Tracing Autism Trends:
Prelude for an Epidemic?

By Julie Herczeg
Mrs. M. Younger
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Table of Contents

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Hypothesis Question

Do Canadian autism diagnostic trends match those of other countries?

Background Information

Susie sat by herself at lunch and was fixated on the clasp on her lunch box. Silently, she opened and closed the clasp incessantly and was equally surprised when the box popped open each time. Susie tended not to notice when her peers ridiculed her for her rocking habits. "You're a cross between a rocking horse and a bird, Susie!" a classmate had said earlier in the day. Susie misinterpreted their nasty comments as jokes. She giggled, and continued to flap her hands. This made her classmates laugh even harder.

Susie is not your typical third-grade student. Susie had been diagnosed with a moderate form of a developmental disorder known as autism, at the age of three. Her parents struggled to track her odd behaviours since her symptoms were so varied. Later, once Susie had been diagnosed, they discovered that their struggle was not uncommon. Autism Spectrum Disorders, often referred to as ASDs, present a wide spectrum behaviours and characteristics, making them extremely difficult to diagnose. No two cases of autism are exactly alike, and range widely in severity. One variant of ASD, Asperger's Syndrome, is associated with having higher than average intelligence, and yet other variants are non-verbal and unable to function properly. Because of this wide range, some autistics have extreme talent and abilities in specified areas like music, physics or software development. Famous autistics, like Glenn Gould, Albert Einstein and Bill Gates, are or were able to contribute positively to our society.

Not everyone who is diagnosed with ASDs is so lucky. Sufferers often experience difficulty in communication, social interaction, sensory impairment and

"abnormal" behavioural tendencies. They may make little or no eye contact, show little or no interest in socializing, appear to be unresponsive to social cues, or appear insensitive to pain. They may experience difficulty with routine changes, rock back and forth or flap their hands, have an obsessive interest in a single object, activity or person, and may have a speech delay. The most severe cases eventually become institutionalized. Autism affects boys four times more frequently than girls, but scientists and researchers are currently unsure why this is. The disorder's causes are largely unknown, although some believe that it is genetically linked.

There is currently no single test to diagnose ASDs. Diagnoses are usually formed through a comparison against a set of standards, which vary from country to country. Treatment is only available for individual symptoms, like speech-language therapy, or interaction workshops. In Canada, a limited amount of additional support is available in public classrooms. Since autism is a developmental disorder, there is no cure. If the time period for development is missed, someone affected by autism will never be able to recover and develop the missing characteristics.

Because ASDs exhibit such a wide variety of symptoms, there are many disorders which overlap with autism. Related disorders include fragile X syndrome, tuberous sclerosis, ADHD, Tourette's Syndrome, and obsessive compulsive disorder. Diagnosing ASDs is complicated by the many related and overlapping disorders.

Children like Susie are becoming increasingly common in today's classrooms. Autism prevalence is rising at a frightening pace, but scientists and researchers are unsure of its causes. Perhaps most importantly for the general public, however, is that the social and societal implications of this increasing prevalence will directly affect us in the near future. In some severe cases, autism sufferers must be institutionalized, or supported in government funded group homes. In many moderate cases, additional support is required in learning and working environments regardless of the age of the person. As well as a huge emotional and financial burden on families, this means an additional strain on the health care system and an increase tax dollars. Average therapy costs $80 000 CDN per

child per year for full support. An increase in the number of autistic people will mean an increase in the amount of tax dollars we are forced to pay.

Definition of Terms:

Autism: "Developmental disability that affects communication and social interaction, adversely affects educational performance, is generally evident before age 3. Children with autism often engage in repetitive activities and stereotyped movements, resist environmental change or change in daily routines, and have unusual responses to sensory experiences."[1]

Autism Spectrum Disorder (ASD): "…an increasingly popular term that refers to a broad definition of autism including the classical form of the disorder as well as closely related disabilities that share many of the core characteristics. ASD includes the following diagnoses and classifications: (1) Pervasive Developmental Disorder—Not Otherwise Specified (PDD-NOS)…; (2) Rett's syndrome…; (3) Asperger syndrome…; (4) Childhood Disintegrative Disorder… Although the classical form of autism can be readily distinguished from other forms of ASD, the terms autism and ASD are often used interchangeably."[2]

Incidence: "the relative frequency of occurrence of something."[3]

Prevalence: "The total number of cases of a disease in a given population at a specific time."[4]

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[1] SchwabLearning.org, *Glossary of Special Education and Legal Terms* (2002). http://pathfinder.minot.com/plaintext/law08.html [28 May 2004].
[2] Dunlap, Glen and Mary-Kay Bunton-Pierce. *Autism and Autism Spectrum Disorder (ASD)* (1999). http://ericec.org/digests/e583.html [28 May 2004]
[3] The American Heritage Dictionary of the English Language, Fourth Edition (2000). http://dictionary.reference.com/search?q=incidence [28 May 2004]
[4] The American Heritage Dictionary of the English Language, Fourth Edition (2000). http://dictionary.reference.com/search?q=prevalence [28 May 2004]

Rate: "a quantity measured with respect to another measured quantity"[5]

Procedure

After several years of experience dealing with autism and exploring its intricacies, I have developed a strong interest in ASDs. Specifically, I am interested in working with those affected by the disorder, and in educating myself about the possible genetic linkages. I am intrigued by the ongoing MMR vaccine and thimerosal preservative debate, and other possible causes. When I realized that autism prevalence was in fact rising, and the opportunity to trace the autism prevalence trends arose, I was excited to investigate these trends. I realized that taking on a current project would make finding statistics difficult, but I was motivated. It was important to me to produce a project of meaning both to the Data Management course and to myself. By taking on a task which sparked my interest, I was able to move towards an important goal.

After developing my hypothesis, I began to search the Internet and Statistics Canada for data. To my surprise, Statistics Canada is currently not collecting data specifically on autism. I was forced to rely on statistics from individual medical studies, mainly published and posted on Internet websites. After many hours of searching, I discovered this lack of government funded statistical studies to be the case for many countries. Since the apparent marked increase in autism prevalence is relatively recent, published data of significance is hard to come by. At the same time, I contacted many smaller Canadian autism societies, who were able to direct me towards meaningful data. I also visited the Geneva Centre for Autism in Toronto and explored their resources.

After dividing the world's countries into similar criteria-based groups, I began to format my data using a combination of Microsoft Excel and Fathom. I created data tables, and graphed my data in a combination of bar graphs, line graphs and histograms. I fitted trendlines to the Excel graphs to visualize the direction of the trends. To estimate

[5] The American Heritage Dictionary of the English Language, Fourth Edition (2000). http://dictionary.reference.com/search?q=rate [28 May 2004].

future trends, I extrapolated the fitted trendlines to a common year between all of my graphs. If outliers occurred, they were removed from the data set, and I re-graphed the data. Where it was meaningless to remove the outliers, I used Fathom to create box and whisker plots to properly visualize the outlying points. When data was presented as autism incidence, I used Excel's formulae to convert the data into autism prevalence. Once I created all of my graphs, I began to analyze my findings. I also used Excel to calculate the coefficient of determination, for both quadratic and linear regression trendlines. Later, I used additional Internet sources to support my findings, and used any anecdotal data for other countries in my conclusions.

Analysis of Findings

The United States of America provided the most ample and detailed data. The graphs below provide a sample of states showing a general increasing trend from the years 1999-2000, 2000-2001 and 2001-2002 (Appendix A).

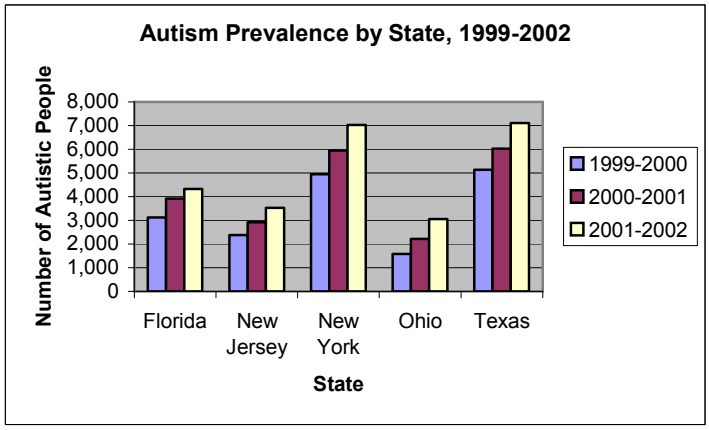

Figure 1.1

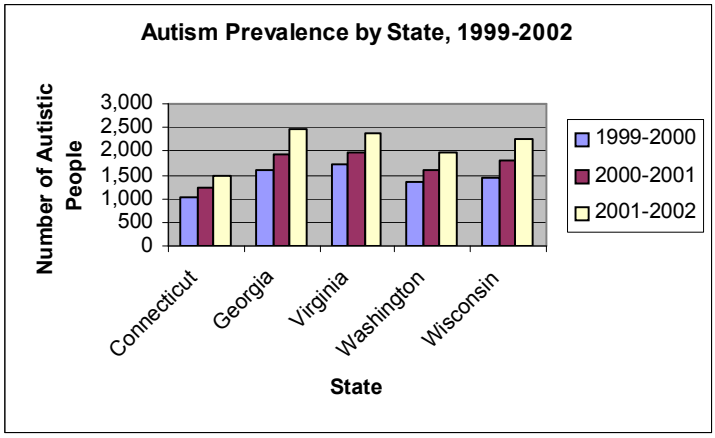

Figure 1.2

While each state demonstrates different prevalence levels, each state still shows a general increasing trend. However, when we look at the United States of America as a whole, it is much more striking to examine the trends of autistic American children (children being defined as age six to age twenty-one) attending American schools (Appendix B).

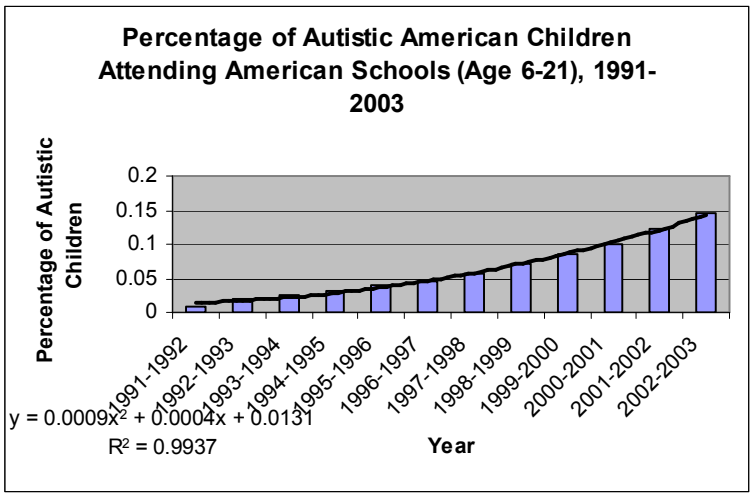

Figure 1.3

Figure 1.3 demonstrates the relative values of autistic American children attending American schools as a percentage of the total American children population attending schools. The increasing trend is cause for concern. Since 1991, when the data was first collected, the percentage of autistic American children has increased from approximately 0.007 percent to 0.146 percent. As a quadratic regression line was fitted to the data, the r^2 value, the coefficient of determination, was 0.9937, demonstrating a very strong correlation. This increase is no accident, and suggests that there is, in fact, a true rise in the amount of autistic children in classrooms in the United States.

At the same time, we must consider all potential hypotheses. Is it possible that prior to 1991, when this data was first collected, autistic children did not attend classes in any type of American school? Perhaps before then, all autistic children were institutionalized or prevented from attending schools. If this is indeed the case, we must consider the possibility of false corollary, since this graph would not represent a true rise in autism cases. This data would then represent an increasing number of accepted autistic children in American schools, as a percentage of the total American children population attending schools.

If autism trends continue to rise at the rate that it is, by 2006-2007, it is likely that the percentage of autistic American children attending American schools as a percentage of the total American children population attending schools will rise to approximately 0.27 percent (see Figure 1.4). This is particularly concerning given the inherent increase in taxation on the general public that will occur due to the rise in the amount of necessary support for the growing autistic population.

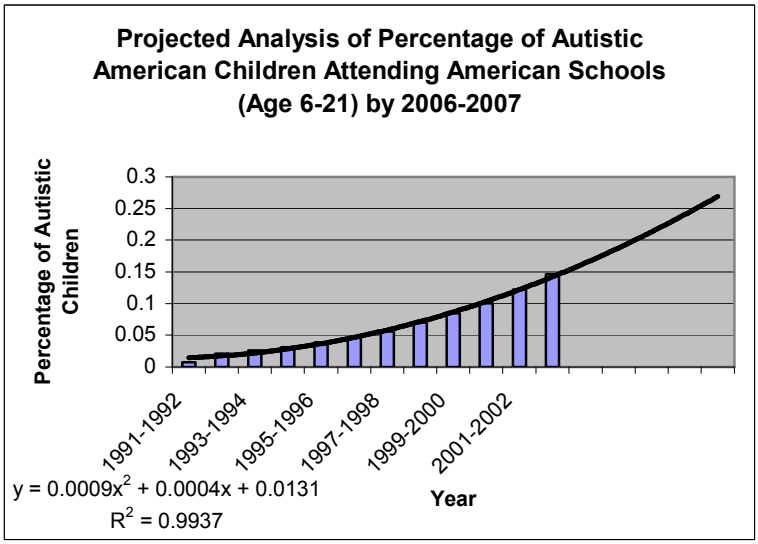

Figure 1.4

Likewise, trends in other countries abroad exhibit similar surges. Western Australia has tracked autism cases in children born in 1980 to 1995 (see Appendix C)

and, once again, demonstrates a clear increase in autism prevalence. Figure 2.1 below reveals this trend.

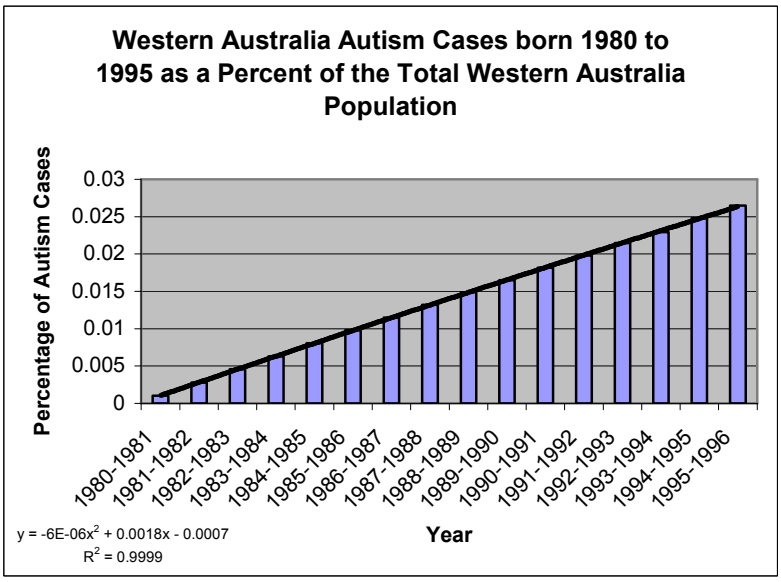

Figure 2.1

With a coefficient of determination of 0.9999, this is a very strong correlation. There has clearly been a surge in autism prevalence in Western Australia over the cited fifteen years. However, since Australia has similar living standards to the United States, an increasing trend is no surprise. If environmental or geographical factors have influenced autism prevalence, the fact that there is a marked increase on another continent, in another hemisphere is significant.

Similarly, Denmark has exhibited a significant increase in autism prevalence from 1970-2000 (see Appendix D).

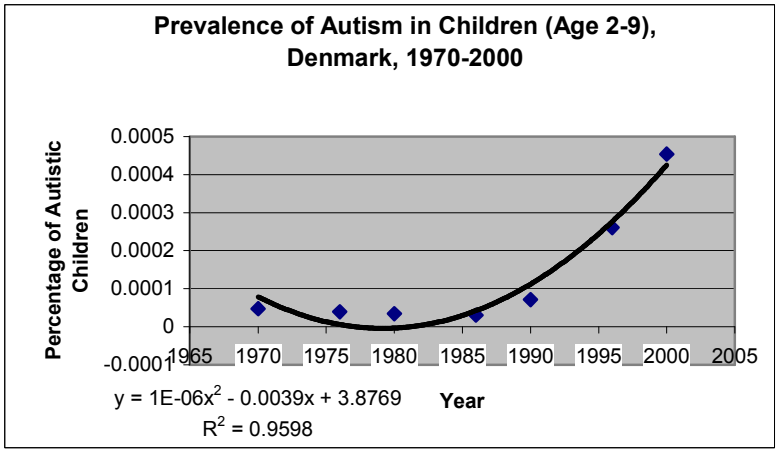

Figure 3.1

Although the coefficient of determination for this graph is not as strong as the past graphs, the r^2 value is still 0.9598, representing very strong correlation. The quadratic regression trendline is slightly misleading since it appears to concave down. In fact, the data is constant until 1986, when it begins its sharp incline.

Anecdotal data from other countries abroad also suggests similar trends. Israeli evidence indicates a sharp increase in autism prevalence, but raw data was not available. "The epidemiological characteristics found in the Haifa area are similar to those reported from non-Israeli communities."[6] A Finnish study suggests that "careful review [reveals] a cumulative incidence of autism in Northern Finland of 12.2/10,000 an alarming increase when compared to the previously reported incidence of 4.75/10,000 in 1991."[7] The Scottish government has examined "the apparent rise in autism in Scotland in the mid/late nineties the Scottish Education service[8]" and suggests that "autism…is now the most common serious childhood condition in Scotland."[9] In Japan, "the prevalence of autism in Japan during the 1980s was 5-16 per 10,000, and 21.1 in 1996.[10]" Discussion implies that the "apparent increase of autism in 1996 was difficult to interpret…[and so] no conclusion has yet been obtained.[11]" As of 2003 in India, "numerous studies have placed the occurrence of autism at a rate of approximately 1 in 500 people…[but] the majority of autistic people in India have not been diagnosed and do not receive the services they need…There is a tremendous lack of awareness and misunderstanding about autism among the medical professionals, who may either misdiagnose or under

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[6] Davidovitch, M., G. Holtzman and E. Tirosh. *Autism in Haifa area—an epidemiological perspective* (2003). http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11303376&dopt=Abstract [23 May 2004].

[7] Yazbak, F. Edward. *Autism: A Recent Serious Rise in Finland* (2001). http://www.garynull.com/Documents/AutismFinnishStudy.htm [23 May 2004].

[8] Welsh, B. *Autism in Scotland* (2004). http://bmj.bmjjournals.com/cgi/eletters/328/7433/226-c#48557 [25 May 2004].

[9] Welsh, B. *Autism in Scotland* (2004). http://bmj.bmjjournals.com/cgi/eletters/328/7433/226-c#48557 [25 May 2004].

[10] Takahashi, Hiroshi, Satoru Arai, Keiko Tanaka-Taya and Nobuhiko Okabe. *Autism Infection/Immunization Episodes in Japan* (2001). http://www.nih.go.jp/JJID/LEC-97.html [22 May 2004].

[11] Takahashi, Hiroshi, Satoru Arai, Keiko Tanaka-Taya and Nobuhiko Okabe. *Autism Infection/Immunization Episodes in Japan* (2001). http://www.nih.go.jp/JJID/LEC-97.html [22 May 2004].

diagnose the condition.[12]" If we look at the anecdotal and statistical data provided, a common increasing trend is present. The inherent ASD increase is prevalent worldwide.

Where, then, does Canada stand amidst these foreign statistics? Reliable Canadian data is difficult to come by, and I was forced to depend upon individual medical studies. "Health Canada says it doesn't have the money to [complete an autism study]. Statistics Canada said it would take 10 years to organize such a survey as part of the census."[13] Independent statistics were only available for the provinces of Quebec and Saskatchewan (see Figures 4.1 and 4.2, respectively, and Appendices E and F).

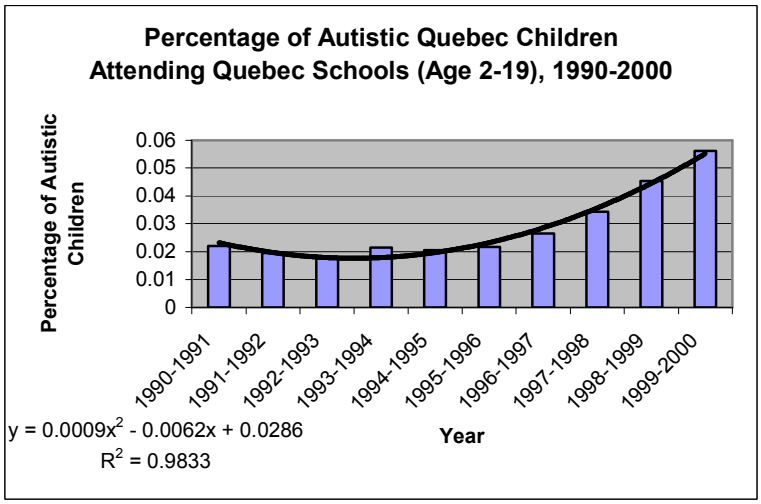

Figure 4.1

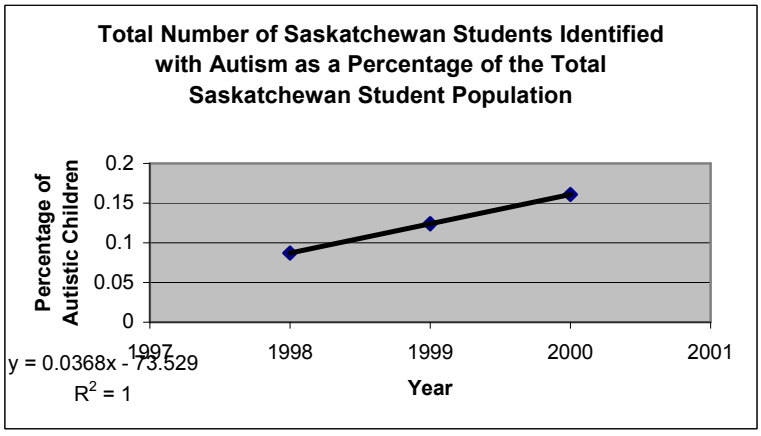

Figure 4.2

[12] Autism India. *Autism in India* (2003). http://autism-india.org/afa_autisminindia.htm [23 May 2004].
[13] Ruttan, Susan. *Autism on the increase but no one knows the exact numbers* (2004). http://www.autismsocietycanada.ca/en/NEWSITEMS/Feb9_2004.html [22 May 2004].

Figure 4.1 has a snugly fit quadratic regression trendline which traces the percentage of autistic Quebecois children attending schools in Quebec. It has a coefficient of determination of 0.9833, which can be classified as being very strong. While Figure 4.2 also demonstrates a very strong correlation, (r^2 of 1), the sample set is far too small to make any valid conclusions. No data was available prior to 1998 for Saskatchewan, but this simply means that there was no interest in obtaining autism statistics at that time.

If we extrapolate these trendlines, we can see that the percentage of autistic Quebecois children attending schools in Quebec will rise to approximately 0.18 percent (Figure 4.3), *ceteris paribus*. This is lower than the estimated percentage in the United States (0.27 percent), but is nonetheless a significant increase. Extrapolating the Saskatchewan data would only produce a meaningless estimation of a future autism trend due to the small sample set.

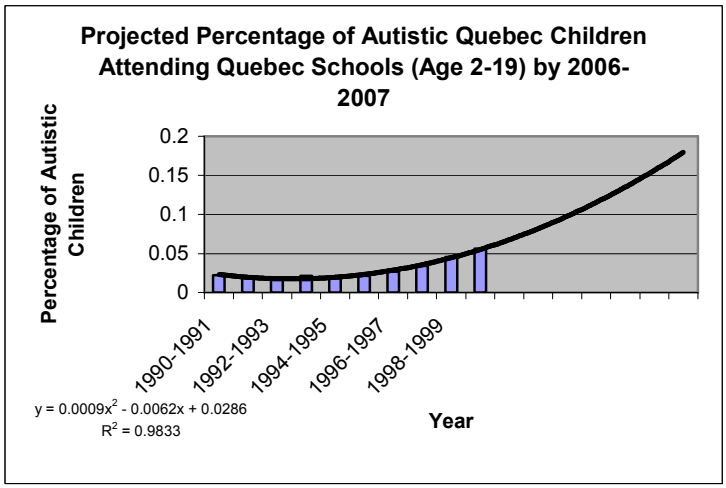

Figure 4.3

Interestingly, Pervasive Developmental Disorder (PDD), an autism-like disorder found on the autism spectrum, appears to be constant across Canada (see Appendix G). Figure 5.1 below demonstrates this trend in 2001.

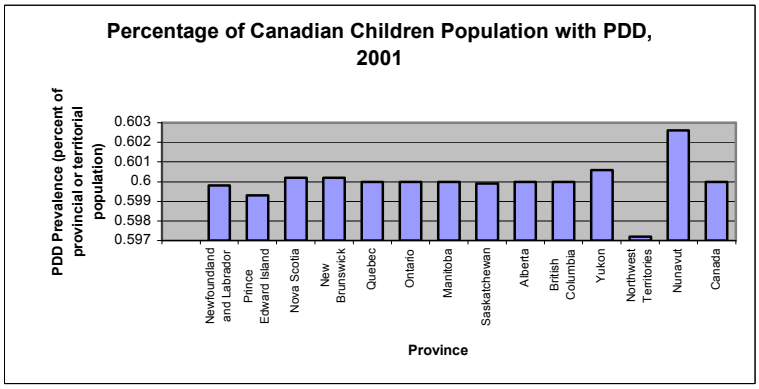

Figure 5.1

The scale, in this case, is misleading, as it exaggerates the differences between provinces and territories. The difference between the percentage of children with PDD in the Northwest Territories and Nunavut is only 0.0053 percent, but it appears to be much larger. Figure 5.2 below allows us to see this trend clearly.

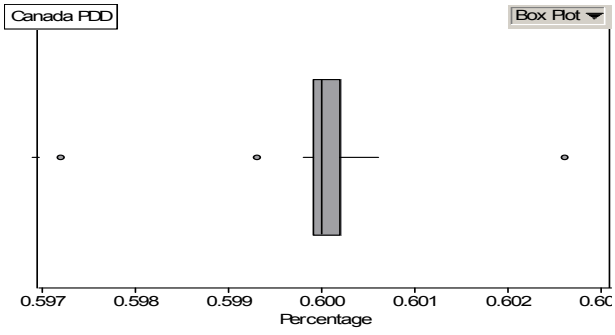

Figure 5.2

Additionally, we must exercise caution in determining the causes for these outliers. If autism (and, by extension, autism spectrum disorders) is caused by an environmental factor, the fact that the Northwest Territories and Nunavut have significantly different percentages of PDD is concerning. Canadian PDD trends appear to be constant across the country, disproving the suggestion that autism trends are localised. However, because the data set only tracks one year across Canada, no conclusions can be made.

How can we determine if Canadian autism diagnostic trends match those of other countries? We know, based on previous analysis, that autism trends worldwide are increasing, but how can we measure this? The underlying query from the hypothesis question asks whether Canadian autism diagnostic rates match those of other countries. In order to adequately assess the diagnostic rates, we must look at autism prevalence in

several nations. By adding a linear trendline, we will be able to measure the slope of the line, and can therefore compare the rate of diagnosis between countries.

The set of graphs below includes linear trendlines for each country.

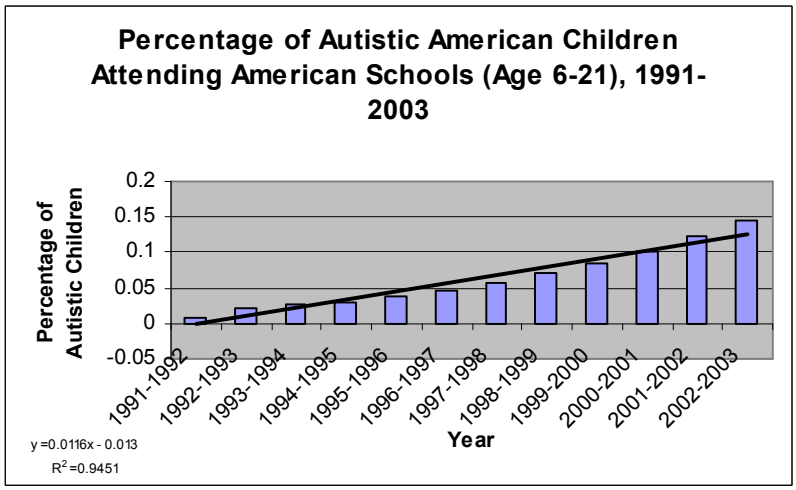

Figure 6.1

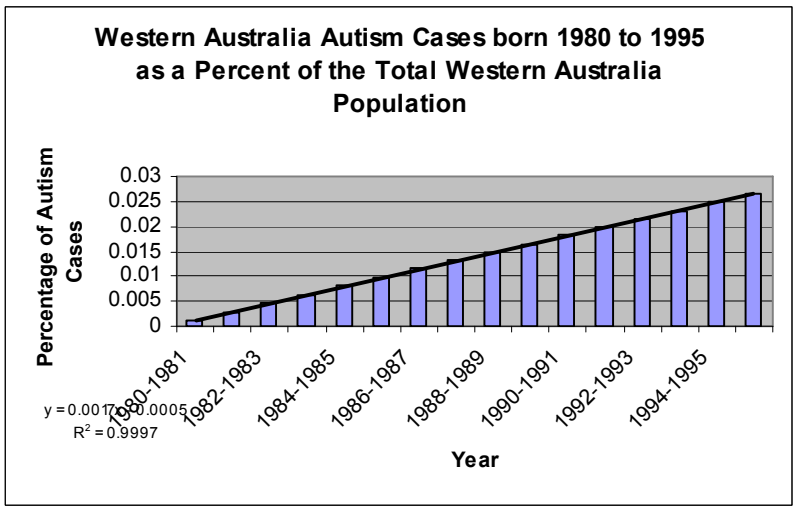

Figure 6.2

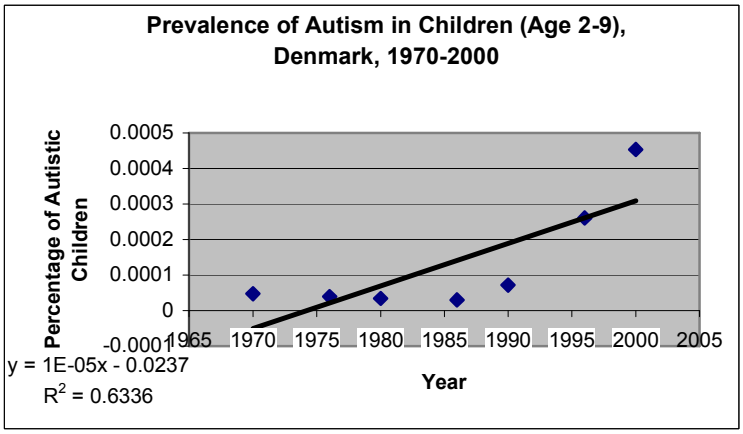

Figure 6.3

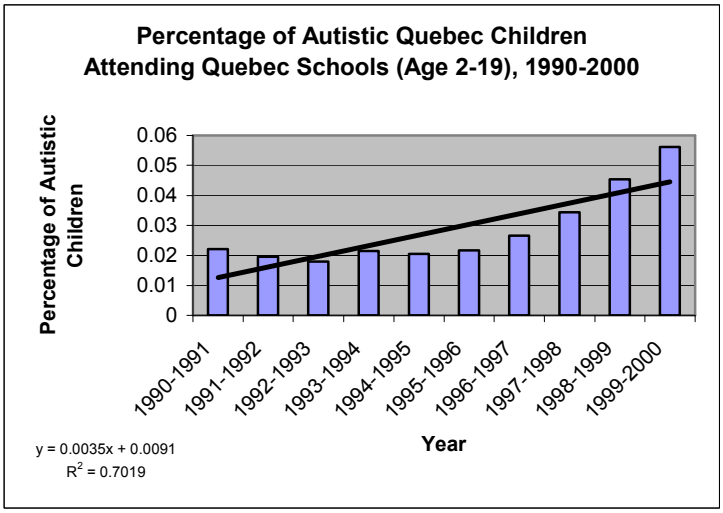

Figure 6.4

In each case, the coefficient of determination is not as strong as it would have been with a different type of regress ional analysis. However, to measure the diagnostic rate of each country, a linear regression is implied. As stated earlier, to compare the diagnostic rates, we must look at the slope of each country's trendline.

Country	**Coefficient of Determination (r^2)**	**Slope**
United States of America	0.9451	0.0116
Western Australia	0.9997	0.0017
Denmark	0.6336	0.00001
Canada	0.7019	0.0035

Table 1.1: Comparison of Coefficient of Determination and Slope by Country from Linear Regression Analyses

Table 1.1 presents some striking results. Each chosen country demonstrates a different diagnostic rate. The number of autistic Americans is rising the fastest, and the number of autistic Danes is rising the slowest. Each graph shows a positive rate, demonstrating that the amount of autism diagnoses is increasing, yet each country's rate is different.

Why, though, is the number of children and adults like Susie increasing? There are several speculations as to why this is occurring. Have we changed our definition of autism in recent memory? Is it possible that we are now accepting far more symptoms as being autistic indicators? A broader range will result in an increase in autism prevalence. Have we, as a society, changed our idea of what is 'normal', leading to an increase in labelling? Are we less accepting of diverse mannerisms? Fifteen or twenty years ago, an observer may have commented that Susie, sitting in the corner playing with the clasp on her lunch box and rocking back and forth, was simply odd. Today, an increased cultural trend has occurred, suggesting the need for a label, and possibly increasing autism prevalence. Another possibility is that autism and ASDs are genetically predisposed disorders, meaning that a specified 'faulty' sequence in DNA must be present in the parent, even if it is not exhibited. Two carriers have the possibility of creating an autistic child, who is homozygous for the autistic gene. Consider the following fictitious example. I have an autistic child, and the probability of this occurring is 0.2%. Let's call this Event (A). The probability that I have an autistic child, given that I am autistic, is 0.5%. Let's call this Event (A given B). I want to know what the probability is that I am autistic myself (Event (B)). Conditional probability applies here, and P(B) = P(A) x P(A given B). Therefore, the probability that I am autistic as well is 0.1%, since 0.2 x 0.5 is 0.1. This theory, however, does not explain why there has been such a marked increase in autism diagnoses.

Many scientists and researchers believe that an environmental influence has caused this drastic increase. The increase in the use of pesticides, gasoline additives, and aluminium additives in water and paint have affected autism prevalence around the world. This could, however, be an accidental relationship and must therefore be re-examined. The use of PET plastics (polyethylene terephthalate plastics, the type of

plastic used in recyclable pop bottles) was introduced around the same time that the world began to see an increase in autism. Again, this could simply be another example of an accidental relationship and should be carefully investigated. Other researchers believe that the autism increase is due to the surge in the amount of prescribed medication. It is entirely possible that we are not challenging our immune systems enough, and so there has been a rise in diagnosed disorders in the last few years.

Experts in the fields of vaccinations and medication have also speculated that there is a strong correlation between the use of thimerosal (a mercury preservative used in vaccines) and the increase in autism prevalence. Specifically, thimerosal has been used in the MMR vaccine (measles, mumps and rubella), and many researchers feel that this preservative is indeed the cause of this marked increase. Yet, Canada has been thimerosal-free since the 1994[14], and we still continue to see an increase in autism prevalence in Canada. Similarly, Denmark removed thimerosal from its vaccines in 1990[15], and again we continue to see a marked increase. This theory has largely been disproven on the basis of recent evidence.

Hypothesis Answer

Due to the noted lack of data, a definite answer cannot be provided to the hypothesis question. Yet, Canadian autism diagnostic trends appear to be increasing, as are those of other countries abroad, but at different rates, based on the available data.

Further Analysis

Upon completion of this study, and based on the available data, it can be concluded that autism prevalence is increasing around the world. The countries with statistical data available have demonstrated that the rates for autism prevalence vary

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[14] Health Canada. *Questions and Answers* (2004). http://www.hc-sc.gc.ca/pphb-dgspsp/dird-dimr/q_a_thimerosal_e.html [25 May 2004].
[15] Eurosurveillance Weekly. *Eurosurveillance Weekly*, (2003) http://www.eurosurveillance.org/ew/2003/031009.asp [22 May 2004].

between countries. Although the coefficients of determination for a linear regression analysis were lower than those of other regression analyses, all were high enough to be cause for concern and to be considered as being statistically significant.

If we remove the apparent outlier from the Danish graph, (2000, 0.00045373), the coefficient of determination actually decreases to 0.4896, meaning that the effect of this outlier on the linear trend is positive.

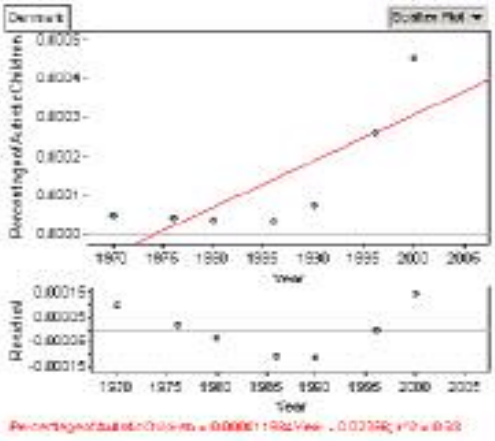

Figure 7.1

However, if we remove the data from the years 1994-1995 and 1995-1996 in the Quebec graph, the coefficient of determination improves to 0.7896, and the slope becomes steeper, changing to 0.005.

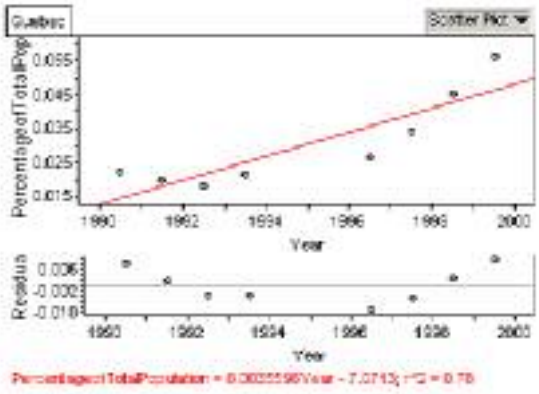

Figure 7.2

If autism prevalence is environmentally related, perhaps the environmental agent was apparent to a lesser degree in those years. There do not appear to be any significant outliers in the Western Australian or the American data.

The Saskatchewan data provided was effectively discarded due to its small sample size. Had there been more than three points on the graph, the analysis would have had more meaning. Within the three years of data available (1998, 1999 and 2000), there was an increase in autism diagnoses, but three years is not enough to make a greater conclusion about autism prevalence trends in Saskatchewan.

Until the root causes of autism and ASDs are discovered, it is unlikely that we will be able to determine why such a marked increase has, and will continue, to occur. Because such limited data was available, we can only assume that Canadian autism diagnostic trends do not match those of other countries in terms of the rate of diagnosis.

Evaluation: Assumptions, Limitations and Bias

Perhaps the largest assumption that was made during this study was that the data collected from the individual medical studies was accurate. It is possible that the data was skewed to prove a point in a medical study, and so my data analysis could therefore also be skewed.

Autism prevalence rates have been estimated from autism incidence rates (i.e. from first diagnosis). We have assumed that autism sufferers diagnosed since the apparent inception of the autism "epidemic" (i.e. circa 1985) have survived to the present and are hence represented in the current prevalence statistics.

Diagnostic criteria vary from country to country. To create an accurate comparison between countries, the same diagnostic criteria should be used, but this is not always the case. In this study, it was assumed that all data collected used the American definition of autism and ASDs unless otherwise marked.

The largest limitation to this study was the restricted amount of data. A more definitive conclusion could have arisen from this study if a longer time series had been readily available for more countries. However, because of the nature of this topic,

interest has only begun to spark within the last ten years and so it is not surprising that there is little available data.

The idea and definition of autism and ASDs varies from country to country. For some countries, data was available, but was based on a different set of criteria than the other data sets from other countries. As a result, some of the data that I discovered was useless for this study. If all of the data discovered was based on the same definition of autism and ASDs, a wider study could have been executed.

One final limitation was that many websites only published the current prevalence or incidence of autism, and the raw data, tracked over several years, was not available. This obstacle made it difficult for me to find a wide range of statistics from multiple nations for a longer period of time.

Bias may have entered the study from the original data collected. Often medical researchers will skew their data to prove a point, and so the title of a graph or chart (from which I collected my data) may have been misleading.

In the past, many right-wing government officials have believed that public health should not be government controlled. As a result, illegalizing mandatory vaccinations have been a large part of this platform. When the possibility of a link between the MMR vaccine and autism was first discussed, right-wing government officials used this idea to support their platforms. Through my research, some of the websites that I stumbled upon were written by individuals attempting to gain a political stand by trying to prove the link between the MMR vaccine and autism. Although I tried to avoid using data from websites similar to these ones, it is possible that I was unable to see the bias in the data that I obtained. This data may have been skewed to prove a political standpoint, and may not be reliable.

Similarly, there seems to be a strong emotional attachment for many authors to finding answers for the mystery of autism and ASDs. Many parents, or authors

connected to autism in some form, appear to be emotionally driven to uncovering the intricacies of autism. When such a large emotional attachment occurs, often imagined trends appear which do not actually exist. Again, I avoided using data from these sources, but it is possible that I was unable to see the bias in the obtained data.

Suggestions for Improvement

Access to current medical journals would have been beneficial to this study. It is likely that medical journals would have had more complete data and clearly identified autism definitions that were used for the data.

Due to the nature of the topic, it would be difficult to eliminate limitations involving differences in diagnostic criteria. However, if data were available, it would be wise to compare autism diagnostic trends in smaller sections of a country (for example, by state in the United States, or by province in Canada) over a longer period of time. This would eliminate the possibility of having varying autism definitions.

Having a copy of Fathom at home would have also been beneficial. With a copy of the programme at home, I would have likely used Excel and Fathom in equal proportions. Fathom is cumbersome to use, and so it requires time and patience. It would have been far more convenient to have a copy of the programme at home.

Extensions of Analysis

With a larger sample set, this study would have been far more effective. It would be beneficial to repeat this study again in five or ten years, after more research has been completed in this area, and more statistics are available. It would also be helpful to contact an autism epidemiologist to gain additional information.

If I were to repeat this study again, it would be interesting to attempt to correlate autism prevalence with the introduction of PET plastics, with the introduction of the

MMR vaccine, or with the removal of thimerosal from the MMR vaccine. However, caution must be exercised since accidental relationships may enter the study and cause bias.

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