Revised

# Autism and Childhood MMR Vaccine
# Analysis Plan

June 18, 2002

## Introduction

Autism is a serious life-long developmental disorder characterized by marked impairments in social interactions, and communication skills; and repetitive, restrictive, or stereotyped behaviors. A recent review of studies conducted since 1985, shows an estimate of the prevalence to be 1-1.4 per 1,000 for classic autism, and possibly as high as 4-5 per 1,000 for all autism spectrum disorders (ASD) combined (Kedesjo et al 1999; Rapin, 1997; Arvidsson et al., 1997). While these rates are 3-4 times higher than rates found in studies conducted 15-20 years ago (Fombonne, 1999), there are several recent studies, including a study done by Baird et al. (2000) and an investigation in Brick Township NJ, which suggested that the rate of autism may be higher still with rates of 3.1 per 1,000 and 4 per 1,000 respectively (CDC 2000; Baird et al. 2000). These higher prevalence rates, coupled with reports of increasing numbers of children with autism being served by schools and service agencies (California Department of Developmental Services,1999) have prompted concerns that the rate of autism may be increasing.

A study published in 1998 in the Lancet (Wakefield et al, 1998) has lead some to hypothesize the MMR vaccine may play a role in the recent trend upward in autism rates. This study was a case series of 12 children who were referred to a pediatric gastroenterology clinic because of chronic enterocolitis and were found to also have autistic behavioral characteristics. Eight of the 12 children were reported by parental interview as first experiencing the onset of autistic-like symptoms following the MMR vaccine, and an additional child's onset occurred after measles infection which lead the investigators to hypothesize that the measles, mumps and rubella vaccine might be associated with the onset of autism. While suggestive, this clinical case study lacked evidence to evaluate a possible causal association between MMR vaccine and the occurrence of ASD (6). More recently, Wakefield and Montgomery (1999) have suggested that the MMR vaccine may alter the immune response for one of the vaccine components due to an interaction with one or more of the other vaccine components. Animal models support the possibility of interference of T-cell responses based on exposure to several viruses simultaneously but to date this has not been demonstrated with the MMR vaccine (IOM, 2001). Wakefield et al., (1998, 2000) have also suggested that exposure to the MMR vaccine may be linked to inflammation-mediated intestinal permeability that results in incomplete breakdown and excessive absorption of gut-derived peptides from certain foods (Wakefield, 2001).

A number of other studies have been designed to try and confirm the alleged association found between autism and the MMR vaccine. A study in Sweden, which used data from the only ongoing population-based registry of autism, showed that the prevalence of autism did not increase after the introduction of the MMR vaccine in 1982. (Gillberg & Heijbel, 1998).

Taylor et al. (1999) identified 498 children with autism (261 with typical autism, 166 with atypical autism, and 71 with Asperger's syndrome) in eight North Thames health districts in the United Kingdom (UK) who were born since 1979. These cases were linked to an independent regional vaccination registry. The investigators examined time trends in rates of autism, compared age at diagnosis for children vaccinated before and after 18 months of age, and performed a case series analyses examining temporal trends between MMR vaccination and age of onset of autism. There were no statistically significant associations between the onset of autism within 1 or 2 years after vaccination with MMR. Further, developmental regression was not clustered in the months following vaccination and no significant temporal clustering for age at onset of parental concern was seen for cases of core autism or atypical autism with the exception of a single interval within 6 months of MMR vaccination. There were several possible weaknesses in the study including failure to confirm ICD10 criteria for diagnosis of ASD and the possibility of incomplete ascertainment.

In a series of large epidemiology studies (Patja A, Davidkin I, Kurki et al, 2000; Peltola H, Patja A, Leinikki P., 1998) a Finnish cohort of 1.8 million individuals with approximately 3 million MMR vaccine doses from 1982 to 1996 was examined. There were 173 potentially serious adverse events that were claimed to be causally associated with MMR vaccination. Of these adverse events, 45% had evidence suggesting other causes or contributing factors (i.e, infectious agents, viruses). The resulting incidence of adverse events was 5.3 per 100,000 MMR vaccinees. There were no cases of autism that were associated with MMR vaccination.

In 2001, Kaye et al. (2001) published a study that examined children 12 years of age or younger from the UK diagnosed with autism between 1988 and 1999 through the use of the UK general practice research database. Because only 3% of children did not receive the MMR vaccine, time trend analyses were carried out to determine whether there was a temporal association between the age of receipt of the MMR vaccine and the diagnosis of autism over time. A total of 305 children with autism aged 12 years or younger whose first recorded diagnosis occurred between 1988 and 1999 were identified from 3,092,742 person year observations. Subsequent analyses were restricted to boys aged 2 to 5 years born between 1988 and 1993. Annual birth cohorts were analyzed separately. There was a significant increase in the rates of autism between 1988 and 1999 from 0.3 per 10,000 person years in 1988 to 2.1 per 10,000 person years in 1999. However, there was no temporal association between MMR prevalence rates and the risk for autism. The major weakness in the study was that diagnosis of autism was not confirmed from original records.

More recently, Dale et al. (2001) published results of a study carried out in California that was conducted to determine if a correlation existed between the trends of MMR vaccine coverage and autism occurrence. The researchers of this study performed retrospective analyses of children from kindergartens who were born in 1980 to 1994 (samples of 600-1900 children each year) and of autism cases derived from the California Department of Developmental Services who were born in the same years. School immunization records were reviewed to determine the age at which children received the first dose of the MMR vaccination. Two main outcome measures were used: the proportion of children in each birth year that received the MMR vaccine by the age of 17 months and the proportion of children that received the vaccine by the age of 24 months. The results of this study showed no correlation between the trend in MMR vaccine

coverage and the occurrence of autism. It was noted that there was a marked increase in autism from 1980 to 1994, 44 per 100.000 in 1980 to 208 per 100,000 in 1994; however, it was also found that changes in MMR immunization coverage were smaller and of shorter duration. The administrative data had limitations especially with the diagnosis of autism.

Finally, in April of this year the Institute of Medicine (2001) reviewed the research examining the association between the receipt of the MMR vaccine and risk for autism. They concluded "The evidence favors the rejection of a causal relationship at the population level between MMR vaccine and autistic spectrum disorder." Although they rejected a causal hypothesis at the population level they strongly encouraged additional studies to examine possible associations between the MMR and certain subgroups of autistic children.

In terms of the suggested link between MMR vaccination, inflammatory bowel disease (IBD) and autism (Wakefield et al.1998, 2000, 2001) several additional studies have been carried out to try and confirm the associations. Fombonne (1998) using two large databases (a clinical database from the Child and Adolescent Psychiatry Services of large teaching hospital in south London with about 9000 clinic records and a second survey of autism in France in school-aged children in three French departments from a population of 325,347 children) examined records of children with autism for the co-occurrence of ulcerative colitis or Crohn's disease. There were no cases that were identified in either database, suggesting that if the two conditions were associated, as suggested by Wakefield et al. (1998) it was a rare occurrence.

Davis, Kramarz, Bohlke et al (2001) carried out a case-control study of individuals from four large health maintenance organizations in the United States. They identified 155 cases with ICD-9 codes for IBD and up to 5 controls matched on sex, age, and HMO. Only 142 cases were subsequently used in the analyses of timing of vaccination and diagnosis of IBD. Of the 142 cases, 75 were Crohn's diseases and 67 had ulcerative colitis (UC). Ninety-four (66%) of cases had been vaccinated with MMR and 38 with other measles containing vaccines (MCV). Ten had never been vaccinated with either MMR or MCV. There were no statistical associations between timing of vaccination and subsequent diagnosis of IBD, Crohn's Diseases or UC at 2, 4, 6, or 12 months after vaccination.

In an effort to resolve the speculation regarding the association between the MMR vaccine and autism, investigators from the CDC have conducted a matched case-control study utilizing the Metropolitan Atlanta Developmental Disabilities Surveillance Program to look at this potential relationship. The main objective of this study is to evaluate the association between the CDC case definition for autism and timing of the receipt of the MMR vaccine.

The CDC's Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) monitors the rate of serious developmental disabilities using records from public school special education and other medical facilities for children with one or more of four developmental disabilities -- mental retardation, cerebral palsy, hearing impairment, and vision impairment. In the 1996 surveillance year autism was added to the MADDSP in response to public concern about the possible increase in the prevalence of autism and related disorders. The first year of prevalence data for autism is completed with over 700 children with autistism identified. The strengths of MADDSP include the multiple source approach to identifying children with

developmental disabilities and the expert clinical review of case information to determine cases status.

Justification for Study

Several limitations of previous investigations examining the association between the MMR vaccine and autism included incomplete case ascertainment and inability to confirm the diagnosis of autism. Most of the studies described above used selected service provider databases to identify children with autism and only the Taylor et al. (1999) study attempted to confirm the diagnosis of autism from original records. These limitations along with the continuing concern surrounding this issue suggested the need for further research to clarify the relationship between MMR vaccine and autism. The benefits of the CDC study include 1) complete ascertainment of known cases from a large population, 2) extensive record review of cases by a panel of autism experts to confirm the case definition for autism, 3) inclusion of a sample of controls matched by age, sex, and school system to compare the distribution of age at MMR vaccination among cases and controls, 4) inclusion of birth records to control for other background variables that may be associated with autism and receipt of MMR vaccine including birth weight, gestational age, maternal age, and maternal education, and 5) because of the extensive clinical information on case children, the ability to examine the case group by the presence or absence of other co-existing conditions, e.g. mental retardation and possible genetic risk factors. It is expected that findings from this study will provide important information regarding the relationship between MMR vaccine and autism.

Study Design

We used a case-control design to examine the distribution of age at receipt of the first dose of the MMR vaccine among children with autism compared to control children. Case children were identified through a population-based surveillance system and control children were selected from the same population as the case children and matched on birth year, gender, and school system.

Objectives:

We did not have information regarding onset of symptoms for most cases in this study and this limited our ability to do certain types of analyses such as case series analyses. In addition, a totally unexposed group (i.e., never received the MMR vaccine or other measles containing vaccine) was not available since measles, mumps, and rubella vaccination are required for school attendance in Georgia. The following objectives are considered the primary objectives for this study.

1) To determine whether the age distribution for receipt of the MMR vaccine differs between cases and controls.
2) To determine whether there was a difference between cases and controls in the proportion of children exposed to their first dose of MMR vaccine before 18 months of age. This objective was based on the fact that ACIP recommends that children be vaccinated between 12 and 15

months of age. In this study, we considered any child vaccinated before 18 months of age to be vaccinated "on-time" according to ACIP recommendations.

3) To determine if case children were more likely than their matched controls to have been vaccinated with their first dose of MMR prior to 24 months of age. The research conducted by Cathy Lord suggests that first parental concern regarding autism symptoms occurs by 24 months of age. Therefore, we used the 24-month cut-off to define an "exposed" and "unexposed" sample.

Study population

MADDSP was established to ascertain all children who have one or more of the five developmental disabilities -- mental retardation, cerebral palsy, autism, hearing impairment, and vision impairment -- who are 3 to 10 years of age and whose parents reside in the five-county metropolitan Atlanta area. In 1996, this area had an estimated population of 2.5 million people, approximately 38,000 live births per year, and 289,456 children 3-10 years of age.

Cases:

Information on potential cases was collected via a multiple-source case finding method of record abstraction. Children's records that contain descriptive behavioral information, diagnostic tests, and other relevant diagnostic information were abstracted at different sites including school systems (special education records) and medical facilities that serve children with autism. Children with Rett's Disorder or Childhood Disintegrative Disorder were excluded as autism cases; however, information on these children was maintained in the database.

An autism case was defined in MADDSP as a child: (1) who was 3-10 years old at any time during 1996 (birth years 1987-1993); (2) whose parent or legal guardian resided in the five-county metropolitan Atlanta area during 1996; and (3) who displayed behaviors (as coded by a qualified professional) consistent with the DSM-IV diagnostic criteria for Autistic Disorder, Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) or Asperger's Disorder [DSM-IV reference]. We will refer to the case definition as autism throughout the rest of the analysis plan.

A coding system based on the social, communication, behavioral, and age criteria, as well as the associated features for autism was developed by a panel of professionals who have extensive experience in the field of autism. The panel consisted of 2 developmental psychologists, a clinical psychologist, and a special education specialist. Children's school and provider records were screened for statements of a broad range of behavioral triggers associated with autism (for example, decreased eye contact, problems with social interactions, rocking, etc ). If a single trigger was present, verbatim behavioral descriptions were abstracted from the medical, psychological, and educational reports.

To determine case status for each child, one of four expert reviewers went through the abstracted records for each child and scored behavioral statements according to DSM-IV criteria. For cases with limited or questionable information, a second reviewer independently scored the record for the DSM-IV criteria and then consensus was reached on whether the child met the case

definition for autism. Cases that were still in question following the second review were scored by Catherine Lord, Ph.D, a clinical psychologist and expert in the diagnosis of children with autism spectrum disorders, to determine final case status. In the absence of described behaviors, children with a previous diagnosis of an autism spectrum disorder by a qualified examiner were classified as suspected cases (then what). Reliability estimates for the scoring system were obtained by randomly selecting 20% of the records and having two reviewers independently score each record. A total of _____ cases were identified and abstracted for the study.

How many potential autism cases did we start with? _____
How many were labeled as suspect? _____

Controls:

Control children were selected from the same population as cases and were matched based on age within 6 months, sex, and school or a school in close proximity to the matched case school. A total of 2,265 controls were abstracted for the study. The ratio of cases to controls was chosen to be 1:3 and for a small number of cases, fewer than 3 controls were obtained. Controls were selected from regular education programs and were not receiving special education services at the time of abstraction.

After controls were abstracted, they were matched against MADDSP and the Georgia Special Education Files to determine if the child had received special education services at some point prior to abstraction. While none of the controls were found in the MADDSP database, 111 (7%) were found in Georgia's Special Education files indicating that they did receive special education services at some time but they did not have one of the MADDSP eligible developmental disabilities. All controls will be included in the analyses independent of whether they received special education services.

Vaccination history:

Trained abstractors collected vaccination histories of cases and controls from the standardized State of Georgia immunization forms that all children are required to provide to attend public schools in Georgia. The immunization form, also referred to as Form 3032, reflects the immunization requirements (minimum standards) for attendance at Georgia schools (See Appendix A). The forms are filed in each student's permanent school record. The child's primary health care provider completes the forms prior to school entry. All childhood vaccines required by Georgia law are recorded on the vaccination forms. During the period of this study, Georgia law required the following vaccines for children: 1) at least 3 doses of either DTP, DT, or DTaP, 2) a combination of at least 3 doses of either trivalent oral polio vaccine (TOPV) or enhanced potency inactivated polio vaccine (EIPV), and 3) at least one dose of measles, mumps, and rubella vaccine in the form of either the MMR, MR, or single antigen vaccines. Effective with the 1994-95 school year, for entrance into the sixth grade of school, a child needed to have received at least one additional dose of the MMR vaccine, for a total of two MMR vaccines administered on or after the child's first birthday and at least one month apart. A child can also meet the measles and rubella requirement with lab confirmation of the presence of protective levels of antibodies. Hepatitis B vaccine and Hib vaccine were not required at any time during

the study. Other information collected from the vaccination forms included location of vaccine administration, the physician or qualified examiner who administered the vaccine, and information regarding the administration of vaccines not required for school entry or additional doses of a vaccine that was required. Data regarding vaccination exemptions (medical and religious) were also available. Only one child in this study had an exemption filed in the school records.

Family Background and Other Data Collection:

Information extracted from the child's school record included child's date of birth, sex, birth state, and race. Subsequently cases and controls born in Georgia were matched to state birth certificate records. The matching criteria used were birth certificate number and child's first and last name. Of the children identified as being born in Georgia, approximately 95% of cases and 88% of controls were successfully matched. For the subset of children with Georgia birth records, sub-analyses will be performed in which potential confounding variables from the birth certificate will be used to adjust the estimated association between the MMR vaccine and autism. The variables that will be assessed as potential confounders will be birth weight, APGAR scores, gestational age, birth type, parity, maternal age, maternal race/ethnicity, and maternal education.

Additional background information was obtained from the MADDSP data set for case children. This included information on the presence of other developmental disabilities (mental retardation, cerebral palsy, vision and hearing impairment, and epilepsy), the presence of a coexisting medical condition (specifically, tuberous sclerosis and fragile X syndrome), intelligence quotient (IQ), as well as prenatal and perinatal conditions (fetal alcohol syndrome, bacterial meningitis, otitis media, etc). In addition, we identified major congenital malformations among the case children by matching with the CDC's Metropolitan Atlanta Congenital Defects Program, a population-based surveillance program of major congenital defects that covers the same geographic area (Edmonds et al, 1981).

MMR Exposure Variables

All children in Georgia must document receipt of the MMR vaccine before school entry or obtain a medical or philosophical exemption. Therefore, for this study there will be too few subjects to define an unvaccinated referent category. The primary exposure of interest in this study will be the age of receipt of the first dose of the MMR vaccine. The DSM-IV criteria for autism requires onset of symptoms before 36 months of age and therefore MMR exposure would need to occur prior to 36 months of age in order to be causally associated with autism. The age of MMR vaccination will be examined in several ways. The first two analyses will examine two alternative age cut-offs for exposure to the MMR vaccine: 18 months and 36 months. The third analysis will examine age of MMR vaccination categorized into six different age groups: 6-11 months; 12-17 months; 18-23 months; 24-29 months; 30-35 months; $\geq$ 36 months. The referent group will be on time vaccination (i.e. 12-17 months).

Other Vaccine Related Exposure Variables

Prior to 1999, thimerosal was included as a preservative in most multi-dose formulations of DTP, hepatitis B and Hib vaccines. The hepatitis B and Hib vaccines were not recommended by ACIP for children aged less than 1 year until 1991. Most children in this study were born prior to 1991 and therefore will not have been exposed to thimerosal from either the hepatitis B or Hib vaccines during the first year of life. In addition, Georgia schools did not require the Hib vaccine at the time of this study and administration of the Hib vaccine appears to have been poorly recorded in the school immunization records. Therefore, the association between thimerosal dose received early in life and subsequent risk for autism will not be addressed with this data.

**Power Calculations – Need to be update numbers.**

We have identified 706 cases of autism and 2143 matched controls for inclusion in the study. If we assume 80% vaccination coverage among controls at 24 months of age and an alpha error of .05, we will have greater than 90% power to detect an odds ratio of 1.5 and greater than 80% power to detect odds ratio of 1.4. If we assume 90% vaccination coverage among controls at 36 months of age and an alpha error of .05, we will have greater than 90% power to detect an odds ratio of 1.7 and greater than 80% power to detect an odds ratio of 1.6.

If we assume that 50% of cases and controls for the analyses will be included in the birth certificate analyses then, with 80% vaccination coverage among controls at 24 months of age and an alpha error of .05, we will have greater than 90% power to detect an odds ratio of 1.7 and greater than 80% power to detect odds ratio of 1.6. If we assume 90% vaccination coverage among controls at 36 months of age and an alpha error of .05, we will have greater than 90% power to detect an odds ratio of 2.0 and greater than 80% power to detect an odds ratio of 2.2.

Statistical Analyses:

We will use conditional logistic regression stratified by matched sets to estimate the odds ratios for the association between age at MMR vaccination and autism. In the main analyses, we will include all autism cases.

Potential confounding variables will be evaluated individually for their association with the autism case definition. Those with an odds ratio p-value $< 0.20$ will be included as covariates in a conditional logistic regression model to estimate adjusted odds ratios for the association between age at vaccination and autism. The only variable available to be assessed as a potential confounder using the entire sample is child's race. For the children born in Georgia for whom we have birth certificate data, several sub-analyses will be carried out similar to the main analyses to assess the effect of several other potential confounding variables. A recent case-control study (CDC, 2001) carried out with a subset of the autism cases from this study found that age matched cases and controls differed on several important background factors including maternal age, maternal education, birth type, and parity. The variables that will be assessed as potential confounders in this study will be birth weight, APGAR scores, gestational age, birth type, parity, maternal age, maternal race/ethnicity, and maternal education. (See Table 2 for how variables will be categorized.)

Analysis of Autism subgroups **(Need to update)**

The IOM (2001) specifically recommended additional research regarding autism subgroups and MMR. We will examine several subtypes of autism in this study. Data from the Metropolitan Atlanta Congenital Defects Program will be included in the sub-analyses to identify particular sub-groups. The following sub-group analyses will be conducted:

1) Matched Subgroup Analyses
    a. No pre-existing conditions prior to age 1: We examined children who had no identified pre-existing conditions in either their previous records or in records complied for the study. We examined cases without an established or presumptive cause for autism, such as tuberous sclerosis, fragile X, and other congenital/chromosomal anomalies. The purpose of doing this analysis was to create a more homogeneous case group that may be more likely to be impacted by the timing of the MMR vaccine. The three objectives from the primary analyses will be replicated in this sub-analysis.
    b. Regression or Plateau: We defined regression or plateau as ....
    c. Low Functioning: We defined low functioning as .....
    d. High Functioning: We defined high functioning as .....
    e. Gender Effects: Males are at substantially higher risk for autism and may be more vulnerable to the exposure associated with the MMR vaccine. We will analyze males and females separately and replicate the main objectives of the primary analyses as well as examine the potential confounders available from Georgia birth certificates.
2) Unmatched Subgroup Analyses
    a. Maternal Age (35 Years)
    b. Maternal Education (16 Years)
    c. Birth Weight (2500 Grams)

Study Strengths and Limitations:

Strengths:

< Population-based study that attempted to ascertain all autism cases in a well-defined geographic area.

< Extensive record review of cases to confirm the diagnosis of autism.

< Standardized form for MMR vaccine exposure information that was completed by the child's primary care provider.

< Matching with birth certificates allows controlling for several potentially confounding factors such as birth weight, gestational age, maternal age, and maternal education.

Limitations:

< Retrospective study with information on cases restricted to what is available in various records.

< Inherent in this type of record review are errors that cannot be rectified through use of an independent data source. Care was taken to record the information accurately with edits done by the computer programmer, the abstractors, and the project coordinator. Several immunization forms contained errors in dates that could be reasonably corrected (e.g., transposition of year digits 98 for 89) whereas the others that could not be corrected will be counted as missing data. This will be reflected by the numbers of case/control children with complete information available for analyses.

< Date of onset or first occurrence of autism behaviors was incompletely recorded.

< Incomplete ascertainment of all autism spectrum disorders, especially Asperger's Syndrome and high functioning autism.

Timeline for Review of Research Protocol, Analyses, and Dissemination of Results

May 15th - Analysis plan sent out for review
June 1st – Completion of Data Collection
June 15th - Comments back from reviewers for analysis plan
July 1st – Completion of Data Cleaning
August 1st – Completion of 1st Round of Statistical Analyses
September 1st – Review and Discussion of Results
October 1st – 1st Draft of Manuscript
December 1st – Manuscript submitted for publication

Table Shells:

**Table X: Flow Chart for Case Identification**

Table 1 Descriptive characteristics of Entire Sample

| Demographic Characteristics | Cases | Controls |
|---|---|---|
| Sex | | |
| Male | n (%) | n (%) |
| Female | n (%) | n (%) |
| Age in 1996 | | |
| 3-5 (1991 - 1993) | n (%) | n (%) |
| 6-8 (1988 - 1990) | n (%) | n (%) |
| 9-10 (1986 - 1987) | n (%) | n (%) |
| Race | | |
| White | n (%) | n (%) |
| Black | n (%) | n (%) |
| Other | n (%) | n (%) |
| Co-existing DD: | | |
| Mental Retardation | n (%) | n (%) |
| Cerebral Palsy | n (%) | n (%) |
| Vision Impairment | n (%) | n (%) |
| Hearing Impairment | n (%) | n (%) |
| Epilepsy | n (%) | n (%) |

Table 2: Descriptive Statistics for Children Born in Georgia with Birth Certificate Records

| Demographic Characteristics | Cases | Controls |
|---|---|---|
| Sex | | |
| Male | n (%) | n (%) |
| Female | n (%) | n (%) |
| Age in 1996 (birth year) | | |
| 3-5 (1991 - 1993) | n (%) | n (%) |
| 6-8 (1988 - 1990) | n (%) | n (%) |
| 9-10 (1986 - 1987) | n (%) | n (%) |
| Race | | |
| White | n (%) | n (%) |
| Black | n (%) | n (%) |
| Other | n (%) | n (%) |
| Birth Weight | | |
| <1500 gms | n (%) | n (%) |
| 1500-2499 gms | n (%) | n (%) |
| 2500+ gms | n (%) | n (%) |
| Gestational Age | | |
| < 38 weeks | n (%) | n (%) |
| 38 – 42 weeks | n (%) | n (%) |
| > 42 weeks | n (%) | n (%) |
| Birth Type | | |
| Singleton | n (%) | n (%) |
| Twin | n (%) | n (%) |
| Triplet+ | n (%) | n (%) |
| Parity | | |
| 1st Born | n (%) | n (%) |
| 2nd or higher | n (%) | n (%) |
| Maternal Age | | |
| <20 | n (%) | n (%) |
| 20 – 29 | n (%) | n (%) |
| 30 – 34 | n (%) | n (%) |
| 35 + | n (%) | n (%) |
| Maternal Race/Ethnicity | | |
| White | n (%) | n (%) |
| Black | n (%) | n (%) |
| Other | n (%) | n (%) |
| Maternal Education | | |
| <12 | n (%) | n (%) |
| 12 | n (%) | n (%) |
| 13-15 | n (%) | n (%) |
| 16 | n (%) | n (%) |
| > 16 | n (%) | n (%) |

Table 3a: Association between MMR vaccination before 18 months of age and autism

| Age vaccinated | Cases | Controls | OR (95 % CI) |
|---|---|---|---|
| < 18 months | n (%) | n (%) | |
| ≥ 18 months | n (%) | n (%) | 1.0 (referent) |

Table 3b: Association between MMR vaccination before 24 months of age and autism

| Age vaccinated | Cases | Controls | OR (95 % CI) |
|---|---|---|---|
| < 24 months | n (%) | n (%) | |
| ≥ 24 months | n (%) | n (%) | 1.0 (referent) |

Table 3c: Association between age at MMR vaccination and autism

| Age vaccinated | Cases | Controls | OR (95 % CI) |
|---|---|---|---|
| 0-11 months | n (%) | n (%) | |
| 12-17 months | n (%) | n (%) | |
| 18-23 months | n (%) | n (%) | |
| 24-29 months | n (%) | n (%) | |
| 30-35 months | n (%) | n (%) | |
| ≥ 36 months | n (%) | n (%) | 1.0 (referent) |

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