if there was a difference in the Asthma and Wheezing rates in the children who had incomplete (less than 5 doses) versus complete DPT/DaPT vaccinations (5 + doses).

TABLE 47: The unadjusted odds ratios of DPT and DaPT vaccination combinations

	Vaccine combinations		# of	asthma	asthma	Odds	95% CI	
	DPT	DaPT	children	cases	%	Ratios	low	high
	1	1	45	3				
incomplete	2	1	150	11	9.17			
	3	1	786	76		1.3001	1.0379	1.6285
	4	1	9869	1139				
complete	5	1	147	23	11.61			
	6	1	3	1				
	Total		11000	1253	11.39			
	DPT	DaPT						
	1	2	26	3				
incomplete	2	2	80	7	9.43			
	3	2	542	50		1.079	0.537	2.1682
complete	4	2	127	17	10.1			
	5	2	4	1				
	Total		779	78	10.01			
	Overall Total		11779	1331	11.29	Note: OR's use complete as "exposed"		

The unadjusted odds ratio (OR) for the first DPT /DaPT combinations where children received 1 DaPT vaccine and between 1 to 6 DPT vaccines (Complete vs. Incomplete) was 1.3001 with a 95% CI of 1.0379 to 1.6285, which is significant. The second group where the children had 2 DaPT vaccines and between 1 to 5 DaPT vaccines had an OR of 1.079 with a 95% CI of 0.537 to 2.1682, not significant.

The following TABLE indicates the group orders of the various vaccine combinations and also shows additional data for the children who were vaccinated with either DPT or DaPT or both but who do not fall in to the given categories. Also shown are the 114 children who had never been immunized with a DPT-type vaccine. These unadjusted Odds Ratios indicate that children who had Complete DPT/DaPT immunizations had higher Asthma rates than children

with Incomplete DPT/DaPT immunizations but only if the majority of the doses received were DPT. There was no difference in the Asthma rates between children who had Complete and Incomplete DPT/DaPT immunizations when a greater proportion of the doses were DaPT.

TABLE 48: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	
	3	1	786	76		4
complete	4	1	9869	1139		
	5	1	147	23	11.61	
	6	1	3	1		
Total			11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	3
complete	3	2	542	50		
	4	2	127	17	10.1	
	5	2	4	1		
Total			779	78	10.01	
	Overall Total		11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated &			2057	230	11.18	2
All the children who have never been vaccinated			114	8	7.02	1
Total			2171	238	10.96	
	Grand Total		13950	1569	11.25	
Note: the 5 groups are used in a logistic regression and group 1 is the reference group						

For this analysis the groups are based on DaPT – Group 4 consists of the vaccine combinations which include 1 dose of DaPT. Group 3 consists of the vaccine combinations which include 2 doses of DaPT.

TABLE 49: The adjusted odds ratios of DPT-type vaccines (groups 1 to 4) and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.62	0.36	1.065
Rx	4 to 11	0.807	0.684	0.951
Rx	1 to 3	0.949	0.829	1.086
Rx	0 (reference)			
MD	152 to 459	19.434	12.881	29.321
MD	67 to 151	8.411	6.744	10.49
MD	50 to 66	4.168	3.33	5.216
MD	36 to 49	2.24	1.775	2.827
MD	0 to 35 (ref.)			
Region	U vs Rural	1.293	1.148	1.457
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.726	1.425	2.09
Income	Low vs H	1.017	0.898	1.153
Dvaccines	4	1.129	0.535	2.382
	3	1.124	0.514	2.459
	2	1.074	0.504	2.292
	1 (ref.)			

For this logistic regression, the reference group (Group #1) was the group of children who were never immunized. As each of the 95%CL crossed over 1.00 there were no significant findings.

Another approach of testing whether or not number of doses of DaPT affects the Asthma and Wheezing rates is to group the vaccination categories according to the number of DaPT doses received.

Vaccine Group	#Asthma Cases / Rate	SAS Group #
No DaPT	206 (206/1731=11.9%)	Group 0
1 dose of DaPT	1267 (1267/11184=11.33%)	Group 1
2+ doses of DaPT	88 (88/921=9.55%)	Group 2
No vaccines	8 (8/114=7.02%)	Group 3

TABLE 50: The adjusted odds ratios of DPT-type vaccines (Groups 0 to 3) and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.623	0.363	1.071
Rx	4 to 11	0.807	0.684	0.951
Rx	1 to 3	0.949	0.829	1.086
Rx	0 (reference)			
MD	152 to 459	19.447	12.89	29.34
MD	67 to 151	8.412	6.744	10.492
MD	50 to 66	4.174	3.335	5.225
MD	36 to 49	2.244	1.779	2.832
MD	0 to 35 (ref.)			
Region	U vs Rural	1.29	1.145	1.454
Gender	M vs F	1.416	1.268	1.582
Mom Hx	Yes vs No	1.723	1.423	2.087
Income	Low vs H	1.016	0.896	1.151
DaPT	0	1.142	0.535	2.441
	1	1.121	0.531	2.364
	2	1.08	0.496	2.354
No vaccines	3 (ref.)			

For this logistic regression, the reference group (Group 3) was the group of children who were never immunized. As each of the 95%CL crossed over 1.00 there were not significant findings.

TABLE 51: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	6
	3	1	786	76		
complete	4	1	9869	1139		
	5	1	147	23	11.61	5
	6	1	3	1		
Total			11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	4
complete	3	2	542	50		
	4	2	127	17	10.1	3
	5	2	4	1		
Total			779	78	10.01	
	Overall Total		11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated with DPT+ or DaPT+orDT			2057	230	11.18	2
All the children who have never been vaccinated			114	8	7.02	1
Total			2171	238	10.96	
	Grand Total		13950	1569	11.25	
Note: the 6 groups are used in a logistic regression and group #1 is used as a reference group and compared to groups 2 to 6						

Although Group 2 has the highest Asthma rate (11.18%), this group is not of interest for this analyses. Groups 3, 4, 5, 6 are of interest because of their vaccination combinations. The following table is of the same data; only the model has been adjusted for possible confounders.

TABLE 52: The adjusted odds ratio of DPT-type vaccines (groups 1 to 6) & Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.62	0.36	1.066
Rx	4 to 11	0.807	0.684	0.952
Rx	1 to 3	0.949	0.829	1.086
Rx	0 (reference)			
MD	152 to 459	19.4	12.856	29.275
MD	67 to 151	8.395	6.727	10.477
MD	50 to 66	4.159	3.321	5.209
MD	36 to 49	2.236	1.772	2.823
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.147	1.457
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.728	1.427	2.092
Income	Low vs High	1.018	0.898	1.154
Dvaccines	6	1.098	0.504	2.389
	5	1.132	0.537	2.389
	4	1.188	0.433	3.253
	3	1.115	0.507	2.453
	2	1.074	0.504	2.292
	1 (ref.)			

Note: the preceding table defines the DVaccine group order.

The odds ratios of the 5 different comparisons and of the 6 different groups indicate that none of the comparisons are significant. Here the 114 children who had never been immunized were used as the reference group (Group # 1). None of the OR's were statistically significant as all of the 95%CL's crossed over 1.00.

To test the possible effects of increasing the number of doses of DaPT and the Asthma rates, all of the children who received 1 dose of DaPT were tested against those who received 2 + doses of DaPT. This was performed to determine if the children who received more doses i.e. 2 + of DaPT were less likely to have asthma than children who only received 1 dose.

# of DaPT doses	# of Children	Percent
0	1836	13.16%
1	11 184	80.17%
2 +	930	6.67%

TABLE 53: The adjusted Odds Ratio of 1 and 2 doses of DaPT and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.623	0.363	1.071
Rx	4 to 11	0.808	0.685	0.952
Rx	1 to 3	0.95	0.83	1.087
Rx	0 (reference)			
MD	152 to 459	19.472	12.908	29.375
MD	67 to 151	8.421	6.752	10.503
MD	50 to 66	4.179	3.339	5.23
MD	36 to 49	2.247	1.781	2.835
MD	0 to 35 (ref.)			
Region	U vs Rural	1.291	1.145	1.455
Gender	M vs F	1.417	1.268	1.582
Mom Hx	Yes vs No	1.723	1.423	2.086
Income	Low vs H	1.016	0.897	1.152
DaPT	0 DaPT	1.011	0.861	1.187
	2 DaPT	0.97	0.766	1.228
	1 DaPT (Ref.)			

The Odds Ratios are not statistically significant, as the 95%CL crosses over 1.00.

PART IV: LONE DPT & DaPT IMMUNIZATIONS AND ASTHMA

When the children in the 1995 cohort are broken into different groups based on those who were immunized with DaPT only or DPT only or neither, there were relatively few children in each group.

TABLE 54: The vaccine combinations / the number of children with Asthma within each group / the asthma rate and the group order

Number	Group	Frequency	Asthma	%Asthma
0	Other	13756	1557	11.32
1	DaPT Only	32	2	6.25
2	DPT Only	48	2	4.17
3	No DPT or DaPT	114	8	7.02
Total		13950	1569	11.25

Note: here the "Other" group would include children who have had the DPT / DaPT immunization combination as well as children who received the DT version.

TABLE 55: The adjusted Odds Ratios of Asthma and DPT / DaPT / No DPT or DaPT / Other

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.617	0.359	1.061
Rx	4 to 11	0.803	0.681	0.947
Rx	1 to 3	0.945	0.826	1.081
Rx	0 (reference)			
MD	152 to 459	19.421	12.871	29.306
MD	67 to 151	8.406	6.741	10.482
MD	50 to 66	4.162	3.326	5.209
MD	36 to 49	2.235	1.771	2.82
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.146	1.456
Gender	M vs F	1.417	1.268	1.583
Mom Hx	Yes vs No	1.723	1.422	2.086
Income	Low vs H	1.016	0.897	1.15
DPT	0	1.126	0.534	2.374
	1	0.621	0.119	3.247
	2	0.449	0.089	2.272
	3 (ref.)			

The adjusted Odds Ratio indicates that when the children in Group # 0 (children immunized with both DaPT and DPT and DT) were compared to the children in Group # 3 (children who had never been immunized with those vaccines), they were more likely to have Asthma. However, the 95%CL did not cross 1, so this trend was not significant statistically. The other two comparisons of Group # 1 and 2 to Group # 3 indicated a trend towards being less likely to develop Asthma. Once again the 95%CL was not statistically significant.

PART V: VARIATIONS OF THE DPT VACCINE & WHEEZING

Research Question Three – *Second Objective*:

3 – Is there a difference in the incidence of wheezing among children who have been immunized with DPT (Diphtheria, whole cell pertussis, tetanus) as opposed to DaPTP (Diphtheria, acellular pertussis, tetanus, polio) or DT (diphtheria and tetanus) or aP (acellular pertussis)?

My research hypothesis is that the combination vaccines containing pertussis as well the acellular pertussis vaccine will be associated with an increase in the incidence of Wheezing.

TABLE 56: The Frequency of Diphtheria / Tetanus Vaccines & Wheezing

The Vaccine Dose and Type and Asthma Rates at 90 months (2790 days)				
Dose	Type	Frequency	Wheeze	Rate%
1 or more	DipT_2790	33	8	24.24
1	DT1_2790	310	147	47.42
2	DT2_2790	47	27	57.45
3	DT3_2790	19	10	52.63
4	DT4_2790	12	5	41.67
Overall Total		421	197	46.79

Note: Dip T was two separate vaccines received by the same individual, combined for the purpose of analyses. DT is a combined vaccine of Diphtheria and Tetanus. DT 1 to 4 indicates the number of doses which were received and 2790 is the number of days after birth (~ 7.5 years).

When the children who had 1 or more DT vaccines (388 children) are grouped together, the OR of the 388 children who received 1 or more DT vaccines and had Wheezing was 1.1340 with a 95% CL of 1.0261 to 1.2532, also significant.

TABLE 57: Logistic Regression of Wheezing and DT (1 or more)

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.68	1.094	2.579
Rx	4 to 11	1.812	1.619	2.027
Rx	1 to 3	1.403	1.289	1.528
Rx	0 (reference)			
MD	152 to 459	10.345	6.696	15.981
MD	67 to 151	5.979	5.301	6.743
MD	50 to 66	3.235	2.885	3.628
MD	36 to 49	2.155	1.92	2.409
MD	0 to 35 (ref.)			
Region	U vs Rural	1.105	1.023	1.194
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.802	1.534	2.116
Income	Low vs High	1.299	1.194	1.413
DT	1+ vs None	1.103	0.886	1.373

Note: here DT includes children who received 1 or more DT vaccination

The adjusted OR was not statistically significant.

PART VI: DT & DPT & DaPT VACCINE COMBINATIONS & WHEEZING RATES

Another approach for analyzing this data was to determine how Wheezing may vary with the variations in DT and DPT and DaPT combinations. For this cohort this was more realistic and testable questions or objectives.

Did the children who received a combination (1 or more of each type of vaccine) of DT with DPT vaccines have a higher incidence of Wheezing when compared to the children who had a combination of DT and DaPT?

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Wheezing when compared to the children who had a combination of DT and DaPT and DPT?

TABLE 58: Part A – Two Vaccine Combinations of DT (1 to 4) and DPT (1 to 6)

Vaccine Combination	Frequency	Wheeze
DT1_DPT1	2	0
DT1_DPT2	8	5
DT1_DPT3	29	11
DT1_DPT4	148	77
DT1_DPT5	2	0
DT1_DPT6	1	1
DT2_DPT1	1	0
DT2_DPT2	4	2
DT2_DPT3	15	8
DT2_DPT4	0	0
DT2_DPT5	0	0
DT2_DPT6	0	0
DT3_DPT1	4	3
DT3_DPT2	8	4
DT3_DPT3	1	0
DT3_DPT4	0	0
DT3_DPT5	0	0
DT3_DPT6	0	0
DT4_DPT1	3	2
DT4_DPT2	0	0
DT4_DPT3	0	0
DT4_DPT4	0	0
DT4_DPT5	0	0
DT4_DPT6	0	0
Total	**226**	**113**
Rate		**50%**

Note: this table presents the different combinations of vaccines. DT1_DPT1 (children who received 1 DT vaccine and 1 DPT vaccine over ~7.5 years). DT2_DPT (children who received 2 DT vaccines and 1 DPT vaccine over ~7.5 years).

TABLE 58: Part B – Two Vaccine Combinations of DT (1 to 4) and DaPT (1 to 6)

Vaccine Combination	Frequency	Wheeze
DT1_DaPT1	0	0
DT1_DaPT2	1	0
DT1_DaPT3	1	1
DT1_DaPT4	0	0
DT1_DaPT5	0	0
DT1_DaPT6	0	0
DT2_DaPT1	1	1
DT2_DaPT2	0	0
DT2_DaPT3	0	0
DT2_DaPT4	0	0
DT2_DaPT5	0	0
DT2_DaPT6	0	0
DT3_DaPT1	0	0
DT3_DaPT2	0	0
DT3_DaPT3	0	0
DT3_DaPT4	0	0
DT3_DaPT5	0	0
DT3_DaPT6	0	0
DT4_DaPT1	5	2
DT4_DaPT2	0	0
DT4_DaPT3	1	0
DT4_DaPT4	0	0
DT4_DaPT5	1	1
DT4_DaPT6	0	0
Total	10	5

Note: here the groups are organized in the same manner as the table above except the DaPT vaccine is presented instead of DPT.

The first part of the new objective could also not be adequately tested due to the very small number of children who received DT and DaPT only (10 children). The TABLE above categorizes DT and DPT and makes it obvious that children who received DT and DPT vaccines only, were more likely to have a higher incidence of Wheezing (50%) when compared to the overall averages of 42.28% for Wheezing.

TABLE 59: Three Vaccine Combinations of DT (1 to 4) / DPT (1 to 6) / DaPT (1 to 2)

Vaccine Combination	Frequency	Wheeze
DT1_DPT1_DaPT1	3	2
DT1_DPT2_DaPT1	9	2
DT1_DPT3_DaPT1	57	27
DT1_DPT4_DaPT1	33	16
DT1_DPT5_DaPT1	0	0
DT1_DPT6_DaPT1	2	0
DT2_DPT1_DaPT1	2	1
DT2_DPT2_DaPT1	14	8
DT2_DPT3_DaPT1	5	4
DT2_DPT4_DaPT1	2	1
DT2_DPT5_DaPT1	0	0
DT2_DPT6_DaPT1	0	0
DT3_DPT1_DaPT1	4	3
DT3_DPT2_DaPT1	0	0
DT3_DPT3_DaPT1	0	0
DT3_DPT4_DaPT1	0	0
DT3_DPT5_DaPT1	0	0
DT3_DPT6_DaPT1	0	0
DT4_DPT1_DaPT1	1	0
DT4_DPT2_DaPT1	0	0
DT4_DPT3_DaPT1	0	0
DT4_DPT4_DaPT1	0	0
DT4_DPT5_DaPT1	0	0
DT4_DPT6_DaPT1	0	0
DT1_DPT1_DaPT2	4	3
DT1_DPT2_DaPT2	5	1
DT1_DPT3_DaPT2	2	1
DT1_DPT4_DaPT2	0	0
DT1_DPT5_DaPT2	0	0
DT1_DPT6_DaPT2	0	0
DT2_DPT1_DaPT2	0	0
DT2_DPT2_DaPT2	1	1
DT2_DPT3_DaPT2	0	0
DT2_DPT4_DaPT2	0	0
DT2_DPT5_DaPT2	1	1
DT2_DPT6_DaPT2	0	0
Total	145	71
Rate		48.97%

DT Combinations	Frequency	Wheeze
Overal Total	381	189
Overal Rate		49.61%

Note: This Table is organized in the same manner as the two prior tables, except all three vaccines are presented in this table (DT / DPT / DaPT).

The Wheezing rates were virtually identical (48.97% compared to 50%).

TABLE 60: UNADJUSTED ODDS RATIOS FOR WHEEZING

WHEEZING					
Vaccine Combinations	Test	Value	95% CL		Statistically
	ODDS RATIO		Lower	Upper	Significant
DT_DPT		1.157	1.0147	1.3191	Yes
DT_DaPT		1.1545	0.6211	2.1461	No
DT_DPT_DaPT		1.1324	0.9649	1.329	No

When the children who received both DT and DPT vaccinations were combined into one group and compared to all other children, there was a significant difference. Children in this group are more likely to have Wheezing when compared to other children in this cohort.

A logistic regression was also performed using the children who received DT_DPT combinations as the reference category and it was tested with children who received DT_DaPT combinations and DT_DPT_DaPT combinations as well as all other children who did not receive any DT vaccines.

Groups	SAS Group #
Other	4
DT_DaPT	3
DT_DPT_DaPT	2
DT_DPT	1

TABLE 61: Logistic Regression of Wheezing and DT_DPT / DT_DaPT / DT_DPT_DaPT

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.681	1.095	2.581
Rx	4 to 11	1.811	1.618	2.027
Rx	1 to 3	1.403	1.288	1.528
RX	0 (reference)			
MD	152 to 459	10.35	6.696	15.988
MD	67 to 151	5.979	5.301	6.743
MD	50 to 66	3.235	2.885	3.628
MD	36 to 49	2.155	1.928	2.408
MD	0 to 35 (ref.)			
Region	U vs Rural	1.105	1.023	1.193
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.802	1.535	2.117
Income	Low vs High	1.299	1.194	1.413
DT	4	0.841	0.633	1.116
	3	0.924	0.24	3.56
	2	0.908	0.577	1.43
	1 (ref.)			

None of the adjusted Odds Ratios were significant for Wheezing.

PART VII

TABLE 62: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	
	3	1	786	76		4
complete	4	1	9869	1139		
	5	1	147	23	11.61	
	6	1	3	1		
Total			11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	3
complete	3	2	542	50		
	4	2	127	17	10.1	
	5	2	4	1		
Total			779	78	10.01	
Overall Total			11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated &			2057	230	11.18	2
All the children who have never been vaccinated			114	8	7.02	1
Total			2171	238	10.96	
Grand Total			13950	1569	11.25	
Note: the 5 groups are used in a logistic regression and group 1 is the reference group						

For this analysis, the groups are based on DaPT – Group 4 consists of the vaccine combinations which include 1 dose of DaPT. Group 3 consists of the vaccine combinations which include 2 doses of DaPT.

Group # s	# of Wheezing Cases	Wheezing Rate (%)
4	4657	42.34%
3	339	43.52%
2	875	42.54%
1	8	23.68%

TABLE 63: The adjusted odds ratios of DPT-type vaccines (groups 1 to 4) and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.661	1.081	2.551
Rx	4 to 11	1.803	1.611	2.017
Rx	1 to 3	1.399	1.284	1.523
Rx	0 (reference)			
MD	152 to 459	10.338	6.691	15.972
MD	67 to 151	5.996	5.315	6.764
MD	50 to 66	3.231	2.88	3.624
MD	36 to 49	2.151	1.925	2.405
MD	0 to 35 (ref.)			
Region	U vs Rural	1.109	1.027	1.198
Gender	M vs F	1.444	1.342	1.553
Mom Hx	Yes vs No	1.805	1.537	2.121
Income	Low vs H	1.294	1.189	1.408
Dvaccines	4	1.512	0.956	2.391
	3	1.758	1.085	2.847
	2	1.488	0.933	2.372
	1 (ref.)			

The comparison groups for the outcome of Wheezing were similar to those of Asthma; however, there was one comparison which was significant. Children who were in Group 3 (received 2 doses of DaPT) were more likely to have Wheezing than children who were in Group 1 (no immunizations).

Another approach of testing whether or not number of doses of DaPT affects the Wheezing rates is to group the vaccination categories according to the number of DaPT doses received.

Vaccine Group	#Wheezing Cases / Rate	SAS Group #
No DaPT	751 (751/1731=43.39%)	Group 0
1 dose of DaPT	1267 (4731/11184=42.3%)	Group 1
2+ doses of DaPT	389 (389/921=42.24%)	Group 2
No vaccines	27 (27/114=23.68%)	Group 3

TABLE 64: The adjusted odds ratios of DPT-type vaccines (groups 1 to 4) and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.668	1.086	2.562
Rx	4 to 11	1.802	1.61	2.016
Rx	1 to 3	1.399	1.284	1.523
Rx	0 (reference)			
MD	152 to 459	10.331	6.687	15.961
MD	67 to 151	5.998	5.317	6.767
MD	50 to 66	3.235	2.884	3.628
MD	36 to 49	2.155	1.927	2.409
MD	0 to 35 (ref.)			
Region	U vs Rural	1.108	1.025	1.197
Gender	M vs F	1.443	1.342	1.552
Mom Hx	Yes vs No	1.804	1.536	2.119
Income	Low vs H	1.293	1.188	1.407
DaPT	0	1.535	0.961	2.451
	1	1.507	0.953	2.384
	2	1.677	1.039	2.705
No vaccines	3 (ref.)			

The comparison groups for the outcome of Wheezing were similar to those of Asthma; however, there was one comparison which was significant. Children who had received 2 or more DaPT doses were more likely to have had Wheezing than children who had never been immunized.

TABLE 65: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	6
	3	1	786	76		
complete	4	1	9869	1139		
	5	1	147	23	11.61	5
	6	1	3	1		
	Total		11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	4
complete	3	2	542	50		
	4	2	127	17	10.1	3
	5	2	4	1		
	Total		779	78	10.01	
	Overall Total		11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated with DPT+ or DaPT+orDT			2057	230	11.18	2
All the children who have never been vaccinated			114	8	7.02	1
	Total		2171	238	10.96	
	Grand Total		13950	1569	11.25	

Note: the 6 groups are used in a logistic regression and group #1 is used as a reference group and compared to groups 2 to 6

Although Group 2 has the highest Asthma rate (11.18%), this group is not of interest for this analyses. Groups 3, 4, 5, 6 are of interest because of their vaccination combinations.

The following table is of the same data, only the model has been adjusted for possible confounders.

TABLE 66: The adjusted odds ratio of DPT-type vaccines (groups 1 to 6) & Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.647	1.072	2.53
Rx	4 to 11	1.796	1.605	2.01
Rx	1 to 3	1.398	1.283	1.522
Rx	0 (reference)			
MD	152 to 459	10.468	6.774	16.177
MD	67 to 151	6.074	5.38	6.856
MD	50 to 66	3.273	2.916	3.674
MD	36 to 49	2.175	1.945	2.432
MD	0 to 35 (ref.)			
Region	U vs Rural	1.113	1.031	1.203
Gender	M vs F	1.444	1.342	1.553
Mom Hx	Yes vs No	1.798	1.531	2.112
Income	Low vs H	1.282	1.177	1.395
Dvaccines	6	1.774	1.1	2.86
	5	1.486	0.939	2.351
	4	1.403	0.75	2.622
	3	1.821	1.12	2.961
	2	1.486	0.932	2.37
	1 (ref.)			

The odds ratios of the 5 different comparisons of the 6 different groups and Wheezing did indicate that two of the comparisons were significant. Once again, the 114 children who were never vaccinated were used as the reference group (Group 1). When Group 6 was compared to Group 1 there was an increased risk for having Wheezing as the adjusted OR was 1.774 with a 95%CL of 1.1 to 2.86. The other comparison which had a significant result was when Group 3 was compared to Group 1. This adjusted OR was 1.821 with a 95%CL of 1.12 to 2.961, which also indicates that children in Group 3 were more likely than children in Group 1 to have had Wheezing.

To test the possible effects of increasing the number of doses of DaPT and the Wheezing rates, all of the children who received 1 dose of DaPT were tested against those who received 2 + doses of DaPT. This was performed to determine if the children who received more doses i.e. 2 + of DaPT were less likely to have Wheezing than children who only received 1 dose.

# of DaPT doses	# of Children	Percent
0	1836	13.16%
1	11 184	80.17%
2 +	930	6.67%

TABLE 67: The adjusted Odds Ratio of 1 and 2 doses of DaPT and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.667	1.086	2.559
Rx	4 to 11	1.807	1.615	2.023
Rx	1 to 3	1.403	1.288	1.528
Rx	0 (reference)			
MD	152 to 459	10.382	6.72	16.039
MD	67 to 151	6.013	5.33	6.783
MD	50 to 66	3.245	2.893	3.64
MD	36 to 49	2.16	1.932	2.415
MD	0 to 35 (ref.)			
Region	U vs Rural	1.109	1.027	1.199
Gender	M vs F	1.445	1.343	1.554
Mom Hx	Yes vs No	1.802	1.534	2.116
Income	Low vs H	1.295	1.19	1.409
DaPT	0 DaPT	0.894	0.751	1.065
	1 DaPT	0.899	0.774	1.043
	2 DaPT (Ref.)			

The Odds Ratios are not statistically significant, as the 95%CL crosses over 1.00.

PART VIII: LONE DPT & DaPT IMMUNIZATIONS & WHEEZING

When the children in the 1995 cohort are broken into different groups based on those who were immunized with DaPT only or DPT only or neither, there were relatively few children in each group.

TABLE 68: The vaccine combinations / the number of children with Wheezing within each group / the Wheezing rate and the group order

Number	Group	Frequency	Wheeze	%Wheeze
0	Other	13756	5850	42.53
1	DaPT Only	32	5	15.63
2	DPT Only	48	16	33.33
3	No DPT or DaPT	114	27	23.68
Total		**13950**	**5898**	**42.28**

TABLE 69: The adjusted Odds Ratios of Wheezing and DPT / DaPT / No DPT or DaPT / Other

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.666	1.085	2.558
Rx	4 to 11	1.801	1.61	2.016
Rx	1 to 3	1.396	1.282	1.52
Rx	0 (reference)			
MD	152 to 459	10.427	6.742	16.125
MD	67 to 151	5.962	5.285	6.724
MD	50 to 66	3.213	2.865	3.604
MD	36 to 49	2.141	1.915	2.393
MD	0 to 35 (ref.)			
Region	U vs Rural	1.107	1.024	1.195
Gender	M vs F	1.444	1.342	1.553
Mom Hx	Yes vs No	1.809	1.54	2.125
Income	Low vs H	1.302	1.197	1.416
DPT	0	1.528	0.966	2.415
	1	0.408	0.135	1.232
	2	1.309	0.592	2.897
	3 (ref.)			

CHAPTER 11: THE MEASLES, MUMPS & RUBELLA VACCINATION AND ASTHMA

This chapter analyzes the variation in the adherence to the immunization schedule for the MMR vaccine in regards to the time of administering / receiving the vaccine and number of MMR doses received over 7.5 years.

Research Objective Four:

Is there a difference in the rates of asthma between those who have been immunized with MMR, and those who have not?

My research hypothesis is that the incidence of asthma will be higher among individuals who have been immunized with MMR than among those who have not been immunized with MMR.

As previously discussed in Chapter 2, at the end point of 7 years there was a slight variation in the distribution of the number of MMR vaccines received among the birth cohort.

TABLE 70: The distribution of MMR vaccines & Asthma

MMR Vaccines	Frequency	Asthma	Asthma%
0	318	23	7.23
1	1645	172	10.46
2	11717	1336	11.4
3+	270	38	14.07
Total	13950	1569	11.25

There were 318 children who did not receive any MMR vaccines and of these children 23 had Asthma which is a rate of 7.23% compared to an average rate of 11.34% among the children who were vaccinated with MMR. The 270 children who had 3 or more MMR vaccines have an Asthma rate of 14.07% compared to 11.19% (1531/13680) of all the other children.

TABLE 71: Chi-square test & the Chi-square test for trend & the unadjusted Odds Ratios of MMR & Asthma

ASTHMA					
Vaccine Combinations	Test				Statistically
	Chi-square	DF	Value	Probability	Significant
MMR 3+		1	2.2039	0.1377	No
MMR (0,1,2,3+) Trend		3	8.6094	0.035	Yes

ASTHMA					
Vaccine Combinations	Test	Value	95% CL		Statistically
	ODDS RATIO		Lower	Upper	Significant
MMR 3+		1.0335	0.9845	1.8391	No

The Chi-Square test for trend for Asthma and MMR (0, 1, 2, 3+) was statistically significant, meaning that the risk of Asthma increased with the number of doses of MMR received.

The following tables are summary tables of Logistic Regressions performed where MMR was entered into the model as an independent variable. The Odds Ratios have been adjusted by controlling for prescription history, medical consults, region (Urban/Rural), gender, maternal history of asthma (Mom Hx), and family income (low income).

TABLE 72: MMR as a continuous independent variable (0, 1, 2, 3+) & Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.62	0.36	1.065
Rx	4 to 11	0.806	0.684	0.951
Rx	1 to 3	0.947	0.828	1.084
Rx	0 (reference)			
MD	152 to 459	19.308	12.795	29.135
MD	67 to 151	8.37	6.71	10.44
MD	50 to 66	4.149	3.314	5.194
MD	36 to 49	2.231	1.768	2.816
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.146	1.456
Gender	M vs F	1.418	1.27	1.584
Mom Hx	Yes vs No	1.728	1.427	2.092
Income	Low vs H	1.02	0.9	1.155
MMR		1.068	0.94	1.213

When MMR is included as a continuous variable that increases in increments, the changes in the Asthma rates are not statistically significant because the 95% CL crosses over 1.00.

MMR Groups	SAS Group #'s
0 MMR	MMR 1
1 MMR	MMR 2
2 MMR	MMR 3
3 or more doses of MMR	MMR 4

TABLE 73: MMR as a categorical independent variable & Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.619	0.36	1.065
Rx	4 to 11	0.805	0.683	0.949
Rx	1 to 3	0.947	0.827	1.083
Rx	0 (reference)			
MD	152 to 459	19.285	12.78	29.103
MD	67 to 151	8.366	6.706	10.436
MD	50 to 66	4.145	3.311	5.19
MD	36 to 49	2.229	1.766	2.814
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.146	1.456
Gender	M vs F	1.418	1.269	1.584
Mom Hx	Yes vs No	1.728	1.427	2.093
Income	Low vs H	1.018	0.899	1.154
MMR	4	1.304	0.74	2.298
	3	1.248	0.8	1.945
	2	1.192	0.745	1.907
	1 (ref.)			

Although the OR's are all above 1.00, all of the 95%CL cross over 1.00, thus the outcome is not statistically significant.

TABLE 74: MMR 1+ as a dichotomous binary (1+ MMR vs. 0 MMR) independent variable & Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.62	0.361	1.066
Rx	4 to 11	0.804	0.682	0.949
Rx	1 to 3	0.947	0.827	1.084
Rx	0 (reference)			
MD	152 to 459	19.34	12.818	29.18
MD	67 to 151	8.39	6.728	10.464
MD	50 to 66	4.158	3.322	5.204
MD	36 to 49	2.235	1.771	2.82
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.146	1.456
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.727	1.426	2.091
Income	Low vs H	1.016	0.897	1.15
MMR all	1+ vs None	1.23	0.796	1.901

Once the model controlled for potential confounding variables, the adjusted OR of MMRall was not statistically significant.

** Additional data on the demographics associated with MMR can be found in Appendix III.

PART II: MMR RECEIVED ON TIME & DELAYED & ASTHMA

MEASLES, MUMPS & RUBELLA:

The measles, mumps, and rubella (MMR) vaccine was analyzed separately from the DPT vaccine. The MMR vaccine is typically given at 12 months of age and then again between 4 to 6 years, as indicated by the Canadian immunization schedule.

TABLE 75: MMR Frequency and Asthma

MMR Vaccines				
Age	# of Vaccines	Frequency	Asthma02	Asthma(%)
1 year	1	1522	192	12.61
	2	4	0	0
1 year 6months	1	12312	1412	11.47
	2	79	13	16.4
	3	1	0	0
6 yrs	1	2513	282	11.22
	2	10849	1223	11.27
	3	217	35	16.13
7 yrs	1	1645	172	10.46
	2	11717	1336	11.4
	3	265	37	13.96
Overall Total (7yrs)		**13627**	**1545**	**11.34**

Note: here 3 doses does not include more than 3 doses i.e. 4

This TABLE is different than the DPT tables. Here each time group or age after birth is separate from one another and the point of interest is the associated asthma rates for each period of time. By 12 months after birth only 1522 children of 13 950 (or 10.91%) were immunized with their first MMR vaccine. This group of children had an asthma rate of 12.61%; however, when compared to the overall asthma rate of 11.25% the Chi-square value was 3.2012 with 1 degree of freedom and a probability of 0.0736, the difference is not significant.

PART III

THE MEASLES, MUMPS & RUBELLA VACCINATION AND WHEEZING

Research Objective Four – *Second Objective*:

Is there a difference in the rates of wheezing between those who have been immunized with MMR, and those who have not?

My research hypothesis is that the incidence of wheezing will be higher among individuals who have been immunized with MMR than among those who have not been immunized with MMR.

As previously discussed, at the end point of 7 years there was a slight variation in the distribution of the number of MMR vaccines received among the birth cohort.

TABLE 76: The distribution of MMR vaccines & Wheezing

MMR Vaccines	Frequency	Wheeze	Wheeze%
0	318	97	30.5
1	1645	694	42.19
2	11717	4974	42.45
3+	270	133	49.26
Total	13950	5898	42.28

There were 318 children who did not receive any MMR vaccines and of these children 97 had Wheezing which is a rate of 30.5% compared to an average rate of 41.88% among the children who were vaccinated with MMR. The 270 children who had 3 or more MMR vaccines have a Wheeze rate of 49.26% compared to 42.28% overall.

TABLE 77: Chi-square test & the Chi-square test for trend & the unadjusted Odds Ratios of MMR & Wheezing

WHEEZING					
Vaccine Combinations	Test				Statistically
	Chi-square	DF	Value	Probability	Significant
MMR 3+		1	5.4962	0.0191	Yes
MMR (0,1,2,3+) Trend		3	23.6083	<.0001	Yes

WHEEZING					
Vaccine Combinations	Test	Value	95% CL		Statistically
	ODDS RATIO		Lower	Upper	Significant
MMR 3+		1.1403	1.013	1.2836	Yes

The Chi-Square test for trend for Wheezing and MMR (0, 1, 2, 3+) was statistically significant, meaning that the risk of Wheezing increased with the number of doses of MMR received. Both the Chi-Square test for MMR 3+ and Wheezing and the unadjusted OR for MMR 3+ and Wheezing were also statistically significant. Thus, children who had 3 or more doses of MMR were more likely to have wheezing.

The following tables are summary tables of Logistic Regressions performed where MMR was entered into the model as an independent variable. The Odds Ratios have been adjusted by controlling for prescription history, medical consults, region (Urban/Rural), gender, maternal history of asthma (Mom Hx), and family income (low income).

TABLE 78: MMR as a continuous independent variable (0, 1, 2, 3+) & Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.62	0.36	1.065
Rx	4 to 11	0.806	0.684	0.951
Rx	1 to 3	0.947	0.828	1.084
Rx	0 (reference)			
MD	152 to 459	19.308	12.795	29.135
MD	67 to 151	8.37	6.71	10.44
MD	50 to 66	4.149	3.314	5.194
MD	36 to 49	2.231	1.768	2.816
MD	0 to 35 (ref.)			
Region	U vs Rural	1.292	1.146	1.456
Gender	M vs F	1.418	1.27	1.584
Mom Hx	Yes vs No	1.728	1.427	2.092
Income	Low vs H	1.02	0.9	1.155
MMR		1.068	0.94	1.213

The adjusted OR of MMR as a continuous independent variables and Wheezing was not significant.

MMR Groups	SAS Group #'s
0 MMR	MMR 1
1 MMR	MMR 2
2 MMR	MMR 3
3 or more doses of MMR	MMR 4

TABLE 79: MMR as a categorical independent variable & Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.676	1.091	2.573
Rx	4 to 11	1.81	1.617	2.025
Rx	1 to 3	1.401	1.286	1.525
Rx	0 (reference)			
MD	152 to 459	10.285	6.657	15.891
MD	67 to 151	5.96	5.282	6.724
MD	50 to 66	3.222	2.872	3.616
MD	36 to 49	2.146	1.92	2.4
MD	0 to 35 (ref.)			
Region	U vs Rural	1.106	1.024	1.195
Gender	M vs F	1.444	1.343	1.553
Mom Hx	Yes vs No	1.804	1.535	2.119
Income	Low vs H	1.296	1.191	1.441
MMR	4	1.392	0.966	2.005
	3	1.236	0.952	1.605
	2	1.294	0.979	1.71
	1 (ref.)			

Once again, the OR's are not statistically significant as the 95%CL's cross over 1.00.

TABLE 80: MMR as dichotomous binary (1+MMR vs.. 0 MMR) independent variable & Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.675	1.091	2.571
Rx	4 to 11	1.81	1.617	2.025
Rx	1 to 3	1.4	1.286	1.525
Rx	0 (reference)			
MD	152 to 459	10.307	6.671	15.924
MD	67 to 151	5.953	5.278	6.715
MD	50 to 66	3.215	2.866	3.606
MD	36 to 49	2.143	1.917	2.396
MD	0 to 35 (ref.)			
Region	U vs Rural	1.107	1.025	1.196
Gender	M vs F	1.445	1.344	1.554
Mom Hx	Yes vs No	1.807	1.538	2.122
Income	Low vs H	1.3	1.195	1.414
MMR all	1+ vs None	1.236	0.954	1.6

Once again the model controlled for potential confounding variables the adjusted OR of MMRall was not statistically significant.

** Additional data on the demographics associated with MMR can be found in Appendix III.

CHAPTER 12: THE BCG VACCINE & ASTHMA / WHEEZING

This chapter analyzes the available data on the BCG vaccine, its frequency of use, and distribution within Manitoba as well as the associated Asthma and Wheezing rates.

Research Question Five:

Is there a difference in the incidence of Asthma / Wheezing between those who have been immunized with the BCG vaccine and those who have not?

My research hypothesis is that the incidence of Asthma / Wheezing will be lower among individuals who have been immunized with BCG than among those who have not been immunized with BCG.

There were only 414 children who received a BCG vaccine from the birth cohort, or 2.97% and only two of these children received 2 BCG vaccinations.

The overall asthma rate (Asthma) among the 414 children was 7.73% or 32 / 414. Although the Asthma rate was lower than the overall population at 11.25% the children who were immunized with BCG had a slightly higher rate of Asthma05 at 47.10% compared to 42.13%. The unadjusted OR for the 414 BCG children and Asthma was 0.9607 with a 95% C.L. of 0.9337 to 0.9885, which indicates a significant difference. The unadjusted OR for the 414 BCG children and Wheezing was 1.0939 with a 95% C.L. of 0.9978 to 1.1994, which is not significant.

TABLE 81: The adjusted OR of the BCG vaccine and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	0.631	0.367	1.085
Rx	4 to 11	0.814	0.69	0.96
Rx	1 to 3	0.952	0.832	1.089
Rx	0 (reference)			
MD	152 to 459	19.447	12.891	29.338
MD	67 to 151	8.398	6.735	10.472
MD	50 to 66	4.155	3.32	5.2
MD	36 to 49	2.233	1.77	2.818
MD	0 to 35 (ref.)			
Region	U vs Rural	1.287	1.139	1.454
Gender	M vs F	1.416	1.268	1.582
Mom Hx	Yes vs No	1.728	1.427	2.092
Income	Low vs H	0.958	0.858	1.071
BCG	1+ vs None	0.872	0.593	1.283

The adjusted OR for Asthma and the BCG vaccine had a Point Estimate less than 1, which indicates that children who were immunized with BCG were less likely to develop Asthma. However, the 95%CL crossed 1 making the outcome not statistically significant.

TABLE 82: The adjusted OR of the BCG vaccine and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	12 to 40	1.643	1.071	2.522
Rx	4 to 11	1.783	1.593	1.996
Rx	1 to 3	1.398	1.284	1.522
Rx	0 (reference)			
MD	152 to 459	10.522	6.812	16.252
MD	67 to 151	6.072	5.382	6.85
MD	50 to 66	3.27	2.915	3.668
MD	36 to 49	2.168	1.939	2.424
MD	0 to 35 (ref.)			
Region	U vs Rural	1.123	1.038	1.215
Gender	M vs F	1.445	1.344	1.554
Mom Hx	Yes vs No	1.804	1.536	2.119
Income	Low vs H	1.235	1.148	1.33
BCG	1+ vs None	1.315	1.056	1.638

When the association between the BCG vaccine and Wheezing was tested using a logistic regression, the adjusted OR value of 1.315 was statistically significant which then indicates that children who received the BCG vaccine were also more likely to have had Wheezing.

CHAPTER 13: DISCUSSION OF MAIN FINDINGS OF INTEREST (CHAPTERS 8 to 12)

TABLE 83: SUMMARY TABLE OF ADJUSTED ODDS RATIOS & ASTHMA

OBJECTIVE	PART	VACCINES IN QUESTION	TEST QUESTION	TABLE #	ADJUSTED ODDS RATIO & 95% CONFIDENCE LIMITS ABOVE OR BELOW 1 OR CROSSED OVER 1	OUTCOME SIGNIFICANT (S) / NON-SIGNIFICANT (NS)
1		DPT/DaPT	*Adherence in #*			
	A		Complete vs None	21	Crossed over 1	NS
	B		Incomplete vs None	21	Crossed over 1	NS
	C		Over vs None	21	Crossed over 1	NS
	D		Complete+Over vs Incomplete+None	22	Crossed over 1	NS
2		DPT	*Adherence in timing*			
	A		Groups0,2-13,18 vs Group1(all on time)	27	Crossed over 1	NS
	B		Group14 (all delayed) vs Group 1	27	Below	S
	C		Group1 (all on time) vs all other	29	Crossed over 1	NS
	D		Group14 vs all other	30	Below	S
	E		Other vs. 1st DPT on time	31	Below	S
	F		1st DPT delayed vs 1st DPT on time	31	Below	S
	G		Other vs. 1st and/or 2nd DPT on time	32	Below	S
	H		1st and 2nd DPT delayed vs. " "	32	Below	S
	I		Other vs. 1st and/or 2nd DPT delayed	33	Below	S
	J		1st and 2nd DPT on time vs. " "	33	Crossed over 1	NS
3		DT / DipT				
Part I	A		DT (one or more) vs No DT	41	Crossed over 1	NS
	B		No DT vs DT_DPT	46	Below	S
	C		DT_DaPT vs DT_DPT	46	Crossed over 1	NS
	D		DT_DPT_DaPT vs DT_DPT	46	Below	S
Part II		DPT / DaPT				
	E		incomplete/complete dif. Combos	50,52,53	Crossed over 1	NS
Part III						
	F		Both DPT/DaPT vs No DPT/DaPT	55	Crossed over 1	NS
	G		DaPT only vs No DPT or DaPT	55	Crossed over 1	NS
	H		DPT only vs No DPT or DaPT	55	Crossed over 1	NS
4		MMR				
	A		MMR (as a continuous variable--0,1,2,3)	72	Crossed over 1	NS
	B		3 or more MMR vs 0 MMR	73	Crossed over 1	NS
	C		2 MMR vs 0 MMR	73	Crossed over 1	NS
	D		1 MMR vs 0 MMR	73	Crossed over 1	NS
	F		MMR (one or more) vs No MMR	74	Crossed over 1	NS
5		BCG				
	A		BCG (one or more) vs No BCG	81	Crossed over 1	NS

TABLE 84: SUMMARY TABLE OF ADJUSTED ODDS RATIOS & WHEEZING

OBJECTIVE	PART	VACCINES IN QUESTION	TEST QUESTION	TABLE #	ADJUSTED OR & 95% CL < 1 < or = 1 CROSSED OVER 1	OUTCOME SIGNIFICANT (S) / NON-SIGNIFICANT (NS)
1		DPT/DaPT	*Adherence in #*			
	A		Complete vs None	25	Above	S
	B		Incomplete vs None	25	Above	S
	C		Over vs None	25	Above	S
2		DPT	*Adherence in timing*			
	A		GroupsO,2-13,18 vs Group1(all on time)	34	Crossed over 1	NS
	B		Group5 (first DPT delayed) vs Group 1	34	Below	S
	C		Group1 (all on time) vs all other	36	Crossed over 1	NS
	D		Group14 vs Group1	37	Crossed over 1	NS
	E		1st DPT delayed vs 1st DPT on time	38	Crossed over 1	NS
	F		Other vs 1st and/or2nd DPT on time	39	Crossed over 1	NS
	G		1st & 2nd delayed vs 1st and/or2nd DPT o	39	Crossed over 1	NS
3		DT / DipT				
Part I	A		No DT vs DT_DPT	61	Crossed over 1	NS
	B		DT_DaPT vs DT_DPT	61	Crossed over 1	NS
	C		DT_DPT_DaPT vs DT_DPT	61	Crossed over 1	NS
		DPT / DaPT				
Part II	D		DPT(1-6)DaPT1 vs No vaccines	63	Crossed over 1	NS
	E		DPT(1-5)DaPT2 vs No vaccines	63	Above	S
	F		Other vs No vaccines	63	Crossed over 1	NS
	G		DPT(1-3)DaPT1 vs No vaccines	66	Above	S
	H		DPT(4-6)DaPT1 vs No vaccines	66	Crossed ocer 1	NS
	I		DPT(1-2)DaPT2 vs No vaccines	66	Crossed over 1	NS
	J		DPT(3-5)DapT2 vs No vaccines	66	Above	S
	K		Other vs No vaccines	66	Crossed over 1	NS
Part III	L		Both DPT/DaPT vs No DPT/DaPT	69	Crossed over 1	NS
	M		DaPT only vs No DPT or DaPT	69	Crossed over 1	NS
	N		DPT only vs No DPT or DaPT	69	Crossed over 1	NS
4		MMR				
	A		MMR (as a continuous variable--0,1,2,3)	78	Crossed over 1	NS
	B		3 or more MMR vs 0 MMR	79	Crossed over 1	NS
	C		2 MMR vs 0 MMR	79	Crossed over 1	NS
	D		1 MMR vs 0 MMR	79	Crossed over 1	NS
	E		MMR (one or more) vs No MMR	80	Crossed over 1	NS
5		BCG				
	A		BCG (one or more) vs No BCG	82	Above	S

Note: The remainder of this Chapter will only discuss findings where the adjusted OR were statistically significant (highlighted in pink on tables above).

CHAPTER 8: The association between immunization & the Asthma / Wheezing

Children who were incomplete, complete, and over immunized were all more likely to have had wheezing when compared to children who had never been immunized with DPT or DaPT, although there was no significant difference for Asthma. The Wheezing rate among the children in the "None" group was 22.31% which was considerable lower than the overall average of 42.28%. Although the Asthma rate was lower for the "None" group (6.61%) compared to the overall average of 11.25%, the difference was not statistically significant. Wheezing also affects more children and thus has a larger (n) which contributes to statistical significance. The effect size is also much larger (~20% difference between the two groups).

CHAPTER 9: DPT immunization delayed & on time & Asthma / Wheezing

The data in this chapter proved to be both very interesting and statistically significant. There was a significant difference between Group 1C (first 4 DPT immunization received on time) and Group 14 C (first 4 DPT immunization not received on time) where children in Group 14C were less likely to develop Asthma (Table 27) and (Table 34).

The adjusted ORs indicate that children who did not have their first DPT on time and who either received 4 or more doses of DPT or those who received less than 4 doses of DPT were less likely to have Asthma than those who did have their first dose of DPT on time and who received at least 4 doses of DPT (Table 31).

The adjusted ORs also indicated that the children who were delayed for their 1st and 2nd DPT vaccine were less likely to develop Asthma than children who either received one or both of their 1st and 2nd DPT vaccine on time. The adjusted OR for the "Other" group also indicated that the children within this group (1st and / or 2nd DPT delayed and a total of less than 4 doses of DPT) were also less likely to develop Asthma than the children who received their 1st and 2nd DPT on time and who received at least 4 doses of DPT.

The adjusted the OR indicates that children who received both their 1st and 2nd DPT immunizations on time and who also received at least 4 doses of DPT were not more or less likely to develop Asthma than children who also received at least 4 doses of DPT and had their 1st and / or 2nd DPT vaccine delayed. The adjusted OR for the "Other" group (had their 1st and / or 2nd DPT on time but had less than 4 doses of DPT) were less likely than children who had at least 4 doses of DPT and who had their 1st and / or 2nd DPT delayed to develop Asthma.

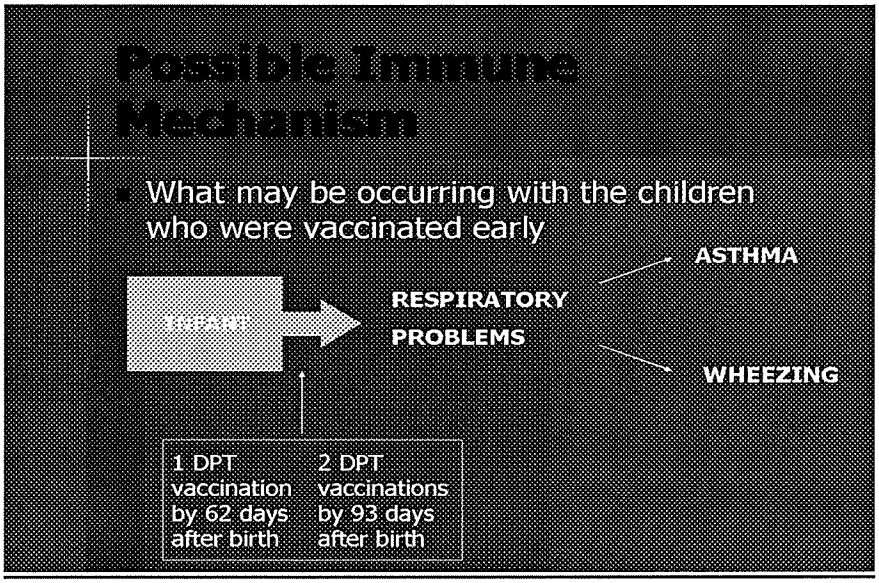
This type of analysis between immunization timing and the development of Asthma / Wheezing is a novel approach and there have not been other studies which have researched this particular association. At this time the reasons for such findings are hypothetical and based on immunological theory. It is known that at the time of birth, infants' immune systems are immature and not fully functional. As presented in the literature review section of this document, there is a tendency for newborn infants to have immune systems which are skewed towards the Th2 pathway (Figure 1). Over time this unbalanced state should balance through the exposure to environmental exposures (bacteria, viruses, pollens etc.) and the maturation of the immune system occurs. It may be possible that a delay in the DPT immunization allows the infant / toddler time for their immune systems to mature on their own and be better able to deal with vaccines, which do affect the immune system in aspects that are both known (enhance Th2 pathway) and unknown.[69,70]

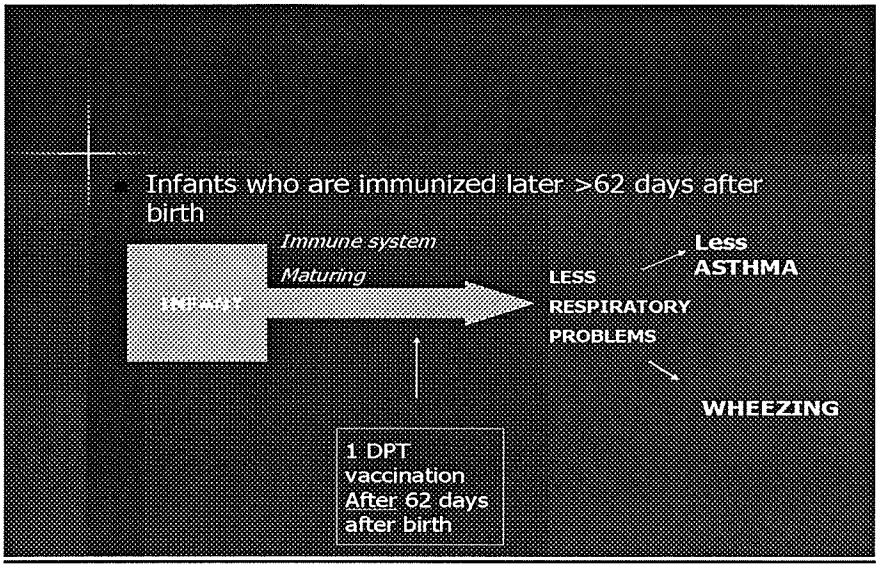
There has been an increase in the research performed on preterm infants and the development of their immune systems. The following research provides a context for how immunizations can affect pre-term infants. Pre-term infants have a high likelihood of not responding well to immunizations because their immune systems are not mature. This evidence can then provide a rational as to why a delay in immunizations for young children may result in lower rates of asthma.

In support of the theory that theTh2 pathway is predominant in neonates, researchers have found that pre-term infants or infants of low birth weight are less likely than full term infants to have mothers with a history of atopy. The rational for this finding is that "allergic" mothers have immune systems which are more heavily weighted towards the TH2 pathway and that this state is more conducive to pregnancy, which is also thought to be a TH2 inducer. Therefore, a mother in an allergic state is more likely to carry a baby to term as her body has been "fixed" that way through her own immunity.[71] From this research it can be hypothesized that pre-term infants are less likely to have a strong genetic component towards developing allergies / atopy later in life.

It is possible that as normal children age, their immune systems react differently to immunizations than they did or would have as infants. A reasonably mature, balanced, well functioning immune system is probably more tolerant of immune challenges such as immunizations – just as a child with a reasonably mature, balanced and well functioning immune system is also less likely to develop asthma. Figure 41 depicts the possible immune mechanism.

FIGURE 40: The possible immune mechanism occurring with delayed immunizations





The children who did not receive their first DPT immunization on time had a lag / delay period of time in which their immature immune systems had more time to develop. Perhaps this additional maturing time allowed their immune systems to better handle the DPT immunization when it was received.

Three studies which were presented in the Literature Review section indicated an association between being vaccinated with DPT-type immunizations and an increased risk of developing Asthma. To re-iterate – In a British retrospective cohort study of 1, 934 people born between 1975 and 1984, researchers reviewed public health and physician practice records and then made temporal records of all immunizations, diagnoses of asthma, hay fever, eczema, maternal atopy and others. Using logistic regression analysis the researchers identified three statistically significant predictors of atopic disease: maternal atopy, immunization with whole cells pertussis and receiving oral antibiotics within the first two years of life. The odds ratio of subsequent atopy in individuals who were exposed to the pertussis immunization alone was 1.76 and the rate for those who were exposed to all three independent variables was 67%.[72]

Pertussis vaccines are made with chemically detoxified pertussis toxin. Pertussis toxin is often used in lab experiments to enhance IgE production in lab animals. A study which was

published in 1998 by Nilsson L, Gruber C. *et.al.* reported that the initial IgE levels were higher in children who received the acellular version of the Pertussis vaccine when compared to children who had received the whole cell version. They hypothesized that this short-term elevation in IgE levels could have been due to adjuvants or other components in the acellular vaccines.[73] Elevated levels of IgE against pertussis toxin have been found in children who had a local adverse reaction to a acellular Pertussis vaccine. It has also been found that children who are atopic or have a family history of atopy will also present higher levels of IgE to pertussis toxin after a pertussis vaccine.[74,75]

The acellular pertussis vaccine was developed because of the overall high rates of adverse reactions recorded to the whole-cell vaccine. The documented adverse events associated with the whole-cell pertussis DPT vaccine were: high-fever, and serious neurological disorders such as; infantile spasms, seizures, encephalopathy, speech disorders and sudden death.[76,77, 78, 79] Today Health Canada advises for the acellular version in the combination vaccine DTaP as opposed to the DTP vaccine. The newer DTaP combination vaccine has been found to be less reactogenic, with lower incidence of adverse events.[80,81] In general the combination of DTaP has been less reactogenic in causing the known side effects of this vaccine. However, in 2000 a US study reported that children and adolescents who had been routinely vaccinated with DTP or plain Tetanus had an increased risk for allergies / respiratory problems and were twice as likely to develop asthma.[82] Another study on tetanus and Diphtheria found that there was a significant increase in the IgE immune response associated with atopic disorders after the children involved in the study received Td vaccines.[83]

The Canadian Childhood Immunization Schedule sets a precedent for the provinces and territories within Canada. Immunization schedules do vary by country for various reasons such as: the different diseases and infections prevalent in different geographical regions and environments; public demand / awareness; the level of health care within each country. The World Health Organization contains immunization information of every country on their web-site

– Vaccines, Immunization, and Biologicals. The immunization schedule for the DPT type / combination immunization also varies by country. France's schedule requires that infants be vaccinated with DPT at 2, 3, 4, 18 months and again at 6, 11, 16 years of age. Hungary and the UK require less DPT type vaccines in infancy – Hungary's schedule indicates that DPT is given at 4 and 5 months of age and again at 3 and 6 years of age. The United Kingdom has a similar schedule to Hungary but includes one additional vaccine in infancy (2, 3, 4 months) and again at 3 and 5 years old.[84] It is also interesting to note that prior the mid-1990's Japanese children were not immunized before the age of two. Today Japan's childhood immunization schedule indicates that children get three doses of DaPT between 6 to 9 months after birth and their fourth dose around 18 months after birth. As a brief aside, it is also interesting to note that in 1982 Japan's childhood asthma rate was approximately 3.17% and by 2002 it was approximately 6.51%. Although it doubled over 20 years it is still below asthma rates seen in North America.[85]

If future research concludes that delaying DaPT reduces asthma then resulting changes may occur in the Canadian Childhood immunization schedule and may take on a schedule more similar to one presented above.

North American childhood immunization schedules which normally include (2, 4, 6 month) intervals date back to the 1950's and 1960's when "well-baby' visits were scheduled with physicians and pediatricians as routine check-ups. The vaccine companies decided that as infants were their target market, they would use the existing "well-baby" schedule to market new vaccines. That way including immunizations as a routine part of childhood would reduce non compliance and increase the overall immunization rates.[86]

The rational for continuing to use this schedule in Canada, aside from the fact that it is well established, is that immunizing infants at 2, 4, and 6 months: 1 – provides protection as quickly as possible in early infancy when the infants' immune systems are not mature and not as effective at combating disease on their own, the same reason why more doses are needed to provide protection in early infancy 2 – to achieve herd immunity requires the majority of the

population to be immunized, which is more likely to occur among infants if they are immunized frequently 3 – two months between vaccinations allows for immune response to occur but at the same time two months is not too long to allow the infant to become susceptible to disease 4 – the schedule is so compact that if infants become delayed in their immunizations they can catch up fairly quickly and do not require additional doses above the total number recommended.[87]

It is surprising how many developed countries still use the whole cell pertussis in their DPT-type vaccines despite the fact that the acellular version of the pertussis vaccine is safer and more effective. Although Manitoba began to phase out the whole cell pertussis DPT vaccine in 1997, the acellular version of DaPT was first developed in Japan in the late 1970's. The change was spurred after there was mass public concern and demand for a change in their childhood immunizations and schedule after two children died of complications after receiving a DPT vaccine (both from the same lot). Japanese researchers responded by developing the DaPT vaccine with the acellular pertussis component and by 1981 the new vaccine was introduced onto the market. The researchers did not patent their new vaccine as they wanted children around the world to benefit from their research and have access to this safer vaccine. There were many studies in the mid to late 1990's which assessed the safety and effectiveness of DPT and the new DaPT vaccine. Both Swedish and Italian studies found DaPT to be more effective and safer than DPT. They also determined that the combination vaccine containing the whole cell pertussis was less than 50% effective.[88]

There are numerous new vaccines that are being added to childhood immunization schedules and are thus pushing the schedules toward giving more vaccines sooner to infants. As post-licensed studies are the only way to determine the safety of a new vaccine in a population, great efforts should be taken in order to insure that this is done. Surveillance needs to be sensitive enough to determine when there are irregularities in what would be considered "normal" adverse-events or reactions and whether or not Asthma / Wheezing could be considered an

"adverse-event" associated with DPT-type immunizations. As it was previously discussed in this chapter – additional research needs to be performed on whether or not the DaPT-type immunization now used in Canada at 2, 4, 6, and 18 months and between 4 to 6 years demonstrates the same pattern that the DPT vaccine and Relative Asthma rate did in this study. It would also be valuable to determined if children who had delayed immunizations but who only received the DaPT version of the vaccine had lower Asthma rates than children who received their DaPT immunizations on time.

CHAPTER 10: Variations of the DPT vaccine and the Asthma / Wheezing Rates

PART II:

Additional Research Question:

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Asthma and Wheezing when compared to the children who had a combination of DT and DaPT?

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Asthma and Wheezing when compared to the children who had a combination of DT and DaPT and DPT?

TABLE 44: Three Vaccine Combinations of DT (1 to 3) / DPT (1 to 6) / DaPT (1 to 2)

The children who received DT and DPT vaccines but in combination with DaPT vaccines had a much lower Asthma rate than the children who received the DT and DPT combinations (11% compared to 19.03%). Although the Wheezing rates were virtually identical (48.97% compared to 50%). This may indicated that the use of DaPT is associated with lower rates of Asthma. The adjusted OR indicated a significant result when children who had not received any DT immunizations were compared to children who had been immunized with DT and DPT. Children who had never received any DT immunizations were less likely to have Asthma than children who had been immunized with both DT and DPT. At the same time children who had

been immunized with a combination of DT, DPT and DaPT were also less likely to have Asthma than children who were immunized with DT and DPT.

The original objective and research hypothesis were very clear and precise; however, as in life nothing is that simple. The children in the 1995 birth cohort had a variety of immunizations in different combinations at different times. Children who received a DT vaccine were more likely to do so after they developed Asthma. By just analyzing the end result a connection may be made between being immunized with DT and having a higher Asthma. However, depending on the order in which the events occur changes the interpretation of the association. DT does not cause high rates of Asthma just because they are associated with one another. Here the temporal association indicates that children who had developed Asthma were more likely to receive a DT vaccine after the fact. There were 41 out of 61 (67.21%) children who received a DT vaccine after they were diagnosed with Asthma. Perhaps this occurred because either their physician or parents were concerned about the possible complications of administering a vaccine containing Pertussis to a child with a respiratory condition. It is also possible that these children had had wild Pertussis and no longer required an immunization for protection as they now had natural immunity.

It is of particular interest that children who received one or more DaPT vaccine were less likely to have Asthma than the children who only received DT and DPT. This may support that the DaPT version of the "classic" DPT vaccine is a safer and also less likely to be associated with the development of Asthma.

TABLES 63 - 65: The adjusted odds ratios of DPT-type vaccines (groups 1 to 4) & Wheezing

Children in Group 3 (DPT[1-5] and DaPT2) were a combination of children who were incomplete and complete for their immunizations; however, all of these children had received 2 doses of DaPT. The children in group 3 were more likely to have had wheezing than the children in group 1 (never been immunized with a DPT-type vaccine). The reason why the children who had received only 1 dose of DaPT were not statistically different, may be due to size (n), the number of children in Groups 1 and 3 were closer than Groups 1 and 4.

TABLE 66: The adjusted odds ratios of DPT-type vaccines (groups 1 to 6) & Wheezing

The reasons as to why Group 3 (DPT[3-5]and DaPT2 / Complete) and Group 6 (DPT[1-3] and DaPT1 / Incomplete) had a significant adjusted ORs indicating a higher risk of Wheezing when they were compared to Group 1 (No vaccines) is not known. Perhaps the children in Group 3 had a "larger relative" exposure to DPT than children in Group 4 but this does not explain the children in Group 6. Perhaps there is a real difference in some aspect of the vaccine combination used or in the time frame in which the children were immunized, which would then explain the variation in the immunizations used. If this is the case, then it may be said that the categorization of the data above was not the best method for data analyses.

Elevated levels of IgE which can influence asthma and currently there is debate whether or not IgE also affects wheezing. Much effort has been placed to identify and categorize the different types of asthma / wheezing which occur throughout childhood. Three phenotypes which are well defined are: 1 – Transient infant wheezing 2 – Non-atopic wheezing of the toddler and early school years, and 3 – Persistent IgE-mediated wheezing / asthma. More recently, a fourth phenotype has been determined – 4 – Late-onset childhood asthma.

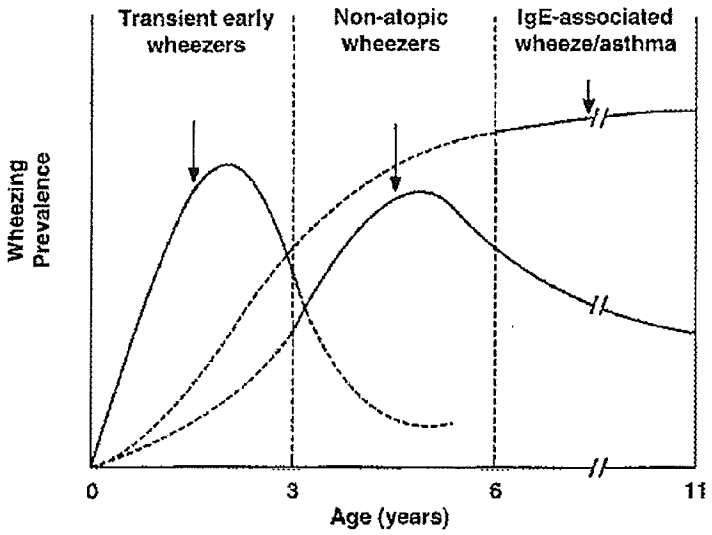
1 – Transient infant wheezing: Children with no family history of wheezing or atopy, wheeze during infancy but not after the age of 3, demonstrate a slight impairment in maximal expiratory flow at 7 years of age.

2 – Non-atopic wheezing of the toddler and early school years: These children wheeze beyond 3 years of age and close to 40% of them are non-atopic. Many of them have a history of lower respiratory tract infections with respiratory syncytial virus (RSV) bronchiolitis.

3 – Persistent IgE-mediated wheezing / asthma: these children go on to have persistent, chronic asthma, these children have high levels of atopy and bronchial responsiveness as well as impaired lung function One main risk factor for this type of wheezing is being genetically predisposed.

4 – Late-onset childhood asthma: This asthma occurs during or after puberty, mainly affects women, and has a low rate of remission.[89]

FIGURE 41: Hypothetical yearly peak prevalence of wheezing according to phenotype in childhood



These groups are not exclusive and the dashed lines suggest that wheezing can be represented by different curve shapes resulting from many different factors.[90]

The Asthma rates did vary with the timing of DPT immunizations (delayed vs. on schedule); however, this did not affect Wheezing. The reason for this may be that IgE is not involved with Wheezing to the same extent it can be involved in Asthma. This may explain why a delay in DPT immunization (all four doses, the first dose, and the first and second dose) is associated with a lower rate of Asthma but not Wheezing. However, this does not explain why

the children who did not receive a DPT / DaPT vaccine were less likely to develop Wheezing when compared to the children who were immunized with DPT / DaPT.

CHAPTER 12: The BCG vaccine and Asthma / Wheezing

TABLE 81-82: The adjusted OR of the BCG vaccine and Wheezing

There is plenty of literature which supports an association between the BCG vaccine and asthma whereby there is a decrease of asthma symptoms in individuals who were immunized with BCG. However, the opposite effect was found with the BCG vaccine and Wheezing in this cohort. The association between the BCG vaccine and Wheezing was tested using a Logistic Regression the adjusted OR value of 1.315 and it was statistically significant which then indicates that children who received the BCG vaccine were also more likely to have experienced Wheezing.

This finding can be explained by the fact that First Nations children are most likely to be the children who are immunized with BCG. It is known that First Nations children who live on or frequently visit First Nations reservations have a higher likelihood (three times higher) than non First Nations children to be exposed to tobacco smoke within the First Nation homes. [91]
It is also known that children who live in Norman, Burntwood, and Parkland are more likely to experience wheezing from Lower Respiratory Infections (LRI) caused by viral infections than children living in other Manitoba RHA's.[92] It is also known that these children are more likely to be First Nations children.

CHAPTER 14: DISCUSSION OF DATA ANALYSIS FROM EACH RESEARCH OBJECTIVE (CHAPTERS 8 to 12)

This chapter will go through each chapter containing results from the research study and discuss the significant and non-statistically significant findings.

CHAPTER 8: Association between immunization status & Asthma / Wheezing rates

The majority of the children in the cohort were Complete (5 + doses) for their DPT/DaPT immunizations (76.87%). In 1995 the Canadian Immunization Schedule stated that children should be vaccinated with a DPT immunization at 2, 4, 6, 18 months and again around 5 years of age. In 1997 Manitoba began to phase out the use of DPT and replaced it with DaPT. Therefore most of the children in this cohort have received a combination of DPT and DaPT and because of this the analyses also combined these two vaccinations together to form one group. When the "Complete" group of children was compared to all other children those in the "Complete" group have an Asthma rate of 11.53% compared to 10.32%.

There were 345 children who received over and above the suggested 5 DPT / DaPT immunizations. Although this is only 2.71% of the cohort population, this was still 378 children who were put at risk of having adverse events as a result of being over immunized.[93]

In 2002 a health survey performed by the Public Health Agency of Canada indicated that by the time children reached 7 years of age (on average) 70.5% were complete for their Diphtheria immunizations (5 doses), 65.3% were complete for their Pertussis immunizations (5 doses), and 65.9% of the children were complete for their Tetanus immunizations (also 5 doses).[94]

Although immunization status varies by Regional Health Authority, there were only 121 children in the cohort who were not immunized at all with DPT or DaPT. This means that less than 1% of the cohort was never immunized with DPT or DaPT.

The reasons as to why the children who were incomplete for their DPT/DaPT immunizations were less likely to visit a physician(s) cannot be determined from this dataset or this research study (Figures in Appendix III). Some questions which could be addressed in future

research are: Are their parents less vigilant when it comes to routine medical exams? Do their parents not agree with parts of or the entire immunization schedule and therefore knowingly skip routine medical visits for immunizations? Or are children who are incomplete for their immunizations healthier children and do not require medical attention as often as other children?

As stated before, it is not possible to answer these questions in this particular portion of the research study. Future research could also include an additional variable from the MIMS database which indicates whether or not missed immunizations were by the parents' or guardians' choice. Other studies have found that parents who do not fully immunize their children do so because they have made a conscious decision not to. This decision can stem from personal beliefs, research or their family physician has advised against it for reasons such as a cold or flu at the time of the doctors visit or other contra-indications.[95,96]

**For additional data on immunization status and Asthma within Manitoba and Winnipeg see Appendix III.

In addition to the differences in the Asthma rates between the different immunization groups, the Wheezing groups also varied. As with Asthma the Wheezing rates also increased with immunization status (from None to Over). Although the adjusted OR's were not statistically significant Asthma (Table 21) the adjusted OR's were significant for Wheezing when the immunized groups were compared to the non immunized group (None) (Table 25). The possible reasons for this outcome are discussed in greater detail in the "Discussion of Main Results Section".

CHAPTER 9: DPT immunization delayed & on time & Asthma / Wheezing

The Canadian immunization schedule for children indicates that Diphtheria, Pertussis, and Tetanus should be given at 2, 4, 6 and 18 months after birth and then again some time between 4 to 6 years. To reiterate the second objective –

2 – Is there a difference in the incidence of asthma in children who have completed their immunizations according to the set schedule and in those whose immunizations are complete but have been delayed for one reason or another?

My research hypothesis is that children who had delayed immunizations will have a lower incidence of asthma.

Table 26:

There were 1005 children who received each of their first four DPT vaccinations on schedule (Group 1C) and of these children there were 145 with Asthma (14.43%). Children in Group 14 C had an Asthma rate of 9.12%, which is considerably lower than the Asthma rate of children in Group 1C. Despite all of the variation in the immunization patterns, only Group 1C and 14C demonstrated significance for both unadjusted and adjusted Odds Ratios.

See the "Discussion of Main Results Section" for a complete discussion of this data.

CHAPTER 10: Variations of the DPT vaccine and the Asthma / Wheezing Rates

Research Question Three –

Is there a difference in the incidence of asthma among children who have been immunized with DPT (Diphtheria, whole cell pertussis, tetanus) as opposed to DaPTP (Diphtheria, acellular pertussis, tetanus, polio) or DT (diphtheria and tetanus) or aP (acellular pertussis)?

My research hypothesis is that the combination vaccines containing pertussis as well the acellular pertussis vaccine will be associated with an increase in the incidence of asthma compared to DT.

TABLE 40: The Frequency of Diphtheria and Tetanus Vaccines

The Asthma rate was higher among the children who received 1 or more DT vaccines, 14.49% compared to 11.25% for the entire population. Although the 33 children who received separate vaccines for each disease did not have Asthma and not many experienced Wheezing (a Wheezing rate of 24.24% compared to 42.29% of the general population). The Asthma rate did increase with an increase in the number of DT vaccines received; however, the cell size of each group (1, 2, 3 and 4) decreased – making comparisons difficult.

The research hypothesis suggested that children who received DT vaccines rather than DaPT or DPT would have a lower incidence of asthma. This research hypothesis was not supported by the data analyses. However, as the majority of the children received more than one type of combination vaccine (DT / DPT / DaPT) and only 7 children received solely DT. Further analyses also determined that of the 421 children who received either a DT or DipT vaccine there were 61 children who developed Asthma. Of these 61 children 41 of them (or 67.21%) had developed Asthma prior to their first DT vaccine.

PART II:

Another approach for analyzing this data was to determine how Asthma and Wheezing may vary with the variations in DT and DPT and DaPT combinations. For this cohort this was a more realistic and testable question or objective.

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Asthma and Wheezing when compared to the children who had a combination of DT and DaPT?

Did the children who received a combination of DT with DPT vaccines have a higher incidence of Asthma and Wheezing when compared to the children who had a combination of DT and DaPT and DPT?

TABLE 42 – 43 and 58: Two Vaccine Combinations of DT (1 to 3) and DPT (1 to 6)

The first part of the new objective could also not be adequately tested due to the very small number of children who received DT and DaPT only (10 children). Table 42 categorizes DT and DPT and makes it obvious that children who received only DT and DPT vaccines were more likely to have a higher incidence of Asthma (19.03%) and Wheezing (50%). It is possible that children who had developed respiratory difficulties prior to their DT / DPT immunization had parents or physicians who requested or decided to use the acellular version (DT) for concerns of exacerbating the respiratory symptoms. It is also possible that these children had been infected with "wild" Pertussis and due to their natural immunity no longer required the Pertussis component of the DTP immunization. This may account for the higher incidence of Asthma and Wheezing in children who received a DT vaccine at some point in their immunization history.

TABLE 44 and 59: Three Vaccine Combinations of DT (1 to 3) / DPT (1 to 6) / DaPT (1 to 2)

The children who received DT and DPT vaccines but in combination with DaPT vaccines had a much lower Asthma rate than the children who received the DT and DPT combinations (11% compared to 19.03%). Although the Wheezing rates were virtually identical (48.97%

compared to 50%). This may indicated that the use of DaPT is associated with lower rates of Asthma.

**Additional information on this data can be found in the "Discussion of Main Findings" section.

Although the unadjusted Odds Ratio for Wheezing indicated statistical significance, the adjusted Odds Ratio did not confirm this. The adjusted Odds Ratios were statistically significant. Thus, when the children who had been immunized with DT / DaPT vaccines and those who had been immunized with DT / DPT / DaPT vaccines and those who had never received any DT vaccines were compared to the children who received DT and DPT vaccines they were all less likely to have Asthma. This indicates that the children who received both DT and DPT were more likely to have Asthma. It was established that most of the children received a DPT vaccine before a DT vaccine and that 41of the 61 children who had Asthma developed it prior to their first DT immunization. Therefore, this may indicate that there is a component of the DPT vaccine that is associated with a higher likelihood of developing Asthma.

PART III: COMPLETE vs. INCOMPLETE DPT/DaPT IMMUNIZATIONS & ASTHMA

TABLES : Unadjusted and adjusted Odds Ratios for the different DPT/DaPT vaccine combinations

The very large difference between group sizes may have played an important role in the inability to find a statistically significant result between the various groups and the development of Asthma. Although the first table (Table 51) indicated a significant result (more likely to have Asthma) when children with a Complete immunization status (DPT[4-6] and DaPT 1) were compared to children with an incomplete immunization status (DPT[1-3] and DaPT 1), these comparisons were not significant when an adjusted OR was performed.

**The adjusted OR for Wheezing can be found in the "Discussion of Main findings" section.

PART IV: LONE DPT & DaPT IMMUNIZATIONS AND ASTHMA

TABLE 65: The vaccine combinations / the number of children with Asthma within each group / the asthma rate and the group order

TABLE 66: The adjusted Odds Ratios of Asthma and DPT / DaPT / No DPT or DaPT / Other

This analysis is difficult as the cell size (n) of each group is very different. It is not fair to compare 13, 756 children to 114 just as it is not fair to compare 48 or 32 children to 114. Although the latter is a much closer comparison in terms of size, no grand sweeping statements can be said about 2 children with Asthma versus 8 children with Asthma. The same could be said for the differences in the number of children with Wheezing.

CHAPTER 11: The Measles, Mumps & Rubella vaccination and Asthma / Wheezing

Research Question Four

Is there a difference in the rates of asthma between those who have been immunized with MMR, and those who have not?

My research hypothesis is that the incidence of asthma will be higher among individuals who have been immunized with MMR than among those who have not been immunized with MMR.

PART I

TABLES 70 – 80: MMR frequencies and Odds Ratios

The majority of the children in the 1995 birth cohort were immunized with MMR (13 632 / 13 950 = 97.72%). This makes it very difficult to find a statistically significant difference which is significant when comparing those who were immunized with MMR to those who were not. The Chi-Square test for trend (difference in the Asthma rate between 0, 1, 2, 3+ MMR received) indicated that there was a significant difference between the MMR groups and Asthma and also for Wheezing (Table 77). Although the unadjusted Odds Ratios indicated a difference for Wheezing, once the OR's were controlled for no statistical difference was found.

There have been other research studies which were presented in the Literature Review section which described associations between the MMR vaccine and an increased risk for Asthma which were statistically significant.

A cross-sectional study by Alm J. Swartz J, *et.al.* of 295 children from two Steiner schools and 380 children from two neighboring schools who found that on average only 52% of the Steiner children had used antibiotics compared to 90% of control school children. They also found that only 18% of the Steiner school children had been immunized against measles, mumps, and rubella (MMR) whereas 93% of the control school children had been immunized with MMR. As a result, 61% of the Steiner children had had measles. Overall the Steiner children had lower rates of atopic disorders, with an average asthma rate of 5.8% compared to the control group's

average of 17%. In conclusion, they found that there was an inverse relationship between the number of anthroposophic lifestyle "features" and the risk of atopy.[97]

In 2001, researchers at The John Hopkins University School of Medicine performed a study involving peripheral blood lymphocyted (PBLs) and the MMR vaccine. They concluded that the viral vaccine has the ability to induce IgE class switching. The researchers then performed the same study with individual vaccines of measles, mumps, and rubella. From this they determined that the rubella vaccine was the most potent inducer of IgE class switching. As was discussed before IgE antibodies are associated with allergic disorders.[98] Another study on allergic reactions to the MMR vaccination found that vaccine seemed to have the ability to exacerbate asthma symptoms in those who were previously diagnosed as being asthmatic.[99]

The preliminary data analyses of the MMR vaccine indicates an increase in the Asthma and Wheezing rates with an increase in the number of MMR doses received. Despite the fact that this was found to not be statistically significant, it does not mean that there is no true association. The fact that there were only 323 children or 2.31% of the cohort did not receive a MMR vaccine and that of the children who were immunized 83.99% received 1 vaccine makes it very difficult to compare groups. It can not be said without a doubt that there is no association and it would be advisable to suggest further research to confidently state that no association exists. Additional research is also needed to confirm that this trend does exist.

CHAPTER 12: The BCG Vaccine and Asthma / Wheezing

Research Question Five:

Is there a difference in the incidence of asthma between those who have been immunized with the BCG vaccine and those who have not?

My research hypothesis is that the incidence of asthma will be lower among individuals who have been immunized with BCG than among those who have not been immunized with BCG.

There were only 414 children who received a BCG vaccine from the birth cohort, or 2.97% and only two of these children received 2 BCG vaccinations. This is not surprising as only infants at high risk of becoming infected with TB are given the BCG vaccine as a preventative measure. Thus, there exists a hypothesis about the demographics of who is more likely to receive the vaccine. Typically, in Canada, the highest number of TB cases is found amongst Aboriginal communities on reserves. It is therefore most likely that the majority of the children who were vaccinated with BCG are Aboriginal. This hypothesis was confirmed by speaking with a nurse from the First Nations Inuit Health Branch (FNIHB) who said that in Manitoba the requirements for infants to be immunized with BCG are either:

1- to be born and live in a rural or northern First Nations community or

2 - an infant who is not born in the First Nations community but will be spending a considerable amount of time visiting there.[100]

TABLE 81: The adjusted OR of the BCG vaccine and Asthma

Although the adjusted OR / Logistic Regression does make allowances or give consideration to variation in group size, the fact that there were only 414 children who were immunized out of 13 950 makes it difficult to compare the two groups (vaccinated / not vaccinated) due to the large size differences.

DEMOGRAPHICS:

FIGURE 29: The distribution of the BCG vaccine across Manitoban RHA's

The three RHA's with the highest number of children who received the BCG vaccine were Interlake, Parkland, and Burntwood. This is not surprising as the requirements for children / infants receiving a BCG vaccination in Manitoba are to be born on a First Nation's reservation or living in an environment at high risk for becoming infected with TB. It is probable that most, if not all of the 414 children born in 1995 and who were immunized with BCG are Aboriginal. It would be ideal to confirm this assumption by referring to additional data; however, the ethical parameters do not allow for this. Although the Asthma rate among the children who received the BCG vaccine was considerably less (7.72%) than the overall Asthma rate of 11.25%, there were only 414 children who received the BCG vaccine.

The children who received the BCG vaccine were very homogenous in terms of social and environmental living conditions. As a result two of the independent variables were very strong confounders for the model. The logistic model which included the following independent variables: gender, maternal history of asthma, income, and antibiotic prescriptions within the first year of life produced an OR which was statistically significant and indicated that children who received one or more BCG vaccines were less likely to develop asthma. However, when the independent variable "Medical consults" was added to the model the OR became non-significant as the 95%CL crossed over 1.00. The same thing occurred when "Region" was added to the model instead of "Medical consults".

The OR produced from the model which included all six independent variables remained non-significant when Region was taken out of the model. The adjusted OR became significant once Medical consults and Region were taken out of the model and the other four independent variables were left in the model. Here the OR was 0.58 with a 95%CL of 0.401 to 0.84.

Table 85: The distribution of Medical Consults among children who received a BCG vaccine

	Medical Consults (#)					
BCG	0 - 35	36 - 49	50 to 66	67 to 151	152 to 459	Total
Yes	145	101	73	90	5	414
Rate (%)	35.02	24.4	17.63	21.74	1.21	100

Children who were immunized with BCG were more likely than children who did not receive a BCG immunization to have fewer Medical consults. Only 5.31% (22 / 414) of the children who were immunized with BCG lived in an urban centre, while 94.69% or (392 / 414) were from a rural household. Children that live in a rural area have less access to healthcare than children who live in Winnipeg or Brandon.

Therefore, once "Medical consults" and "Region" were controlled for the OR was no longer significant.

Possible reasons for the large variation in asthma rates among rural RHA's:

1 – children who live in these RHAs have less asthma than children who live in other RHA's genetics, less air pollution.

2 – children who live in this RHA have less access to health care facilities and workers and are therefore less likely to be diagnosed with asthma (in this case Asthma).

3 – there may be a significant number of aboriginal children i.e. Burntwood, who seek health care from nursing stations. These medical visits would not be recorded by Manitoba Health.[101,102]

CHAPTER 15: POST HOC POWER ANALYSIS

Throughout this research project there have been significant issues related to the size differences of various groups in question (i.e. immunization groups). Although the relevance of conducting a post hoc power analysis is a point for debate among biostaticians, it is of importance in this study as the birth cohort size was pre-determined and non-negotiable. The post hoc power analysis was used to demonstrate what "sample" size would have been required to detect the maximum power level with the significance level, original "sample" size, and actual observed difference (i.e. odds ratio [OR]) from the original Logistic Regression. In many cases the Power level is not impressive and does strengthen the argument that – often the size difference of the immunized group is far too great to be able to detect any significant differences among those who were not vaccinated.

In Chapter 8 there was a very large difference between the number of children who were immunized with DPT/DaPT and those who were not. There were only 121 children who were never immunized with DPT/DaPT compared to 13 829 children who were. The post hoc power analysis of the "none" group of children using a significance level of 0.548, an OR of 0.782, and an original sample size of 121 indicated that the power to detect a difference in the odds of asthma between the two groups as large as this was only 9 percent. For the "Over-immunized" group of children using a significance level of 0.5106, an OR of 1.029 was obtained with a significance level of 0.5106 with a sample size of 345. The power to detect a difference in the odds of asthma between the two groups as large as this was only 10 percent, and the sample size that would be required to detect an effect of this magnitude is 3062 children.

In Chapter 9 there were 1005 children in Group #1 – these children had each of their first four DPT immunizations on time. The post hoc power analysis of the children in Group #1 using a significance level of 0.1619, an OR of 1.147, and original sample size of 1005 indicated that the power to detect a difference in the odds of asthma between the two groups as large as this was 29 percent and the sample size that would be required to detect an effect of this magnitude is 1975

children. While, the post hoc power analysis of the children in Group #15 (the 3708 children who had each of their first four DPT vaccines delayed) using a significance level of 0.0575, an OR of 0.907, and original sample size of 3708 indicated that the power to detect a difference in the odds of asthma between the two groups as large as this was 48 percent and the sample size that would be required to detect an effect of this magnitude is 3948.

Chapter 10 indicated that there were only 421 children who received a DT / D / T vaccines and that on the whole, these children had higher Asthma rates (average Asthma rate of 14.49%). The post hoc power analysis of these 421 children using a significance level of 0.2617, an OR of 1.179, and original sample size of 420 indicated that the power to detect a difference in the odds of asthma between the two groups as large as this was 20 percent and the sample size that would be required to detect an effect of this magnitude is 1281 children.

Chapter 12 indicated that there were only 414 children who received a BCG vaccine and that the Asthma rate among these children was 7.73%. The post hoc power analysis of these 414 children using a significance level of 0.4879, an OR of 0.872, and original sample size of 414 indicated that the power to detect a difference in the odds of asthma between the two groups as large as this was 10 percent and the sample size that would be required to detect an effect of this magnitude is 3305 children.[103]

CHAPTER 16: DISCUSSION OF ADDITIONAL POINTS OF INTEREST & CONCLUSION

Although the majority of the 5898 children who experienced Wheezing probably outgrew these symptoms, they did place an enormous burden of care on society during the time of their illness. This type of asthma-like condition is rarely, if ever, taken into account when assessing the impact of asthma on the health care system. The fact that the only code of interest in the extraction of health data was 493 (asthma = 493) also raises the question – are physicians accurately diagnosing asthma?

The SAGE project is still underway and analysis is continuous. As a result, the definition of asthma that will be used in future publications and presentations will not be exactly the same as the definition used for Asthma in this document. A medication used to treat asthma symptoms was removed from the prescription list used when extracting medication data on the children in the birth cohort. Therefore, the number of children with Asthma is 1591 instead of the 1599 used in this project. Upon receiving this information and re-running the logistic regression on several of the objectives (using the new asthma definition) the final adjusted Odds Ratios and 95%CL did not change enough to result in a change of the final outcomes. This did not warrant the revision of this document, but is important to mention and be aware of in future publications and presentations of particular sections of this thesis.

STRENGTHS OF THE RESEARCH

This project presented a unique opportunity to perform an in-depth analyses of both childhood asthma and childhood immunizations within Manitoba. Although the end date for this project was 2002, there were over seven years of health data for each of the 13, 980 children in the 1995 Birth Cohort. The magnitude of resources available for this research project is rare for both asthma and immunization studies and especially for a combined study.

Many of the current studies on the possible association between immunizations and childhood asthma have been criticized for not being able to determine if immunizations played a

causal role in the development of asthma or exacerbated asthma that already existed. This study minimized this conflict by removing children from the cohort who developed asthma or asthma like symptoms (Wheezing) prior to their first immunization. It was determined that of the1599 children who had Asthma, 30 of these children were removed as they displayed asthma symptoms prior to their first immunization. There were 6087 children who experienced Wheezing; however, 189 of these children developed these symptoms prior to their first immunization and were also removed from the cohort.

LIMITATIONS OF THE STUDY:

The limitations of this study would involve certain limitations of the MIMS data whereby the true rates of immunizations are not known because of the following events: there are some cases where physicians give immunizations and then miscode on their physician claims, or not at all; other possibilities may include nurses who give immunizations, but they are not reported to MIMS; the lower rates among the Status Aboriginal children may be due to Manitoba Health having inaccurate records with regards to the population registry of Treaty status children. Although, these will most likely not be significant limitations in this study as another study using MIMS data by Roberts J. et.al. found that when comparing MIMS data to physician records they matched 98% of the time. The rate at which physicians failed to bill for immunizations was estimated at 0.2% for urban areas and 6.6% for rural. This study also reported that the immunization levels among Treaty Status children were in fact much higher when they consulted the Federal Health Department.[104] Another limitation was the inability to definitely determine whether or not the BCG immunizations were only or mainly received by First Nations children.

Another limitation of this study would be the loss of cohort members due to emigration out of the province or moving to another region / Health Authority in the province and their guardians do not notify Manitoba Health of their address change. This study is also limited in that the environmental exposures of the children cannot be directly measured. Although lower respiratory infections cause by RSV were also not directly included in the analysis or controlled

for, other independent variables (Medical consults, and antibiotics) served as proxy measures.

FUTURE RESEARCH & CONCLUSION:

This study was able to answer many questions / objectives that were set out in the beginning of this research and this study also raised many new questions which could spur future research.

As Canada no longer uses DPT the same analyses should be performed on children who have been completely immunized with DaPT to determine if the same association with Asthma and Wheezing exists. Although Canada no longer uses DPT and it would seem that this may be of historical significance only, many countries around the world still use the whole cell Pertussis DPT vaccine today. Therefore, this finding may be of interest world-wide.

Another finding which was of great interest and could definitely be followed up with additional research was that children who had each of their first four DPT vaccines delayed had a lower risk of developing Asthma when compared to children who had each of their first four DPT immunizations on time. It was also of interest that children who had their first and second DPT immunization on time had a higher Asthma rate when compared to children who did not receive these immunizations on time. Again, this finding should be repeated with children who have only received the DaPT version of the vaccine to determine if this is still the outcome.

There also exists the possibility of future research between the immunization status (Over, Complete, Incomplete, and None) with DaPT and wheezing, whereby children who received various levels of immunization with DaPT-type vaccines also have a higher rate of Wheezing when compared to children who have never been immunized.

The high rate at which Wheezing was experienced by the cohort emphasizes the importance of future research involving the use of appropriate diagnostic codes and asthma. The Wheezing cases in this cohort were coded in the administrative data as 493, which is the code for asthma. According to the validated definition most of these children where not considered to actually have asthma but rather experienced respiratory difficulties categorized as Wheezing.

From this preliminary finding there now exists the opportunity to further investigate this with future research.

This research answered or met the objectives that were set out at the beginning of this project. Although every objective / question could not be answered exactly as asked, there was enough data available to perform a fairly in depth analysis of the situation. In addition to the various preliminary questions in this research project, many new questions arose throughout the analysis. This chapter as well as those before, have highlighted many areas where future asthma / immunization research could venture. The title of this thesis is "Is there an association between childhood immunizations & childhood asthma?" and the answer to this question is – yes, there is. Many aspects of the degree and length to which this or these associations exist remain a question; however, the last one hundred and ninety-three pages of this document provide a good start.

Some additional questions which were raised are: whether or not the parents / guardians of the children who were not immunized, made this a conscious decision. The MIMS database does contain this information and it would be interesting to analyze it.[105] Another question which was raised was whether or not the individuals (physicians, nurses) administering vaccines have access to the MIMS database to make properly informed decisions on when and how to immunize their patients if they do not have accurate immunization records in their office. A research study on the current and possible future uses of MIMS data by health care professionals would be valuable.

Conclusion:

As it was stated in the literature review section of this document – in Canada in 1997 asthma was listed as the primary diagnosis for 12% of all admissions for children age 0 to 4 and 10% for children age 5 to 14. In 1990 the direct cost of asthma was estimated at $504 million and the indirect cost at $648 million. Just imagine the cost today, fifteen years later! In addition to the financial cost of childhood asthma, the personal and emotional cost of a chronic health condition can be very taxing to both the children who suffer from the disease and their parents

and siblings who suffer with them. There are documents that date back thousands of years which describe asthma-like symptoms. Unfortunately in the year 2005, there is still no cure for asthma and the exact cause(s) are not known. The continuation of thorough and multi-faceted asthma research remains essential. Immunizations are one piece of the puzzle that is asthma. Although there are debates about the association of childhood immunizations and childhood asthma, it is important to remember the following:

> *It is for us, and for those who come after us, to see that the sword which vaccines and antisera have put into our hands is never allowed to tarnish through over-confidence, negligence, carelessness, or want of foresight on our part.*
>
> *Sir Graham S. Wilson*
> *M.D., LL.D., F.R.C.P., D.P.H.*
> *University of London, 1967*

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APPENDIX I
VARIABLES USED IN THE
1995 BIRTH COHORT ASTHMA & IMMUNIZATION DATABASE

VARIABLES IN THE ASTHMA/IMMUNIZATION DATA SET:

Data Set Name: WORK.KARA Observations: 13950
Member Type: DATA Variables: 1085

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
103	Apr1995	Num	8	152		*the number of asthma cases per month*
115	Apr1996	Num	8	248		
127	Apr1997	Num	8	344		
139	Apr1998	Num	8	440		
151	Apr1999	Num	8	536		
163	Apr2000	Num	8	632		
175	Apr2001	Num	8	728		
187	Apr2002	Num	8	824		
107	Aug1995	Num	8	184		
119	Aug1996	Num	8	280		
131	Aug1997	Num	8	376		
143	Aug1998	Num	8	472		
155	Aug1999	Num	8	568		
167	Aug2000	Num	8	664		
179	Aug2001	Num	8	760		
191	Aug2002	Num	8	856		
3	COUNT	Num	8	8		*Frequency Count*
82	DATEPRVD	Char	8	8315		*date provided CCYYMMDD*
86	DATESEP	Char	8	8333		*DATE OF DISCHARGE/SEPARATION YYMMDD*
995	DPT1DaPT1_620	Num	8	7288		*Children who had 1DPT and 1DaPTvaccine at 620 days after birth*
959	DPT1DaPT1_2790	Num	8	7000		
965	DPT1DaPT2_2790	Num	8	7048		
971	DPT1DaPT3_2790	Num	8	7096		
977	DPT1DaPT4_2790	Num	8	7144		
983	DPT1DaPT5_2790	Num	8	7192		
989	DPT1DaPT6_2790	Num	8	7240		
524	DPT1_31	Num	8	3520		*children who had 1 DPT vaccine at 31 days after birth*
512	DPT1_62	Num	8	3424		
500	DPT1_93	Num	8	3328		
488	DPT1_124	Num	8	3232		
476	DPT1_155	Num	8	3136		
464	DPT1_186	Num	8	3040		
452	DPT1_217	Num	8	2944		
440	DPT1_248	Num	8	2848		
428	DPT1_279	Num	8	2752		
416	DPT1_310	Num	8	2656		
408	DPT1_341	Num	8	2592		
402	DPT1_365	Num	8	2544		
396	DPT1_558	Num	8	2496		
384	DPT1_744	Num	8	2400		
376	DPT1_1116	Num	8	2336		
364	DPT1_1488	Num	8	2240		

352	DPT1_1860	Num	8	2144
340	DPT1_2232	Num	8	2048
338	DPT1_2790	Num	8	2032
996	DPT2DaPT1_620	Num	8	7296
960	DPT2DaPT1_2790	Num	8	7008
966	DPT2DaPT2_2790	Num	8	7056
972	DPT2DaPT3_2790	Num	8	7104
978	DPT2DaPT4_2790	Num	8	7152
984	DPT2DaPT5_2790	Num	8	7200
990	DPT2DaPT6_2790	Num	8	7248
526	DPT2_31	Num	8	3536
514	DPT2_62	Num	8	3440
502	DPT2_93	Num	8	3344
490	DPT2_124	Num	8	3248
478	DPT2_155	Num	8	3152

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
466	DPT2_186	Num	8	3056		
454	DPT2_217	Num	8	2960		
442	DPT2_248	Num	8	2864		
430	DPT2_279	Num	8	2768		
418	DPT2_310	Num	8	2672		
634	DPT2_341	Num	8	4400		
638	DPT2_365	Num	8	4432		
642	DPT2_558	Num	8	4464		
386	DPT2_744	Num	8	2416		
378	DPT2_1116	Num	8	2352		
366	DPT2_1488	Num	8	2256		
354	DPT2_1860	Num	8	2160		
342	DPT2_2232	Num	8	2064		
328	DPT2_2790	Num	8	1952		
997	DPT3DaPT1_620	Num	8	7304		
961	DPT3DaPT1_2790	Num	8	7016		
967	DPT3DaPT2_2790	Num	8	7064		
973	DPT3DaPT3_2790	Num	8	7112		
979	DPT3DaPT4_2790	Num	8	7160		
985	DPT3DaPT5_2790	Num	8	7208		
991	DPT3DaPT6_2790	Num	8	7256		
528	DPT3_31	Num	8	3552		
516	DPT3_62	Num	8	3456		
504	DPT3_93	Num	8	3360		
492	DPT3_124	Num	8	3264		
480	DPT3_155	Num	8	3168		
468	DPT3_186	Num	8	3072		
456	DPT3_217	Num	8	2976		
444	DPT3_248	Num	8	2880		
432	DPT3_279	Num	8	2784		
420	DPT3_310	Num	8	2688		
410	DPT3_341	Num	8	2608		
404	DPT3_365	Num	8	2560		
398	DPT3_558	Num	8	2512		
388	DPT3_744	Num	8	2432		
380	DPT3_1116	Num	8	2368		

368	DPT3_1488	Num	8	2272
356	DPT3_1860	Num	8	2176
344	DPT3_2232	Num	8	2080
330	DPT3_2790	Num	8	1968
998	DPT4DaPT1_620	Num	8	7312
962	DPT4DaPT1_2790	Num	8	7024

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
968	DPT4DaPT2_2790	Num	8	7072		
974	DPT4DaPT3_2790	Num	8	7120		
980	DPT4DaPT4_2790	Num	8	7168		
986	DPT4DaPT5_2790	Num	8	7216		
992	DPT4DaPT6_2790	Num	8	7264		
530	DPT4_31	Num	8	3568		
518	DPT4_62	Num	8	3472		
506	DPT4_93	Num	8	3376		
494	DPT4_124	Num	8	3280		
482	DPT4_155	Num	8	3184		
470	DPT4_186	Num	8	3088		
458	DPT4_217	Num	8	2992		
446	DPT4_248	Num	8	2896		
434	DPT4_279	Num	8	2800		
422	DPT4_310	Num	8	2704		
636	DPT4_341	Num	8	4416		
640	DPT4_365	Num	8	4448		
644	DPT4_558	Num	8	4480		
390	DPT4_744	Num	8	2448		
646	DPT4_1116	Num	8	4496		
370	DPT4_1488	Num	8	2288		
358	DPT4_1860	Num	8	2192		
346	DPT4_2232	Num	8	2096		
332	DPT4_2790	Num	8	1984		
999	DPT5DaPT1_620	Num	8	7320		
963	DPT5DaPT1_2790	Num	8	7032		
969	DPT5DaPT2_2790	Num	8	7080		
975	DPT5DaPT3_2790	Num	8	7128		
981	DPT5DaPT4_2790	Num	8	7176		
987	DPT5DaPT5_2790	Num	8	7224		
993	DPT5DaPT6_2790	Num	8	7272		
532	DPT5_31	Num	8	3584		
520	DPT5_62	Num	8	3488		
508	DPT5_93	Num	8	3392		
496	DPT5_124	Num	8	3296		
484	DPT5_155	Num	8	3200		
472	DPT5_186	Num	8	3104		
460	DPT5_217	Num	8	3008		
448	DPT5_248	Num	8	2912		
436	DPT5_279	Num	8	2816		
424	DPT5_310	Num	8	2720		
412	DPT5_341	Num	8	2624		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
406	DPT5_365	Num	8	2576		
400	DPT5_558	Num	8	2528		
392	DPT5_744	Num	8	2464		
382	DPT5_1116	Num	8	2384		
372	DPT5_1488	Num	8	2304		
360	DPT5_1860	Num	8	2208		
348	DPT5_2232	Num	8	2112		
334	DPT5_2790	Num	8	2000		
1000	DPT6DaPT1_620	Num	8	7328		
964	DPT6DaPT1_2790	Num	8	7040		
970	DPT6DaPT2_2790	Num	8	7088		
976	DPT6DaPT3_2790	Num	8	7136		
982	DPT6DaPT4_2790	Num	8	7184		
988	DPT6DaPT5_2790	Num	8	7232		
994	DPT6DaPT6_2790	Num	8	7280		
534	DPT6_31	Num	8	3600		
522	DPT6_62	Num	8	3504		
510	DPT6_93	Num	8	3408		
498	DPT6_124	Num	8	3312		
486	DPT6_155	Num	8	3216		
474	DPT6_186	Num	8	3120		
462	DPT6_217	Num	8	3024		
450	DPT6_248	Num	8	2928		
438	DPT6_279	Num	8	2832		
426	DPT6_310	Num	8	2736		
414	DPT6_341	Num	8	2640		
394	DPT6_744	Num	8	2480		
690	DPT6_1116	Num	8	4848		
374	DPT6_1488	Num	8	2320		
362	DPT6_1860	Num	8	2224		
350	DPT6_2232	Num	8	2128		
336	DPT6_2790	Num	8	2016		
89	DRvisits	Num	8	56		*The number of physician visits*
1001	DT1_2790	Num	8	7336		
1007	DT1_DPT1DaPT1_2790	Num	8	7384		*One DT and one DPT and one DaPT vaccine at 2790 days*
1013	DT1_DPT1DaPT2_2790	Num	8	7432		
1055	DT1_DPT1_2790	Num	8	7768		
1008	DT1_DPT2DaPT1_2790	Num	8	7392		
1014	DT1_DPT2DaPT2_2790	Num	8	7440		
1056	DT1_DPT2_2790	Num	8	7776		
1009	DT1_DPT3DaPT1_2790	Num	8	7400		
1015	DT1_DPT3DaPT2_2790	Num	8	7448		

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#	Variable	Type	Len	Pos	Format	Label
1057	DT1_DPT3_2790	Num	8	7784		
1010	DT1_DPT4DaPT1_2790	Num	8	7408		
1016	DT1_DPT4DaPT2_2790	Num	8	7456		
1058	DT1_DPT4_2790	Num	8	7792		
1011	DT1_DPT5DaPT1_2790	Num	8	7416		
1017	DT1_DPT5DaPT2_2790	Num	8	7464		
1059	DT1_DPT5_2790	Num	8	7800		
1012	DT1_DPT6DaPT1_2790	Num	8	7424		
1018	DT1_DPT6DaPT2_2790	Num	8	7472		
1060	DT1_DPT6_2790	Num	8	7808		
1079	DT1_DaPT1_2790	Num	8	7960		
1080	DT1_DaPT2_2790	Num	8	7968		
1081	DT1_DaPT3_2790	Num	8	7976		
1082	DT1_DaPT4_2790	Num	8	7984		
1083	DT1_DaPT5_2790	Num	8	7992		
1084	DT1_DaPT6_2790	Num	8	8000		
1003	DT2_2790	Num	8	7352		*Two DT vaccines at 2790 days*
1019	DT2_DPT1DaPT1_2790	Num	8	7480		
1025	DT2_DPT1DaPT2_2790	Num	8	7528		
1061	DT2_DPT1_2790	Num	8	7816		
1020	DT2_DPT2DaPT1_2790	Num	8	7488		
1026	DT2_DPT2DaPT2_2790	Num	8	7536		
1062	DT2_DPT2_2790	Num	8	7824		
1021	DT2_DPT3DaPT1_2790	Num	8	7496		
1027	DT2_DPT3DaPT2_2790	Num	8	7544		
1063	DT2_DPT3_2790	Num	8	7832		
1022	DT2_DPT4DaPT1_2790	Num	8	7504		
1028	DT2_DPT4DaPT2_2790	Num	8	7552		
1064	DT2_DPT4_2790	Num	8	7840		
1023	DT2_DPT5DaPT1_2790	Num	8	7512		
1029	DT2_DPT5DaPT2_2790	Num	8	7560		
1065	DT2_DPT5_2790	Num	8	7848		
1024	DT2_DPT6DaPT1_2790	Num	8	7520		
1030	DT2_DPT6DaPT2_2790	Num	8	7568		
1066	DT2_DPT6_2790	Num	8	7856		
1004	DT3_2790	Num	8	7360		
1031	DT3_DPT1DaPT1_2790	Num	8	7576		*Three DT vaccines and one DPT and one DaPT vaccine at 2790 days after birth*
1037	DT3_DPT1DaPT2_2790	Num	8	7624		
1067	DT3_DPT1_2790	Num	8	7864		
1032	DT3_DPT2DaPT1_2790	Num	8	7584		
1038	DT3_DPT2DaPT2_2790	Num	8	7632		
1072	DT3_DPT2_2790	Num	8	7904		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
1033	DT3_DPT3DaPT1_2790	Num	8	7592		
1039	DT3_DPT3DaPT2_2790	Num	8	7640		
1068	DT3_DPT3_2790	Num	8	7872		
1034	DT3_DPT4DaPT1_2790	Num	8	7600		
1040	DT3_DPT4DaPT2_2790	Num	8	7648		
1069	DT3_DPT4_2790	Num	8	7880		
1035	DT3_DPT5DaPT1_2790	Num	8	7608		
1041	DT3_DPT5DaPT2_2790	Num	8	7656		
1070	DT3_DPT5_2790	Num	8	7888		
1036	DT3_DPT6DaPT1_2790	Num	8	7616		
1042	DT3_DPT6DaPT2_2790	Num	8	7664		
1071	DT3_DPT6_2790	Num	8	7896		
1043	DT4_DPT1DaPT1_2790	Num	8	7672		
1049	DT4_DPT1DaPT2_2790	Num	8	7720		
1073	DT4_DPT1_2790	Num	8	7912		
1044	DT4_DPT2DaPT1_2790	Num	8	7680		
1050	DT4_DPT2DaPT2_2790	Num	8	7728		
1074	DT4_DPT2_2790	Num	8	7920		
1045	DT4_DPT3DaPT1_2790	Num	8	7688		
1051	DT4_DPT3DaPT2_2790	Num	8	7736		
1075	DT4_DPT3_2790	Num	8	7928		
1046	DT4_DPT4DaPT1_2790	Num	8	7696		
1052	DT4_DPT4DaPT2_2790	Num	8	7744		
1076	DT4_DPT4_2790	Num	8	7936		
1047	DT4_DPT5DaPT1_2790	Num	8	7704		
1053	DT4_DPT5DaPT2_2790	Num	8	7752		
1077	DT4_DPT5_2790	Num	8	7944		
1048	DT4_DPT6DaPT1_2790	Num	8	7712		
1054	DT4_DPT6DaPT2_2790	Num	8	7760		
1078	DT4_DPT6_2790	Num	8	7952		
1005	DT4ormore_2790	Num	8	7368		*4 or more vaccines at 2790 days after birth*
523	DaPT1_31	Num	8	3512		
511	DaPT1_62	Num	8	3416		*1 DaPT vaccine at 62 days after birth*
499	DaPT1_93	Num	8	3320		
487	DaPT1_124	Num	8	3224		
475	DaPT1_155	Num	8	3128		
463	DaPT1_186	Num	8	3032		
451	DaPT1_217	Num	8	2936		
439	DaPT1_248	Num	8	2840		
427	DaPT1_279	Num	8	2744		
415	DaPT1_310	Num	8	2648		
407	DaPT1_341	Num	8	2584		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
401	DaPT1_365	Num	8	2536		
395	DaPT1_558	Num	8	2488		
383	DaPT1_744	Num	8	2392		
375	DaPT1_1116	Num	8	2328		
363	DaPT1_1488	Num	8	2232		
351	DaPT1_1860	Num	8	2136		
339	DaPT1_2232	Num	8	2040		
337	DaPT1_2790	Num	8	2024		
525	DaPT2_31	Num	8	3528		
513	DaPT2_62	Num	8	3432		
501	DaPT2_93	Num	8	3336		
489	DaPT2_124	Num	8	3240		
477	DaPT2_155	Num	8	3144		
465	DaPT2_186	Num	8	3048		
453	DaPT2_217	Num	8	2952		
441	DaPT2_248	Num	8	2856		
429	DaPT2_279	Num	8	2760		
417	DaPT2_310	Num	8	2664		
633	DaPT2_341	Num	8	4392		
637	DaPT2_365	Num	8	4424		
641	DaPT2_558	Num	8	4456		
385	DaPT2_744	Num	8	2408		
377	DaPT2_1116	Num	8	2344		
365	DaPT2_1488	Num	8	2248		
353	DaPT2_1860	Num	8	2152		
341	DaPT2_2232	Num	8	2056		
327	DaPT2_2790	Num	8	1944		
527	DaPT3_31	Num	8	3544		
515	DaPT3_62	Num	8	3448		
503	DaPT3_93	Num	8	3352		
491	DaPT3_124	Num	8	3256		
479	DaPT3_155	Num	8	3160		
467	DaPT3_186	Num	8	3064		
455	DaPT3_217	Num	8	2968		
443	DaPT3_248	Num	8	2872		
431	DaPT3_279	Num	8	2776		
419	DaPT3_310	Num	8	2680		
409	DaPT3_341	Num	8	2600		
403	DaPT3_365	Num	8	2552		
397	DaPT3_558	Num	8	2504		
387	DaPT3_744	Num	8	2424		
379	DaPT3_1116	Num	8	2360		

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#	Variable	Type	Len	Pos	Format	Label
367	DaPT3_1488	Num	8	2264		
355	DaPT3_1860	Num	8	2168		
343	DaPT3_2232	Num	8	2072		
329	DaPT3_2790	Num	8	1960		
529	DaPT4_31	Num	8	3560		
517	DaPT4_62	Num	8	3464		
505	DaPT4_93	Num	8	3368		
493	DaPT4_124	Num	8	3272		
481	DaPT4_155	Num	8	3176		
469	DaPT4_186	Num	8	3080		
457	DaPT4_217	Num	8	2984		
445	DaPT4_248	Num	8	2888		
433	DaPT4_279	Num	8	2792		
421	DaPT4_310	Num	8	2696		
635	DaPT4_341	Num	8	4408		
639	DaPT4_365	Num	8	4440		
643	DaPT4_558	Num	8	4472		
389	DaPT4_744	Num	8	2440		
645	DaPT4_1116	Num	8	4488		
369	DaPT4_1488	Num	8	2280		
357	DaPT4_1860	Num	8	2184		
345	DaPT4_2232	Num	8	2088		
331	DaPT4_2790	Num	8	1976		
531	DaPT5_31	Num	8	3576		
519	DaPT5_62	Num	8	3480		
507	DaPT5_93	Num	8	3384		
495	DaPT5_124	Num	8	3288		
483	DaPT5_155	Num	8	3192		
471	DaPT5_186	Num	8	3096		
459	DaPT5_217	Num	8	3000		
447	DaPT5_248	Num	8	2904		
435	DaPT5_279	Num	8	2808		
423	DaPT5_310	Num	8	2712		
411	DaPT5_341	Num	8	2616		
405	DaPT5_365	Num	8	2568		
399	DaPT5_558	Num	8	2520		
391	DaPT5_744	Num	8	2456		
381	DaPT5_1116	Num	8	2376		
371	DaPT5_1488	Num	8	2296		
359	DaPT5_1860	Num	8	2200		
347	DaPT5_2232	Num	8	2104		
333	DaPT5_2790	Num	8	1992		

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#	Variable	Type	Len	Pos	Format	Label
533	DaPT6_31	Num	8	3592		
521	DaPT6_62	Num	8	3496		
509	DaPT6_93	Num	8	3400		
497	DaPT6_124	Num	8	3304		
485	DaPT6_155	Num	8	3208		
473	DaPT6_186	Num	8	3112		
461	DaPT6_217	Num	8	3016		
449	DaPT6_248	Num	8	2920		
437	DaPT6_279	Num	8	2824		
425	DaPT6_310	Num	8	2728		
413	DaPT6_341	Num	8	2632		
393	DaPT6_744	Num	8	2472		
689	DaPT6_1116	Num	8	4840		
373	DaPT6_1488	Num	8	2312		
361	DaPT6_1860	Num	8	2216		
349	DaPT6_2232	Num	8	2120		
335	DaPT6_2790	Num	8	2008		
111	Dec1995	Num	8	216		*count of asthma cases occurring in December 1995*
123	Dec1996	Num	8	312		
135	Dec1997	Num	8	408		
147	Dec1998	Num	8	504		
159	Dec1999	Num	8	600		
171	Dec2000	Num	8	696		
183	Dec2001	Num	8	792		
195	Dec2002	Num	8	888		
1002	DipT1_2790	Num	8	7344		*children who had either a single vaccine of diphtheria or tetanus*
1006	DipT2_2790	Num	8	7376		
101	Feb1995	Num	8	136		
113	Feb1996	Num	8	232		
125	Feb1997	Num	8	328		
137	Feb1998	Num	8	424		
149	Feb1999	Num	8	520		
161	Feb2000	Num	8	616		
173	Feb2001	Num	8	712		
185	Feb2002	Num	8	808		
100	Jan1995	Num	8	128		
112	Jan1996	Num	8	224		
124	Jan1997	Num	8	320		
136	Jan1998	Num	8	416		
148	Jan1999	Num	8	512		
160	Jan2000	Num	8	608		
172	Jan2001	Num	8	704		

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#	Variable	Type	Len	Pos	Format	Label
184	Jan2002	Num	8	800		
106	Jul1995	Num	8	176		
118	Jul1996	Num	8	272		
130	Jul1997	Num	8	368		
142	Jul1998	Num	8	464		
154	Jul1999	Num	8	560		
166	Jul2000	Num	8	656		
178	Jul2001	Num	8	752		
190	Jul2002	Num	8	848		
105	Jun1995	Num	8	168		
117	Jun1996	Num	8	264		
129	Jun1997	Num	8	360		
141	Jun1998	Num	8	456		
153	Jun1999	Num	8	552		
165	Jun2000	Num	8	648		
177	Jun2001	Num	8	744		
189	Jun2002	Num	8	840		
535	MMR1_372	Num	8	3608		*children who had 1 measles/mumps/rubella vaccine at 372 days after birth*
536	MMR1_558	Num	8	3616		
541	MMR1_2232	Num	8	3656		
542	MMR1_2604	Num	8	3664		
537	MMR2_372	Num	8	3624		
538	MMR2_558	Num	8	3632		
543	MMR2_2232	Num	8	3672		
544	MMR2_2604	Num	8	3680		
539	MMR3_372	Num	8	3640		
540	MMR3_558	Num	8	3648		
545	MMR3_2232	Num	8	3688		
546	MMR3_2604	Num	8	3696		
547	MMR4_2232	Num	8	3704		
548	MMR4_2604	Num	8	3712		
102	Mar1995	Num	8	144		
114	Mar1996	Num	8	240		
126	Mar1997	Num	8	336		
138	Mar1998	Num	8	432		
150	Mar1999	Num	8	528		
162	Mar2000	Num	8	624		
174	Mar2001	Num	8	720		
186	Mar2002	Num	8	816		
104	May1995	Num	8	160		
116	May1996	Num	8	256		
128	May1997	Num	8	352		

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#	Variable	Type	Len	Pos	Format	Label
140	May1998	Num	8	448		
152	May1999	Num	8	544		
164	May2000	Num	8	640		
176	May2001	Num	8	736		
188	May2002	Num	8	832		
110	Nov1995	Num	8	208		
122	Nov1996	Num	8	304		
134	Nov1997	Num	8	400		
146	Nov1998	Num	8	496		
158	Nov1999	Num	8	592		
170	Nov2000	Num	8	688		
182	Nov2001	Num	8	784		
194	Nov2002	Num	8	880		
29	OBPHIN	Char	9	8046		*MH Scrambled PHIN - mother*
109	Oct1995	Num	8	200		
121	Oct1996	Num	8	296		
133	Oct1997	Num	8	392		
145	Oct1998	Num	8	488		
157	Oct1999	Num	8	584		
169	Oct2000	Num	8	680		
181	Oct2001	Num	8	776		
193	Oct2002	Num	8	872		
4	PERCENT	Num	8	16		*Percent of Total Frequency*
88	SERVDATE	Num	4	8016	YYMMDD8.	*date of service / date that the medical consult occurred*
108	Sep1995	Num	8	192		
120	Sep1996	Num	8	288		
132	Sep1997	Num	8	384		
144	Sep1998	Num	8	480		
156	Sep1999	Num	8	576		
168	Sep2000	Num	8	672		
180	Sep2001	Num	8	768		
192	Sep2002	Num	8	864		
84	Y02azcat	Char	6	8327		*used in the coding of Rx data*
85	Y02drug	Num	8	40		
196	Year1995	Num	8	896		*children who presented with asthma for the first time in 1995*
197	Year1996	Num	8	904		
198	Year1997	Num	8	912		
199	Year1998	Num	8	920		
200	Year1999	Num	8	928		
201	Year2000	Num	8	936		
202	Year2001	Num	8	944		
203	Year2002	Num	8	952		

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#	Variable	Type	Len	Pos	Format	Label
306	apr2003	Num	8	1776		
97	asthma02	Num	8	104		
325	asthma95	Num	8	1928		
91	asthma1599	Num	8	64		*old asthma definition*
623	asthma10m1	Num	8	4312		*child had asthma at 10 months after birth and after 1 DPT vaccine*
625	asthma10m2	Num	8	4328		
627	asthma10m3	Num	8	4344		
629	asthma10m4	Num	8	4360		
631	asthma10m5	Num	8	4376		
839	asthma10m1da	Num	8	6040		*child had asthma at 10 months after birth and after 1 DaPT vaccine*
624	asthma10m1sbfa	Num	8	4320		*child had asthma at 10 months after birth and after 1 DPT vaccine but here was confirmed*
840	asthma10m1sbfaDaPT	Num	8	6048		
841	asthma10m2da	Num	8	6056		
626	asthma10m2sbfa	Num	8	4336		
842	asthma10m2sbfaDaPT	Num	8	6064		
843	asthma10m3da	Num	8	6072		
628	asthma10m3sbfa	Num	8	4352		
844	asthma10m3sbfaDaPT	Num	8	6080		
845	asthma10m4da	Num	8	6088		
630	asthma10m4sbfa	Num	8	4368		
846	asthma10m4sbfaDaPT	Num	8	6096		
847	asthma10m5da	Num	8	6104		
632	asthma10m5sbfa	Num	8	4384		
848	asthma10m5sbfaDaPT	Num	8	6112		
849	asthma10m6da	Num	8	6120		
850	asthma10m6sbfaDaPT	Num	8	6128		
226	asthma10months	Num	8	1136		
647	asthma11m1	Num	8	4504		
649	asthma11m2	Num	8	4520		
651	asthma11m3	Num	8	4536		
653	asthma11m4	Num	8	4552		
655	asthma11m5	Num	8	4568		
851	asthma11m1da	Num	8	6136		
648	asthma11m1sbfa	Num	8	4512		
852	asthma11m1sbfaDaPT	Num	8	6144		
853	asthma11m2da	Num	8	6152		
650	asthma11m2sbfa	Num	8	4528		
854	asthma11m2sbfaDaPT	Num	8	6160		
855	asthma11m3da	Num	8	6168		
652	asthma11m3sbfa	Num	8	4544		
856	asthma11m3sbfaDaPT	Num	8	6176		
857	asthma11m4da	Num	8	6184		

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#	Variable	Type	Len	Pos	Format	Label
654	asthma11m4sbfa	Num	8	4560		
858	asthma11m4sbfaDaPT	Num	8	6192		
859	asthma11m5da	Num	8	6200		
656	asthma11m5sbfa	Num	8	4576		
860	asthma11m5sbfaDaPT	Num	8	6208		
861	asthma11m6da	Num	8	6216		
862	asthma11m6sbfaDaPT	Num	8	6224		
227	asthma11months	Num	8	1144		
657	asthma12m1	Num	8	4584		
659	asthma12m2	Num	8	4600		
661	asthma12m3	Num	8	4616		
663	asthma12m4	Num	8	4632		
665	asthma12m5	Num	8	4648		
863	asthma12m1da	Num	8	6232		
658	asthma12m1sbfa	Num	8	4592		
864	asthma12m1sbfaDaPT	Num	8	6240		
865	asthma12m2da	Num	8	6248		
660	asthma12m2sbfa	Num	8	4608		
866	asthma12m2sbfaDaPT	Num	8	6256		
867	asthma12m3da	Num	8	6264		
662	asthma12m3sbfa	Num	8	4624		
868	asthma12m3sbfaDaPT	Num	8	6272		
869	asthma12m4da	Num	8	6280		
664	asthma12m4sbfa	Num	8	4640		
870	asthma12m4sbfaDaPT	Num	8	6288		
871	asthma12m5da	Num	8	6296		
666	asthma12m5sbfa	Num	8	4656		
872	asthma12m5sbfaDaPT	Num	8	6304		
873	asthma12m6da	Num	8	6312		
874	asthma12m6sbfaDaPT	Num	8	6320		
228	asthma12months	Num	8	1152		
229	asthma13months	Num	8	1160		
230	asthma14months	Num	8	1168		
231	asthma15months	Num	8	1176		
232	asthma16months	Num	8	1184		
233	asthma17months	Num	8	1192		
667	asthma18m1	Num	8	4664		
669	asthma18m2	Num	8	4680		
671	asthma18m3	Num	8	4696		
673	asthma18m4	Num	8	4712		
675	asthma18m5	Num	8	4728		
875	asthma18m1da	Num	8	6328		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
668	asthma18m1sbfa	Num	8	4672		
876	asthma18m1sbfaDaPT	Num	8	6336		
877	asthma18m2da	Num	8	6344		
670	asthma18m2sbfa	Num	8	4688		
878	asthma18m2sbfaDaPT	Num	8	6352		
879	asthma18m3da	Num	8	6360		
672	asthma18m3sbfa	Num	8	4704		
880	asthma18m3sbfaDaPT	Num	8	6368		
881	asthma18m4da	Num	8	6376		
674	asthma18m4sbfa	Num	8	4720		
882	asthma18m4sbfaDaPT	Num	8	6384		
883	asthma18m5da	Num	8	6392		
676	asthma18m5sbfa	Num	8	4736		
884	asthma18m5sbfaDaPT	Num	8	6400		
885	asthma18m6da	Num	8	6408		
886	asthma18m6sbfaDaPT	Num	8	6416		
234	asthma18months	Num	8	1200		
235	asthma19months	Num	8	1208		
217	asthma1months	Num	8	1064		*Asthma diagnosed 1 month after birth*
236	asthma20months	Num	8	1216		*Asthma diagnosed 20 months after birth*
237	asthma21months	Num	8	1224		
238	asthma22months	Num	8	1232		
239	asthma23months	Num	8	1240		
677	asthma24m1	Num	8	4744		
679	asthma24m2	Num	8	4760		
681	asthma24m3	Num	8	4776		
683	asthma24m4	Num	8	4792		
685	asthma24m5	Num	8	4808		
687	asthma24m6	Num	8	4824		
887	asthma24m1da	Num	8	6424		
678	asthma24m1sbfa	Num	8	4752		
888	asthma24m1sbfaDaPT	Num	8	6432		
889	asthma24m2da	Num	8	6440		
680	asthma24m2sbfa	Num	8	4768		
890	asthma24m2sbfaDaPT	Num	8	6448		
891	asthma24m3da	Num	8	6456		
682	asthma24m3sbfa	Num	8	4784		
892	asthma24m3sbfaDaPT	Num	8	6464		
893	asthma24m4da	Num	8	6472		
684	asthma24m4sbfa	Num	8	4800		
894	asthma24m4sbfaDaPT	Num	8	6480		
895	asthma24m5da	Num	8	6488		

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#	Variable	Type	Len	Pos	Format	Label
686	asthma24m5sbfa	Num	8	4816		
896	asthma24m5sbfaDaPT	Num	8	6496		
897	asthma24m6da	Num	8	6504		
688	asthma24m6sbfa	Num	8	4832		
898	asthma24m6sbfaDaPT	Num	8	6512		
240	asthma24months	Num	8	1248		
241	asthma25months	Num	8	1256		
242	asthma26months	Num	8	1264		
243	asthma27months	Num	8	1272		
244	asthma28months	Num	8	1280		
245	asthma29months	Num	8	1288		
569	asthma2m1	Num	8	3880		
571	asthma2m2	Num	8	3896		
751	asthma2m1da	Num	8	5336		
570	asthma2m1sbfa	Num	8	3888		
752	asthma2m1sbfaDaPT	Num	8	5344		
753	asthma2m2da	Num	8	5352		
572	asthma2m2sbfa	Num	8	3904		
754	asthma2m2sbfaDaPT	Num	8	5360		
218	asthma2months	Num	8	1072		
246	asthma30months	Num	8	1296		
247	asthma31months	Num	8	1304		
248	asthma32months	Num	8	1312		
249	asthma33months	Num	8	1320		
250	asthma34months	Num	8	1328		
251	asthma35months	Num	8	1336		
691	asthma36m1	Num	8	4856		
693	asthma36m2	Num	8	4872		
695	asthma36m3	Num	8	4888		
697	asthma36m4	Num	8	4904		
699	asthma36m5	Num	8	4920		
701	asthma36m6	Num	8	4936		
899	asthma36m1da	Num	8	6520		
692	asthma36m1sbfa	Num	8	4864		
900	asthma36m1sbfaDaPT	Num	8	6528		
901	asthma36m2da	Num	8	6536		
694	asthma36m2sbfa	Num	8	4880		
902	asthma36m2sbfaDaPT	Num	8	6544		
903	asthma36m3da	Num	8	6552		
696	asthma36m3sbfa	Num	8	4896		
904	asthma36m3sbfaDaPT	Num	8	6560		
905	asthma36m4da	Num	8	6568		

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#	Variable	Type	Len	Pos	Format	Label
698	asthma36m4sbfa	Num	8	4912		
906	asthma36m4sbfaDaPT	Num	8	6576		
907	asthma36m5da	Num	8	6584		
700	asthma36m5sbfa	Num	8	4928		
908	asthma36m5sbfaDaPT	Num	8	6592		
909	asthma36m6da	Num	8	6600		
702	asthma36m6sbfa	Num	8	4944		
910	asthma36m6sbfaDaPT	Num	8	6608		
252	asthma36months	Num	8	1344		
253	asthma37months	Num	8	1352		
254	asthma38months	Num	8	1360		
255	asthma39months	Num	8	1368		
573	asthma3m1	Num	8	3912		
575	asthma3m2	Num	8	3928		
755	asthma3m1da	Num	8	5368		
574	asthma3m1sbfa	Num	8	3920		
756	asthma3m1sbfaDaPT	Num	8	5376		
757	asthma3m2da	Num	8	5384		
576	asthma3m2sbfa	Num	8	3936		
758	asthma3m2sbfaDaPT	Num	8	5392		
759	asthma3m3da	Num	8	5400		
760	asthma3m3sbfaDaPT	Num	8	5408		
761	asthma3m4da	Num	8	5416		
762	asthma3m4sbfaDaPT	Num	8	5424		
763	asthma3m5da	Num	8	5432		
764	asthma3m5sbfaDaPT	Num	8	5440		
765	asthma3m6da	Num	8	5448		
766	asthma3m6sbfaDaPT	Num	8	5456		
219	asthma3months	Num	8	1080		
256	asthma40months	Num	8	1376		
257	asthma41months	Num	8	1384		
258	asthma42months	Num	8	1392		
259	asthma43months	Num	8	1400		
260	asthma44months	Num	8	1408		
261	asthma45months	Num	8	1416		
262	asthma46months	Num	8	1424		
263	asthma47months	Num	8	1432		
703	asthma48m1	Num	8	4952		
705	asthma48m2	Num	8	4968		
707	asthma48m3	Num	8	4984		
709	asthma48m4	Num	8	5000		
711	asthma48m5	Num	8	5016		

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#	Variable	Type	Len	Pos	Format	Label
713	asthma48m6	Num	8	5032		
911	asthma48m1da	Num	8	6616		
704	asthma48m1sbfa	Num	8	4960		*At 48 months after birth there was 1 DaPT vaccine before the asthma was diagnosed in that month*
912	asthma48m1sbfaDaPT	Num	8	6624		
913	asthma48m2da	Num	8	6632		
706	asthma48m2sbfa	Num	8	4976		
914	asthma48m2sbfaDaPT	Num	8	6640		
915	asthma48m3da	Num	8	6648		
708	asthma48m3sbfa	Num	8	4992		
916	asthma48m3sbfaDaPT	Num	8	6656		
917	asthma48m4da	Num	8	6664		
710	asthma48m4sbfa	Num	8	5008		
918	asthma48m4sbfaDaPT	Num	8	6672		
919	asthma48m5da	Num	8	6680		
712	asthma48m5sbfa	Num	8	5024		
920	asthma48m5sbfaDaPT	Num	8	6688		
921	asthma48m6da	Num	8	6696		
714	asthma48m6sbfa	Num	8	5040		
922	asthma48m6sbfaDaPT	Num	8	6704		
264	asthma48months	Num	8	1440		
265	asthma49months	Num	8	1448		
577	asthma4m1	Num	8	3944		
579	asthma4m2	Num	8	3960		
581	asthma4m3	Num	8	3976		
767	asthma4m1da	Num	8	5464		
578	asthma4m1sbfa	Num	8	3952		
768	asthma4m1sbfaDaPT	Num	8	5472		
769	asthma4m2da	Num	8	5480		
580	asthma4m2sbfa	Num	8	3968		
770	asthma4m2sbfaDaPT	Num	8	5488		
771	asthma4m3da	Num	8	5496		
582	asthma4m3sbfa	Num	8	3984		
772	asthma4m3sbfaDaPT	Num	8	5504		
773	asthma4m4da	Num	8	5512		
774	asthma4m4sbfaDaPT	Num	8	5520		
775	asthma4m5da	Num	8	5528		
776	asthma4m5sbfaDaPT	Num	8	5536		
777	asthma4m6da	Num	8	5544		
778	asthma4m6sbfaDaPT	Num	8	5552		
220	asthma4months	Num	8	1088		
266	asthma50months	Num	8	1456		
267	asthma51months	Num	8	1464		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
268	asthma52months	Num	8	1472		
269	asthma53months	Num	8	1480		
270	asthma54months	Num	8	1488		
271	asthma55months	Num	8	1496		
272	asthma56months	Num	8	1504		
273	asthma57months	Num	8	1512		
274	asthma58months	Num	8	1520		
275	asthma59months	Num	8	1528		
583	asthma5m1	Num	8	3992		
585	asthma5m2	Num	8	4008		
587	asthma5m3	Num	8	4024		
779	asthma5m1da	Num	8	5560		
584	asthma5m1sbfa	Num	8	4000		
780	asthma5m1sbfaDaPT	Num	8	5568		
781	asthma5m2da	Num	8	5576		
586	asthma5m2sbfa	Num	8	4016		
782	asthma5m2sbfaDaPT	Num	8	5584		
783	asthma5m3da	Num	8	5592		
588	asthma5m3sbfa	Num	8	4032		
784	asthma5m3sbfaDaPT	Num	8	5600		
785	asthma5m4da	Num	8	5608		
786	asthma5m4sbfaDaPT	Num	8	5616		
787	asthma5m5da	Num	8	5624		
788	asthma5m5sbfaDaPT	Num	8	5632		
789	asthma5m6da	Num	8	5640		
790	asthma5m6sbfaDaPT	Num	8	5648		
221	asthma5months	Num	8	1096		
715	asthma60m1	Num	8	5048		
717	asthma60m2	Num	8	5064		
719	asthma60m3	Num	8	5080		
721	asthma60m4	Num	8	5096		
723	asthma60m5	Num	8	5112		
725	asthma60m6	Num	8	5128		
923	asthma60m1da	Num	8	6712		
716	asthma60m1sbfa	Num	8	5056		
924	asthma60m1sbfaDaPT	Num	8	6720		
925	asthma60m2da	Num	8	6728		
718	asthma60m2sbfa	Num	8	5072		
926	asthma60m2sbfaDaPT	Num	8	6736		
927	asthma60m3da	Num	8	6744		
720	asthma60m3sbfa	Num	8	5088		
928	asthma60m3sbfaDaPT	Num	8	6752		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
929	asthma60m4da	Num	8	6760		
722	asthma60m4sbfa	Num	8	5104		
930	asthma60m4sbfaDaPT	Num	8	6768		
931	asthma60m5da	Num	8	6776		
724	asthma60m5sbfa	Num	8	5120		
932	asthma60m5sbfaDaPT	Num	8	6784		
933	asthma60m6da	Num	8	6792		
726	asthma60m6sbfa	Num	8	5136		
934	asthma60m6sbfaDaPT	Num	8	6800		
276	asthma60months	Num	8	1536		
277	asthma61months	Num	8	1544		
278	asthma62months	Num	8	1552		
279	asthma63months	Num	8	1560		
280	asthma64months	Num	8	1568		
324	asthma65months	Num	8	1920		
281	asthma66months	Num	8	1576		
282	asthma67months	Num	8	1584		
283	asthma68months	Num	8	1592		
284	asthma69months	Num	8	1600		
589	asthma6m1	Num	8	4040		
591	asthma6m2	Num	8	4056		
593	asthma6m3	Num	8	4072		
595	asthma6m4	Num	8	4088		
791	asthma6m1da	Num	8	5656		
590	asthma6m1sbfa	Num	8	4048		
792	asthma6m1sbfaDaPT	Num	8	5664		
793	asthma6m2da	Num	8	5672		
592	asthma6m2sbfa	Num	8	4064		
794	asthma6m2sbfaDaPT	Num	8	5680		
795	asthma6m3da	Num	8	5688		
594	asthma6m3sbfa	Num	8	4080		
796	asthma6m3sbfaDaPT	Num	8	5696		
797	asthma6m4da	Num	8	5704		
596	asthma6m4sbfa	Num	8	4096		
798	asthma6m4sbfaDaPT	Num	8	5712		
799	asthma6m5da	Num	8	5720		
800	asthma6m5sbfaDaPT	Num	8	5728		
801	asthma6m6da	Num	8	5736		
802	asthma6m6sbfaDaPT	Num	8	5744		
222	asthma6months	Num	8	1104		
285	asthma70months	Num	8	1608		
286	asthma71months	Num	8	1616		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
727	asthma72m1	Num	8	5144		
729	asthma72m2	Num	8	5160		
731	asthma72m3	Num	8	5176		
733	asthma72m4	Num	8	5192		
735	asthma72m5	Num	8	5208		
737	asthma72m6	Num	8	5224		
935	asthma72m1da	Num	8	6808		
728	asthma72m1sbfa	Num	8	5152		
936	asthma72m1sbfaDaPT	Num	8	6816		
937	asthma72m2da	Num	8	6824		
730	asthma72m2sbfa	Num	8	5168		
938	asthma72m2sbfaDaPT	Num	8	6832		
939	asthma72m3da	Num	8	6840		
732	asthma72m3sbfa	Num	8	5184		
940	asthma72m3sbfaDaPT	Num	8	6848		
941	asthma72m4da	Num	8	6856		
734	asthma72m4sbfa	Num	8	5200		
942	asthma72m4sbfaDaPT	Num	8	6864		
943	asthma72m5da	Num	8	6872		
736	asthma72m5sbfa	Num	8	5216		
944	asthma72m5sbfaDaPT	Num	8	6880		
945	asthma72m6da	Num	8	6888		
738	asthma72m6sbfa	Num	8	5232		
946	asthma72m6sbfaDaPT	Num	8	6896		
287	asthma72months	Num	8	1624		
288	asthma73months	Num	8	1632		
289	asthma74months	Num	8	1640		
290	asthma75months	Num	8	1648		
291	asthma76months	Num	8	1656		
292	asthma77months	Num	8	1664		
293	asthma78months	Num	8	1672		
294	asthma79months	Num	8	1680		
597	asthma7m1	Num	8	4104		
599	asthma7m2	Num	8	4120		
601	asthma7m3	Num	8	4136		
603	asthma7m4	Num	8	4152		
803	asthma7m1da	Num	8	5752		
598	asthma7m1sbfa	Num	8	4112		
804	asthma7m1sbfaDaPT	Num	8	5760		
805	asthma7m2da	Num	8	5768		
600	asthma7m2sbfa	Num	8	4128		
806	asthma7m2sbfaDaPT	Num	8	5776		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
807	asthma7m3da	Num	8	5784		
602	asthma7m3sbfa	Num	8	4144		
808	asthma7m3sbfaDaPT	Num	8	5792		
809	asthma7m4da	Num	8	5800		
604	asthma7m4sbfa	Num	8	4160		
810	asthma7m4sbfaDaPT	Num	8	5808		
811	asthma7m5da	Num	8	5816		
812	asthma7m5sbfaDaPT	Num	8	5824		
813	asthma7m6da	Num	8	5832		
814	asthma7m6sbfaDaPT	Num	8	5840		
223	asthma7months	Num	8	1112		
295	asthma80months	Num	8	1688		
296	asthma81months	Num	8	1696		
297	asthma82months	Num	8	1704		
298	asthma83months	Num	8	1712		
299	asthma84months	Num	8	1720		
301	asthma85months	Num	8	1736		
303	asthma86months	Num	8	1752		
305	asthma87months	Num	8	1768		
307	asthma88months	Num	8	1784		
309	asthma89months	Num	8	1800		
605	asthma8m1	Num	8	4168		
607	asthma8m2	Num	8	4184		
609	asthma8m3	Num	8	4200		
611	asthma8m4	Num	8	4216		
815	asthma8m1da	Num	8	5848		
606	asthma8m1sbfa	Num	8	4176		
816	asthma8m1sbfaDaPT	Num	8	5856		
817	asthma8m2da	Num	8	5864		
608	asthma8m2sbfa	Num	8	4192		
818	asthma8m2sbfaDaPT	Num	8	5872		
819	asthma8m3da	Num	8	5880		
610	asthma8m3sbfa	Num	8	4208		
820	asthma8m3sbfaDaPT	Num	8	5888		
821	asthma8m4da	Num	8	5896		
612	asthma8m4sbfa	Num	8	4224		
822	asthma8m4sbfaDaPT	Num	8	5904		
823	asthma8m5da	Num	8	5912		
824	asthma8m5sbfaDaPT	Num	8	5920		
825	asthma8m6da	Num	8	5928		
826	asthma8m6sbfaDaPT	Num	8	5936		
224	asthma8months	Num	8	1120		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
739	asthma90m1	Num	8	5240		
741	asthma90m2	Num	8	5256		
743	asthma90m3	Num	8	5272		
745	asthma90m4	Num	8	5288		
747	asthma90m5	Num	8	5304		
749	asthma90m6	Num	8	5320		
947	asthma90m1da	Num	8	6904		
740	asthma90m1sbfa	Num	8	5248		
948	asthma90m1sbfaDaPT	Num	8	6912		
949	asthma90m2da	Num	8	6920		
742	asthma90m2sbfa	Num	8	5264		
950	asthma90m2sbfaDaPT	Num	8	6928		
951	asthma90m3da	Num	8	6936		
744	asthma90m3sbfa	Num	8	5280		
952	asthma90m3sbfaDaPT	Num	8	6944		
953	asthma90m4da	Num	8	6952		
746	asthma90m4sbfa	Num	8	5296		
954	asthma90m4sbfaDaPT	Num	8	6960		
955	asthma90m5da	Num	8	6968		
748	asthma90m5sbfa	Num	8	5312		
956	asthma90m5sbfaDaPT	Num	8	6976		
957	asthma90m6da	Num	8	6984		
750	asthma90m6sbfa	Num	8	5328		
958	asthma90m6sbfaDaPT	Num	8	6992		
311	asthma90months	Num	8	1816		
313	asthma91months	Num	8	1832		
315	asthma92months	Num	8	1848		
317	asthma93months	Num	8	1864		
319	asthma94months	Num	8	1880		
321	asthma95months	Num	8	1896		
323	asthma96months	Num	8	1912		
613	asthma9m1	Num	8	4232		
615	asthma9m2	Num	8	4248		
617	asthma9m3	Num	8	4264		
619	asthma9m4	Num	8	4280		
621	asthma9m5	Num	8	4296		
827	asthma9m1da	Num	8	5944		
614	asthma9m1sbfa	Num	8	4240		
828	asthma9m1sbfaDaPT	Num	8	5952		
829	asthma9m2da	Num	8	5960		
616	asthma9m2sbfa	Num	8	4256		
830	asthma9m2sbfaDaPT	Num	8	5968		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
831	asthma9m3da	Num	8	5976		
618	asthma9m3sbfa	Num	8	4272		
832	asthma9m3sbfaDaPT	Num	8	5984		
833	asthma9m4da	Num	8	5992		
620	asthma9m4sbfa	Num	8	4288		
834	asthma9m4sbfaDaPT	Num	8	6000		
835	asthma9m5da	Num	8	6008		
622	asthma9m5sbfa	Num	8	4304		
836	asthma9m5sbfaDaPT	Num	8	6016		
837	asthma9m6da	Num	8	6024		
838	asthma9m6sbfaDaPT	Num	8	6032		
225	asthma9months	Num	8	1128		
98	asthmabfimmun	Num	8	112		*Asthma before any imunizations*
314	aug2003	Num	8	1840		
77	birthsas	Num	8	24		*new born sas birthdate*
207	bmApr1995	Num	8	984		*Birth Month April 1995*
211	bmAug1995	Num	8	1016		
215	bmDec1995	Num	8	1048		
205	bmFeb1995	Num	8	968		
204	bmJan1995	Num	8	960		
210	bmJul1995	Num	8	1008		
209	bmJun1995	Num	8	1000		
206	bmMar1995	Num	8	976		
208	bmMay1995	Num	8	992		
214	bmNov1995	Num	8	1040		
213	bmOct1995	Num	8	1032		
212	bmSep1995	Num	8	1024		
216	bmYear1995	Num	8	1056		
90	cat	Char	4	8341		*Category of asthma diagnosis (diagnosed by hospital / Md claim / Rx claim*
73	chquint	Char	2	8306		*Child Health Income Quintile (pc)*
74	class	Char	2	8308		*urban(U)/rural(R)/not ranked(N) flag*
6	cntb730	Num	3	8356		*BCG immunization count over 2 yrs*
7	cntd365	Num	3	8359		*DPT immunization count over 1 yr*
8	cntd730	Num	3	8362		*DPT immunization count over 2 yrs*
9	cnth365	Num	3	8365		*HiB immunization count over 1 yr*
10	cnth730	Num	3	8368		*HiB immunization count over 2 yrs*
11	cntm730	Num	3	8371		*MMR immunization count over 2 yrs*
12	cnto365	Num	3	8374		*Polio immunization count over 1 yr*
13	cnto730	Num	3	8377		*Polio immunization count over 2 yrs*
14	compb730	Num	3	8380		*BCG 2yr imm schedule complete - yes(1)/no(0)*
15	compd365	Num	3	8383		*DPT 1yr imm schedule complete - yes(1)/no(0)*
16	compd730	Num	3	8386		*DPT 2yr imm schedule complete - yes(1)/no(0)*

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
17	comph365	Num	3	8389		*HiB 1yr imm schedule complete - yes(1)/no(0)*
18	comph730	Num	3	8392		*HiB 2yr imm schedule complete - yes(1)/no(0)*
19	compm730	Num	3	8395		*MMR 2yr imm schedule complete - yes(1)/no(0)*
20	compo365	Num	3	8398		*Polio 1yr imm schedule complete - yes(1)/no(0)*
21	compo730	Num	3	8401		*Polio 2yr imm schedule complete - yes(1)/no(0)*
78	consults	Num	8	32		*# of hosp or physician visits from birth to age 7*
32	dateim01	Char	8	8064		1st immunization date
33	dateim02	Char	8	8072		2nd immunization date
34	dateim03	Char	8	8080		3rd immunization date
35	dateim04	Char	8	8088		4th immunization date
36	dateim05	Char	8	8096		5th immunization date
37	dateim06	Char	8	8104		6th immunization date
38	dateim07	Char	8	8112		7th immunization date
39	dateim08	Char	8	8120		8th immunization date
40	dateim09	Char	8	8128		9th immunization date
41	dateim10	Char	8	8136		10th immunization date
42	dateim11	Char	8	8144		11th immunization date
43	dateim12	Char	8	8152		12th immunization date
44	dateim13	Char	8	8160		13th immunization date
45	dateim14	Char	8	8168		14th immunization date
46	dateim15	Char	8	8176		15th immunization date
47	dateim16	Char	8	8184		16th immunization date
48	dateim17	Char	8	8192		17th immunization date
49	dateim18	Char	8	8200		18th immunization date
50	dateim19	Char	8	8208		19th immunization date
51	dateim20	Char	8	8216		20th immunization date
94	dateim01a	Num	8	88		
550	dateim02a	Num	8	3728		
551	dateim03a	Num	8	3736		
552	dateim04a	Num	8	3744		
553	dateim05a	Num	8	3752		
554	dateim06a	Num	8	3760		
555	dateim07a	Num	8	3768		
556	dateim08a	Num	8	3776		
557	dateim09a	Num	8	3784		
558	dateim10a	Num	8	3792		
559	dateim11a	Num	8	3800		
560	dateim12a	Num	8	3808		
561	dateim13a	Num	8	3816		
562	dateim14a	Num	8	3824		
563	dateim15a	Num	8	3832		
564	dateim16a	Num	8	3840		

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
565	dateim17a	Num	8	3848		*date of immunization in sas date*
566	dateim18a	Num	8	3856		
567	dateim19a	Num	8	3864		
568	dateim20a	Num	8	3872		
93	dateprvda	Num	8	80		*date provided with Rx*
92	datesepa	Num	8	72		*date left hospital*
322	dec2003	Num	8	1904		
2	earlyasthma	Num	8	0		*Asthma before vaccines*
302	feb2003	Num	8	1744		
81	first_nat	Char	1	8314		
1085	firstdt	Num	8	8008		
549	firstmmr	Num	8	3720		*Kids who had MMR vaccine before DPT vaccines*
326	flag02	Num	8	1936		
99	flag95	Num	8	120		
28	fn_flag	Char	1	8045		Dakota Tipi,The Pas,Fort Alexander flag 1/0
87	hsp_493	Num	8	48		
24	inreg	Num	3	8407		*in registry flag - yes(1)/no(0)*
300	jan2003	Num	8	1728		
312	jul2003	Num	8	1824		
310	jun2003	Num	8	1808		
304	mar2003	Num	8	1760		
308	may2003	Num	8	1792		
31	muncb	Char	3	8061		*new born municipal code at birth*
79	nb_allergy	Char	1	8312		*new born allergy flag - yes(1)/no(0)*
75	nb_asthma	Char	1	8310		*new born asthma flag - yes(1)/no(0)*
23	nbbirth	Char	8	8029		*new born birthdate*
26	nbinit	Char	1	8038		*new born first initial*
25	nbsex	Char	1	8037		*new born gender*
320	nov2003	Num	8	1888		
5	npres_sum	Num	3	8353		*# of antibiotics received within 1 yr after birth*
80	ob_allergy	Char	1	8313		*mothers allergy flag - yes(1)/no(0)*
76	ob_asthma	Char	1	8311		*mothers asthma flag - yes(1)/no(0)*
318	oct2003	Num	8	1872		
1	phin2	Char	9	8020		*new born Provincial health Id/Phin*
27	postal	Char	6	8039		*new born postal code in June 2001*
30	postalb	Char	6	8055		*new born postal code at birth*
72	rha	Char	2	*8304*		*regional health authority*
316	sep2003	Num	8	1856		
95	servdate1	Char	8	8345		
96	servdatea	Num	8	96		
52	tarimm01	Char	4	8224		1st tariff code
53	tarimm02	Char	4	8228		2nd tariff code

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
54	tarimm03	Char	4	8232		3rd tariff code
55	tarimm04	Char	4	8236		4th tariff code
56	tarimm05	Char	4	8240		5th tariff code
57	tarimm06	Char	4	8244		6th tariff code
58	tarimm07	Char	4	8248		7th tariff code
59	tarimm08	Char	4	8252		8th tariff code
60	tarimm09	Char	4	8256		9th tariff code
61	tarimm10	Char	4	8260		10th tariff code
62	tarimm11	Char	4	8264		11th tariff code
63	tarimm12	Char	4	8268		12th tariff code
64	tarimm13	Char	4	8272		13th tariff code
65	tarimm14	Char	4	8276		14th tariff code
66	tarimm15	Char	4	8280		15th tariff code
67	tarimm16	Char	4	8284		16th tariff code
68	tarimm17	Char	4	8288		17th tariff code
69	tarimm18	Char	4	8292		18th tariff code
70	tarimm19	Char	4	8296		19th tariff code
71	tarimm20	Char	4	8300		20th tariff code
22	urbrha	Num	3	8404		*urban(1)/rural(0) flag*
83	year	Char	4	8323		

APPENDIX II
SAS PROGRAMS CREATED FOR THE CHILDHOOD IMMUNIZATIONS & ASTHMA DATA

Note: This Appendix is available upon request

APPENDIX III: ADDITIONAL RESULTS & DISCUSSION

TABLE 1: Income level & Asthma

	Asthma02		
Income	No	Yes	Total
Average - High income	9318	1152	10470
	89.00%	**11.00%**	75.05%
Low income	3063	417	3480
	88.02%	**11.98%**	24.95%
Total	12381	1569	13950

The difference in the Asthma rates between children from low income and average / high income homes is only .98%. A Chi-square test gave a value of 2.5123 with 1 degree of freedom and a probability of 0.113, not significant. An unadjusted Odds Ratio test gave a value of 1.0111 with a 95% C.L. of 0.9971 to 1.0254, also not significant.

TABLE 2: Income level & Wheezing

	Wheezing		
Income	No	Yes	Total
Average - High income	6228	4242	10470
	59.48%	**40.52%**	75.05%
Low income	1824	1656	3480
	52.41%	**47.59%**	24.95%
Total	8052	5898	13950

The difference in the Wheezing rate between the low income children and those from average / high income homes is 7.02%. The Chi-square test gave a value of 53.5039 with 1 degree of freedom and a probability of <.0001, which is significant. The unadjusted Odds Ratio value is 1.1349 with a 95%C.L. of 1.0954 to 1.1758, also significant.

TABLE 3: Gender & Asthma

	Asthma		
Gender	No	Yes	Total
Female	6219	630	6849
	90.80%	**9.20%**	49.10%
Male	6162	939	7101
	86.78%	**13.22%**	50.90%
Total	12381	1569	13950

Among asthma researchers and physicians it is commonly known that male infants and children are more likely to develop asthma than girls. Therefore, it is no surprise that there is a significant difference in Asthma rate between boys and girls. Here the Asthma difference between the males and females is 4.02%. The Chi-square value is 56.5833 with 1 degree of freedom and a probability of <.0001 and the unadjusted Odds Ratio is 1.0464 with a 95%C.L. of 1.0341 to 1.0588, both of which are significant.

TABLE 4: Gender & Wheezing

	Wheezing		
Gender	No	Yes	Total
Female	4308	2541	6849
	62.90%	**37.10%**	49.10%
Male	3744	3357	7101
	52.72%	**47.28%**	50.90%
Total	8052	5898	13950

Once again, the difference between gender and Wheezing is quite significant (10.18%). The Chi-square test gave a value of 147.8964 with 1 degree of freedom and a probability of <.0001, which is significant. The unadjusted Odds Ratio is 1.1930 with a 95%C.L. of 1.1594 to 1.2275, which is also significant.

TABLE 5: Maternal history of asthma & Child Asthma

Maternal	Asthma		
History	No	Yes	Total
No	11777	1409	13186
	89.31%	**10.69%**	94.52%
Yes	604	160	764
	79.06%	**20.94%**	5.48%
Total	12381	1569	13950

The Asthma rate among children with a maternal history of asthma was 20.94% compared to 10.69% (a difference of 10.25%). The Chi-square test gave a value of 76.1077 with 1 degree of freedom and a probability of <.0001, significant. The unadjusted Odds Ratio value is 1.1297 and a 95%C.L. of 1.0887 to 1.1723, also significant. Although the paternal history (mother and father) of asthma was not included in this database there are plans to include this information in future SAGE (Study of Asthma Genes and Environment) research.

TABLE 6: The Maternal history of asthma & Wheezing

Maternal History	Wheezing		
	No	Yes	Total
No	7760	5426	13186
	58.85%	**41.15%**	94.52%
Yes	292	472	764
	38.22%	**61.78%**	5.48%
Total	8052	5898	13950

Once again children who have mothers with a history of asthma were more susceptible to developing Wheezing. Here the difference is 20.63% and the Chi-square test gave a value of 125.9469 with 1 degree of freedom and a probability of <.0001, which is significant. The unadjusted Odds Ratio is 1.5398 with a 95%C.L. of 1.4055 to 1.6869, also significant.

Although only 5.48% or 764 children in the cohort had mothers with a history of asthma, these children had much higher rates for both Asthma and Wheezing. Therefore, children who have a maternal asthma influence seem to have a higher risk of developing asthma. However, only a relatively small number of children in this cohort had a maternal genetic influence. The majority of children with both Asthma and Wheezing did not have a strong genetic or maternal genetic component. Perhaps if the paternal history had been included in the data set the numbers would be different.

FIGURE 1:

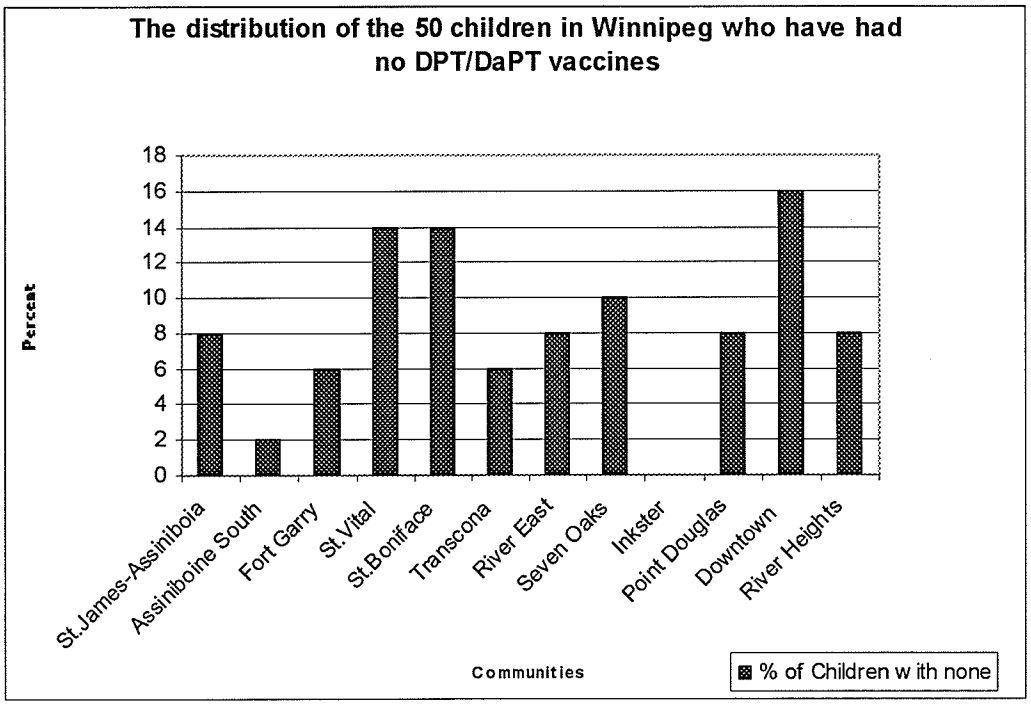
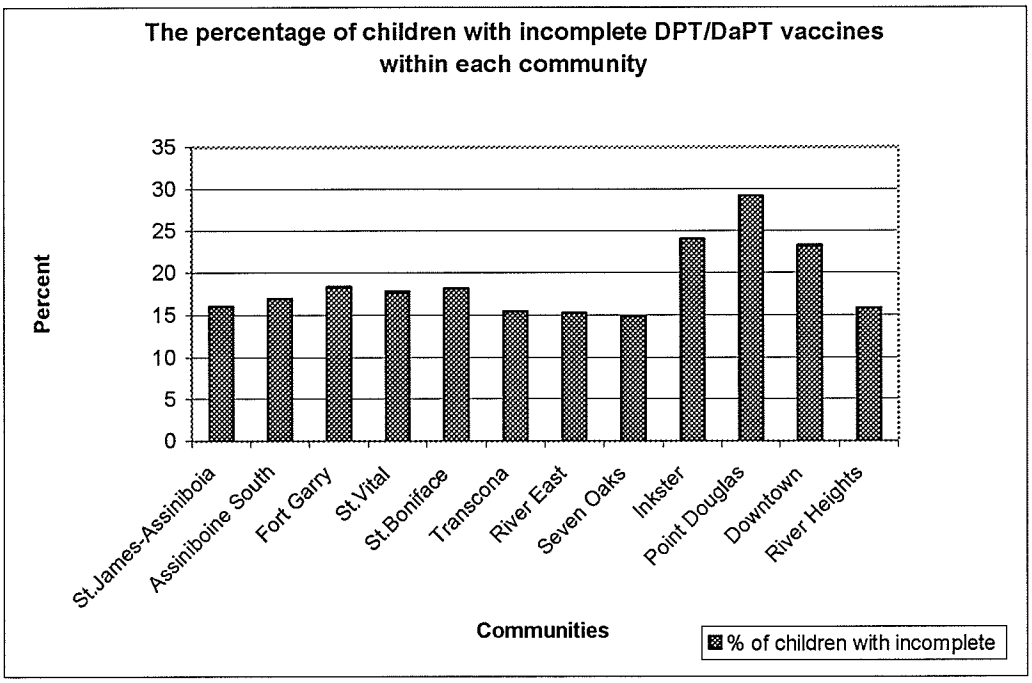


Figure 1 above indicates that a large number of the 50 children who have never had any DPT/DaPT immunizations reside in the Downtown area as well as St. Vital and St. Boniface. Inkster, Point Douglas and Downtown are the three communities which have the highest percentage of children who have "incomplete" DPT/DaPT immunizations, compared to the other Winnipeg communities. FIGURE 3 demonstrates the opposite trend compares to FIGURE 1 – whereby Inkster, Point Douglas and Downtown are the three Winnipeg communities with the lowest percentage of children with "complete" DPT/DaPT immunizations.

FIGURE 2:

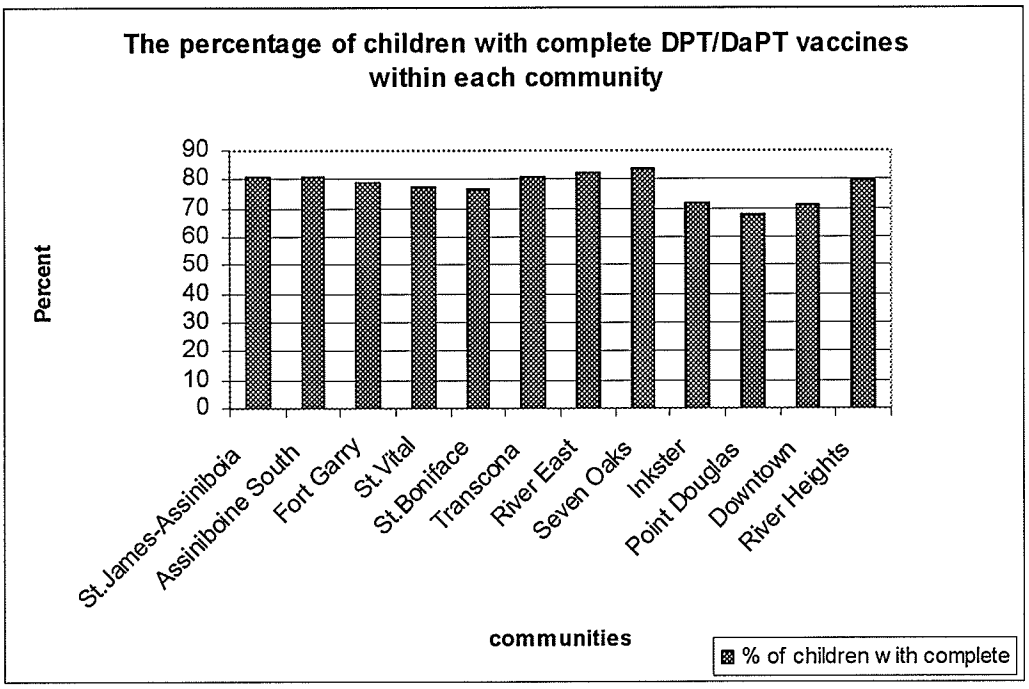


The number or percentage of children within each community who have incomplete DPT/DaPT immunizations peaks with Inkster, Point Douglas, and Downtown. There is also a slight increase in the percentages among Fort Garry, St. Vital and St. Boniface.

Overall a fairly large number of Manitoban children in the 1995 birth cohort were incomplete with their DPT/DaPT vaccines. The average was 19.79% but it ranged from a low of 6.01 in South Westman to a high of 38.85% in Burntwood. For many of the rural communities this may be due to access of care, or a lack of it. This may also be partially due to the fact that aboriginal children living in rural and northern First Nations communities receive their health care / immunizations from nursing stations. However, six of the rural RHA's have a lower rate of incomplete than Winnipeg. This is of interest as children who live in Winnipeg have a greater access to health care than children who reside in rural and northern areas.

Although immunization status varies by Regional Health Authority, there were only 121 children in the cohort who were not immunized at all with DPT or DaPT. This means that less than 1% of the cohort was never immunized with DPT or DaPT.

FIGURE 3:

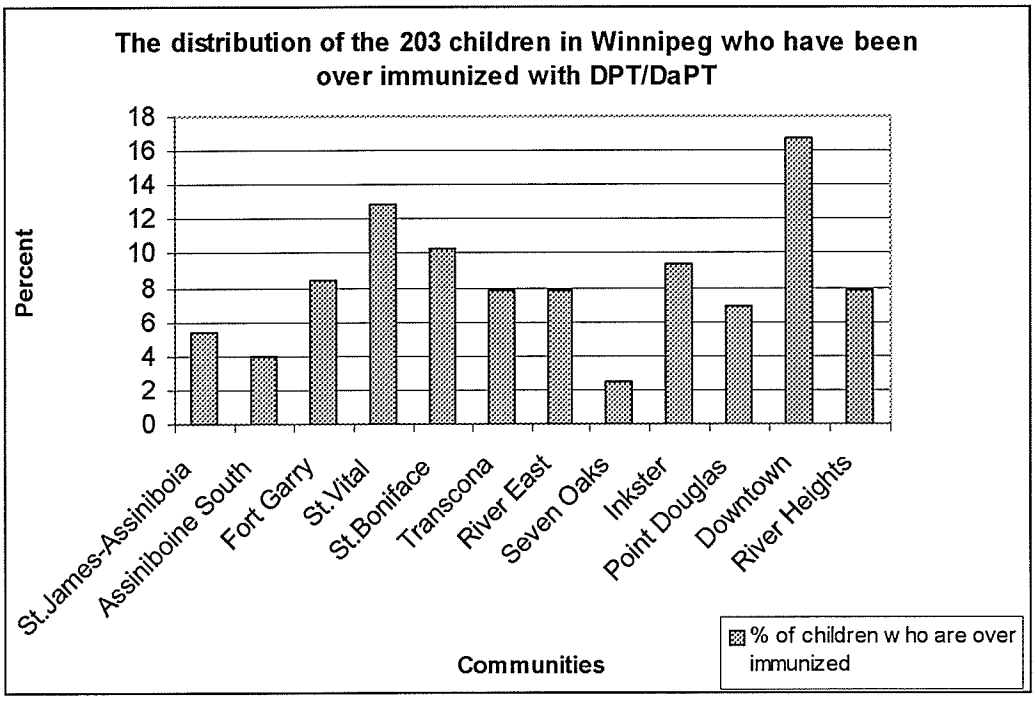


This last FIGURE is almost the reverse of the previous FIGURE.

An average of 76.86% of children in Manitoba completed their 5 DPT/DaPT vaccines, although this ranged from a low of 57.32% in Burntwood to a high of 92.79% in South Westman. This is a huge variation, particularly with Burntwood. The large difference seen with Burntwood may be due to the fact that there are many First Nations communities within Burntwood and the Federal government is responsible for their health care. Thus, the immunization records for these children in the MIMS database would be incomplete.[i]

In 2002 a health survey performed by the Public Health Agency of Canada indicated that by the time children reached 7 years of age (on average) 70.5% were complete for their Diphtheria immunizations (5 doses), 65.3% were complete for their Pertussis immunizations (5 doses), and 65.9% of the children were complete for their Tetanus immunizations (also 5 doses).[ii]

FIGURE 4:



This FIGURE is some what of a surprise as the Downtown area has the highest number of children within Winnipeg who have been over immunized. The Downtown area also had the highest number of children within Winnipeg who were under immunized. It may be that children in this community do not have regular family physicians who keep accurate records of their immunization status. These children may be more likely to visit walk in clinics and thus, have a decreased continuity of care. As a result children living in this community are more likely to either be "under" or "over" immunized. If this is the case a program or improved surveillance measures could be put into place to better monitor these children's adherence to the set immunization schedule.

TABLE 7: The number of children in the "Complete" group by Regional Health Authority

Regional Health Authorites	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	Total
Complete													
No	270	158	102	212	73	69	446	5	98	74	24	1695	**3227**
Yes	1012	336	578	695	281	377	599	23	403	321	309	5787	**10721**
Rate (%)	78.94	68.02	85	76.63	79.38	84.53	57.32	79.31	80.44	81.27	92.79	77.35	**76.86%***
Overall**	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

* the average % of children who belong to the "complete" category

** the average % of children within each RHA who contribute to the overall "complete" category

An average of 76.86% of children completed their 5 DPT/DaPT vaccines, although this ranged from a low of 57.32% in Burntwood to a high of 92.79% in South Westman.

TABLE 8: The number of children in the "Over" group by Regional Health Authority

Regional Health Authorites	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	Total
Over													
No	1265	483	664	880	342	431	1010	29	492	394	330	7250	**13570**
Yes	17	11	16	27	12	15	35	0	9	1	3	232	**378**
Rate (%)	1.33	2.23	2.35	2.98	3.39	3.36	3.35	0	1.8	0.25	0.9	3.1	**2.71%***
Overall**	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

*the average % of children who are belong in the "Over" group

Although the rural areas have less access to health care this has not stopped most of the rural RHA's from over immunizing their children. Winnipeg accounts for the majority of children who were over immunized although Winnipeg did not have the highest rate, Norman did at 3.39%. Looking at the actual number of children who were over-immunized, Burntwood had 35 children.

TABLE 9:The number of children in the "Incomplete" group by Regional Health Authority

gional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
complete													
)	1051	351	601	723	294	393	639	23	414	328	313	6057	**11187**
s	231	143	79	184	60	53	406	6	87	67	20	1425	**2761**
te (%)	18.02	28.95	11.62	20.29	16.95	11.88	38.85	20.69	17.37	16.96	6.01	19.05	**19.79%***
erall**	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

* the average % of children who are belong in the "Incomplete" group

Manitoba had an average of 19.79% of its children in the "incomplete" group but the range was from a low of 6.01 in South Westman to a high of 38.85% in Burntwood.

TABLE 10: The number of children in the "None" group by Regional Health Authority

egional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
one													
o	1257	490	671	901	353	444	1038	29	499	389	332	7424	**13827**
s	25	4	9	6	1	2	7	0	2	6	1	58	**121**
te (%)	1.95	0.81	1.32	0.66	0.28	0.45	0.67	0	0.4	1.52	0.3	0.78	***0.87%**
verall**	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

* The average % of children who are belong in the "None" group.

Relative to the size of the birth cohort very few children did not receive any DPT or DaPT vaccines.

TABLE 11: The number of Medical Consults & children in the "Complete" group

	Medical Consults (#)					
Complete	**0 - 35**	**36 - 49**	**50 to 66**	**67 to 151**	**152 to 459**	**Total**
No	1079	729	637	743	39	3227
Yes	2494	2906	2622	2605	96	10723
Rate	69.8	79.94	80.45	77.81	71.11	*76.87
Overall rate	25.61	26.06	23.36	24	0.97	100

* The average % of children who were in the "Complete" group.

Also, the Overall rate is each column's or group's contribution (%) to the overall population of the cohort.

TABLE 12: The number of Medical Consults & children in the "Over" group

	Medical Consults (#)					
Complete	0 - 35	36 - 49	50 to 66	67 to 151	152 to 459	Total
No	3500	3548	3169	3230	125	13572
Yes	73	87	90	118	10	378
Rate (%)	2.04	2.39	2.76	3.52	7.41	*2.71%
Overall rate	25.61	26.06	23.36	24	0.97	100%

* The average of children who were in the "Over" group.

TABLE 13: The number of Medical Consults & children in the "Incomplete" group

	Medical Consults (#)					
Incomplete	0 - 35	36 - 49	50 to 66	67 to 151	152 to 459	Total
No	2624	3009	2719	2730	107	11189
Yes	949	626	540	618	28	2761
Rate (%)	26.56	17.22	16.57	18.46	20.74	*19.79%
Overall rate	25.61	26.06	23.36	24	0.97	100%

* The average of children who were in the "Incomplete" group.

TABLE 14: The number of Medical Consults & children in the "None" group

	Medical Consults (#)					
None	0 - 35	36 - 49	50 to 66	67 to 151	152 to 459	Total
No	3509	3611	3245	3330	134	13829
Yes	64	24	14	18	1	121
Rate (%)	1.79	0.66	0.43	0.54	0.74	*0.87%
Overall rate	25.61	26.06	23.36	24	0.97	100%

*The average of children who were in the "None" group.

The TABLEs above indicate that the children who have completed their DPT/DaPT immunizations have a "medical consult distribution" where the peak or the most children fall into the (36 to 49 medical consults) group. As this group contains "48" – the median number of medical consults for the cohort this group was considered to be the norm by which to compare the other groups of medical consults.

Tables 11 to 14 indicate that the children who have completed their DPT/DaPT immunizations have a "medical consult distribution" where the majority of the children fall into the group of (36 to 49 medical consults). As this group contains "48" – the median number of medical consults for the cohort this group was considered to be the norm by which to compare the other groups of medical consults. Thus, the children who were in the "Complete" immunization

group were also more likely to have visited a physician(s) the average number of times. Only 23.36% of the children in the "Complete" group were below the norm for the number of medical consults in the first 7 years of life.

The medical consults distribution for the children who were in the "Over" group for DPT/DaPT immunizations peaked at the (67 to 151 medical consults) group. This indicates that children who received more than the required or suggested number of DPT/DaPT vaccines also went to see their physicians much more frequently than children in the other groups. The "Over" group only had 19.31% of their children in the lowest medical consult category of (0 to 35 medical consults).

There were 949 children in the "Incomplete" group who fell into the lowest category of (0 to 35 medical consults) or 34.37% of the children in the "Incomplete" group. This suggests that children who were incomplete for their immunizations visited their physician or had a medical consult less frequently. Finally, there were 121 children who had no DPT or DaPT vaccines and among these children 52.89% or 64 of them also fell within the lowest medical consult category.

TABLE 15: The percentage of children within each Winnipeg community when divided into various groups based on the number of medical consults

		Number of Medical Consults from birth to ~7.5 years					
Communities	# of Children	0 to 35	36 to 49	50 to 66	67 to 151	152 to 459	Total %
St.James-Assiniboia	543	0.92	25.41	30.76	28.36	14.55	100
Assiniboine South	365	1.37	23.29	25.48	34.52	15.34	100
Fort Garry	615	0.98	24.72	27.8	32.2	14.31	100.01
St.Vital	652	0.61	27.91	26.38	29.29	15.8	99.99
St.Boniface	506	1.58	22.53	26.68	33.4	15.81	100
Transcona	434	1.38	25.35	26.73	28.8	17.74	100
River East	969	1.14	28.07	27.04	29.93	13.83	100.01
Seven Oaks	601	1	31.61	29.12	26.29	11.98	100
Inkster	433	0.92	35.8	28.41	22.17	12.7	100
Point Douglas	515	1.75	36.7	24.66	24.47	12.43	100.01
Downtown	713	1.68	33.66	29.17	23.98	11.5	99.99
River Heights	424	1.18	24.76	27.12	29.48	17.45	99.99
Total	6770						

Note: The cells highlighted in blue are the peaks of the medical consults distribution within each community.

A previous question asked "Are children who are incomplete for their immunizations healthier children and do not require medical attention as often as other children?". This question was referring to the high number of children in Fort Garry, St. Vital and St. Boniface who were incomplete in their DPT/DaPT immunizations. From viewing TABLE 34 it is evident that this hypothesis can be answered by saying this is not correct. Children living within these three communities are more likely to be in the second highest medical consult category of (67 to 151 visits). This then poses the question – Have these children suffered from other illnesses or health conditions whereby they have had their immunizations delayed or it was advisable not to administer them at all? Once again this question can not be answered; however, it does raise a potentially valid point.

TABLE 16: The number of children from Low and Average/High Income homes in Winnipeg

Communities	# of Children	INCOME %	
		Low	Average/High
St.James-Assiniboia	543	13.44	86.56
Assiniboine South	365	9.32	90.68
Fort Garry	615	12.85	87.15
St.Vital	652	15.95	84.05
St.Boniface	506	12.06	87.94
Transcona	434	10.6	89.4
River East	969	26.42	73.58
Seven Oaks	601	17.47	82.53
Inkster	433	41.34	58.66
Point Douglas	515	56.7	43.3
Downtown	713	60.03	39.97
River Heights	424	14.86	85.14
	6770		

The variations in socioeconomic status or income were compiled for the various communities within Winnipeg. The following communities had over 25% of its residents classified as Low Income: River East, Inkster, Point Douglas, and Downtown. It is well known among people working in and researching Public Health that individuals from low income families are less likely to have a steady family physicians (continuity of care) and are more likely to have poor health.

TABLE 17: The Asthma rates by the communities within Winnipeg

Communities	# of Children	# of Asthma02	Asthma02 Rate (%)
St.James-Assiniboia	543	63	11.6
Assiniboine South	365	42	11.51
Fort Garry	615	102	16.59
St.Vital	652	68	10.43
St.Boniface	506	63	12.45
Transcona	434	57	13.13
River East	969	129	13.31
Seven Oaks	601	109	18.14
Inkster	433	81	18.71
Point Douglas	515	66	12.82
Downtown	713	132	18.51
River Heights	424	50	11.79
	6770	**962**	**14.21**

Winnipeg had a higher Asthma rate when compared to the overall average of the province – 14.21% compared to 11.25%. There was also considerable variation in the Asthma rates between the various Winnipeg communities. St. Vital had a low at 10.43% to a high of over 18% amongst Seven Oaks, Inkster, and Downtown. It is also interesting that of the four communities who had more than 25% low income families only Inkster and Downtown had unusually high Asthma rates. River East and Point Douglas were above the provincial average and below the overall city average. Does socioeconomic status or income level in Winnipeg play a significant role in the development of Asthma? From the data presented in the last few TABLEs it would seem that socioeconomic status does not strongly influence the development of Asthma.

TABLE 18: The Wheezing rates by the communities within Winnipeg

Communities	# of Children	# of Asthma95	Asthma95 Rate (%)
St.James-Assiniboia	543	243	44.75
Assiniboine South	365	150	41.1
Fort Garry	615	301	48.94
St.Vital	652	239	36.66
St.Boniface	506	197	38.93
Transcona	434	167	38.48
River East	969	465	47.99
Seven Oaks	601	314	52.25
Inkster	433	255	58.89
Point Douglas	515	270	52.43
Downtown	713	413	57.92
River Heights	424	184	43.4
	6770	**3198**	**47.24**

Winnipeg had a higher Wheezing rate when compared to the provincial average (47.24% compared to 42%). As with Asthma there was also a lot of variation in the Wheezing rates between the various Winnipeg communities. St. Vital had a low with 36.66% to a high of 57.92% in the Downtown area. Although children living in the Downtown area did not have a high number of medical consults, they did have high Asthma and Wheezing rates. This may indicate that although these children consult physicians less often – when they do they are more likely to have respiratory difficulties i.e. Asthma and Wheezing.

TABLE 19: The Wheezing rates by Regional Health Authority

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
None													
No	861	281	449	493	215	261	716	16	302	261	219	3976	**8050**
Yes	421	213	231	414	139	185	329	13	199	134	114	3506	**5898**
Rate (%)	32.84	43.12	33.97	45.64	39.27	41.48	31.48	44.83	39.72	33.92	34.23	46.86	**42.99%**
Overall**	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

TABLE 21: The number of DPT immunizations received between 2 to 12 months after birth (1^{st} year of life) & the number of Asthma cases which occurred within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
2	DPT	6					6
3	DPT	29					29
4	DPT	22	6	1			29
5	DPT	13	36				49
6	DPT	5	31	4			40
7	DPT	2	12	34			48
8	DPT	4	6	46	1		57
9	DPT		3	35			38
10	DPT	2	2	34			38
11	DPT	2	4	23	1		30
12	DPT	2	1	29			32
Total		87	101	206	2		396
Total (%)		21.97	25.51	52.02	0.5		100

The number of months that have passed since birth are under the (Months of Age) column. The vaccine of concern is the DPT vaccine. At each month after birth the number of DPT vaccines from 1 to 5 is examined and the number of children who have developed Asthma within the same month after receiving their X DPT vaccine are indicated in the cells within the middle section of the TABLE. For example, at 4 months after birth of the children who were immunized with a DPT vaccine there were 29 children who went on to develop Asthma within the 4^{th} month. There were 22 of these children who received their 1^{st} DPT vaccine, 6 children who received their second vaccine, and 1 child who received his or her 3^{rd} DPT vaccine.

TABLE 22: The number of DPT immunizations received between 13 to 24 months after birth (2nd year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
13	DPT			25			25
14	DPT		3	24	1		28
15	DPT	1	1	27			29
16	DPT	2	2	27			31
17	DPT			24			24
18	DPT	1		17	4		22
19	DPT			11			11
20	DPT		2	5	14	1	22
21	DPT	1	1	4	18		24
22	DPT		1	5	19		25
23	DPT	1		3	9		13
24	DPT			1	15		16
Total		6	10	173	80	1	270
Total (%)		2.22	3.7	64.07	29.63	0.37	100

TABLE 23: The number of DPT immunizations received between 25 to 36 months after birth (3rd year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
25	DPT		1	3	13		17
26	DPT			2	16		18
27	DPT		2	1	16		19
28	DPT			2	12	1	15
29	DPT			1	8		9
30	DPT				14		14
31	DPT			3	11	1	15
32	DPT			1	4	1	6
33	DPT			1	17		18
34	DPT	1	1	2	6		10
35	DPT			1	9	2	12
36	DPT			1	20		21
Total		1	4	18	146	5	174
Total (%)		0.57	2.29	10.34	83.91	2.87	100

TABLE 24: The number of DPT immunizations received between 37 to 48 months after birth (4th year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
37	DPT			2	7		9
38	DPT			1	9	1	11
39	DPT	1		1	18		20
40	DPT			2	8		10
41	DPT			1	10		11
42	DPT			2	12		14
43	DPT	1		2	10		13
44	DPT			1	15	1	17
45	DPT				6		6
46	DPT		1	1	11		13
47	DPT			1	9	1	11
48	DPT			3	10	1	14
Total		2	1	17	125	4	149
Total (%)		1.34	0.67	11.41	83.89	2.68	100

TABLE 25: The number of DPT immunizations received between 49 to 60 months after birth (5th year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
49	DPT			2	5		7
50	DPT			2	6	1	9
51	DPT			2	16		18
52	DPT			2	20		22
53	DPT				10		10
54	DPT					8	8
55	DPT	1		1	5		7
56	DPT		1	1	8		10
57	DPT				11		11
58	DPT				5		5
59	DPT			1	8		9
60	DPT			1	3		4
Total		1	1	12	97	9	120
Total (%)		0.83	0.83	10	80.83	7.5	100

TABLE 26: The number of DPT immunizations received between 61 to 72 months after birth (6th year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
61	DPT				10	2	12
62	DPT				4		4
63	DPT				9		9
64	DPT			1	12		13
65	DPT				6	1	7
66	DPT				3	1	4
67	DPT				7		7
68	DPT			2	9		11
69	DPT				7		7
70	DPT			1	6		7
71	DPT			1	3		4
72	DPT			1	5	1	7
Total				6	81	5	92
Total (%)				6.52	88.04	5.43	100

TABLE 27: The number of DPT immunizations received between 73 to 84 months after birth (7th year of life) & the number of Asthma cases within this time period

Months of Age	Vaccine Type	Number of Vaccines					
		1	2	3	4	5	Total
73	DPT		1	1	11	1	14
74	DPT			3	10		13
75	DPT		1	1	9		11
76	DPT			1	13		14
77	DPT			4	15	2	21
78	DPT			5	11	2	18
79	DPT			1	15		16
80	DPT			1	9		10
81	DPT			4	22	1	27
82	DPT			5	13		18
83	DPT			1	20		21
84	DPT				13		
Total			2	27	161	6	196
Total (%)			1.02	13.78	82.14	3.06	100

TABLE 28: The Grand Total of Asthma cases per number of DPT vaccines

Vaccine Type	Number of Vaccines					Grand Total
	1	2	3	4	5	
DPT	97	119	459	692	30	1397

Note: 89.04% of the 1569 children with Asthma in this cohort are accounted for in the above tables.

There were 97 children who developed Asthma within the same month after they received their first DPT vaccine. There were 119 children who developed Asthma within the same month after receiving their second vaccine. There were 459 out of 1397 children or 32.86% who developed Asthma within the same month after receiving their 3rd DPT vaccine. There were 692 out of 1397 children or 49.53% who developed Asthma within the same month after receiving their 4th DPT vaccine. The tables above present the number of children who received X number of DPT vaccines prior to the onset of Asthma.

TABLE 29: Immunization timing Group 1 – 18 A

Group 1 A						
Onsched & Over			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		50	11	22
1	X		62			
2	X		124			
3	X		186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 2 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		33	9	27.27
1	X		62			
2	X		124			
3	X		186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 3 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		21	1	4.76
1	X		62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 4 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		50	6	12
1	X		62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 5 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		19	0	0
1		X	62			
2	X		124			
3	X		186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 6 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		21	0	0
1		X	62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT5_2790 = 5						

Group 7	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		60	8	13.33
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 8	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		26	7	26.92
1	X		62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 9	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		11	2	18.18
1		X	62			
2	X		124			
3	X		186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 10	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		9	0	0
1	X		62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 11	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		17	2	11.76
1		X	62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 12	A		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		14	3	21.43
1	X		62			
2	X		124			
3		X	186			
4	X		558			
Note: here complete is DPT5_2790 = 5						

Group 13 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		14	0	0
1		X	62			
2		X	124			
3	X		186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 14 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		94	9	9.57
1		X	62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 15 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 16 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT5_2790 = 5						
Group 17 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1		X	62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT5_2790 = 5						
Group 18 A			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		8	1	12.5
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT5_2790 = 5						

TABLE 30: Immunization timing Group 1 – 18 B

Group 1	B					
Onsched & Over			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		955	134	14.03
1	X		62			
2	X		124			
3	X		186			
4	X		558			

Note: here complete is DPT4_2790 = 4

Group 2	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		908	130	14.32
1	X		62			
2	X		124			
3	X		186			
4		X	558			

Note: here complete is DPT4_2790 = 4

Group 3	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		625	88	14.08
1	X		62			
2	X		124			
3		X	186			
4		X	558			

Note: here complete is DPT4_2790 = 4

Group 4	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		1304	169	12.96
1	X		62			
2		X	124			
3		X	186			
4		X	558			

Note: here complete is DPT4_2790 = 4

Group 5	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		347	44	12.68
1		X	62			
2	X		124			
3	X		186			
4	X		558			

Note: here complete is DPT4_2790 = 4

Group 6	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		250	31	12.4
1		X	62			
2		X	124			
3	X		186			
4	X		558			

Note: here complete is DPT4_2790 = 4

Group 7	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		937	109	11.63
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4						
Group 8	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		417	50	11.99
1	X		62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4						
Group 9	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		331	36	10.88
1		X	62			
2	X		124			
3	X		186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 10	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		200	29	14.5
1	X		62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4						
Group 11	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		331	33	9.97
1		X	62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 12	B		DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		362	49	13.54
1	X		62			
2	X		124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4						

Group 13 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		318	40	12.58
1		X	62			
2		X	124			
3	X		186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 14 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		3614	329	9.1
1		X	62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 15 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2	X		124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 16 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1	X		62			
2		X	124			
3		X	186			
4		X	558			
Note: here complete is DPT4_2790 = 4						
Group 17 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		0	0	0
1		X	62			
2		X	124			
3	X		186			
4	X		558			
Note: here complete is DPT4_2790 = 4						
Group 18 B			DAYS	Frequency	Asthma02	Rate02(%)
Vaccines	Onsched	Delayed		173	23	13.29
1		X	62			
2		X	124			
3		X	186			
4	X		558			
Note: here complete is DPT4_2790 = 4						

Note: Group 1 – 18 C is the combination of A and B.

TABLE 31: The Chi-Square test of GroupC # 1 & 14 and Asthma and Wheezing

CHI-SQUARE TESTS				
ASTHMA				Statistically
GROUP C #	DF	Value	Probability	Significant
1	1	10.9752	0.0009	YES
14	1	22.9946	<.0001	YES
WHEEZE				Statistically
GROUP C #	DF	Value	Probability	Significant
1	1	5.4103	0.02	YES
14	1	16.8251	<.0001	YES

TABLE 32: The unadjusted Odds Ratio of Group C # 1 & 14 and Asthma and Wheezing

ODDS RATIO				
ASTHMA		95%CL		Statistically
GROUP C #	Value	Lower	Upper	Significant
1	1.0401	1.0133	1.0676	YES
14	0.9681	0.9561	0.9802	YES
WHEEZE		95%CL		Statistically
GROUP C #	Value	Lower	Upper	Significant
1	1.0694	1.0085	1.134	YES
14	0.9359	0.9073	0.9654	YES

TABLE 33: The Chi-Square Tests of various vaccine groups and Asthma and Wheezing

CHI-SQUARE TESTS				
ASTHMA				Statistically
Vaccine Delayed	DF	Value	Probability	Significant
FIRST	1	13.7824	0.0002	YES
SECOND	1	2.9553	0.0856	NO
THIRD	1	1.0341	0.3092	NO
FOURTH	1	0.0771	0.7813	NO
FIRST & SECOND	1	13.6552	0.0002	YES
Vaccine On Sched.				
FIRST & SECOND	1	20.8248	<.0001	YES
WHEEZE				Statistically
Vaccine Delayed	DF	Value	Probability	Significant
FIRST	1	7.7762	0.0053	YES
SECOND	1	2.4843	0.115	NO
THIRD	1	0.0007	0.9786	NO
FOURTH	1	1.4799	0.2238	NO
FIRST & SECOND	1	9.4722	0.0021	YES
Vaccine On Sched.				
FIRST & SECOND	1	9.9667	0.0016	YES

TABLE 34: The unadjusted Odds Ratios of various vaccine groups and Asthma and Wheezing

ODDS RATIO				
ASTHMA		95%CL		Statistically
Vaccine Delayed	Value	Lower	Upper	Significant
FIRST	0.9778	0.9664	0.9894	YES
SECOND	0.9897	0.978	1.0015	NO
THIRD	0.9938	0.9819	1.0058	NO
FOURTH	0.9983	0.9865	1.0103	NO
FIRST & SECOND	0.9775	0.966	0.9892	YES
Vaccine On Sched.				
FIRST & SECOND	1.0409	1.0213	1.061	YES
WHEEZE		95%CL		Statistically
Vaccine Delayed	Value	Lower	Upper	Significant
FIRST	0.9604	0.9335	0.988	YES
SECOND	0.9773	0.9498	1.0056	NO
THIRD	0.9996	0.9713	1.0288	NO
FOURTH	1.0179	0.9893	1.0474	NO
FIRST & SECOND	0.9556	0.9285	0.9835	YES
Vaccine On Sched.				
FIRST & SECOND	1.0697	1.0245	1.117	YES

The following TABLEs present adjusted odds ratios of vaccine groups which had statistically significant unadjusted odds ratio.

TABLE 35: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	5
	3	1	786	76		
complete	4	1	9869	1139		
	5	1	147	23	10.1	4
	6	1	3	1		
	Total		11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	3
complete	3	2	542	50		
	4	2	127	17	10.1	2
	5	2	4	1		
	Total		779	78	10.01	
	Overall Total		11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated & All the children who have never been vaccinated			2057	230	11.18	1
			114	8	7.02	
	Total		2171	238	10.96	
	Grand Total		13950	1569	11.25	
Note: the 5 groups are used in a logistic regression and group 1 is the reference group						

Note: the 114 children have never been immunized with DPT / DaPT or DT

Once again, the following TABLE is of the same data, only the model has been adjusted for possible confounders.

TABLE 36: The adjusted odds ratios of DPT-type vaccines (Groups 1 to 5) & Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	4	0.62	0.361	1.066
Rx	3	0.808	0.685	0.953
Rx	2	0.95	0.83	1.086
Rx	1 (ref.)			
MD	5	19.415	12.867	29.296
MD	4	8.399	6.73	10.481
MD	3	4.161	3.323	5.211
MD	2	2.238	1.773	2.824
MD	1 (ref.)			
Region	U vs Rural	1.293	1.147	1.457
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.727	1.426	2.092
Income	Low vs H	1.018	0.898	1.155
Dvaccines	5	1.025	0.785	1.338
	4	1.057	0.906	1.232
	3	1.108	0.554	2.217
	2	1.04	0.774	1.398
	1 (ref.)			

The odds ratios of the 4 different comparisons of the 5 different groups indicate that none of the comparisons were significant. Here the 2171children who did not fall into the other categories and those who were never vaccinated were combined and used as the reference group (Group 1). Although the reference group's (n) or size was increased, the OR's of the vaccine combinations remained non-significant.

Group #'s	Wheezing Rates
1	41.53%
2	44.43%
3	37.74%
4	42.4%
5	41.69%

TABLE 37: The adjusted odds ratio of DPT-type vaccines (groups 1 to 6) & Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	4	1.645	1.071	2.527
Rx	3	1.802	1.61	2.017
Rx	2	1.402	1.287	1.526
Rx	1 (ref.)			
MD	5	10.519	6.807	16.256
MD	4	6.087	5.392	6.871
MD	3	3.282	2.924	3.684
MD	2	2.18	1.949	2.437
MD	1 (ref.)			
Region	U vs Rural	1.115	1.032	1.204
Gender	M vs F	1.445	1.343	1.554
Mom Hx	Yes vs No	1.796	1.529	2.109
Income	Low vs H	1.283	1.179	1.397
Dvaccines	5	1.216	1.027	1.439
	4	1.018	0.919	1.128
	3	0.961	0.62	1.487
	2	1.248	1.031	1.51
	1 (ref.)			

Although the Wheezing rates for each group are not present in the TABLE above the adjusted OR TABLE there were significant results. The two outcomes which were significant were the (Group 5 vs. 1) comparison and the (Group 2 vs. 1) comparison. The reference group (Group 1) included the 114 children who were never immunized and the 2057 children who did not fit into one of the assigned categories. The comparison group – Group 5 included children who were incomplete for both of their DPT / DaPT immunizations. The other comparison group – Group 2 included children who were complete for their DPT / DaPT immunizations.

TABLE 38: The vaccine combinations / the number of children with Asthma within each group / the Asthma rate and the group order

	Vaccine combinations		# of children	asthma cases	asthma %	Group order
	DPT	DaPT				
incomplete	1	1	45	3		
	2	1	150	11	9.17	5
	3	1	786	76		
complete	4	1	9869	1139		
	5	1	147	23	11.61	3
	6	1	3	1		
	Total		11000	1253	11.39	
	DPT	DaPT				
incomplete	1	2	26	3		
	2	2	80	7	9.43	1
complete	3	2	542	50		
	4	2	127	17	10.1	4
	5	2	4	1		
	Total		779	78	10.01	
	Overall Total		11779	1331	11.29	
All other children who do not fit into the groups above but who have been vaccinated &			2057	230	11.18	2
All the children who have never been vaccinated			114	8	7.02	
	Total		2171	238	10.96	
	Grand Total		13950	1569	11.25	
Note: the 5 groups are used in a logistic regression and group 1 is the reference group						

TABLE 39: The adjusted odds ratios of DPT-type vaccines (groups 1 to 5) and Asthma

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	4	0.62	0.361	1.066
Rx	3	0.808	0.685	0.953
Rx	2	0.95	0.83	1.086
Rx	1 (ref.)			
MD	5	19.415	12.867	29.296
MD	4	8.399	6.73	10.481
MD	3	4.161	3.323	5.211
MD	2	2.238	1.773	2.824
MD	1 (ref.)			
Region	U vs Rural	1.293	1.147	1.457
Gender	M vs F	1.417	1.269	1.583
Mom Hx	Yes vs No	1.727	1.426	2.092
Income	Low vs H	1.018	0.898	1.155
Dvaccines	5	0.924	0.452	1.89
	4	0.939	0.454	1.941
	3	0.953	0.482	1.887
	2	0.902	0.451	1.805
	1 (ref.)			

For this logistic regression the reference group (Group #1) was the group of children who were incomplete for their immunizations but they had had 2 DaPT vaccinations. For this TABLE the combinations of interest were Groups # 3, 4 and 5. Although the OR's indicate that the children who are not in the comparison group (Group 1) are less likely to have had Asthma, their 95%CL's crossed over 1 making the outcomes non-significant.

TABLE 40: The adjusted odds ratios of DPT-type vaccines (groups 1 to 5) and Wheezing

ODDS RATIO ESTIMATES				
Effect		Point Estimate	95% Confidence Limits	
Rx	4	1.645	1.071	2.527
Rx	3	1.802	1.61	2.017
Rx	2	1.402	1.287	1.526
Rx	1 (ref.)			
MD	5	10.519	6.807	16.256
MD	4	6.087	5.392	6.871
MD	3	3.282	2.924	3.684
MD	2	2.18	1.949	2.437
MD	1 (ref.)			
Region	U vs Rural	1.115	1.032	1.204
Gender	M vs F	1.445	1.343	1.554
Mom Hx	Yes vs No	1.796	1.529	2.109
Income	Low vs H	1.283	1.179	1.397
Dvaccines	5	1.266	0.808	1.982
	4	1.299	0.821	2.054
	3	1.059	0.689	1.628
	2	1.041	0.672	1.612
	1 (ref.)			

Note: Here Group 1 = DPT(1 or 2) and DaPT (2).

The comparison groups for the outcome of Wheezing were similar to those of Asthma, none were significant.

TABLE 41: Regional Health Authorities & MMR immunizations

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
MMR vaccines													
0	43	13	17	16	4	4	33	0	7	12	2	172	**323**
1	131	82	50	111	34	23	224	5	37	37	16	884	**1645**
2 or more	1108	399	613	780	316	419	788	24	446	346	315	6426	**11980**
Total	1282	494	680	907	354	446	1045	29	501	395	333	7482	**13948**

Note: 2 children are missing RHA data

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
MMR vaccine coverage in % per column													
0	3.35	2.63	2.5	1.76	1.13	0.9	3.16	0	1.4	3.04	0.6	2.3	**2.32**
1	10.22	16.6	7.35	12.24	9.6	5.16	21.44	17.24	9.58	9.37	4.8	11.82	**11.79**
2 or more	86.43	80.77	90.15	85.99	89.26	93.94	75.41	82.76	89.02	87.6	94.59	85.88	**85.88**
Total	9.19	3.54	4.88	6.5	2.54	3.2	7.49	0.21	3.59	2.83	2.39	53.64	**100**

Note: here the totals are not the sum of the columns and rows but rather the distribution of the children from the cohort relative to the other RHA's. While the 2nd total is of the distribution of the number of MMR vaccines among the cohort.

The distribution of MMR throughout Manitoba's Regional Health Authorities did vary from a low of 75.41% of children in Burntwood who received 2 or more MMR vaccines to a high of 94.59% of children in South Westman who received 2 or more MMR vaccines by the age of seven.

MMR DEMOGRAPHICS:

The number of children in the 1995 birth cohort who did not receive a MMR vaccine is relatively small, as 97.68% of the population had 1 or more MMR vaccines during the study period. In terms of adherence to the vaccine requirements for MMR this percentage of coverage demonstrates efficacy for herd immunity. There were 11982 children or 85.89% of the cohort who received the required 2 or more MMR vaccine by the age of 7. There was only a slight variation in the number or percent coverage between male and female children for each category of MMR immunization. Overall 97.68% of male children received 1 or more MMR vaccines while 97.69% of female children received 1 or more MMR vaccines.

The distribution of MMR throughout Manitoba's Regional Health Authorities did vary from a low of 75.41% of children in Burntwood who received 2 or more MMR vaccines to a high of 94.59% of children in South Westman who received 2 or more MMR vaccines by the age of seven. Although the overall rate of MMR coverage for the birth cohort was relatively high, when broken down into each RHA discrepancies become more obvious. The pattern of MMR immunization rates across the province is also similar to what is seen with other vaccines such as DPT. The latest MIMS report from Manitoba Health from immunization data obtained in 2003 indicated that (80.7% to 94.7%) of Manitoban children at age 7 were immunized with 1 or more MMR.[iii]

Once again the variation in Immunization rates could be due to access to health care, such that northern rural and remote communities do not have the same access to health care as Winnipegers. It is also possible that the health care data is incomplete for children who live on First Nations reserves – RHA's that have many children living on First Nations reserves would have lower immunization rates because of this. Perhaps the true MMR immunization rate for Burntwood is higher than 75.41%; however, this cannot be confirmed with the data available for this project but this should still be taken into consideration when analyzing the data.

Statistically there is no association between MMR immunization status and Asthma or Wheezing. Referring back to Asthma and Wheezing rates by RHA and comparing those rates to the MMR immunization rates by RHA there is also no obvious association.

TABLE 42: The distribution of the BCG vaccine across Manitoban RHA's

Regional Health Authorites													Total
	Central	North Eastman	South Eastman	Interlake	Norman	Parkland	Burntwood	Churchill	Brandon	Marquette	South Westman	WPG	
BCG vaccines													
0	1228	477	680	828	304	350	956	23	500	305	333	7459	13534
1 or more	54	17	0	79	50	88	89	3	1	10	0	23	414
Total	1282	494	680	907	354	446	1045	29	501	395	333	7482	13948

The three RHA's with the highest number of children who received the BCG vaccine were Interlake, Parkland and Burntwood.

FINAL DISCUSSION of ADDITIONAL DATA

Nearly all of the children in the cohort were immunized with 1 or more DPT or DaPT vaccines (99.13%). Only 121 children out of 13 950 had never received a DPT or DaPT vaccine. Although the actual rates of children who were complete in their DPT/DaPT immunizations did vary by Regional Health Authority and ranged from a low of 57.83% in Burntwood to a high of 92.79% in South Westman. As was discussed earlier, the possible reasons for such a low "Complete" DPT/DaPT immunization rate for Burntwood may be due to the fact that there are many children in Burntwood who live on First Nations reserves. The Federal Government is responsible for their health care and the provincial health database does not keep record of this. It is also probable that the access to health care in rural, remote and northern communities is much more difficult and therefore the true immunization rates in these areas are in fact lower. This may also account for the fact that Asthma rates in rural, remote and northern communities are lower than they are in urban environments – because access to health care is difficult more asthma cases go undiagnosed. It was determined that of all the 114 children from the birth cohort who had not received any DPT / DaPT / DT vaccinations, 59.65% of them had not received any prescriptions for antibiotics in their first year of life. Of the 98.61% of the children who were immunized only 33.24% of them had not received even 1 prescription for antibiotics in their first year of life.

Either the children who were not immunized were healthier children in general or they did not access health care as often.

Not having adequate or reliable access to health care does not explain the number of children living within urban centers who were not immunized. These children obviously live in areas where they and their parents had adequate access to health care facilities (Family Medicine clinics / GP's, walk in clinics, urgent care facility, hospital etc.). The exact reasons why these children were not immunized are unknown. Perhaps their parents or guardians did not keep track of their children's medical appointments or vaccine schedule. Perhaps this was because their children were healthy and they did not frequent medical facilities often and forgot about their immunizations. Perhaps they were negligent or perhaps they did not want their children to be immunized and knowingly prevented them from being vaccinated. Or perhaps there were errors in the record keeping and some or all of these children were immunized but their records fail to show so.

One aspect of equal concern is the fact that there were 378 children who were over-immunized for DPT/DaPT. Although there may have been errors in record keeping, the possibility remains that far too many children received more than the 5 DPT/DaPT immunizations listed on the Canadian Childhood Immunization Schedule.[iv] The likelihood of adverse events/reactions to DPT/DaPT vaccines increases with the number of immunizations received. Although the most common adverse event(s) / reaction(s) listed are swelling and fever, more complex and severe neurological complications can occur.[v] This raises the following questions: if a child does not have a regular pediatrician or family physician and chart, do physicians consult the child's MIMS record prior to administering a vaccine? Does the current system allow for a health professional to easily access this information? Do physicians / nurses bother to do so now and would they in the future? Do physicians understand the potential dangers of over-immunizing a child? Do infant / children patients and their parents / guardians keep tract of each vaccine given to their child? If a child's mother is their main care -giver and

their father took them to the doctor's office – does the father know the child's immunization history as well as the mother (or vice versa)? What type of errors can occur within the healthcare system / MIMS which would account for either a loss of data or a mistake in a child's immunization history? All of these are important questions, which should be answered in the future to allow for an improved quality of care in Manitoba and Canada.

Immunization records for DPT were analyzed to determine if there was a relationship between the number of vaccination received and the time of Asthma diagnosis. It was determined that regardless of whether or not children in the cohort were on schedule, there was a higher likelihood of children to develop Asthma after receiving 3 or 4 DPT vaccines compared to 1 or 2. This is the first time that such results have been mapped in such a manner to observe this pattern.

Another form or combination vaccine that was analyzed was DT (Diphtheria and Tetanus). It was originally thought or hypothesized that the DT vaccine would be associated with a lower incidence of asthma due primarily to the absence of the pertussis portion of the vaccine; however, this did not prove to be the case. In fact the children who had received 1 or more DT vaccine were more likely to have Asthma (Asthma rate of 14.67%). Although it could have been then postulated that DT vaccines increased the likelihood of developing Asthma, further temporal analysis determined that the majority of children who received a DT vaccine did so after they were already diagnosed with Asthma. Of the 409 children who received 1 or more DT vaccine, 60 had Asthma and 41 of the 60 developed Asthma prior to their first DT immunization. Therefore, the reason for using DT as opposed to DPT or DaPT may have been a conscious decision of the children's physicians / nurses in attempt to reduce the possibility of exacerbating the pre-existing asthma condition.

The Measles, Mumps, and Rubella vaccine was another important vaccine in question. The majority of the children in the birth cohort had received 1 or more MMR vaccine (13 627 children or 97.68%). Only 12% of the 13 627 children did not receive the 2 doses recommended by the Canadian Childhood Immunization Schedule. The BCG vaccine was also analyzed, only

the opposite was found. There were 414 children or 2.97% of the cohort who received a BCG vaccine. Although the test hypothesis did present themselves in the findings (children's incidence of Asthma would increase with the number of MMR vaccines) and (children who received a BCG would have a lower incidence of Asthma) these findings were not of a large enough magnitude to hold up to statistical significance.

The majority of children in this cohort were immunized with the number of doses and types of vaccines recommended by Health Canada / Manitoba Health between the years of 1995 to 2002 (the exception being the BCG vaccine). As a result any difference in the incidence of Asthma or Wheezing and the different immunization groups (none, incomplete, complete etc.) would have to have been very large to be statistically significant using a Logistic Regression and adjusted Odds Ratio.

ADDITIONAL REFERENCES

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