

SUPPLEMENTAL DATA

1. Target Population

The target population included all 55,266, 7- to 12-year-old children in Ilsan District, Goyang City, who were identified through the elementary school system and a government disability registry. Ilsan is located near Seoul in Kyunggi province and was selected as the target area because its population is stable and representative of the general Korean population. Ilsan is part of the capital region that includes Seoul, Incheon and Kyunggi province and in which 49% of the total population of South Korea resides (1).

- a. Elementary Schools in Ilsan: There are 41 regular (mainstream) education elementary schools in Ilsan District and three special education elementary schools in Goyang City as a whole (two in Ilsan District and one in Dukyang District). Elementary and middle school education is mandatory in Korea and all children are assigned to schools by the government offices in the district in which they reside. All children are accounted for as school registration is checked against birth records. As a result, all school-aged children can be identified through school system.

In order to gain admission to a special education school, a student must apply for and receive a certificate of disability registry enrollment. A student can also obtain admission if the principal from the student's referring school makes an official recommendation for special education services. The government does not require students to attend a special education school in the same district in which the child receives disability certification. For the purposes of this study, only children actually residing in the target area were included, irrespective of school attended. The percentage of students who attended special education schools or classes was 0.8% in the target area; this is comparable to the rate of special education enrollment nationally (0.73%–75%) for South Korean elementary school-aged children during the study period (2).

Since home schooling is rare in Korea (there are fewer than 5,000 home-schooled children in the entire country (3)), these children were not specifically sampled unless they were also in the disability registry.

- b. Disability Registry (DR): The Goyang Department of Welfare maintains the Ilsan DR, a confidential list of children with physical disabilities (e.g., cerebral palsy, hearing and visual deficits, etc), psychiatric disabilities (e.g., schizophrenia, Autism Spectrum Disorder (ASD), etc), and cognitive deficits. The type and severity of disability is recorded in the DR after clinical assessments by psychiatrists (for ASD or Intellectual Disability (ID)), or rehabilitation doctors (for ID), with standardized tests, such as IQ measures. In order to remain on the registry, a child must be re-evaluated every 2 years. Families must initiate the process of enrollment in the DR and can request to be removed at any time. Based on a family's economic resources and the level of disability, enrolled families may receive modest financial support for daily living, educational and medical services, and public transportation (4).

2. Establishment of Community Partnership

Investigators cultivated relationships with research participants and established enduring community partnerships through ethnographic interviewing, meetings and informational lectures.

- a. Board of Education of Goyang City: Investigators contacted the Board of Education of Goyang City to explain the research aims and protocol in September 2005, and subsequently established what is now a long-standing, research partnership. With the Educational Board's guidance and support, investigators subsequently met with the teachers' union, principals, vice-principals and health education teachers at the schools in order to introduce the survey and address their questions and concerns. While the survey was progressing, the investigators maintained regular contact with the Educational Board to discuss and resolve any concerns about parent or teacher participation, to report on the survey progress and preliminary findings, and to provide educational sessions for the staff.
- b. Goyang City Hall: In May 2008, investigators contacted the public officials in City Hall who were responsible for the DR in order to describe our survey and asked for assistance. They agreed to provide the number of children born between 1993 and 1999 who were enrolled in the DR, under the categories of ASD and/or ID, and to send letters to these children and their families inviting them to participate in the research study.
- c. Parents and teachers in Goyang City: Investigators led by the anthropologist on the team (RRG) conducted a series of focus group meetings with parents and teachers to assess potential problems, to identify local beliefs that might influence symptom reporting, and to address stigma and misunderstandings related to ASD. The groups discussed the purposes of the study, risks and benefits to the participants, the language used in the research protocol and informed consent forms, and the specific instruments to be used. Feedback from the focus groups was used to guide and revise study procedures in order to ensure maximal participation and success.
 - 1) *Parent Focus Group Meetings*: Three meetings with parents were conducted in December 2005, including parents of the children with ASD, referred from local hospitals and parents in support groups for children with ASD (N=16). These meetings yielded suggestions about how investigators conveyed the purposes of the research, most of which were implemented: i) Given the stigma associated with psychiatric disorders, we communicated about the study with colloquial language, such as "difficulties in social relationships" or "peer relationships" and we limited the use of medical terminology, including "autism" and "ASD;" ii) we made a substantial effort to repeatedly and explicitly state how confidentiality of the data would be maintained; and, iii) we communicated the results of the screening and diagnostic tests to the families during feedback sessions.
 - 2) *Teacher Focus Group Meetings*: Four meetings were also conducted with teachers from three regular (regular education schools: RES) and one special education school (SES) (N=31). Teachers expressed their concerns about three issues: i) confidentiality of the test results; ii) increase in workload associated with completing screening questionnaires for all students in their classes; and, iii) lack of intervention assistance in their classrooms for children with confirmed diagnoses. We addressed each of these concerns with teachers during the survey processes and provided follow-up sessions regarding medication and basic behavioural management on request.

3. Incentives for the Study Participation

Focus groups indicated that payment for participation would be culturally inappropriate. Instead, study participants were provided with following incentives:

- a. Screening results with general interpretation of the scores were provided to the parents who consented to participate in the study. This was done at no cost to the family.
- b. A complimentary feedback session was provided for the parents who completed the comprehensive diagnostic assessment. During this feedback session, results of the tests, including ADOS, ADI-R and IQ, were explained, and information about ASD, including available resources for services and intervention in the community, was provided.

4. Translation and Validation of Screening and Diagnostic Instruments

Many survey questionnaires and diagnostic instruments developed and used in the US and/or Europe have been translated, back-translated and adapted for use in the Korean population without difficulty (5–7).

- a. Autism Spectrum Screening Questionnaire (ASSQ): During the screening stage, parents and teachers at participating schools completed the ASSQ for their students/children. The ASSQ has 27 items that measure social interaction, communication problems, restricted and repetitive behaviors, motor clumsiness and associated features (8). The ability of the ASSQ to distinguish autism from other diagnoses is well-established, with cut-off scores of 13 for parent ratings and 11 for teacher ratings, as established for European children(9). The ASSQ was translated and back-translated by the investigators. To maximize screening sensitivity, for our study, the cut-off scores were: Parental ASSQ scores \geq upper 5th percentile; Teacher ASSQ scores ≥ 10 .
- b. Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS): The current gold-standard diagnostic assessment for ASD includes both the ADI-R and the ADOS. These instruments make independent, additive contributions to the judgment of clinicians that result in a more consistent and rigorous application of diagnostic criteria (10). The ADI-R is a standardized, clinician-administered interview of caregivers for individuals with autism. The ADOS is a clinician-administered, semi-structured, patient observation that is designed to elicit specific social and communicative behaviors. The ADI-R and ADOS were translated into Korean and back-translated by the investigators, including child psychiatrists, clinical psychologists and developmental psychologists. The back-translated versions were reviewed and reconfirmed by a team of US child psychiatrists and psychologists who have extensive experience with the instrument. A pilot study of 71 ADOS and 63 ADI-R administrations was performed with Korean children with ASD; it resulted in kappa values for diagnostic validity of 0.795 and 0.714, respectively, indicating very good agreement between expert clinical judgment and our Korean versions of the ADOS and ADI-R (11). These results are comparable to US and UK studies (12, 13).
- c. IQ measures: The Korean-Wechsler Intelligence Scale for Children-III (K-WISC-III) for verbal children and the Leiter International Performance Scale-Revised (Leiter-R) for nonverbal children were administered to assess level of cognitive function. These instruments have been standardized and their reliability and validity were established; they are widely used to examine Korean children for clinical and research purposes (14, 15). To avoid the problem of using misleading, full scale IQ scores for children with scattered skills and significant differences between verbal and performance IQ scores, performance

IQ scores were used to represent cognitive level of the subjects. This method is analogous to using nonverbal intelligence measures, such as the Leiter -R for nonverbal, speech delayed, or hearing or speech-impaired children.

5. Screening

- a. School Systems: For this study, the Goyang Board of Education sent two separate formal letters inviting the principals and vice principals in all forty-four elementary schools in the target area to participate in the research; ultimately, thirty of 41 RES and all three SES agreed to participate in the study.

Participating schools sent an informational letter to parents, describing the ASD survey, along with a copy of the ASSQ. Parents were asked to return the completed ASSQ report on their child and to give written consent and permission for the research team to contact them if their children were “screen-positive.”

In addition, our research team provided informational lectures on ASD during weekly in-service teacher training programs at the participating schools. These included videotapes and information on the clinical manifestations of ASD. Teachers were also given an opportunity to discuss the study and their students with the research team. In order to increase response rates, validity and efficiency of the survey, teacher ASSQ’s were completed immediately after the educational sessions. For each child who fit even a single ASSQ item, teachers were asked to complete the ASSQ. No ASSQ return was required for those children who did not fit any item in ASSQ. For the purposes of this study, children for whom we did not receive a teacher ASSQ were automatically considered to be “screen-negative,” unless parent data or other information were received and suggested otherwise.

There were 311 children with both parent and teacher ASSQ scores. These scores were only modestly correlated ($r=0.36$, $p<0.01$); agreement for a positive screen between teachers and parents was only 46%, affirming the value of multi-informant screening because each reporter provides distinct information.

- b. DR: Invitation letters were mailed from the Goyang City Hall to the families of the children on the Disability Registry. The letter asked parents to give written consent and permission for the researchers to contact them directly or for the parents to contact the research center, if they wanted to participate in the study.

6. Quality Control of Best Estimate Diagnoses:

- a. ADOS and ADI-R: An independent, University of Michigan Autism and Communication Disorder Center (UMACC)-certified ADOS and ADI-R trainer (YSK) trained and established reliability for the administration and coding of the ADOS and ADI-R with two other Korean investigators (YJK and ECL). Optimal reliability for the ADOS and ADI-R (80% and 90% coding agreement, respectively) was monitored and maintained throughout the survey by holding annual on-site booster training sessions, and randomly checking reliability of one ADOS/ADI-R out of every 10–15 administrations.
- b. Best Estimate Diagnoses: Two Korean teams, who were independent of the original evaluators, generated best estimate diagnoses. Clinicians on each team had an average of 10 years of experience working in the area of ASD, three were ADOS and ADI-R research reliable with the gold-standard, UMACC, and one completed ADOS and ADI-R research training. YS Kim and SJ Kim were trained in the US and Korea and have 16

years and 11 years of clinical experience in ASD, respectively. KA Cheon and YJ Koh were trained in Korea and have 11 years and 8 years of clinical experience in ASD, respectively. The experts who reviewed the seven cases (2%) for which there was persisting disagreement were North American senior investigators (BLL and EF). BLL has 35 years of clinical and research experience in ASD, leads state-wide ASD program in Illinois (The Autism Program: TAP) that provides clinical service for patients and training for service providers, and is a member of the research team that developed the ADOS. EF is an ADI-R and ADOS trainer, has 25 years of clinical and research experience in the field and leads a busy clinical service in a tertiary pediatric hospital. Thus, best-estimate diagnoses were made by skilled, experienced clinicians who were reliable to the UMACC standard. North American experts on the team were established clinical and academic leaders in the field of autism.

In addition, 49 randomly selected cases completed by the two Korean diagnostic teams were blindly reviewed by the North American experts on the team for validation of the diagnoses. Written case summaries in English were prepared for each of the 49 cases, including developmental, medical and school histories, as well as ASSQ, IQ, ADOS and ADI-R scores. Descriptive vignettes from the ADI-R and ADOS were also provided to the experts to assist in determining best estimate diagnoses.

For these reviewed cases, there was complete diagnostic agreement between the two North American experts with regard to the presence of any ASD; there were minor discrepancies in the classification of ASD subtypes with 86.5% overall agreement for both AD and the OASD subtype. There was 93.9% diagnostic agreement regarding the presence or absence of any ASD between Korean diagnostic teams and the North American experts, with a kappa of 0.75, indicating very good agreement (see Table S1).

TABLE S1. Agreement of Best-Estimate Autism Spectrum Disorder (ASD) Diagnosis Between South Korean and North American Diagnosticians (N=49)

North American Team	South Korean Team		Total
	Any ASD	No ASD	
Any ASD	36	1	37
No ASD	2	10	12
Total	38	11	49

7. Missing data - ASSQ

Values for the missing pages were imputed using the scores from the completed page in three different ways:

- Simple Weighted Average - by multiplying the mean item score of their completed page by 27 (number of items in ASSQ);
- Regression - for each grade and sex, data from complete ASSQ forms were used to obtain a regression on the mean score for page 2, as a function of the mean scores on page 1, and vice versa. These were used to impute the missing ASSQ scores for subjects with incomplete data.
- Hot-Deck Imputation - all subjects were divided into two groups, complete questionnaire or incomplete questionnaire with a missing page. These groups were further subdivided by

their grade and sex. For each grade and sex, subjects with complete ASSQ data were matched to subjects with incomplete data, based on the similarities of the scores on their completed pages, and the scores from the matching complete data were assigned as the scores of the missing page for incomplete data.

The correlations between ASSQ total scores computed with these three imputation methods were statistically significant ($r=0.998$ for 1st and 2nd method, 0.898 for 2nd and 3rd method, and 0.897 for 1st and 3rd method).

Among the computed ASSQ scores from these three methods, the highest score was used as the imputed ASSQ scores. The strategy was designed to maximize the sensitivity of the screening process. To the upper 5th percentile screen-positive subjects already identified among ASSQ completed without missing pages, we added a total of 264 subjects whose imputed value exceeded the cut-point of 14.

8. Adjustment for Nonrespondents in Participating Schools

Only grade information was available for nonrespondents in participating schools. Nonparticipation by grade ranged from 28% to 46%. Since grade was not a significant predictor of being screen-positive, consenting, or diagnoses of ASD (see 10, below), it is considered acceptable to use a simple weigh-back procedure to adjust for nonrespondents in participating schools.

9. Adjustment for Children in Nonparticipating Schools

There were no significant differences between participating and nonparticipating schools, thus allowing a simple weigh-back procedure. Similarities between participating and nonparticipating schools included the total number of students (including male and female students), number of students attending resource classrooms for special needs children and, the number of teachers working in these classrooms, and the number of low income families.

10. Adjustment for Screen-Positive Nonparticipants in RES

Only a subset of the screen-positive children was fully evaluated because some parents either declined to give consent or, if they gave consent, they did not come for the confirmative evaluation. To determine how to handle these missing data in estimating RES prevalence, it was hypothesized that there exists in each child's parents a latent variable that cannot be directly measured but represents parental willingness to further participate in the diagnostic process. If this variable is independent of disease status, then the observed ASD diagnosis rates in the group of children completing confirmative diagnostic assessments provides a reasonable basis for a suitably weighted estimate of prevalence in the entire screen-positive group in RES.

Observed behaviors clearly related to the "parental willingness latent variable" are 1) consenting to the full evaluation; and 2) participating in the full evaluation. A logistic regression model was fit for each of these binary outcomes, using parental ASSQ scores and child's sex and age as covariates. The results were:

$$\begin{aligned}\text{Log(Prob(Consent|Screen Positive))} &= -2.71 + 0.13^* \text{ASSQ} + 0.19^* \text{Sex} - 0.05 \text{Age} \\ \text{Log(Prob(Evaluation|Consent))} &= -1.23 + 0.03^* \text{ASSQ} + 0.13 \text{Sex} - 0.14 \text{Age}\end{aligned}$$

Coefficients marked with an asterisk are statistically significantly different from zero (using Wald test with two-tailed alpha level 0.05). A higher ASSQ score and being a boy, among screen-positive children, predicted a higher likelihood of parental consent to participate in the study. Among those children for whom consent was given, a higher ASSQ score predicted a higher likelihood of completing a confirmative evaluation.

Two predictive scores, surrogate measures of the latent variable, were computed for each child by substituting their ASSQ score, sex and age into the logistic regressions. A logistic regression model was fit to predict whether a child who was fully evaluated had a diagnosis of ASD or not, using parental ASSQ scores, child's sex, age, and the two surrogate measures of the latent variable predicted from the two previous logistic regressions as covariates. None of the regression coefficients differed statistically from zero. That is, the probability of an ASD diagnosis does not depend on the parents' latent variable, the ASSQ score, child's sex or grade. Thus, while the value of the latent variable measuring parental willingness to expose their child to the risk of a positive ASD diagnosis may vary, it is uninformative as to whether the child has the diagnosis among the screen-positive (RES upper 5th percentile on ASSQ score) population. Thus, it is reasonable to infer that the likelihood of diagnoses of ASD among those children who were not definitively evaluated is not different from those 234 children who had a full confirmative diagnostic assessment. As a consequence, a simple, proportional weigh-back procedure was used to compute the estimate of prevalence for the RES.

The pattern of consenting and coming to the full assessment for those individuals whose ASSQ scores were imputed, and fell within the screen-positive range, was substantially different from those whose ASSQ were completed without missing pages. Nevertheless, among those with imputed scores who completed full assessment, the rate of caseness was essentially identical to those whose ASSQ was complete. This further reinforces the independence of the caseness and the parent's latent trait of willingness to participate in the diagnostic process. Therefore, these screen-positive individuals, based on their imputed ASSQ scores were included in the rate used to estimate the population prevalence for the RES.

11. Adjustment for Sampling Procedure

- 1) No weigh-back procedure for sampling was required for screen-positive DR/SES children, all teacher-screen-positive children, and/or all children in the top 2nd percentiles of parental ASSQ scores.
- 2) A two-fold weigh-back procedure was required for students in the 3rd percentile of parental ASSQ scores because we only sampled 50% of this group.
- 3) A three-fold weigh-back procedure was required for students in the 4th and 5th percentiles of parental ASSQ scores because we only sampled 33% of this group.

TABLE S2. Mean Age of Children at Time of Screening, by Cohort Year

Cohort Year	Children in Disability Registry/Special Education Schools (N=103)		Children in Regular Schools (N=23,234)		Total (N=23,337)	
	Mean	SD	Mean	SD	Mean	SD
1993	12.0	0.0	11.9	0.3	11.9	0.3
1994	11.7	0.5	11.2	0.5	11.2	0.5
1995	10.7	0.7	10.3	0.5	10.3	0.5
1996	9.8	0.4	9.3	0.5	9.3	0.5
1997	8.8	0.4	8.3	0.5	8.3	0.5
1998	7.6	0.5	7.3	0.5	7.3	0.5
1999	7.0	0.0	6.5	0.5	6.5	0.5
Total	9.5	1.7	9.1	1.7	9.1	1.7

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