Female Protective Effect
The female protective effect (FPE) has been hypothesized to explain the sex ratio discrepancy (i.e., 4:1) in prevalence estimates of ASD. While there is general consensus regarding the presence of an FPE, how it manifests early in development is unknown. We examined whether the FPE exerts influence in an all-or-nothing type manner as opposed to exerting influence along a gradient in 6-24 month-olds. More specifically, we compared adaptive behavior development across groups stratified by sex, diagnostic status, and concerning social-communicative behaviors. We analyzed data from 481 children recruited from the IBIS network, who contributed a total of 1665 assessments.

Does sex differentially influence behavioral trajectories in HR infant siblings with ASD, social-communicative concern, and typical outcomes?

Sample Stratification
Clinically informed outcomes were defined using 24-month data:

- Autism Spectrum Disorder (ASD)
  - ASD/PDD-NOS DSM-IV Clinical Best Estimate Diagnoses
- Non-ASD
- Typical Development (TD)
- Subthreshold Social-Communicative Concern (SCC)
  - Mullen Scales of Early Learning
    - Expressive Language T < 40 or…
    - Receptive Language T < 40 or…
  - Autism Diagnostic Observational Schedule
  - Social Affect > 6

Vineland Adaptive Behavioral Scales (VABS)
Each infant had repeated parent report measures of child's adaptive level of functioning across multiple domains including communication, socialization, daily living, and motor skills.

Analytic Approach
- FPEs may be evident developmentally through:
  - Sex-specific differences in subgroup behavior
  - Distinct relative-risk ratio patterns
- Five Linear Mixed Effects (LME) models were fit to each VABS subscale and composite to capture development of adaptive behavior
  - Predictors: age, group, sex, and their interactions

\[ \text{VABS}_{abc} = \beta_0 + \beta_1(\text{sex}) + \beta_2(\text{group}) + \beta_3(\text{month}) + \beta_4(\text{group}) + \beta_5(\text{month}) + \epsilon \]

- Benjamini-Hochberg correction for pairwise comparisons
- Relative Risk (RR) Ratios comparing emergent sex ratios of the outcome groups HR-ASD and HR-SCC to HR-TD

The sex discrepancy between in ASD is maintained in our HR sample, supporting a FPE hypothesis. There is only a trend towards a sex discrepancy for SCC, despite developmentally distinguishable differences between groups by 12 months in multiple adaptive behavior domains and entirely distinguishable across all adaptive domains by 24 months. There was no group x sex interaction.

Sex may protect from diagnostic-levels, but not subclinical-levels, of concern

Next Steps
- Compare with empirically driven stratification through growth mixture models
- Extend to subcortical and cortical measures of brain growth