**Obstetric\_Complications.R\_ReadMe**

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ReadMe Sections:

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Purpose of Code:

The purpose of this code is to flag each participant with psychosis-associated Obstetric Complications, based on the risk categories from this article (Mittal et al., 2008): <https://academic.oup.com/schizophreniabulletin/article/34/6/1083/1939509#29826173>

Researcher-Facing Explanation of Code:

1. BACKGROUND:
   1. There are 3 categories: Association with Hypoxia, Prenatal Maternal Infection, and Maternal Stress Exposure.
   2. Of the complications associated with those three categories, the following had variables available in the ABCD 5.0 archive:
      1. Hypoxia
         1. Born by Caesarian Section
         2. Bleeding during Pregnancy
         3. Pre-Eclampsia
         4. Blue at Birth
         5. Required Resuscitation
         6. Neonatal Apnea
      2. Maternal Stress Exposure
         1. Unplanned/Unwanted pregnancy
      3. Prenatal Maternal Infection
         1. Genital Tract Infection / UTI
         2. Rubella
         3. Upper Respiratory Infections, Flu, Toxoplasmosis, Herpes Simplex type 2
            1. While there were no direct yes/no variables for these illnesses, use of Antibiotic/Antiviral medications by the mother during pregnancy were provided. These will be systematically searched through and the presence of infections will be inferred from the use of medications used to treat those infections.
            2. ***It should be noted that some antibiotics may have been prescribed for conditions other than those listed in the above article as associated with psychosis. These should be scrutinized on a case-by-case basis, as necessary. The proportion of antibiotics prescribed for conditions other than these should be noted in the final publication, and columns to count Antibiotics/Non-Antibiotics have been added for thoroughness of analysis.***
2. All columns of interest are enumerated below in the Explanation of Variables section, in order of appearance.

1. Obstetric Complication data (ph\_p\_dhx.tsv) and ABCD medication lookup tables (Full\_Meds\_LUT.csv, OC\_FilledIn\_Meds.csv) were imported. Full\_Meds\_LUT.csv contains medication classification information and category flags for most of the medications used in the ABCD study, and OC\_FilledIn\_Meds.csv was created in a previous iteration of this code to identify the medications in ABCD 5.0 that were not included in Full\_Meds\_LUT.csv.
2. Isolate Relevant Variables
   1. Relevant Obstetric complication variables were isolated and the two medication lookup tables were combined into a single dataframe called “Meds”.
3. Isolate List of Parental Medications
   1. Medications prescribed to the mother during pregnancy—up to 4 prior to knowing they were pregnant, and up to 4 after knowing they were pregnant—were isolated and renamed for human readability.
   2. They were then reformatted longform into Long\_Meds\_ID so that each medication would be on its own line, and those without classification descriptors could be identified and classified.
   3. Common medications were systematically searched and classified (Celexa = SSRI, Ambien = Sedative, etc.)
4. Fill in Remaining Medications
   1. n = 38 medications still needed manual classification and/or medication code lookup on RxNav
   2. These were Isolated, exported, manually filled in, then imported with classifier information. They were then merged into a full dataframe of classified medications called Explained\_Meds
5. Flag Medications if related to: Upper Respiratory Infection, Influenza, Toxoplasmosis, Herpes Simplex type 2
   1. “Antibiotic” was flagged if medications were described as antibiotics
   2. “Not\_Antibiotic” was flagged for the use of a flu-specific antiviral (TamiFlu), herpes medications, or a herpes-specific antiviral that was just described as “antiviral” (Acyclovir)
   3. “Relevant\_Med”Y1N0” was flagged if any of these were present.
6. Clean/Rename Columns For Clarity & Readability, Simplify Patient Data to one row per subject
   1. Non-medication obstetric complication columns were renamed for readability
   2. Participants reported medication data at ses-00A and ses-04A. Because these refer to pre-study experiences, where both reports refer to the same occurrence, data can be combined into a single row for ease of analysis.
      1. Endorsements for each flag during ses-04A were copied into ses-00A. Once checks were performed that no participant had ses-04A data and lacked ses-00A data (and would thus be fully removed from analysis), all ses-04A rows were removed, leaving 1 row per participant.
7. Merge Medication info/Flags into Full Obstetric Complications data frame
   1. Medication information is currently in longform, and needs to be converted to wide, so that all of a subject’s medications can be in the same row.
      1. The number of medications for each subject was counted, so that enough columns would be made
      2. Medication data was converted to wide, with each medication getting a column for its name (Med#), classification (Explanation\_#), antibiotic status (Antibiotic#\_Y1N0), non-antibiotic status (Not\_Antibiotic#\_Y1N0), and relevance to obstetric complications (Relevant\_Med\_#\_Y1N0).
      3. These were all combined and simplified into a single row, and unnecessary rows and columns were removed.
8. Flag each row/subject for Hypoxia, Prenatal Maternal Infection, & Maternal Stress Exposure
   1. Categorical Flags were applied to the category structure noted in 1.2 of this researcher-facing explanation.
9. Count the number of categories Present
   1. Number of relevant medications and number of categories present were counted
10. Data were cleaned and organized for export to csv
11. Data were exported to csv:
    1. All\_OCs 🡪 Obstetric\_Complications\_9\_12\_25.csv

Explanation of Variables:

|  |  |
| --- | --- |
| participant\_id | ABCD Participant ID |
| session\_id | ABCD name of visit; baseline, year1, etc. |
| ph\_p\_dhx\_\_birth\_002  C\_Section\_Y1N0 | Yes = 1, No = 0; Was your child born by Caesarian section? |
| ph\_p\_dhx\_\_med\_002  Bleeding\_Preg\_Y1N0 | Yes = 1, No = 0; Heavy bleeding [during pregnancy] requiring bed rest or special treatment? |
| ph\_p\_dhx\_\_med\_003  Pe\_E\_T\_Y1N0 | Yes = 1, No = 0; Pre-eclampsia, eclampsia, or toxemia? |
| ph\_p\_dhx\_\_med\_014  Pre\_Eclampsia\_Y1N0 | Yes = 1, No = 0; Pre-Eclampsia? |
| ph\_p\_dhx\_\_birth\_003  Blue\_at\_Birth\_Y1N0 | Yes = 1, No = 0; Blue at Birth? |
| ph\_p\_dhx\_\_birth\_005  Required\_Resusc\_Y1N0 | Yes = 1, No = 0; Required Resuscitation/Did not breathe at first? |
| ph\_p\_dhx\_\_birth\_008  NeoNatal\_Apnea\_Y1N0 | Yes = 1, No = 0; Neonatal Apnea/Required Oxygen? |
| ph\_p\_dhx\_006  Planned\_Preg\_Y1N0 | Yes = 1, No = 0; Was your pregnancy with this child a planned pregnancy? |
| ph\_p\_dhx\_\_med\_008  UTI\_Y1N0 | Yes = 1, No = 0; Genital Tract Infection / UTI? |
| ph\_p\_dhx\_\_med\_006  Rubella\_Y1N0 | Yes = 1, No = 0; Rubella (First 3 months of pregnancy)? |
| ph\_p\_dhx\_\_med\_013  OtherConditions\_Y1N0 | Yes = 1, No = 0; Any other conditions requiring medical care? |
| ph\_p\_dhx\_\_rx\_\_label\_001a  Med1 | Medication name 1: Before knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_002a  Med2 | Medication name 2: Before knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_003a  Med3 | Medication name 3: Before knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_004a  Med4 | Medication name 4: Before knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_001b  Med5 | Medication name 1: After knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_002b  Med6 | Medication name 2: After knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_003b  Med7 | Medication name 3: After knowing about pregnancy |
| ph\_p\_dhx\_\_rx\_\_label\_004b  Med8 | Medication name 4: After knowing about pregnancy |
| Med\_Name  Med# | Name (or RxNav code) of medication |
| ‘Other Explanation’  Explanation\_# | Explanation/classification of the medication in Med\_Name |
| Antibiotic  Antibiotic#\_Y1N0 | Yes = 1, No = 0; Is the (relevant) medication an antibiotic? |
| Not\_Antibiotic  Not\_Antibiotic#\_Y1N0 | Yes = 1, No = 0; Is the (relevant) medication not an antibiotic? |
| Relevant\_Med\_Y1N0  Relevant\_Med\_#\_Y1N0 | Yes = 1, No = 0; Is the medication relevant to Obstetric Complications? |
| nummeds | Number of medications a subject’s mother was on when pregnant |
| Antibiotic\_Count | Number of Antibiotics each subject’s mother was on when pregnant |
| Not\_Antibiotic\_Count | Number of relevant non-antibiotic medications each subject’s mother was on when pregnant |
| All\_Relevant\_Med\_Count | Number of medications relevant to obstetric complications each subject’s mother was on when pregnant |
| Hypoxia\_Flag | Number of hypoxia-related obstetric complications present in each subject’s medical history |
| Infection\_Flag | Number of infection-related obstetric complications present in each subject’s medical history |
| Stress\_Flag | Number of stress-related obstetric complications present in each subject’s medical history |
| FlaggedCategories | Number of Flagged Categories (Hypoxia, Infection, Stress) present in each subject’s medical history |

Methods Section Summary:

To identify the presence and extent of psychosis-associated obstetric complications based on extant literature (Mittal et al., 2008), ABCD data (ph\_p\_dhx.tsv) were systematically searched and flagged for relevant occurrences during pregnancy and the perinatal period. The following relevant variables pertaining to three main categories were isolated from available ABCD data:

Associations with Hypoxia—Born by Caesarian Section, Bleeding during Pregnancy, Pre-Eclampsia, Blue at Birth, Required Resuscitation, Neonatal Apnea; Maternal Stress Exposure—Unplanned/Unwanted Pregnancy; Prenatal Maternal Infection—Genital Tract Infection/UTI, Rubella.

To additionally screen for relevant Prenatal Maternal Infections—Upper Respiratory Infections, Influenza, Toxoplasmosis, & Herpes simplex type 2—the reported use of medications typically used to treat those specific infections were assumed to imply the presence of those infections. In the case that such medications were prescribed for a bacterial or viral infection other than those enumerated here, it was assumed that the need to prescribe and take such a medication was the result of an illness that caused similar proinflammatory cytokine spikes to these illnesses. Such spikes in pregnant mothers are known to result in increased incidence of schizophrenia in progeny (Brown et al., 2004; Buka er al, 2001).

References:

Brown, A. S., Hooton, J., Schaefer, C. A., Zhang, H., Petkova, E., Babulas, V., Perrin, M., Gorman, J. M., & Susser, E. S. (2004). Elevated maternal interleukin-8 levels and risk of schizophrenia in adult offspring. *The American journal of psychiatry*, *161*(5), 889–895. <https://doi.org/10.1176/appi.ajp.161.5.889>

Buka, S. L., Tsuang, M. T., Torrey, E. F., Klebanoff, M. A., Bernstein, D., & Yolken, R. H. (2001). Maternal infections and subsequent psychosis among offspring. *Archives of general psychiatry*, *58*(11), 1032–1037. <https://doi.org/10.1001/archpsyc.58.11.1032>

Mittal, V. A., Ellman, L. M., & Cannon, T. D. (2008). Gene-environment interaction and covariation in schizophrenia: the role of obstetric complications. *Schizophrenia bulletin*, *34*(6), 1083–1094. <https://doi.org/10.1093/schbul/sbn080>