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Science Advances

Dear Editor

Please find enclosed the revised manuscript entitled "**Reduced False Positives in Autism Screening Via Digital Bio-markers Inferred from Deep Co-morbidity Patterns**" for your consideration for publication in Science Advances as an original article. We have meticulously addressed the points raised by the reviewers, and highlighted changes in the main and Supplementary text in red.

Autism spectral disorder (ASD) is currently screened for in toddlers using standard questionnaires, *.e.g.* M-CHAT/F with a high number of false positives (85%) and a low sensitivity (38%) – translating to long wait-times for confirmatory diagnosis ($\approx$ 1 year). Children lose crucial time within which interventions are the most effective. Additionally, questionnaires are prone to interpretive biases leading to systematic under-diagnosis in diverse communities.

Here we report an orthogonal methodology that requires **no questionnaires or blood-work**. Using novel stochastic learning on individual diagnostic codes already recorded during past doctor's visits, we design a risk estimator significantly out-performing the state-of-the-art. Without pre-selecting co-morbid disorders, we learn hidden patterns in medical histories to enable cutting down false positives by upto half without losing specificity. Additionally, we get new insights into co-morbid risk that might shed light into ASD pathobiology.

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We are led by a multi-disciplinary team of machine learning experts (Chattopadhyay PH. 8145315312) and clinical practitioners with substantial scholarly work in pediatric developmental psychology and autism: 1) Peter J. Smith, Professor of Pediatrics and **Executive Committee Chair, American Academy of Pediatrics' Section on Developmental & Behavioral Pediatrics**, and 2) Prof. Michael Msall, **Section Chief of Developmental & Behavioral Pediatrics, UChicago, and Fellow of Joseph P. Kennedy Research Center on Intellectual & Neurodevelopmental Disabilities, UChicago**.

We look forward to, and humbly hope for, your positive response.

Sincerely,

Ishanu Chattopadhyay
Chicago, IL

Thursday 1st April, 2021