FIGURE LEGENDS

Figure 1. Percent of women who had selected demographic characteristics whose children were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Women who identified as Black, did not graduate from high school, and/or were eligible for government-provided healthcare (public) insurance gave birth to children who later had ASD-/ID+ or ASD+/ID+ more frequently than other women. *Infants may be in more than one category*]

Figure 2. Percent of women who had selected pregnancy characteristics or exposures whose children were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [Children whose mother *reported a vaginal/cervical infection, and/or a periodontal infection during this pregnancy, had ASD+/ID+ more frequently than children of other women. By contrast, children of women who consumed antibiotics less frequently received a diagnosis of ASD+/ID- compared to the children of other women, whereas ASD-/ID+ occurred more frequently among children born to women who reported fever during this pregnancy than in children of other women.*]

Figure 3. Percent of women who had selected pregnancy complications whose children were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Irrespective of their IQ, children whose mother had preeclampsia and/or received magnesium sulfate for seizure prophylaxis developed ASD more frequently than children of other mothers. Children born to women who had placental abruption, and those whose mother had fever within 48 hours before or after delivery, more frequently developed ASD unaccompanied by ID (ASD+/ID-) than children of other mothers.*]

Figure 4. Percent of newborns with selected characteristics who were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Boys had ASD+/ID+ and ASD+/ID- twice as frequently as girls. The prevalence of ASD increased with decreasing gestational age and, to a lesser extent, with decreasing birth weight, regardless of IQ. Children who had birth head circumference Z-score < -2 also received ASD diagnoses more frequently than other children, irrespective of IQ. Children with the most severe fetal growth restriction (i.e., birth weight Z-score < -2) had the highest percent of ASD+/ID- diagnoses. Antecedents of ID unaccompanied by ASD (ASD-/ID+) included male sex, low gestational age, and fetal growth restriction (including microcephaly).*]

Supplement Figure 1. Study participant flow diagram [*Of the 1198 children from the original ELGAN birth cohort who survived to 10 years of age, 232 children were not recruited to participate in this study (for lack of newborn blood samples), and 77 were recruited to participate, but did not. As previously reported,[39] children who did not participate did not differ from those who did participate on newborn variables, including sex, gestational age, and fetal growth restriction, but non-participants were more likely to have indicators of social disadvantage, which has been associated with increased risk of preterm birth[77] and ASD.[78,79]*]

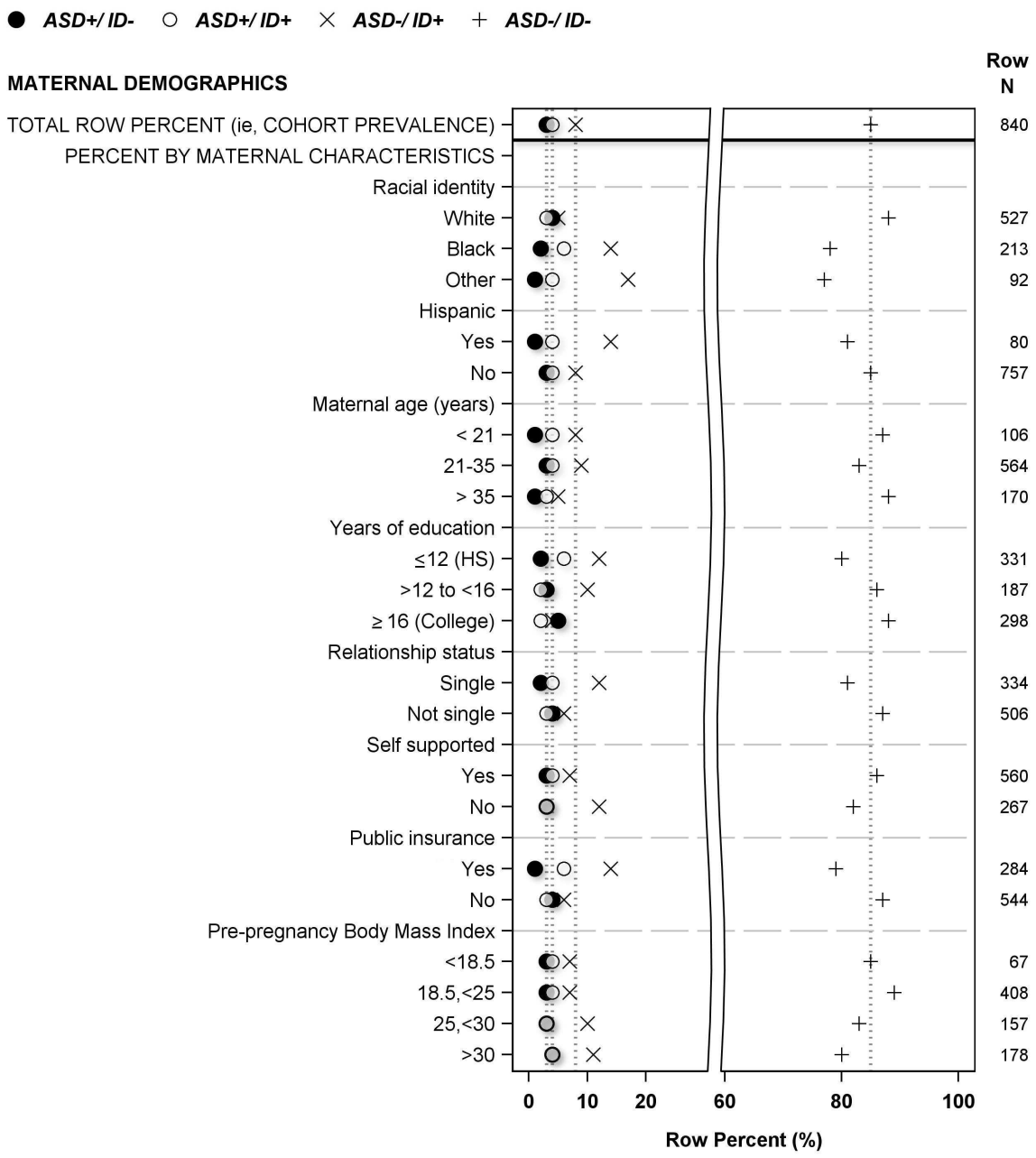
Supplement Figure 2. Percent of children who had placentas with selected characteristics who were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Regardless of IQ, ASD was not diagnosed more frequently among*

children whose placenta harbored microbes than among their peers whose placenta appeared to be sterile. Children whose placenta had umbilical cord vasculitis and/or fetal stem vessel thrombosis had ASD+/ID- more frequently than others, whereas children whose placenta had decidual hemorrhage/fibrin deposition were ASD+/ID+ less frequently than others. Children with infarcts in their placentas, by contrast, were ASD+/ID+ less frequently than children whose placenta did not have a placental infarct. ID unaccompanied by ASD (ASD-/ID+) occurred more frequently in the presence than in the absence of placental Mycoplasma and skin flora.]

Supplement Figure 3. Percent of children who had selected early postnatal characteristics who were classified at age 10 years as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Children whose PaO_2 was in the lowest quartile on either day 7 or day 14 developed ASD+/ID- more frequently than other children. Children who had documented bacteremia had a higher prevalence than others of ASD+/ID+, and to a lesser extent a higher prevalence of ASD+/ID-. ID unaccompanied by ASD (ASD-/ID+) was associated with tracheal colonization during the first postnatal month, early and late documented bacteremia, and mechanical ventilation on days 7, 14, 21, and 28.*]

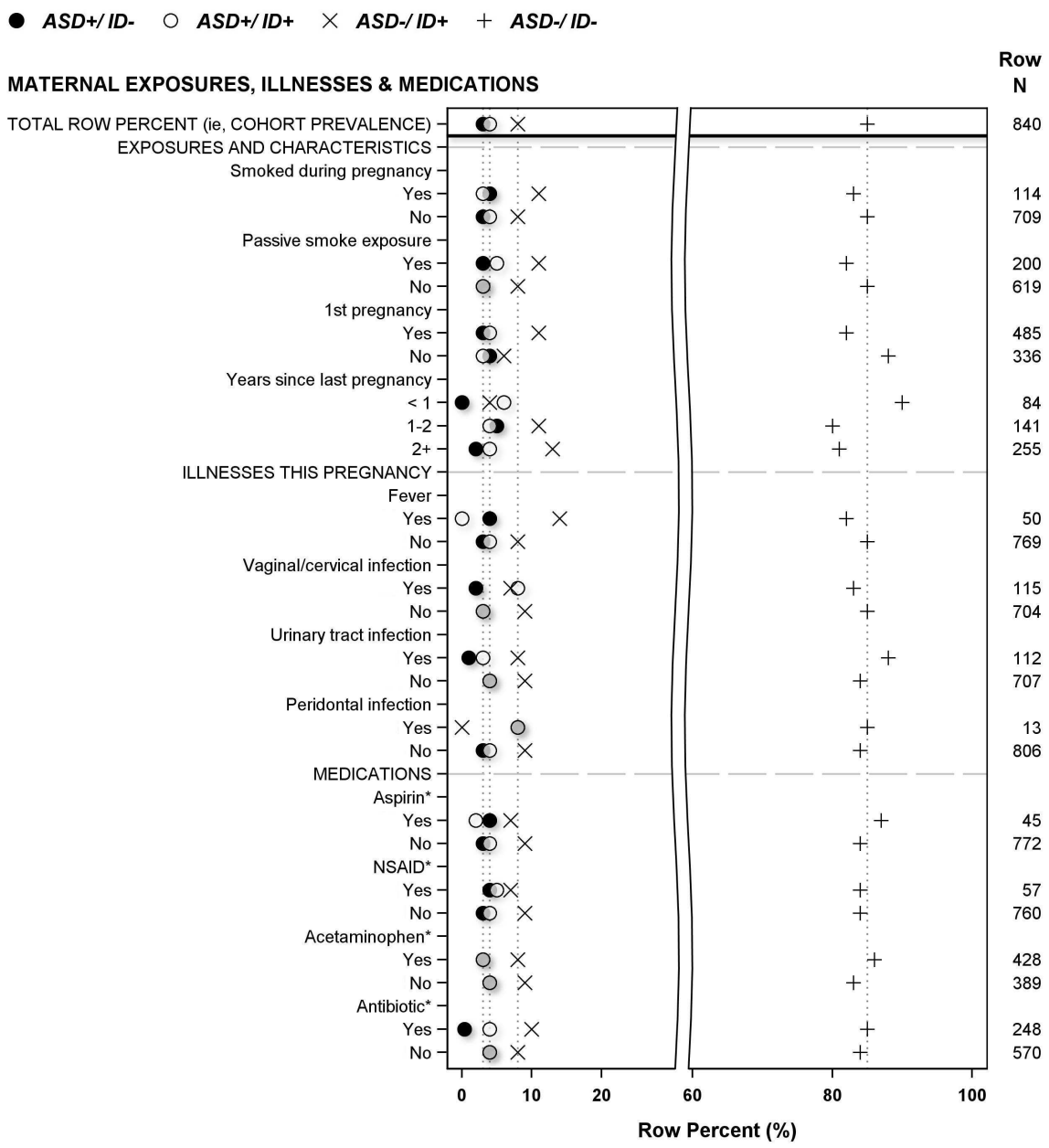
Supplement Figure 4. Percent of children who had selected postnatal diagnoses and dysfunctions who at age-10 years were classified as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Infants who received methylxanthine for 15+ days (usually caffeine) developed ASD less frequently than other children. Children who received hydrocortisone, dexamethasone, or a sedative during the first postnatal month, a transfusion of packed cells or whole blood during 3 of the first 4 postnatal weeks, and an antibiotic during postnatal weeks 2 through 4, had a modestly higher ASD prevalence than children who did not receive these drugs or blood. Children who received postnatal steroids, analgesics, blood transfusions during the first postnatal month, and antibiotics during weeks 2-4 were at increased risk of ID without ASD (ASD-/ID+).*]

Supplement Figure 5. Percent of children who had selected diagnostic and classification entities who at age-10 years were classified as ASD+/ID-, ASD+/ID+, ASD-/ID+ or ASD-/ID- [*Elevated frequencies of ASD+/ID+ and ASD+/ID- were observed among children who had a pneumothorax, early and persistent pulmonary disease, necrotizing enterocolitis, retinopathy of prematurity, and bronchopulmonary dysplasia (also called chronic lung disease of prematurity), especially if severe (defined as receiving ventilator assistance at 36 weeks post-menstrual age). Elevated frequencies of ASD-/ID+ occurred among children who had a persistent ductus arteriosus, pneumothorax, pulmonary interstitial emphysema, early and persistent pulmonary disease or pulmonary deterioration, isolated intestinal perforation, retinopathy of prematurity, and bronchopulmonary dysplasia, compared to those who did not.*]



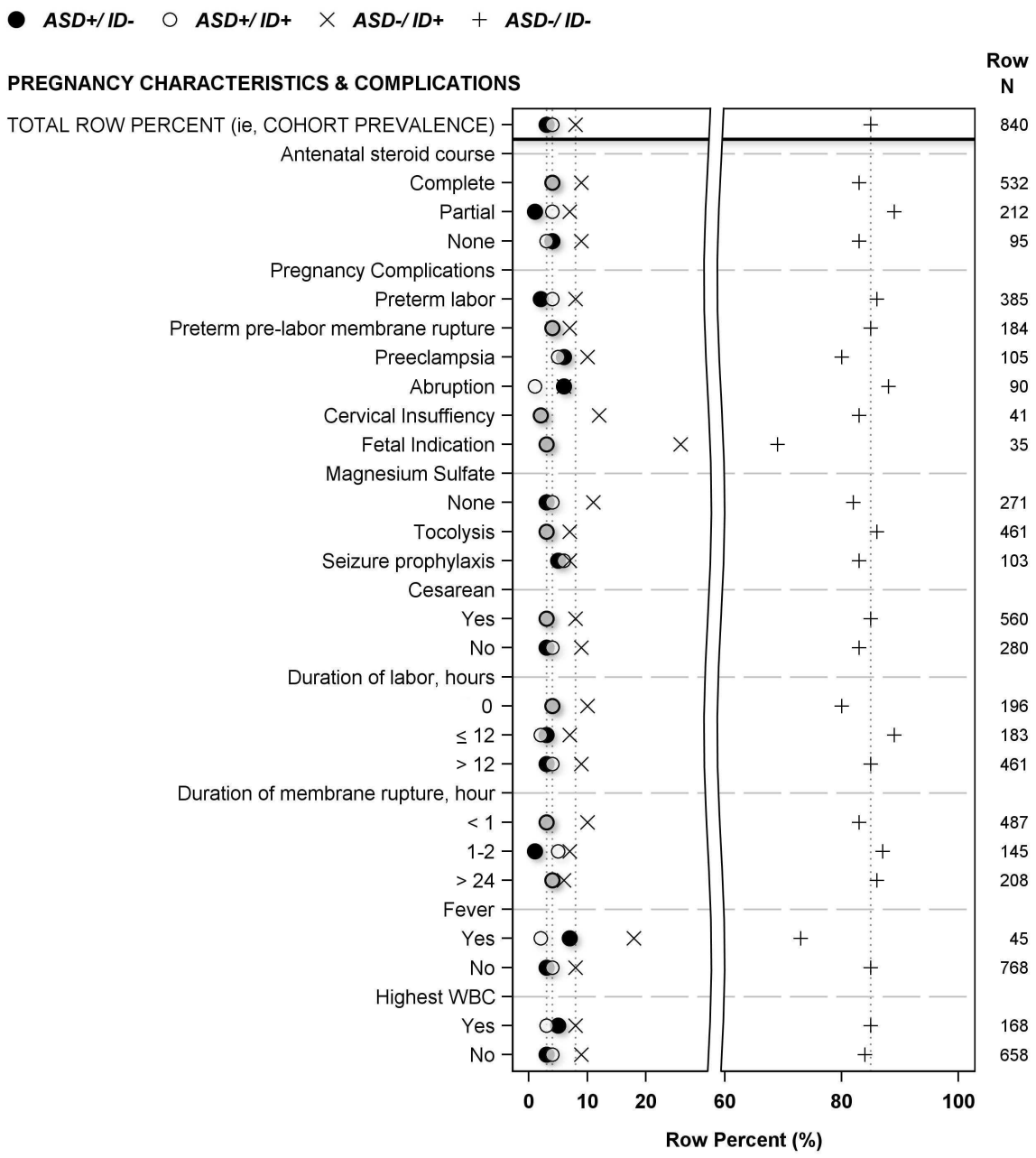
Percent of Children Exposed to What is Described on Left

Each Row Sums to 100%; Gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70)



Percent of Children Exposed to What is Described on Left

Each Row Sums to 100%; gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70);
** categories are not mutually exclusive*



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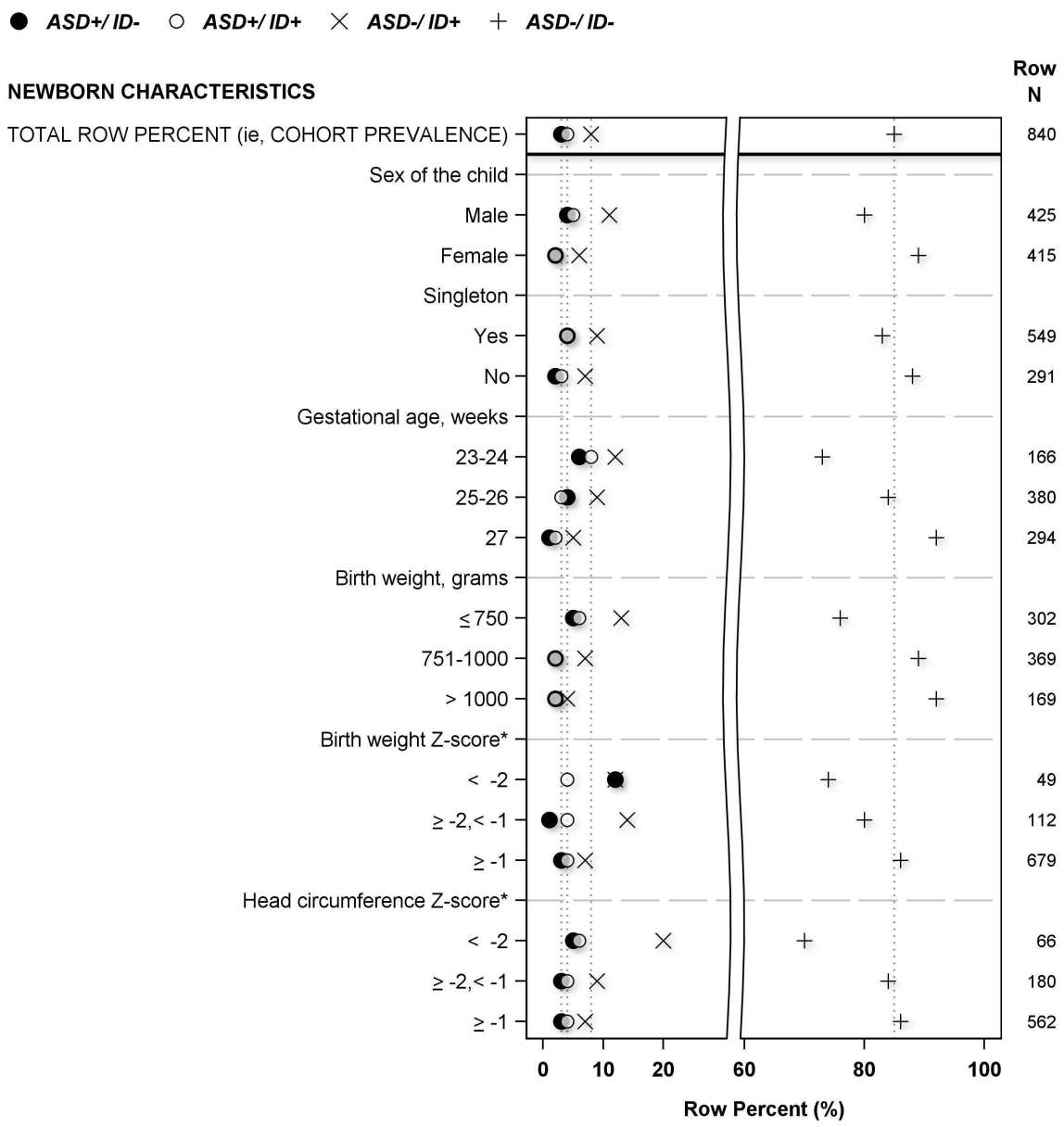

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Each Row Sums to 100%; gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70)

**External standard (Yudkin et al., 1987)*

Supplemental Methods. Antenatal, Perinatal, and Neonatal Variable Methods and Data Collection

Demographic, pregnancy, and delivery variables

After delivery, a trained research nurse interviewed each mother following a structured procedure. Maternal report of personal history, socio-demographics, exposures during pregnancy, and sequence of events leading to preterm delivery were accepted as the primary source when discrepant information was reported in the medical record. Previous research has shown that such information gained through self-report is more accurate than that obtained from medical records or birth certificates.(1-4) Following the mother's discharge, the research nurse reviewed the maternal chart using a structured data collection form to collect information about events after admission. The six initiators of preterm delivery (preterm labor, preterm premature rupture of the fetal membranes, placental abruption, cervical insufficiency, preeclampsia, and delivery for fetal indications) are defined elsewhere.(5)

Gestational age

The gestational age (GA) estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the dates of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14^{th} week (62%). When these were unavailable, reliance was placed sequentially on a fetal ultrasound at 14 or more weeks (29%), last menstrual period (7%), and GA recorded in the log of the neonatal intensive care unit (1%).

Birth weight Z-score

Birth weight Z-scores were calculated as the number of standard deviations each infant's birth weight was above or below the median birth weight in a referent sample that excluded pregnancies delivered for preeclampsia or fetal indications.(6, 7)

Score for Neonatal Acute Physiology II (SNAP-II^{TM})

We collected all the physiology, laboratory and therapy data for the first 12 neonatal hours needed to calculate a Score for Neonatal Acute Physiology II (SNAP-II^{TM}).(8)

Placentas

Delivered placentas were placed in a sterile exam basin and biopsied under sterile conditions. Eighty-two percent of the samples were obtained within 1 hour of delivery. The microbiologic procedures are described in detail elsewhere,(9, 10) as are the histologic.(9, 11)

Mode of ventilation

Mode of ventilation was defined as the highest level of support on each day and ranged from no support, increased ambient oxygen in a hood, nasal cannula, nasal continuous positive airway pressure, and conventional mechanical ventilation to high frequency ventilation. After the first week, this information was collected on days 7, 14, 21, and 28, and at 36 weeks post-menstrual age (PMA). We also recorded the number of days each infant received supplemental oxygen, continuous positive airway pressure (CPAP), and conventional mechanical ventilation (including high frequency ventilation). Details about blood gases obtained during the first three postnatal days and on postnatal days 7 and 14 are provided elsewhere,(12, 13) as are details about the three mutually exclusive respiratory dysfunction groups: consistently low fraction of inspired oxygen, pulmonary deterioration (PD), and early and persistent pulmonary dysfunction.(14)

Bacteremia

Documented early bacteremia was defined as recovery of an organism from blood drawn during the first week, and late bacteremia as recovery of an organism from blood drawn

during weeks 2, 3 or 4.(15, 16) We did not collect data on specific organisms recovered from blood. A diagnosis of a tracheal infection required the recovery of a pathogen from a tracheal aspirate. An infection (whether blood, trachea or CSF) was identified as clinically suspected if no organism was recovered and a clinician treated the baby with antibiotics.

Patent Ductus Arteriosis (PDA)

The diagnosis of PDA was assigned by clinicians without uniformity of definition; confirmation by echocardiography was recorded. Diagnoses of pneumothorax, pulmonary interstitial emphysema, and pulmonary hemorrhage were those made by the clinicians caring for the ELGAN.

Neonatal medications

Medications were recorded if given on any day during the first 28 days of life and included methylxanthines (aminophylline, theophylline, caffeine), analgesics (i.e., morphine, fentanyl, or methadone), sedatives (i.e., lorazepam, midazolam, or chloral hydrate), and steroids (i.e., hydrocortisone and dexamethasone). Information on class and dosage of medications was not collected.

Respiratory care

After discharge, details were collected about the apparent need for respiratory care at 36 weeks post-menstrual age (PMA) along with discharge diagnoses. The diagnosis of bronchopulmonary dysplasia/chronic lung disease (BPD/CLD) was based on receipt of supplemental oxygenation at 36 weeks PMA. Severe BPD was defined as receipt of both supplemental oxygen and mechanical ventilation assistance.(17, 18)

Necrotizing enterocolitis

The child's necrotizing enterocolitis status was classified according to the modified Bell staging system.(19)

Retinopathy

Retinopathy was defined within the 31st to 33rd post-menstrual week according to the guidelines of the International Committee for Classification of Retinopathy of Prematurity (ROP).(20) Follow-up exams were conducted as clinically indicated until normal vascularization began in zone lll of the retina.

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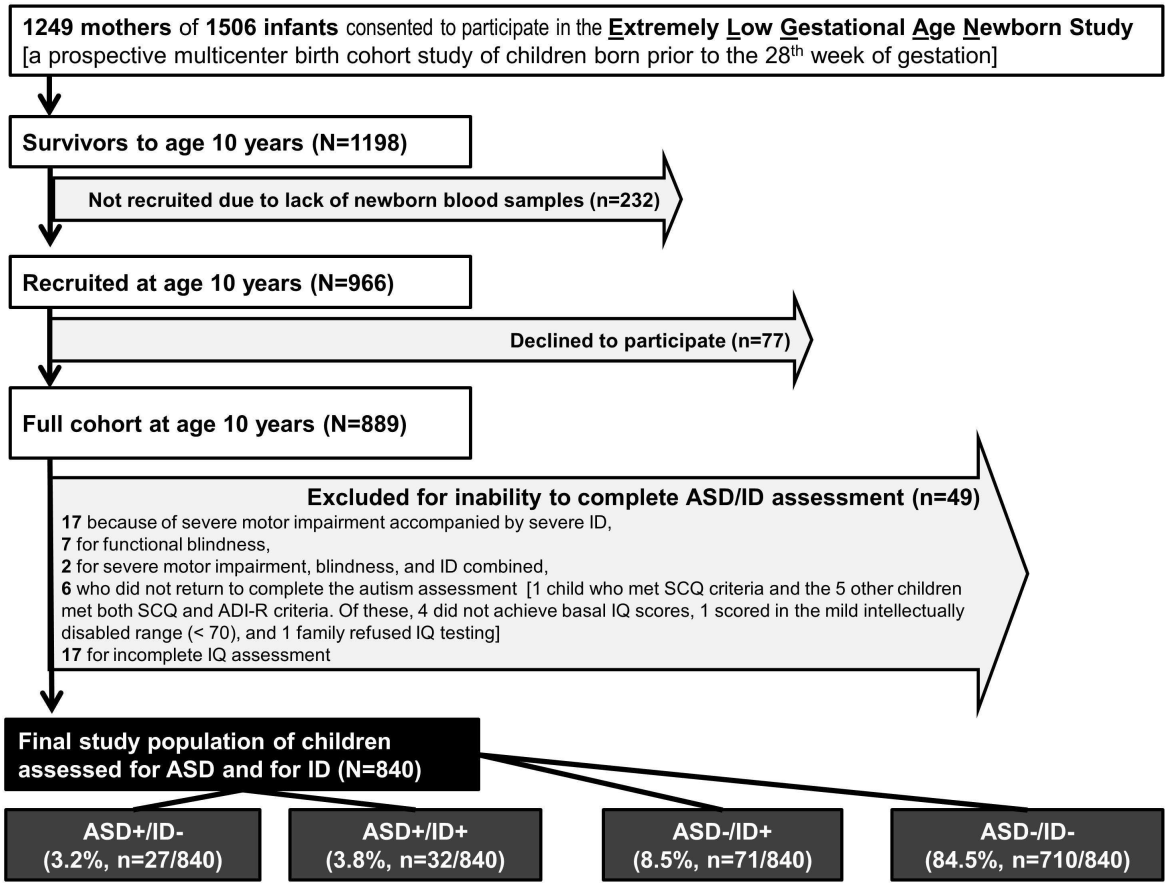
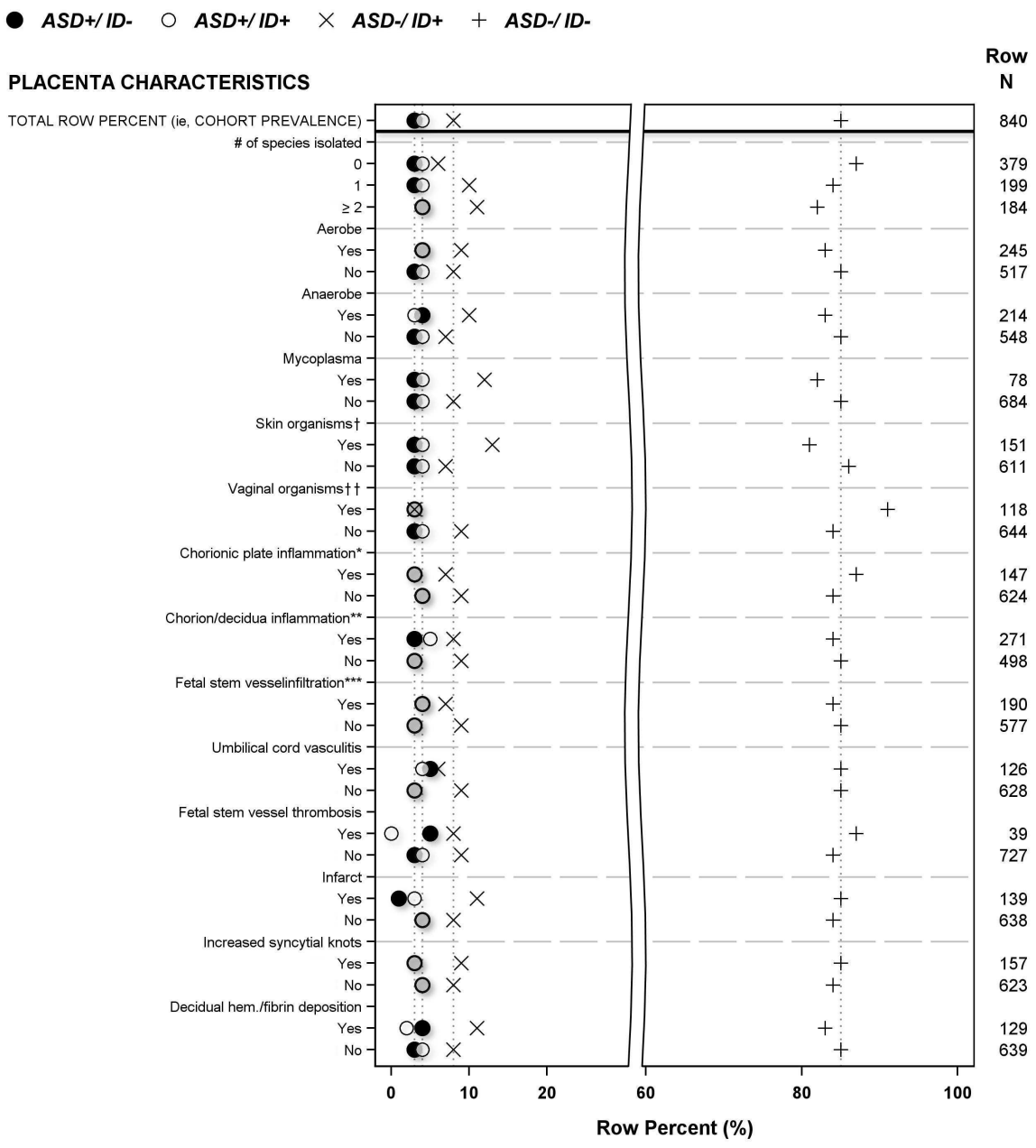

1249 mothers of 1506 infants consented to participate in the Extremely Low Gestational Age Newborn Study
[a prospective multicenter birth cohort study of children born prior to the 28th week of gestation]
Survivors to age 10 years (N=1198)
Not recruited due to lack of newborn blood samples (n=232)
Recruited at age 10 years (N=966)
Declined to participate (n=77)
Full cohort at age 10 years (N=889)
Excluded for inability to complete ASD/ID assessment (n=49)
17 because of severe motor impairment accompanied by severe ID,
7 for functional blindness,
2 for severe motor impairment, blindness, and ID combined,
6 who did not return to complete the autism assessment [1 child who met SCQ criteria and the 5 other children met both SCQ and ADI-R criteria. Of these, 4 did not achieve basal IQ scores, 1 scored in the mild intellectually disabled range (< 70), and 1 family refused IQ testing]
17 for incomplete IQ assessment
Final study population of children assessed for ASD and for ID (N=840)
ASD+/ID-
(3.2%, n=27/840)
ASD+/ID+
(3.8%, n=32/840)
ASD-/ID+
(8.5%, n=71/840)
ASD-/ID-
(84.5%, n=710/840)

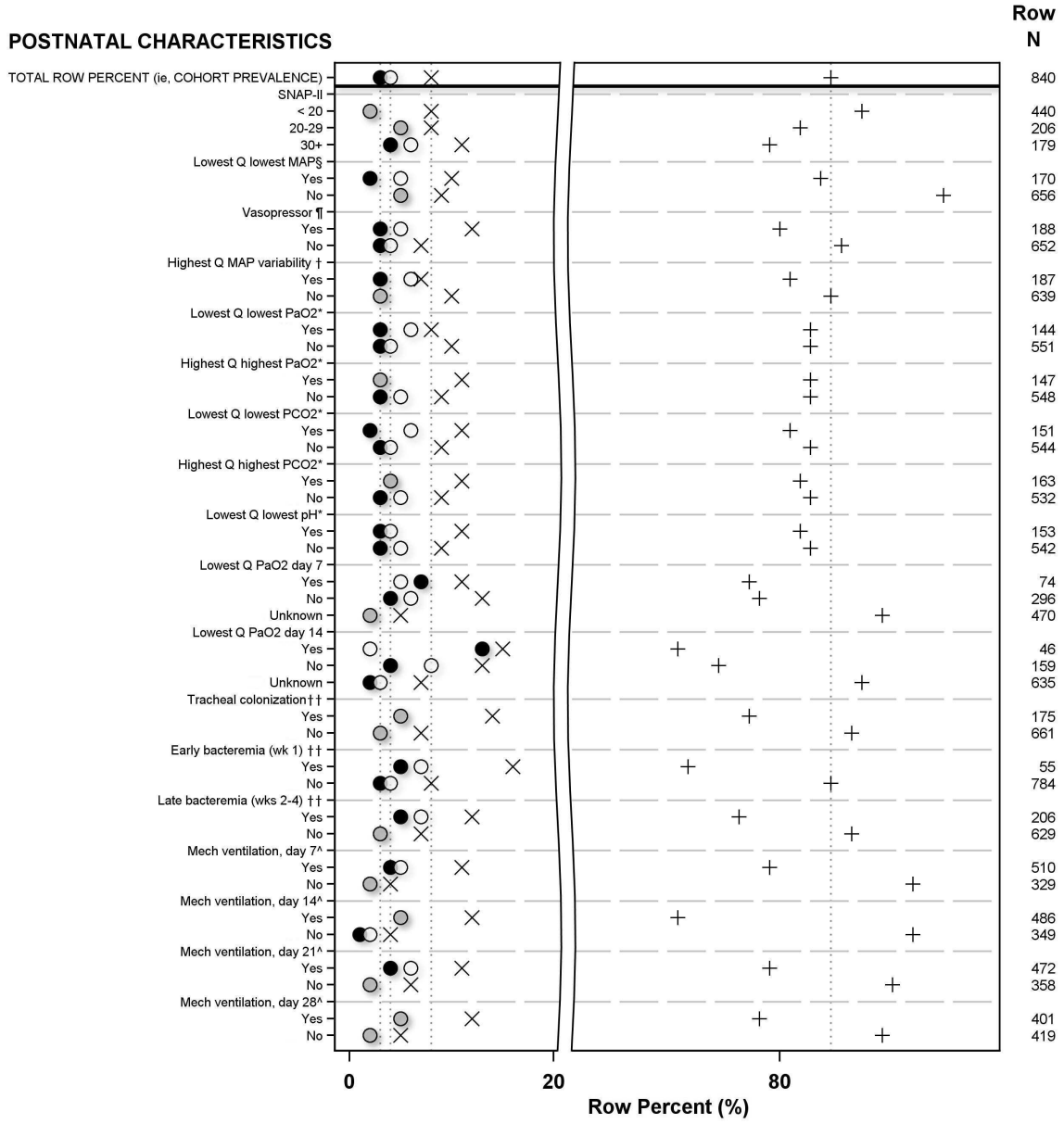


Percent of Children Exposed to What is Described on Left

*†Corynebacterium sp, Propionebacterium sp, Staphylococcus sp;††Prevotella bivia, Lactobacillus sp, Peptostrep magnus, Gardnerella vaginalis; *stage 3 and severity 3;** grades 3 and 4;***grades 3, 4 and 5*

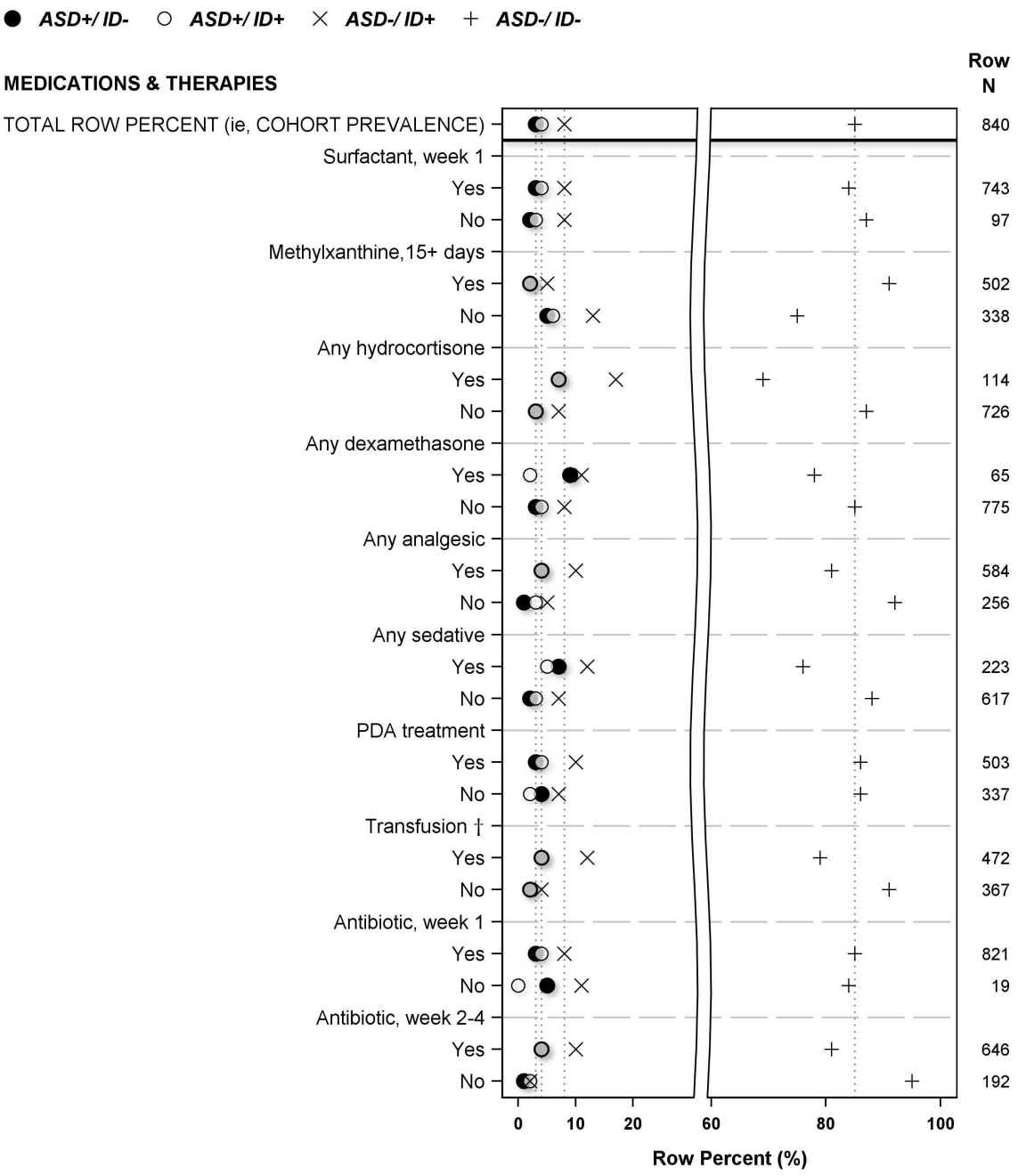
Each Row Sums to 100%; Gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70)

● *ASD+/ ID-* ○ *ASD+/ ID+* × *ASD-/ ID+* + *ASD-/ ID-*



Percent of Children Exposed to What is Described on Left

*§ Lowest MAP recorded in first 24 hours, in the lowest quartile for gestational age; ¶ Vasopressor treatment for hypotension in the first 24 hours(dopamine, dobutamine, epinephrine); †Labile MAP: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP; *extreme quartile for gestational age on two of the first three postnatal days;†† Definite/culture proven; ^Includes conventional and high frequency ventilation*
Each Row Sums to 100%; Gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70)



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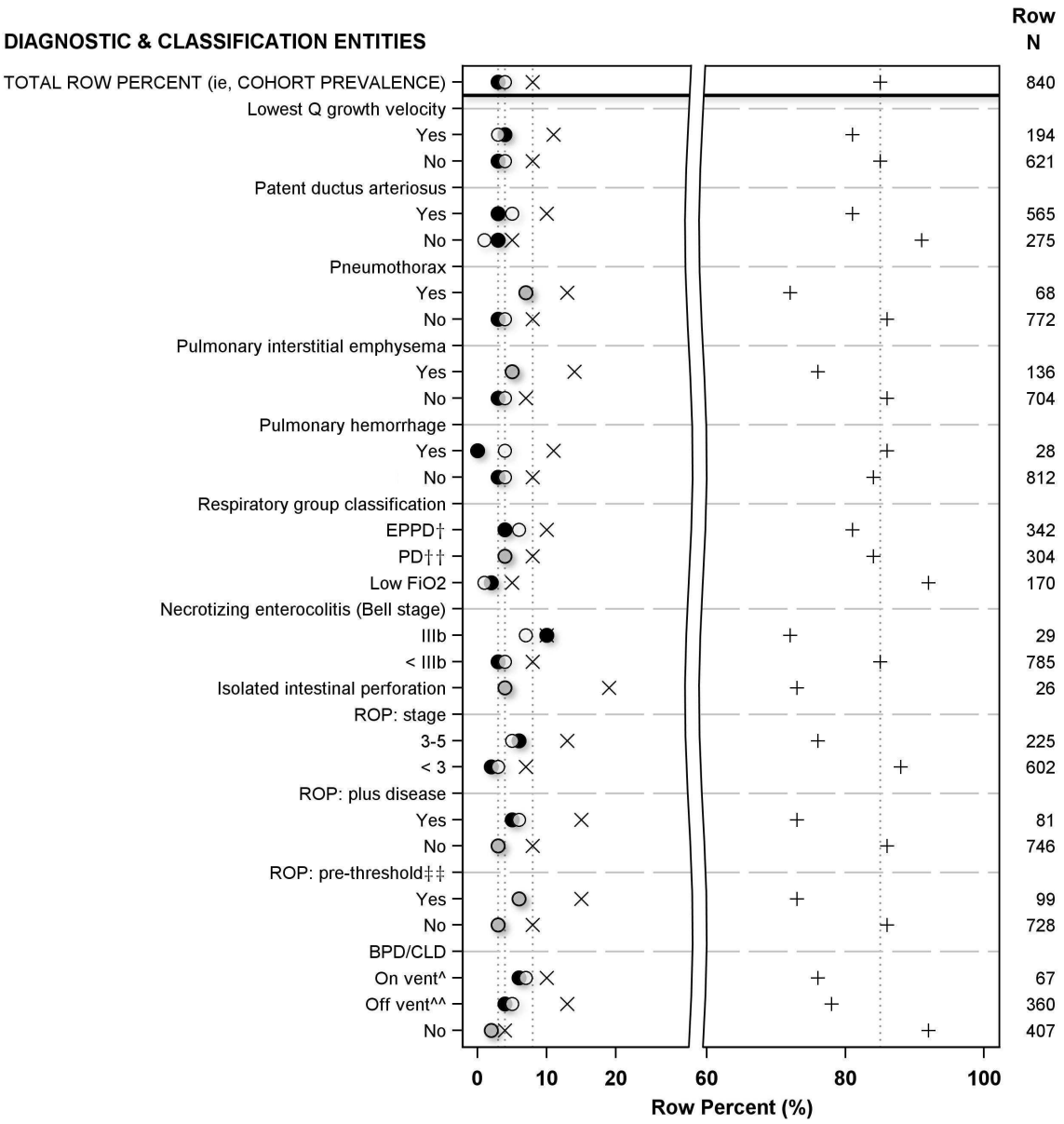
● *ASD+/ ID-* ○ *ASD+/ ID+* × *ASD-/ ID+* + *ASD-/ ID-*



Percent of Children Exposed to What is Described on Left

§ Pulmonary interstitial emphysema; † early and persistent pulmonary dysfunction;†† pulmonary deterioration; ‡‡ satisfied ET-ROP criteria for ablative surgery (pre-threshold disease);^ on ventilator as well as oxygen at 36 weeks post-menstrual age;^^on oxygen, but not on ventilator at 36 weeks post-menstrual age

Each Row Sums to 100%; Gray circles indicate overlap;ASD, autism spectrum disorder; ID, intellectual disability (IQ<70)