April 27, 2001

To Do List for MMR/Autism Analysis Plan

1) Agreed we would use term autism for case definition.

2) Clarification on Methods
   a. Selected diagnosed cases from 1996 MADDSP
   b. In 1996, case children aged 3 to 10 years
   c. Followed up case children between 1996 and 2001
   d. Selected controls at same time cases were abstracted (within 2 weeks)
   e. At time of abstraction, case children aged 5 – 13 years

3) Review Cathy's revision of case identification

4) Recent publication of IOM report
   a. Added biological plausibility arguments to analysis plan
   b. Agreed we would add other studies/references after external review

5) Added discussion of Case-Control Study showing several confounding variables
   a. Maternal Education
   b. Maternal Age
   c. Multiplicity
   d. Parity

6) Hypotheses – we will all review and comment

7) Sample sizes
   a. Currently 755 Cases, 2265 Controls
   b. Will update these numbers on June 1

8) Power calculations
   a. Will be based on 18 months cut-off (Taylor et al)

9) Case Review for first evaluation type variable
   a. Meeting May 9 to discuss record reviews

10) Add references currently in analysis plan

11) Timeline
   a. External Review May 15th
      i. Reviewers - Bob Davis, Susan Hyman, Eric Fombonne
      ii. Methodologist- David Savitz (UNC), Craig Newschaffer, Nigal Paneth
   b. Internal Review – agreed to send out current draft to Roger Bernier

May 4, 2001

To Do List for MMR/Autism Analysis Plan

1) Hypotheses

2) Add references

3) Case Review for parental concern type variable
   a. Proposal currently say first evaluation date
   b. Meeting May 9 to discuss record reviews

Schedule May 9 meeting

4) Upcoming Deadlines

   a. External Review May 15th
      i. Reviewers - Bob Davis, Susan Hyman, Eric Fombonne
      ii. Methodologist- David Savitz (UNC) or Craig Newschaffer or Nigal Paneth

   b. Data collection completed June 1

Word File Date June 26, 2001

Autism Analysis Notes

1) Use Race and Sex
2) Race Recode
   a. 1 = white
   b. 2 = black
   c. 3 – 6 = other
   d. 90,99 = unknown
3) Cases
   a. Casestat = confirmed case
   b. Ausdiag = MADDSP dx
4) Coexisting Developmental Disabilities
   a. Cpcasedf - confirmed
   b. Cpanyoth – not confirmed
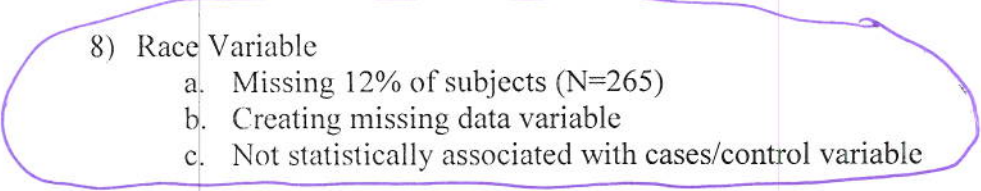
For Total Sample

Roscoe

Fetch tsk.filename
A
Export dsn=wct2.pds.mmr2(mmrname)

Agendas Ps

Data Analysis Issues   8/1/2001

1) MADDSP Case versus MMR/AUTISM CASE
   a. Clarification
      i. 567 MMR/Autism Cases
      ii. 540 MADDSP Cases
   b. 29 subjects are listed as cases in study – but not MADSSP cases
   c. 2 subjects are listed as controls in study – listed as MADDSP case

2) Missing Data on Matching Variable
   a. 22 subjects have no matched subjects

3) Sex Variable
   a. No Missing Data

4) Age Variable
   a. 1 control subject born in 1994
   b. 2 subjects are missing birth year

5) School System Variable
   a. 7 subjects missing School System Variable
   b. Should we check or should we wait for update?

6) MMR Exposure Variable
   a. MMR vaccination data missing for 63 cases
   b. Similar missing across cases and controls
   c. Can we check these values ?????
   d. Vaccination Dates
      i. Unusual values ??
      ii. Changed categories – see handout

7) Vaccine Exemption Variables – no positive values in the current data set
   a. Excode1
   b. Excode2
   c. Excode3

8) Race Variable
   a. Missing 12% of subjects (N=265)
   b. Creating missing data variable
   c. Not statistically associated with cases/control variable

9) Birth weight is normally distributed - reasonable

Examined Race Before Sept 5, 2001 Final Protocol

10) Gestational Age Variable
    a. Data for last menses
        i.   Incorrect data
        ii. Outliers will not be used

11) Preliminary Analyses
    a. MMR Age of Vaccination
        i.   Categorical Age Distribution   +
        ii. < 18 Months   NS
        iii. < 36 Months   +
    b. RACE   NS
    c. Birth Certificate Variables
        i.   Maternal Age   +
        ii. Maternal Race   NS
        iii. Maternal Education   NS
        iv. Birth Weight   +

Data Analysis Issues   8/22/2001

1) Use the confirmed autism case definition for cases
2) Age in 1996 for cases was based on end of year calculation
   a. 1 control 2 years of age
   b. 2 controls 11 years of age
3) State Variable
4) Birth Certificate Variable
5) Missing Data Issues
   a. Entire Sample
      i. Cases with missing state variable that have Birth Cert (N=10)
   b. Sample with Birth Certificates
6) SES -- should we pursue the zipcode matching?

Data Analysis Issues   9/5/2001

1) Confirmed Cases = 620
2) Birth Day
   a. Outliers - Day = 91
3) MMR Variable
   a. Negative vaccination dates N=2
   b. Probably due to incorrect birth date
4) All EXCODE data missing
5) Race Variable
   a. Race
   b. C_Race
   c. M_Race
   d. CDCRace
6) H_Plive
   a. Outliers = 198
7) H_lbordr
   a. Outliers = 199
8) School System
   a. N=7 Controls = 900
9) SES – should we pursue the zipcode matching?
   a. Coleen Boyle suggested we should pursue
10) Statistically Significant Effects
   a. Born in GA
   b. MMR 36+ Months

Agendas #7

Coding Variables For Race for Total Sample and Birth Certificate Sample

Agenda 10/31/2001

1) Data Privacy Issues

2) Update on availability of Final Database

3) Analysis/Data entry for preexisting conditions and parental concern

4) Draft Intro and Methods for Paper

5) Discussion of Preliminary Descriptive Statistics

discussing analyses

Agenda 12/05/2001

1) Data Privacy Issues

2) December 13 Seminar

3) Update on availability of Final Database

4) Analysis/Data entry for preexisting conditions and parental concern

5) Draft Intro and Methods for Paper

6) Discussion of Preliminary Descriptive Statistics

discussing analyses

Agenda 12/12/2001

1) Data Privacy Issues

2) Update on Final Database

    a. Original controls are in database
    b. Exclusion criteria
        i. Cases
        ii. Controls
    c. Missing immunization forms and/or data
        i. Tanya will be following up on missing forms
        ii. Will get both MMR data as well as other vaccine data
    d. Birth certificate matching
    e. Missing data by School System

3) Discussion of Preliminary Descriptive Statistics
    a. Total Sample
    b. Birth Certificate Sample

4) Additional Analyses
    a. Run analyses examining influence of school systems
    b. Others

MMR/Autism Agenda

Date: January 9, 2002

1) Data Privacy Issues

2) Update on Data Checks / Final Database

    a. Original controls are in database
    b. Missing immunization forms/data
        i. Tanya will be following up on missing forms
        ii. Will be getting both MMR data as well as other vaccine data
    c. Will review exclusionary criteria once new data is available
    d. Check why Isolated Autism cases without Delay < 1 all appear to be vaccinated < 36 months
    e. New Variables Added
        i. Developmental Delay < 1
        ii. Plateau/Regression – will not be very useful for analyses
        iii. Pre-existing Condition – was previously subset of DD < 1
        iv. Age of 1st Concern – uncorrelated with age of vaccination

3) Discussion of Preliminary Descriptive Statistics
    a. Total Sample
    b. Birth Certificate Sample

4) Additional Analyses
    a. Run analyses examining influence of each school system
    b. Delay < 1
    c. Age of 1st Concern

running Analyses

MMR/Autism Agenda

Date: January 23, 2002

1) Data Privacy Issues

2) Update on Data Checks / Final Database

    a. Original controls are in database
    b. Missing immunization forms/data
        i. Tanya will be following up on missing forms
        ii. Will be getting both MMR data as well as other vaccine data
    c. Will review exclusionary criteria once new data is available
    d. Check why Isolated Autism cases without Delay < 1 all appear to be vaccinated < 36 months
    e. New Variables Added
        i. Developmental Delay < 1
        ii. Plateau/Regression – will not be very useful for analyses
        iii. Pre-existing Condition – was previously subset of DD < 1
        iv. Age of 1st Concern – uncorrelated with age of vaccination

3) Discussion of Preliminary Descriptive Statistics
    a. Total Sample
    b. Birth Certificate Sample

4) Additional Analyses
    a. Run analyses examining influence of each school system
    b. Delay < 1
    c. Age of 1st Concern

Running analyses

MMR/Autism Agenda

Date: February 13, 2002

1) Data Privacy Issues

2) Update on Data Checks / Final Database
   a. Original controls are in database
   b. Missing immunization forms/data
      i. Tanya will be following up on missing forms
      ii. Will be getting both MMR data as well as other vaccine data
   c. Will review exclusionary criteria once new data is available
   d. Check why Isolated Autism cases without Delay < 1 all appear to be vaccinated < 36 months
   e. New Variables Added
      i. Developmental Delay < 1
      ii. Plateau/Regression – will not be very useful for analyses
      iii. Pre-existing Condition – was previously subset of DD < 1
      iv. Age of 1st Concern -- uncorrelated with age of vaccination

3) Discussion of Preliminary Descriptive Statistics
   a. Total Sample
   b. Birth Certificate Sample

4) Additional Analyses
   a. Isolated Autism
   b. Delay < 1
   c. Pre-existing Condition
   d. Age of 1st Concern
   e. Examine influence of each school system

seeing statistically significant effects

running analyses

MMR/Autism Agenda

Date: February 20, 2002

1) Data Privacy Issues
    a. 308(d) Exemption
    b. Will we be creating a public use database?
    c. What variables will be included in that database?

2) Update on Data Checks / Final Database
    a. Original controls are in database
    b. Review exclusionary criteria
    c. Isolated autism cases without Delay < 1 all vaccinated < 36 mo ???

3) Discussion of Preliminary Descriptive Statistics
    a. Total Sample
    b. Birth Certificate Sample

4) Analyses
    a. Discussion of MMR Exposure Variable
    b. Analysis of Total Sample
        i. Isolated
        ii. Non-Isolated
        iii. Delay < 1 and Pre-existing Condition
        iv. Age of 1st Concern
    c. Analysis of Birth Certificate Sample
        i. Isolated
        ii. Non-Isolated
        iii. Delay < 1 and Pre-existing Condition
        iv. Age of 1st Concern
    d. Examine influence of each school system

① Analyzing Total Sample

② Analyzing Birth-Certificate Sample

MMR/Autism Agenda

Date: April 16, 2002

1) Update on Data Checks / Final Database
   a. Original controls are in database
   b. Added new data from Marshalyn/Tanya on pre-existing conditions

2) Discussion of Descriptive Statistics
   a. Total Sample
   b. Birth Certificate Sample

3) Analyses
   a. Discussion of MMR Exposure Variable
   b. Analysis of Total Sample
      i. Isolated
      ii. Non-Isolated
      iii. Delay < 1 and Pre-existing Condition
      iv. Age of 1st Concern
   c. Analysis of Birth Certificate Sample
      i. Isolated
      ii. Non-Isolated
      iii. Delay < 1 and Pre-existing Condition
      iv. Age of 1st Concern

Total Sample

Birth Certificate Sample

MMR/Autism Agenda

Date: May 22, 2002

1) Update on Data Checks / Final Database
   a. Added new data on pre-existing conditions

2) Descriptive Statistics
   a. Cases
   b. Total Sample
   c. Birth Certificate Sample

3) Statistical Analyses
   a. Analysis of Total Sample
      i. 18 Months
         1. All Cases
         2. Cases with No Delay or Pre-existing Condition
         3. Regression Cases
      ii. 24 Months
         1. All Cases
         2. Cases with No Delay or Pre-existing Condition
         3. Regression Cases
   b. Analysis of Birth Certificate Sample
      i. 18 Months
         1. All Cases
         2. Cases with No Delay or Pre-existing Condition
      ii. 24 Months
         1. All Cases
         2. Cases with No Delay or Pre-existing Condition

Total Sample

Finding Statistically Significant Effects at 24 months and at 36 months

Date: June 28th, 2002

Agenda

1) Review Analysis Plan
   a. Update Power Calculations
      i. Birth Certificate Sample
         1. Original Controls with Birth Certificate N=1049
         2. Matched Controls with Birth Certificate N=576
      ii. Subgroup Analyses
         1. Matched Analyses
         2. Unmatched Analyses
2) Review Data Issues
   a. Sample Selection – See Table
   b. Descriptive Data for Cases – Table 2
      i. Subgroups
      ii. Dropped epilepsy from table
3) Preliminary Results
   a. Table 4 – Primary Analyses
   b. Table 5 – Unmatched Subgroup Analyses
4) Creation of Public Use Data Set
   a. Data privacy Issues
      i. NCHS Model
      ii. Other Model
   b. Code Book
   c. SAS Programs
5) Select Data to Present Preliminary Results to Bob Chen and David Shay

[handwritten annotations:]

Analysis of Whites and Blacks

Want to present results to

Bob Chen → Branch Chief
David Shay → Team Lead

National Immunization Program Immunization Safety Branch

Date: October 2nd, 2002

Agenda

1) Update on Data Analysis and Statistical Issues
    a. Started to rewrite and document SAS programs for public use database
    b. Reviewed Statistical Analyses with Margarette Kolczak
        i. Suggested testing demographic subgroups as interactions with exposure similar to earlier analyses of race
    c. Corrected MMR vaccination data
        i. 1st MMR Vaccination and 2nd MMR Vaccination had coding errors
            1. Coding errors were fixed
            2. Results change slightly
2) Review Preliminary Results
    a. Results are very similar to previous analyses
    b. Any MMR < 36 Months: OR = 1.476 (prev OR=1.53)
    c. Any Measles < 36 Months: OR = 1.492
    d. Any Measles, Mumps, and Rubella: OR = 1.482
3) Review Case Selection Models and Results
    a. See Tanya Handout
4) Revise analysis plan to include:
    a. Any measles containing vaccines
    b. Any measles, mumps, or rubella containing vaccines
5) Select Date to Present Preliminary Results to Bob Chen and David Shay

Examining Results by Type
of MMR Vaccine
        Single Dose vs Multi Dose

— we kept pushing this date back
— Bob Chen had been reprimanded
        on Sept 18th, 2002

Date: October 9th, 2002

Agenda

1) Update on Data Analysis and Statistical Issues
    a. Started to rewrite and document SAS programs for public use database
    b. Reviewed Statistical Analyses with Margarette Kolczak
        i. Suggested testing demographic subgroups as interactions with exposure similar to earlier analyses of race
    c. Corrected MMR vaccination data
        i. 1st MMR Vaccination and 2nd MMR Vaccination had coding errors
            1. Coding errors were fixed
            2. Results change slightly
2) Review Preliminary Results
    a. Results are very similar to previous analyses
    b. Any MMR < 36 Months: OR = 1.476 (prev OR=1.53)
    c. Any Measles < 36 Months: OR = 1.492
    d. Any Measles, Mumps, and Rubella: OR = 1.482
3) Review Case Selection Models and Results
    a. See Tanya Handout
4) Revise analysis plan to include:
    a. Any measles containing vaccines
    b. Any measles, mumps, or rubella containing vaccines
5) Select Date to Present Preliminary Results to Bob Chen and David Shay

Kept pushing back

Margarette Kolczak, Phd reviewed my SAS programs and suggested additional analyses

= suggested testing Race by MMR interaction rather than stratify as we had been doing for 9 months