**ON-LINE APPENDICES**

**Appendix 1 – Codes used to define comorbid psychiatric conditions and mental health visits**



**Appendix 2 – List of targeted psychotropic medications in this study, by class**

Includes medications not observed. Only generic names provided; brand name products, combination products, and minor variations in formulation (e.g., valproate, valproic acid, divalproex) were included in the study, but are not necessarily listed below, for simplicity.



**Appendix 3 – Detailed results on use in 2010 of the 4 major therapeutic categories, by ASD vs no ASD, age, and sex.**



Notes: \* small cell count, <6 individuals.

**Appendix 4 – Specific medications most frequently dispensed to children with ASD in 2010, overall and by sex**



Additional specific drug entities observed but each representing less than 0.2% of all fills received were: clozapine; chlorpromazine; paliperidone; alprazolam; haloperidol; zolpidem; clorazepate; modafinil; thioridazine; loxapine; pregabalin; temazepam; perphenazine; asenapine; divalproex; eszopiclone; pimozide; prochlorperazine; thiothixene; tiagabine; triazolam.

**Appendix 5 – Sensitivity analyses considering earlier ASD diagnoses**

Our main study cohorts used a relatively strict, short-view design for cohort assignment, requiring 2 ASD dx (cases) or no ASD dx (controls) in 2009-2010. By considering only recent diagnoses, our intent was to better ensure that ASD cases were valid and current. All study design decisions trade off advantages and disadvantages. One limitation of the short-view design we selected was that we likely excluded many still-valid ASD cases whose diagnoses were recorded in earlier years. Qualifying diagnoses in our main design include both first-time and follow-up ASD diagnoses.

Our sensitivity analyses, by contrast, used a longer-view design with diagnostic qualification based on all available records between 2000 and 2010. Subjects were all required to have enrollment and 2 health system contacts in 2009-2010, as in the main analyses. In addition, ASD cases were required to have one diagnosis of ASD in 2000-2009 and at least one additional ASD diagnosis in 2000-2010. Controls had no ASD diagnoses in 2000-2010. We attempted to match children 10:1 (non-ASD to ASD) on age, sex, 2009 enrollment quarters, and total 2000-2009 enrollment quarters. A full complement of 10 matches was not available for every case; we retained all 12,633 cases and 124,443 available matches. We repeated all study analyses using these longer-view cohorts.

The longer-view cohorts were each 60% larger than the cohorts in the main analyses presented in the paper. As we expected *a priori*, more older children, in particular, with ASD were identified: those aged 8-17 represented 78.5% of the added cases. We further observed that 771 children (out of 79,010) classified in our main analyses as having no ASD had actually received one or more ASD diagnoses prior to 2009. To the extent that those 771 ASD cases may have still been valid in 2010, their misclassification in our main analyses represents an additional study limitation. We present the sensitivity analyses in this appendix with an aim to be transparent, instructive, and balanced.

Appendix Table 5.a. – Characteristics of shorter- and longer-view cohorts compared



In general, study results were similar and remained statistically significant in the longer-view cohort analyses, though differences between children with and without ASD were attenuated. This was expected, because the case definition was relaxed. The more flexible qualification period was likely to have added, in particular, cases with less severe autism symptoms, cases in less need of medical treatment of any kind (zero or only 1 ASD diagnosis recorded in 2009-2010), cases receiving ASD-related services only in other settings outside of the health system site, and cases whose earlier ASD diagnoses had been revised or resolved.

Appendix Table 5.b. – Selected results compared between shorter- and longer view cohorts



As context for these cohort designs, the population of all children aged under 18 with any 2010 enrollment at the 5 study sites was 1,928,858. Based on all available medical and billing records (some as far back as 1996), the lifetime completeness of which varies greatly among individuals, and based on the same case algorithm as used in the study (2+ ASD diagnoses, or 1+ KPNC autism clinic diagnosis), a total of 18,951 ASD cases were identified, for a crude prevalence rate of 9.7 per 1000, which is consistent with other epidemiological research on ASD. Only 12,633 cases qualified for the sensitivity analyses described above because of additional criteria required (e.g., post-1999 ASD diagnoses; community-dwelling; minimum months enrolled and clinical contacts in 2009-2010).