# To add to notes

* Genetics
  + MDD GWAS: (Howard et al., 2019)
  + PTSD GWAS: (Nievergelt et al., 2024)
* Methods
  + (Zheng et al., 2024)
  + (Hoggart et al., 2024)
  + (Ruan et al., 2022)
  + (Ahern et al., 2023)
  + (Schultz et al., 2022)
  + (Ding et al., 2023)
* Add info on brain changes only
  + (Qiu & Liu, 2023)
  + (Wainberg et al., 2022)
  + (Lahey et al., 2024)
  + (Smith et al., 2024)
  + (Teeuw et al., 2023)
  + (Simpson-Kent et al., 2023)
  + (Arcego et al., 2024)
  + (Gilgoff et al., 2024)
  + (Merz et al., 2024)

# To read (high priority)

* General review
  + Stress: (Boyce, 2016)
  + Stress: (Boyce & Ellis, 2005)
  + Stress: (Herman, 2013)
  + Stress: (Kemeny, 2003)
  + Stress: (Liu, 2015)
  + Stress: (McLaughlin et al., 2010)
  + Stress: (Nelson & Gabard-Durnam, 2020)
  + Stress: (Teicher et al., 2022)
  + Stress: (Russell & Lightman, 2019)
  + Adolescent mental health: (Centers for Disease Control and Prevention, 2023)
* Stress → brain changes and psychopathology
* Stress and psychopathology in ABCD
* Stress → brain changes
  + (Miller et al., 2024)
  + (Cardoner et al., 2024)
  + (Chat et al., 2022)
  + (Huggins et al., 2022)
  + (Barrett et al., 2024)
  + (Miller et al., 2022)
* Stress and genetics → brain changes in ABCD
* Stress and genetics → brain changes
  + (Bolhuis et al., 2022)
  + (Zhang et al., 2021)
* Stress and genetics → psychopathology
  + (Cao & Rijlaarsdam, 2023)
  + (Haberstick et al., 2005)
  + (Huizink et al., 2007)
  + (Pagliaccio et al., 2015)
  + (Starr & Huang, 2019)
* Stress and genetics → psychopathology in ABCD
* Brain changes, psychopathology and ABCD
  + (Blok et al., 2023)
  + (Dall’Aglio et al., 2021)
* Stress, gender, and sex
  + (Bath, 2020)
* Psychopathology and ABCD
* Genetics and brain changes and ABCD
  + (Miles et al., 2024)
* Genetics and psychopathology and ABCD
* Genetics and ABCD
* Glucocorticoids
  + (Bernard et al., 2017)
  + (Dunlop & Wong, 2019)
  + (Ellis & Boyce, n.d.)
  + (Miller et al., 2007)
  + (Starr et al., 2021)
  + (Stroud et al., 2016)
  + (Wang et al., 2018)
  + (Chat et al., 2022)
  + (Hankin et al., 2015)
  + (Laurent et al., 2015)
  + (Daskalakis et al., 2014)
  + (Ouellet-Morin et al., 2021)
  + (Choi et al., 2024)
  + (Brown et al., 2024)
* Gender, SGM, and ABCD
* ABCD
* Genetics
  + (Murray et al., 2021)
  + (Zheutlin & Ross, 2018)
  + (Levey et al., 2020)
  + (Ge et al., 2019)
  + MDD GWAS: (Meng et al., 2024)
* Brain changes and psychopathology
* Exposome
  + (Barzilay et al., 2021)
  + (Department of Psychiatry, University of Health Sciences Ankara Diskapi Training and Research Hospital, Ankara, Turkey et al., 2021)
  + (Wild, 2012)
* Methods
* Other

# Adversity and stress

## General

* About 50% of children in US experience one or more types of adversity and 20% two or more types by adulthood (McLaughlin et al., 2019) from Green 2010, Kessler 2010, Mclaughlin 2012; (Hoffman et al., 2019) from Child and Adolescent Health Measurement Inititative 2013
* Definitions
  + “Negative environmental experiences that are likely to require significant adaptation by an average child and that represent a deviation from the expectable environment” (McLaughlin et al., 2019) from McLaughlin 2016
  + Must be chronic or single acute event “severe enough to require significant emotional, cognitive, or neurobiological adaptation by an average child” (McLaughlin et al., 2019)
  + Expectable environment: caregiver responsiveness and sensitivity, percpetual and sensory input (McLaughlin et al., 2019)
  + Stress: both ‘stressors’ ie adverse events and resulting biological and behavioral responses (Hoffman et al., 2019)
  + “experiences that lead to high psychological distress during childhood, adolescence, and beyond” (Zhang et al., 2023) from Felitti 1998
* Exposure to ACEs negative corr with SES (Barnhart et al., 2022)
* “lower rates of ACEs found among White, non-Latinx children and youth compared to those belonging to other racial and ethnic groups” (Barnhart et al., 2022)
* Decreased ‘family economic status’ linked with increased number of life events reported as negative from caregiver and from youth reported based on LES at year 2, relationship was stronger for families with higher levels of conflict but “for youth-reported models that included either (a) only ACEs that were related to the non-familial environment (e.g., excluding family-specific ACEs; Supplemental Fig. 6) or (b) a PCA-derived family environment score that included other indices of family environment (e.g., parental monitoring, parental acceptance; Supplemental Fig. 7), while the major of results replicated, family economic status no longer strongly interacted with family conflict to predict ACEs.” [but study did nto control for psychopathology or baseline negative event exposure] (Barnhart et al., 2022)
* stressful event scores ie number events perceived as negative + intensity positively corr with having at least one caregiver with 4-year degree (M. A. Botdorf, 2021)
* In ABCD at baseline ten factors identified by factor analysis based on variety of measures: “1) caregiver psychopathology, 2) socioeconomic disadvantage and lack of neighborhood safety, 3) secondary caregiver lack of support, 4) primary caregiver lack of support, 5) child report of family conflict, 6) caregiver substance use and separation from biological caregivers, 7) family anger and arguments, 8) family aggression, 9) physical trauma exposure, and 10) caregiver lack of supervision” (A. Brieant et al., 2023)
* In ABCD at baseline three dimensions of ‘early-life adversity’ as measured by variety of measures identified: ‘acts of omission/commission’ e.g. “physical trauma and family verbal/physical aggression” vs “socioeconomic disadvantage…lack of enighborhood safety, caregiver supervision, and caregiver support”, ‘environmental uncertainty’ e.g. “episodic” vs more chronic experiences, ‘perspective’ ie youth vs parent report (A. Brieant et al., 2023)
* In ABCD at baseline four factors comprising ‘environemtnal stressors’: family dynamics (e.g. family conflict, financial adversity, experiencing traumatic events), interpersonal support (e.g. relationship with teachers, parent, etc), neighborhood SES deprivation, urbanicity (Jeong et al., 2023)
* In abcd at baseline black children had higher exposure to traumatic events as measured with KSADS compared to white children (Dumornay et al., 2023)

## ABCD domains related to adversity

* ABCD domains related to adversity (Hoffman et al., 2019) table 1, categories from Kaiser ACE Study ie abuse, household challenges, neglect (Felitti et al., 1998)
* Original categories (see table 1) from (Felitti et al., 1998)
  + Based on 1988 National Health Interview Survey, Wyatt, Conflict Tactics Scale (Felitti et al., 1998)
  + Used cutoff of 4+ ACEs to compare outcomes (Felitti et al., 1998)
  + Abuse
    - Psychological abuse: swear at/insult/put down; act in a way that made you afraid you would be physically hurt
    - Physical abuse: push, grab, shove, slap; hit so hard had marks or were injured
    - Sexual abuse: touch/fondle in sexual way; have you touch their body in a sexual way; attempt oral, anal, or vaginal intercourse with you; actually have oral, anal, or vaginal intercourse with you
  + Household dysfunction
    - Substance abuse: problem drinker or alcoholic; used street drugs
    - Mental illness: depressed or mentally ill; attempt suicide
    - Mother treated violently – mother or stepmother: pushed, grabbed, slapped, had something thrown at her; kicked, bitten, hit with fist or something hard; repeatedly hit over at least a few minutes; threatened with or hurt by a gun or knife
    - Criminal behavior: household member go to prison
* “no rationale for inclusion of those specific adversities, or for not including others, was given in the original Felitti paper (1998)” (Lacey & Minnis, 2020)
* Different questionnaires all reporting to measures ACEs include different questions and items (Lacey & Minnis, 2020)
* Since original Felitti 1998 article “More recently, experiences such as severe illness and hospitalizations, bullying victimization, and exposure to community violence have also been identified as ACEs” (Barnhart et al., 2022)
* Question as to whether poverty is risk factor for ACE or is an ACE itself (Barnhart et al., 2022)
* Abuse
  + Emotional: not assessed (Hoffman et al., 2019)
  + Physical: KSADS-5 PTSD parent module and parent and youth Family Environment Scale (Hoffman et al., 2019)
  + Sexual: KSADS-5 PTSD parent module (Hoffman et al., 2019)
* Household challenges
  + Mother treated violently: KSADS-5 PTSD parent module (Hoffman et al., 2019)
  + Household substance abuse: Family History Assessment, adult self-report from parent (Hoffman et al., 2019)
  + Household mental illness: Family History Assessment, adult self-report from parent (Hoffman et al., 2019)
  + Parental separation/divorce: Demographics Survey from parent (Hoffman et al., 2019)
  + Criminal household member: Family history assessment from parent (Hoffman et al., 2019)
* Neglect
  + Emotional: CRPBI Acceptance Subscale from youth (Hoffman et al., 2019)
  + Physical: Parental Monitoring from youth, Demographics Survey from parent (Hoffman et al., 2019)
* Other measures
  + Delinquency Scale from youth (Hoffman et al., 2019)
  + Family Environment Scale, Family Conflict Subscale from youth (Hoffman et al., 2019)
  + Neighborhood Safety/Crime Survey from youth (Hoffman et al., 2019)
  + School Risk and Protective Factors Survey from youth (Hoffman et al., 2019)
  + Juvenile Victimization Questionnaire from youth and parent (Hoffman et al., 2019)
  + Peer Delinquent Behavior Survey from youth (Hoffman et al., 2019)
  + Parental separation/divorce added by Anda 1999 (Lacey & Minnis, 2020)
  + Physical and emotional neglect added by Dong 2004 (Lacey & Minnis, 2020)
* Parental separation (9.4%) and financial hardship (18.6%) most common ACEs (Webster, 2022)
* Exposome variables often corr with each other eg pos corr for neighborhood crime variables, for pollution variables, for SES variables (Simpson-Kent et al., 2023)
* Urbanome: like exposome but specifically for urban settings, includes both risk and protective factors (Cardenas-Iniguez et al., 2024)

## Genetics

* In ABCD
  + Abuse but not other kinds of early life stress moderated relationship between educational attainment polygenic score from European ancestry only and brain morphometry (and brain morphometry significantly directly affected total intelligence based on NIH toolbox neurocognitive battery) (Wang et al., 2024)
  + Interaction between abuse and educational attainment polygenic score based on European ancestry only such that if abuse higher polygenic score linked to fewer behavioral problems ie polygenic score potentially protective (Wang et al., 2024)
  + SES but not family environment, maternal substance use, school environment, developmental adversity, or parental psychopathology correlated with PRS calculated via basic/standard method for autism, anxiety, social anxiety, panic disorder, bipolar disorder, MDD, schizophrenia (Qiu & Liu, 2023)
  + PRS calculated via basic/standard method for panic disorder, schizophrenia correlated with child psychosis (Qiu & Liu, 2023)
  + PRS calculated via basic/standard method for MDD correlated with maternal substance use (Qiu & Liu, 2023)
  + MDD PRS from (Howard et al., 2019) for white non-Hispanic participants only sig pos associated with CBCL scores for anxious/depressed, somatic, social, thought, attention, rule-breaking but not aggressive or withdrawn/depressed after correction for multiple tests, no change if only used participants of European ancestry (Wainberg et al., 2022)
  + No relationship between bipolar disorder PRS or schizophrenia PRS or anorexia PRS for any CBCL dimensions for white non-Hispanic participants only, no change if only used participants of European ancestry (Wainberg et al., 2022)
  + ADHD PRS from (ADHD Working Group of the Psychiatric Genomics Consortium (PGC) et al., 2019) for white non-Hispanic participants only sig pos associated with attention subscale in CBCL but no other subscales, no change if only used participants on European ancestry (Wainberg et al., 2022)
  + Externalizing disorder PRS calculated with PRS-CS for participants of European ancestry only prospectively (baseline to wave 1 or wave 2) positively predicted ADHD and conduct problems and negatively predicted internalizing symptoms measured based on selected CBCL items; externalizing disorder PRS did not predict rate of change in any of these problems from baseline to wave 1 or wave 2 (Lahey et al., 2024)
  + Youth internalizing as measured with CBCL at age 12-13 controlling for internalizing at age 11-12 65% explained by nonshared environment (E) and 35% by shared environmental effects (C) based on twin study, E moderated by family cultural values as reported by youth but not parents (Rea-Sandin et al., 2024)
  + Youth externalizing as measured with CBCL at age 12-13 controlling for externalizing at age 12-13 62% explained by nonshared environmental (E) and 38% additive genetic (A) effects based on twin study, E moderated by family cultural values as reported by parents but not youth(Rea-Sandin et al., 2024)
  + ADHD with comorbid disruptive behavior disorder PRS, antisocial behavior PRS, irritability PRS, and self-regulation/addiction PRS calculated with basic/standard PRS for subjects of European ancestry only all significantly associated with externalizing, aggressive, and rulebreaking CBCL subscales (Teeuw et al., 2023)
  + “Additive genetic factors accounted for most of the variability in the volumes of a minority of cortical and in most of subcortical ROIs” at baseline (Bustamante et al., 2022)
  + Relationship between psych-related PRS and ACE exposure could be due to child’s behavior (genetic) leading to ‘harsh parenting or stress responses in their parents’ ie gene by environment correlation or due to common genetics between parent with psychopathology and child with psychopathology (Baldwin et al., 2022)
  + Odds ratio 1.09 for experiencing ACEs based on PRS for overall mental health problems, strongest for PRS for schizophrenia, depression, and ADHD compared to other mental health PRS, did not differ based on specific kind of ACE (Baldwin et al., 2022)
  + “observed” mental health PRS explained 3% internalizing and 5% externalizing problems but genetic sensitivity analysis found “genetic confounding accounted for a large average proportion of the associations between ACEs and internalizing problems (68.6%...” and 60.3% for externalizing (Baldwin et al., 2022)
  + Relationship between ACE and internalizing or externalizing explained by genetic in some things but not others: genetic confounding explains large part of relationship for parent separation, criminality and substance abuse but nor for parental mental illness or child maltreatment (Baldwin et al., 2022)
  + Models with genetic, environmental (life events, proximal contextual, broad contextual), and gene x environment interactions (with life events and proximal context but not broad context) best fit internalizing and externalizing scores on CBCL using novel genetics-based REML approach with matrices and environmental exposure measures at baseline (or life events scale at year 1) for subjects of european ancestry, in American admixed group gene x environment effects sig for ext but not int, in african ancestry group larger gene x environment effects compared to european (Choi et al., 2022)
  + Adding environmental exposome effects to model of internalizing which already included genetic effects had little/no impact suggesting independence but adding environmental exposure sig decreased genetic effects on externalizing so environment could mediate genetic effects or genetic effects could affect both environment and externalizing (Choi et al., 2022)
  + PRS for MDD calculated with PRS-CS with summary stats from (Howard et al., 2019) and (Levey et al., 2020) sig pos related to allostatic load defined as composite measure of salivary DHEA, blood cholesterol, glycemia, blood pressure, waist circumference for European but not african ancestry adolescents; sig pos related to psychopathology for European but not African ancestry youth partially mediated by allostatic load for European ancestry youth; no sig increase in variance explaining allostatic load when added MDD-PRS to model already including exposome; interaction between MDD-PRS and exposomic burden such that stronger relationship between exposomic burden and allostatic load if higher MDD-PRS [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
  + PRS for PTSD calculated with PRS-CS and exposomic burden both individually but not interaction sig pos related to allostatic load in European ancestry participants and allostatic load sig mediated relationship between PRS for PTSD and total problems CBCL score, results not reported for African ancestry [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
* Not in ABCD
  + Dexamethasone (glucocorticoid receptor agonist) study
    - Identify SNPs in genes related to stress response ie that ‘changes their activity upon dex treatment and were termed dex-responsive regulatory elements (DREs)’ as proxy for genes that might be related to responses to adverse events (Penner-Goeke et al., 2022)
    - “DRE and dex SNP-DRE associated etranscripts are enriched in genes differentially expressed in post-mortem cerebral cortex of affected subjects across five neuropsychiatric disorders (SCZ, autism spectrum disorder (ASD), MDD, bipolar disorder (BPD), and alcohol abuse disorder (AAD)) as cpmared to control subjects” (Penner-Goeke et al., 2022)
    - “dex SNP-DREs are more specific to psychiatric traits than the veh SNP-DREs, which are enriched for various non-psychiatric disorders” (Penner-Goeke et al., 2022)
    - Functional gene scores for DRE genes associated with ‘differences in physiological stress measures’, sig pos corr cortisol change following psychological stress task, impaired eyeblink startle habituation and increased eyeblink startle magnitude (Penner-Goeke et al., 2022)
    - Out of range of SNPs chose one related to transcriptional regulation of NUAK2 and another to regulation of FOXC1 (Penner-Goeke et al., 2022)
  + Polygenic score based on four HPA-axis genes (FKBP5, NR3C2, NR3C1, GRHR1) not associated with anxiety or depression symptoms but interaction between polygenic score and maltreatment such that if higher polygenic score then more maltreatment associated with higher risk severe vs mild comorbid depression/anxiety symptoms, mainly due to effects of emotional neglect and abuse rather than other types maltreatment, no difference based on gender (Cao et al., 2024)
  + Interaction between maltreatment and recent interpersonal stress such that recent interpersonal stress associated with stronger changes in depressive symptoms if childhood maltreatment if high but not low stress-related polygenic score as above (Sun & Cao, 2024)
  + MDD PRS and bipolar disorder PRS created with PRS-CS and validation with PRSice2, participants of European ancestry only, MDD PRS sig related to cumulative number of stressful life events before most severe depressive episode, no sig effect of bipolar PRS (Hosang et al., 2024)
  + Antisocial behavior PRS calculated using PRS-CS from GWAS with adults sig linked to nonaggressive conduct issues and from GWAS with children/adolescents sig associated with physical aggression in sample of adolescents of European ancestry only, either PRS interacted with environmental variables or predicted changes in antisocial behavior over time (Acland et al., 2024)
  + Depression PRS from (Howard et al., 2019) anxiety PRS calculated using basic/standard PRS methods for subjects of European ancestry only, depression PRS sig associated with dep symptoms and anxiety PRS sig associated with anxiety symptoms, interaction between dep PRS and stress such that stronger effect of PRS on dep or anx symptoms if more stressfult life events, childhood trauma (only for dep, not anxiety), loneliness, long-term difficulties, or dec social support (Wang et al., 2023)
* Biological sensitivity to context theory: genetic variations that lead to increased stress reactivity cause individual to be more sensitive to their environment (context), probably “domain general reather than domain specific”, alleles with these variations may be “plasticity alleles” – see Ellis & Boyce 2008 from (Cao et al., 2024) or references from (Sun & Cao, 2024)

## Life Events Scale (LES)

* Part of ABCD as described by (Barch et al., 2021) which references (Tiet et al., 2001) which says “the measure of adverse life events in this study was based on Johnson’s revision (Brand & Johnson, 1982; Johnson & mcCutcheon, 1980) for a measure developed by Coddington (1972a, 1972b)”; also references (Grant et al., 2004) which is just review and does not give any additional meaningful information about scale
* Tiet et al study (Tiet et al., 2001)
  + Did not adjust p-values
  + Too few subjects reported new brother/sister as negative event so excluded
  + Controlled for age, SES, ethnicity, and “cumulative effect of the remaining adverse life events”
  + Items with correlation > 0.3: parental separation and parental divorce (r=0.51), death of a close friend and loss of a close friend (r=0.47), parent going to jail and family member arrested (0.37), parental separation and parent away from home more (r=0.33), family member drug/alcohol problem and family member arrested (0.30)
  + Some disorders were significantly associated with most of 25 events: dysthymia (17/25), MDD (19/25), ODD (21/25),dfdf CD (22/25)
  + Other disorders significantly associated with very few events: social phobia (family member drug/alcohol problem), ADHD (seriously sick/injured; saw crime/accident; started new school), agoraphobia (family member drug/alcohol problem; parents argued more than previously; one parent away from home more often)
  + 16/25 events have odds ratio of at least 4 with at least one of studied psychiatric disorders
  + Sex differences: different items associated with same disorder for boys and girls, true of all disorders studied
* Johnson & McCutcheon 1980 study (Johnson & McCutcheon, 1980)
  + Used revised version of Life Events Survey from Coddington 1972 which Johnson & McCutcheon called the Life Events Checklist
  + LEC: 46 items and 4 blank spaces, asks whether event occurred in past year, whether ‘good’ or ‘bad’, how much impacted life from 0 ‘no effect’ to 3 ‘great effect’
  + Small sample size: 97 total, 46 male, 51 female, all from Seattle area, race/ethnicity/other demographics not reported
  + Mean ± SD negative life events: 5.18 ± 5.30 for males, 5.91 ± 5.84 for females
  + Averaged across all subjects number negative life events sig pos corr with depression symptoms, general maladjustment, external locus of control, A-trait (anxiety), number pos life events sig neg corr with locus of control
  + For males only number negative life events not sig corr depression, A-triat, locus of control or general maladjustment; for females only number of negative life events sig pos corr only with general maladjustment
  + Number of neg events and negative change score ie accounting for intensity corr 0.92 so impact ratings did not matter that much
* Sarason et al 1978 (Sarason et al., 1978)
  + Describes development of Life Experiences Survey: 57 items, (47 for all, 10 more for students), items “chosen to represent life changes frequently experienced by individuals in the general population”, some based on SRE, asks about past year, experienced as positive vs neg, and impact rating
  + Test-retest reliability in two very small samples over 5-6 weeks for neg score were 0.56 and 0.88
  + Negative but not positive score assicated with state and trait anxiety, neg events sig corr depression and locus of control
  + Mean ± SD neg scores from full scale ie both parts 6.22 ± 6.28 for males and 7.04 ± 7.90 for females
* Tiet et al 1998 used 25 question version of LES, gives table of prevalence for each item (table 2), focuses on resilience (Tiet et al., 1998)
* Brand & Sarason 1982 (Brand & Johnson, 1982): test-retest for total number neg events 0.72, mean ± SD number neg events at baseline 13.7 ± 9.6 and time two 13 ± 8.9
* Administered in ABCD beginning in year 1 ie not at baseline, in year 4 added questions (caregiver deported, foster care, seeing someone beaten up/shot at, lockdown at school) (Barch et al., 2021)
* Cronbach’s alpha reported as 0.85 and 0.87 at year 1 and year 2 in (Weiss et al., 2023)
* “internal consistency among youth rates was 0.62 and 0.58 for parent/caregiver raters” for number of life events reported as negative (Barnhart et al., 2022)
* See descriptive statistics for ABCD data in table 3.3 from (M. A. Botdorf, 2021)
* For item endorsement frequence in ABCD see table 3.5 from (M. A. Botdorf, 2021)
* Positively skewed in ABCD data, see fig 3.3 from (M. A. Botdorf, 2021)
* Stressful events score ie number life events perceived as negative + intensity not different for males vs females but increased score if higher SES and differed sig based on race, see table 3.4 in (M. A. Botdorf, 2021)

## Potential behavioral / psychopathology outcomes

* + General / other outcomes
    - Can differ based on chronic vs acute (Hoffman 2019 from McEwen 2007), stress responses can be beneficial in short-term and harmful in longer-term (Hoffman et al., 2019) from Chetty 2016, Marmot 1991, Mersky 2013
    - “Stressors that may be more universally experienced in adolescence, such as perceived valuation from one’s peers, can also impact stress burden and thus future health” (Hoffman et al., 2019) from McEwen 2007
    - Adversity linked to impaired academic achievement and social and economic function, chronic disease, early mortality (McLaughlin et al., 2019)
    - Increased exposure to adverse events decreases amount of time 9 and 10 year-olds persists on behavioral task ie learned helplessness (Evans et al., 2013)
    - High school students more likely to smoke if increased exposure to adverse events (Evans et al., 2013)
    - Increased exposure to adverse events associated with lower scores on standardized reading test (Evans et al., 2013)
    - number of life events reported as negative inversely related to episodic memory (M. A. Botdorf, 2021)
  + Physical health outcomes
    - Chronic disease (Nelson et al., 2020)
    - Increased infections (Nelson et al., 2020)
    - Sleep difficulties (Nelson et al., 2020)
    - Sexually transmitted disesases (Metzler et al., 2017) (Felitti et al., 1998)
    - Heart disease (Lacey & Minnis, 2020)
    - Cancer (Lacey & Minnis, 2020)
    - Stroke (Lacey & Minnis, 2020)
    - Hepatitis (Lacey & Minnis, 2020)
  + Social/academic outcomes
    - High school attendance and graduation (Nelson et al., 2020) (Metzler et al., 2017)
    - Teenage pregnancy (Nelson et al., 2020)
    - Unemployment as adult (Metzler et al., 2017)
    - School achievement and grades (Webster, 2022)
  + Increased psychopathology
    - As adversity inc likelihood of developing psychopathology also inc (McLaughlin et al., 2019)
    - Childhood adversity responsible for about 1/3 world’s mental disorders (McLaughlin et al., 2019)
    - If experience childhood adversity then chance of developing mental disorder approximately double (McLaughlin et al., 2019)
    - Increased exposure to traumatic events as measured with the KSADS associated with increased anxiety as measured with the CBCL (Marusak et al., 2022)
    - Greater levels of neighborhood poverty as measured with the ADI linked to higher externalizing symptoms as measured with the CBCL (Maxwell et al., 2021)
    - Attention problems and withdrawn/depressed CBCL scores decreased “during the COVID-19 pandemic” but scores were still within “normal” ranges (Hamatani et al., 2023)
    - Exposure to “childhood trauma” [do not say how measured] associated with increased time on emotional stroop task (Lepow et al., 2021)
    - Increased aggression (Nelson et al., 2020)
    - Increased risk taking (Nelson et al., 2020)
    - Suicidality, suicidal ideation, self-harm (Nelson et al., 2020) (Metzler et al., 2017) (Felitti et al., 1998)
    - Depression (Nelson et al., 2020) (Metzler et al., 2017) (Lacey & Minnis, 2020) (Felitti et al., 1998)
    - Smoking (Metzler et al., 2017) (Felitti et al., 1998)
    - Alcoholism, drug abuse (Felitti et al., 1998)
    - Positive emotion-driven impulsivity only ie not negative emotion-driven impulsivity at baseline predicted what study refers to as ‘childhood trauma’ based on LES at year 2 follow-up, no sex diff (Goncharenko, 2022) (Weiss et al., 2023)
    - increased lifetime negative life event exposure as measured with LES at year 1 associated with increased negative and positive emotion-driven impulsivity at year 2 (Weiss et al., 2023)
    - both lifetime as assessed at year 1 with LES and past year as assessed at year 2 with LES negative event exposure associated with negative and positive emotion-driven impulsivity, no sex diff (Goncharenko, 2022) (Weiss et al., 2023)
    - increased number of life events reported as being negative associated with increased number of psychotic-like experiences (Karcher et al., 2022)
    - Increased exposure to ACEs as 11-12 predicted increased externalizing and internalizing ‘in later adolescence among a sample of African American youth’ (Barnhart et al., 2022)
    - Higher number of life events reported as negative by parent and by youth based on LES associated with increased internalizing and externalizing symptoms but “for youth-reported models that included either (a) only ACEs that were related to the non-familial environment (e.g., excluding family-specific ACEs; Supplemental Fig. 6) or (b) a PCA-derived family environment score that included other indices of family environment (e.g., parental monitoring, parental acceptance; Supplemental Fig. 7), while the major of results replicated, family economic status no longer strongly interacted with family conflict to predict ACEs.” [but study did nto control for psychopathology or baseline negative event exposure] (Barnhart et al., 2022)
    - increased number life events reported as engative associated with increased internalizing and externalizing symptoms (A. E. Brieant et al., 2021)
    - In abcd at baseline black children had higher exposure to traumatic events as measured with KSADS compared to white children (Dumornay et al., 2023)
    - Exposure to negative life events as measured with LES part of one of “two multidimensional factors [which] were significantly inversely and positively associated with greater curiosity about alcohol use, respectively: 1) low internalizing and externalizing symptomatology coupled with low impulsivity, perceived neighborhood safety, negative parental history of alcohol use problems, and fewer adverse life experiences and family conflict…” (Wade et al., 2021)
    - Higher adjusted odds ratio ie more likely to have depression, suicidality, PTSD, ODD, CD, ADHD, anxiety measured based on KSADS if more potentially traumatic events measured with KSADS-5 PTSD module even if account for polyvictimization (Thompson et al., 2022)
    - Exposure to potentially traumatic events as measured with KSADS-5 PTSD module tended to increase risk for both internalizing and externalizing disorders (not just one or the other) suggesting transdiagnostic effects, more likely to have comorbid psych disorders as number of potentially traumatic events increases (Thompson et al., 2022)
    - Type of traumatic event can matter for risk of psychopathology
      * Some potentially traumatic events eg witnessing domestic violence were linked with increased risk of psychopathology but others were not (Thompson et al., 2022)
      * After accounting for other potentially traumatic events and polyvictimization, exposure to accidents requiring serious medical attention linked to increased odds ADHD, PTSD; natural disasters linked to anxiety, PTSD, ADHD, internalizing disorder + PTSD; sudden death of a loved one linked to anxiety, PTSD, ADHD, PTSD + comorbid externalizing and/or internalizing; witnessing community violence not linked to any specific disorder; witnessing domestic violence linked to anxiety, ADHD, ODD, CD, PTSD, PTSD + comorbid externalizing and/or internalizing disorder; physical victimization linked to CD, PTSD + internalizing + externalizing; sexual trauma linked to depression, PTSD, PTSD + internalizing and/or externalizing (Thompson et al., 2022)
      * Above relationships not significantly impacted based on sex (Thompson et al., 2022)
      * Supports multifinality meaning that one type of stress can lead to different psych disorders (Thompson et al., 2022)
    - 35.1% of youth with 3+ potentially traumatic events as measured with KSADS-5 PTSD module met criteria for PTSD (Thompson et al., 2022)
    - Overall weaker relationships between potential traumatic event exposure and psychopathology based on youth vs parent reports in ABCD data (Thompson et al., 2022)
    - Developmental adversity associated with increased risk of psychosis (Qiu & Liu, 2023)
    - Increased family conflict, maternal substance use, parental psychopathology, structural connectivity in attentional network and decreased school engagement, SES, structural connectivity in posterior cerebellar network linked with increased externalizing problems (Qiu & Liu, 2023)
    - Increased maternal substance use, parental psychopathology, structural connectivity in salience network and decreased school engagement linked with increased internalizing problems (Qiu & Liu, 2023)
    - Increased developmental adversity and family conflict and decreased structural connectivity in anterior default mode network and SES linked with increased psychosis (Qiu & Liu, 2023)
    - Household income and parental education (collinear, together 2.3% variance), marital status, race, sex (1.5% variance) sig related to externalizing measured with CBCL, higher externalizing scores if white vs black or Hispanic or Asian, effect of externalizing based mostly on aggressive subscale (Teeuw et al., 2023)
    - Increased comorbid anxiety and depression symptoms if childhood maltreatment, more likely for girls compared to boys (Cao et al., 2024)
    - History of ACEs more common in individuals with schizophrenia vs controls (Misiak et al., 2024)
    - School risk, neighborhood safety, household income, early life stress and area crime (but not air pollution, population density and not family conflict because correlated with early life stress) significantly affected anxiety and depression symptoms as measured based on selected items from the CBCL (Thapaliya et al., 2021)
    - Allostatic load defined as composite measure of salivary DHEA, blood cholesterol, glycemia, blood pressure, waist circumference ie theoretically physical markers of stress linked with increase symptoms of psychopathology even after adjusting for parental education, household income, race, ethnicity, sex, and age; allostatic load partially mediated relationship between exposomic burden and symptoms of parent but not self-reported psychopathology [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
  + Measures from ABCD
    - \*Child Behavior Checklist from parents for psychopathology and “adaptive functioning” (Hoffman et al., 2019)
    - Brief Problem Monitor from teachers for psychopathology and “adaptive functioning” (Hoffman et al., 2019)
    - UPPS Impulsive Behavior Scale from youth for impulsivity (Hoffman et al., 2019)
    - Behavioral Inhibition System/Behavioral Activation System from youth for impulsivity (Hoffman et al., 2019)
  + Brain changes
    - Mechanisms
      * HPA axis activation shaped by stress exposure, causes glucocorticoid release which causes changes in brain, major but not only explanation for brain changes (McLaughlin et al., 2019) also LHPA axis (limbic HPA) (Gee & Casey, 2015)
      * Synaptic pruning in cortex esp on dendritic spines (McLaughlin et al., 2019) , when synapse activated postsyn cell releases trophic factors that strength syn but if not freq activated then not weakened and may be pruned (McLaughlin et al., 2019)
    - “Given a highly heterogeneous sample, identifying more homogeneous subgroups may be an optimal strategy before performing brain-phenotype association analyses” (Hong et al., 2021)
    - Changes in grey matter volume (Hong et al., 2021)
    - Changes in myelination (Hong et al., 2021)
    - Survivors of mass trauma from subway arson in South Korea had inc DLPFC thickness one year later, thicker DLPFC associated with fewer PTSD symptoms in later years, suggests “greater neural recruitment of this region early on may have led to more pronounced symptom improvements” (Hoffman et al., 2019) from Lyoo 2011
    - Deprivation could result in brain changes eg dec cortical thickness via “accelerated and exaggerated pruning”, pruning imp part of experience-dependent plasticity (McLaughlin et al., 2019) from Hensch 2005 and McLaughlin 2017
    - If deprivation then dec volume and thickness in frontoparietal areas ie superior parietal cx and dlPFC; dec frontopariental activity during emotional processing; decreased striatal activity during reward processing but not true if threat (McLaughlin et al., 2019)
    - Lack of caregiver responsivity and sensitivity linked to accelerated dev of fronto-amygdala circuits “potentially to compensate for the absence of species-expectant maternal buffering of emotional reactivity” – stress acceleration hypothesis (McLaughlin et al., 2019) from Callaghan 2016b
    - Resting state connectivity in cingulo-opercular, dorsal attention, and default mode network associated with internalizing as measured with Brief Problem Monitor (Kliamovich et al., 2023)
    - Volume of left amygdala and youth/caregiver feelings of safety mediate relationship between neighborhood poverty and externalizing (Maxwell et al., 2021)
    - “Neighborhood disadvantage” associated with changes in functional connectivity and decreased cognitive functioning but some changes in connectivity attenuated “in the context of positive family and school environments” (Rakesh et al., 2021)
    - Increased number of negative life events as measured with LES associated with smaller DG and smaller CA4 if male and parental education 4 year degree or if female and parental education no 4 year degree; larger DG and CA4 if male and parental education no 4 year degree or if female and parental education 4 year degree – three-way interaction between parental education, sex, and LES (M. Botdorf et al., 2020)
    - Decreased bilateral vmPFC activity associated with decreased CBCL withdrawn/depressed scores in subjects with both exposure to “childhood trauma” [does not say how measured] and prenatal drug exposure but no sig effect on behavior but still decreased vmPFC activity if only exposure to “childhood trauma” (Lepow et al., 2022)
    - Exposure to threat affects morph and fn of hippocampus eg dec hippo volume via synaptic pruning which affects learning and memory (McLaughlin et al., 2014) , dec hippo volume in adults but not kids so maybe delayed effect (McLaughlin et al., 2014)
    - Exposure to threat affects amygdala function eg processing of facial emotions, can generalize fear learning to neutral stim so hypervigilance (McLaughlin et al., 2019) , no diff in amygdala morph in children (McLaughlin et al., 2014)
    - Exposure to threat affects vmPFC emotional processing, coupling with amygdala, and thickness via synaptic pruning (McLaughlin et al., 2014)
    - Subtype (subtype 3) of subjects from ABCD with increased internalizing, externalizing, and total problem symptoms compared to other subtypes, also inc cortical thickness, dec parental monitoring and caregiver support, ‘less favorable’ school environment, inc family history of psychopathology, inc family conflict (Hong et al., 2021)
    - Subtype of participants (subtype 1) [not in ABCD but diff dataset] with differences in orbitofrontolimbic network connectivity for control vs trauma exposed and dec PTSD prevalence in trauma gp at time point 1 vs other groups, diff subtype (subtype 2) with dec connectivity in salience/cingulo-opercular network for control vs trauma exposed and dec PTSD prevalence over time, diff subtype (subtype 3) with persistent inc connectivity in default mode network for control vs trauma exposed over time and persistant high prevalence PTSD (Lee et al., 2023)
    - stressful event score ie number of events reported as bad + intensity associated with increased subiculum volume but no diff in CA1, CA3, or thalamus overall (M. A. Botdorf, 2021)
    - for males but not females with high SES, stressful event score ie number of events reported as bad + intensity associated with decreased CA4/DG volume (M. A. Botdorf, 2021)
    - higher number life events reported as negative associated with weaker positive or stronger negative cinguloopercular-left or right amygdala and cinguloopercular-right [but not left] hippocampus connectivity which was mediator for changes in internalizing [but not externalizing] behavior, however “higher levels of adversity were associated with more mature patterns of functional connectivity between the CO network and left and right amygdala and right hippocampus…more mature functional connectivity was associated with lower elvels of internalizing symptomatology, corroborating the idea that these adaptations may be beneficial for psychosocial adjustment” but may be harmful in long-term (A. E. Brieant et al., 2021)
    - “There is negligible evidence that the volumes of brain ROIs are associated with the indirect effects of TEs [traumatic events as measured by KSADS] on PTSDsx [PTSD symptoms as measured by KSADS] at this age [baseline]”, instead “environmental factors accounted for more of the variation in TEs and PTSDsx” (Bustamante et al., 2022)
    - At baseline in ABCD increased exposure to trauma as measured using latent measure [based on factor analysis] based on KSADS linked to decreased cortical thickness in right caudal middle frontal gyrus and left isthmus cingulate and posterior cingulate, also link with smaller right amygdala and right putamen gray matter volume (Jeong et al., 2021)
    - At baseline in ABCD overall ‘enironemntal stress’ comprised of multiple measures linked with decreased cortical thickness ‘across widespread regions’ and decreases in cortical and subcortical grey matter volume (Jeong et al., 2023)
    - At baseline in ABCD family dynamics related to decreased grey matter volume in some areas and linked to overall increased psychoapthology (Jeong et al., 2023)
    - At baseline in ABCD neighborhood socioeconomic status related to decreased grey matter volume in some areas and linked to increases in conduct and ADHD symptoms (Jeong et al., 2023)
    - At baseline in ABCD urbanicity related to increases in cortical and subcortical grey matter volume and increased cortical thickenss in frontoparietal areas and linked to ADHD symptoms (Jeong et al., 2023)
    - In abcd at baseline trauma history as measured with KSADS positive related to lateral orbitofrontal cortex grey matter volume (Dumornay et al., 2023)
    - Interaction between trauma exposure and variant of fatty acid amide hydroxylase [FAAH, related to endocannabinoids and development] on fractional anisotropy in parahippocampal cingulum and fornix (Marusak et al., 2022)

## Potential moderators and/or mediators

* Potential moderators and/or mediators (life events --moderator or mediator→ psychopathology)
* Individual
  + Executive function: fMRI ie Stop Signal Task, Emotional N-Back Task and Monetary Incentive Delay Task from youth for executive fn (Hoffman et al., 2019)
  + Resilience: low resilience mediates relationship between ACEs and “negative health outcomes” (Morgan et al., 2021), youth resilience scale (Hoffman et al., 2019), for review of resilience see (Zhang et al., 2023)
  + Exercise (Hoffman et al., 2019)
  + Sleep quality (Hoffman et al., 2019)
  + Use of electronic devices (Hoffman et al., 2019)
  + Gender (Evans et al., 2013)
  + Sex
    - Higher allostatic load defined as composite measure of salivary DHEA, blood cholesterol, glycemia, blood pressure, waist circumference for females compared to males in ABCD study [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
    - Higher “exposomic burden” for females compared to males in ABCD study [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
  + Race/ethnicity (Evans et al., 2013)
    - Lower allostatic load defined as composite measure of salivary DHEA, blood cholesterol, glycemia, blood pressure, waist circumference for non-Hispanic white adolescents compared to non-Hispanic black or Hispanic adolescents but not diff between Hisapnic and non-Hispanic black [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
    - But no difference in “exposomic burden” based on race in ABCD study [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]
  + Age (Evans et al., 2013)
  + Attachment (Evans et al., 2013)
  + IQ/cognitive competence (Evans et al., 2013)
  + Genetics (Nelson et al., 2020)
  + Temperament (Nelson et al., 2020)
* Family
  + Parental monitoring/supervision (Hoffman et al., 2019)
  + Parenting style (Evans et al., 2013) (A. E. Brieant et al., 2021)
  + Parent psychopathology (Evans et al., 2013)
  + Household education (Hoffman et al., 2019) (Evans et al., 2013)
  + Income/SES (Hoffman et al., 2019) (Evans et al., 2013)
  + Family structure (Hoffman et al., 2019)
  + Family history of psychopathology (Hoffman et al., 2019)
  + Family conflict (Evans et al., 2013) (Barnhart et al., 2022)
* Community/society
  + Social support (Hoffman et al., 2019) (Nelson et al., 2020)
  + Exposure to environmental toxins (Hoffman et al., 2019)
  + “Substandard” housing (Evans et al., 2013)
  + Noise exposure (Evans et al., 2013)
  + Residential crowding (Evans et al., 2013)
  + Urbanicity (Evans et al., 2013)
  + Food insecurity (Nelson et al., 2020)
  + “having a trusting adult present in childhood” (Webster, 2022)
* Exposome: “interconnected network of nongenetic exposures an individual is exposed to across their lifetime”, includes “internal (e.g., inflammation) as well as external (e.g., chemical, lifestyle, psychosocial) domains” (Pries et al., 2022); “totality of environmental exposures that an individual experiences from conception throughout the lifespan” (Moore et al., 2022); “many inter-connected features of an individual’s environment and experience” (A. Keller et al., 2022)
  + Three categories – general external e.g. stress, urbanicity; specific external e.g. smoking; internal e.g. oxidative stress (Department of Psychiatry, University of Health Sciences Ankara Diskapi Training and Research Hospital, Ankara, Turkey et al., 2021)
  + “sum of weighed exposure based on coefficients from each model”, for more on calculation in non ABCD study see (Pries et al., 2019)
  + P-factor most associated with day-to-day experiences but also associated with household adversity, state-level environment, pregnancy/birth complication and family values but not neighborhood environment, including five sig exposome factors explained 40.1% variance in p-factor (Pries et al., 2022)
  + Overall psychopathology associated with exposome [as defined based on 348 environmental variables including LES but not any genetic data], psychopathology most strongly linked with day-to-day experiences subfactor, including general exposome rather than just parental education and demographics greatly increased variance explained in overall psychopathology, no diff based on sex, some diff based on race/ethnicity, (Moore et al., 2022)
  + “a critical step to increase generalizability of findings is for the field to aspire to reach a consensus regarding which factors are needed to be controlled for (as potential confounders). We further suggest that until that consensus is reached, researchers should attempt to account for as many environmental measures as are available (accounting for their collinearity), test how these affect their findings, and to report this to enhance replicability.” (Barzilay et al., 2022)
  + Unclear if (A. Keller et al., 2022) used LES in study of exposome with ABCD data
  + Increased adversity as measured with exposome in ABCD year 3 linked with increased allostatic load defined as composite measure of salivary DHEA, blood cholesterol, glycemia, blood pressure, waist circumference and BMI even after accounting for sex, race, ethnicity, parental education, income and age [(Hoffman et al., 2023) as preprint, full text not available but actually published as (Hoffman et al., 2024)]

## Models

* + Cumulative risk approach: count number of discrete types of adversity experienced by child (McLaughlin et al., 2019) from Evans 2013
    - For review of many studies of cumulative risk see (Evans et al., 2013)
    - “All CR investigators should begin with an assessment of CR, statistically controlling for each singular risk factor to ensure that the CR term is not sigmply reflecting the operation of one powerful, singular risk factor” (Evans et al., 2013)
    - Assumes similar effect regardless of specific type, chronic vs acute, severity (McLaughlin et al., 2019) from Evans 2013
    - Multiplicative and not additive? (Sun & Cao, 2024)
    - Theoretical bases
      * Allostatic load (“index of cumulative wear and tear on the body caused by repeated mobilizations of multiple physiological systems over time in response to environmental demains” (Evans et al., 2013)): overall allostatic load leads to changes in stress and regulatory responses as common mechanism for effects of adversity (McLaughlin et al., 2019) from Evans 2013 and Evans 2007 (Evans et al., 2013)
      * Broffenbrenner’s ecological model (Lacey & Minnis, 2020): “exchanges of energy between the developing organism and the persons and objects immediately surrounding the child. In order for human development to be successful, these proximal processes must be reciprocal, continuous, and become increasingly complex as the child matures” (Evans et al., 2013) p 1344
    - Most common method of quantifying exposure to adverse experiences (Evans et al., 2013)
    - About same number of studies found relationship between adverse event exposure and outcomes to be linear vs nonlinear (Evans et al., 2013)
    - Typically standardize scores before adding if measuring different types of exposures with different units originally (Evans et al., 2013)
    - “When risk factors are independent or have minimum overlap, combining these various factors into a summary score is not a good idea because having one risk factor does not influence having a second one” (Evans et al., 2013) p 1342, could be that cumulative measure mostly measures effects of one or a few types of exposures (Evans et al., 2013)
    - “OLS model provides better fit when a small number of vairables are related to the outcome; however, the CR [cumulative risk] index is a better predictor when multiple, correlated predictors are related to the outcome of interest” (Evans et al., 2013)
    - Downsides
      * Typically does not account for exposure intensity (Evans et al., 2013)
      * Does not allow for analysis of interactions between effects of different exposures (Evans et al., 2013)
      * When compared to OLS regression with multiple variables for distinct exposures large review found that using multiple variables “does a slightly better job of predicting outcomes” broadly defined including social/psychopathology (Evans et al., 2013) but cumulative risk was better for “prospective prediction” (Evans et al., 2013)
      * Does not led itself to investigations of underlying mechanisms (Lacey & Minnis, 2020)
    - Upsides
      * Increased statistical power compared to studying one exposure at a time (Evans et al., 2013)
      * Does not have to deal with collinearity of different exposures as different terms (Evans et al., 2013)
      * Accounts for common co-occurent of ACEs (Lacey & Minnis, 2020)
      * May increase validity compared to studying one adverse exposure at a time because no single event is likely to capture overall experience of adverse event exposure (Evans et al., 2013)
      * Interpretability (Evans et al., 2013) (Lacey & Minnis, 2020)
  + Dimensional: diff types of adversity result from diff enviro circumstances and can have diff neurodev effects (McLaughlin et al., 2019) from McLaughlin 2016/2014a, Sheridan 2014
    - Diff types of adversity result from set of common enviro circumstances eg threat and deprivation (McLaughlin et al., 2019)
    - Diff types adversity have diff neurodev effects (McLaughlin et al., 2019) from McLaughlin 2016
    - Studies of mixed threat and deprivation exposure on brain volume, thickness, activity have inconsistent results – suggests important to distinguish (McLaughlin et al., 2019)
    - Dimensions not necessarily independent (McLaughlin et al., 2019)
    - Also other dimensions eg harshness and unpredictability (Lacey & Minnis, 2020)
    - Upsides: larger effects when measure adverse exposure based on dimensions rather than cumulative (Evans et al., 2013), can test for interaction between domains (Evans et al., 2013),
    - Threat: experience or threat of harm eg abuse, domestic or community violence (McLaughlin et al., 2019)
      * Affects emotional regulation, learning, threat detection and salience (McLaughlin et al., 2019) from McLaughlin 2014a, Sheridan 2014
      * Exposure to violence associated with altered emotional regulation, reactivity, perception, salience and aversive learning esp if stim is neg (McLaughlin et al., 2019)
      * If threat then dec mPFC, hippocampal, amygdala volume and inc amygdala activation; changes in salience network eg dACC and anterior insula; inc frontopariental activation during emotional processing; inc striatal activation during reward processing but not true if deprivation (McLaughlin et al., 2019)
    - Deprivation: lack of expected enviro input eg “support, nurturance, and cognitive and social stimulation” eg neglect, parental absence, potentially but not necessarily associated with lower SES (McLaughlin et al., 2019)
      * Dec social and cog input liked to changes in executive fn, lang, other cog dev (McLaughlin et al., 2019)
      * If lack caregiver support and attn then also likely to lack social, sensory, motor, linguistic stim (McLaughlin et al., 2019)
      * Lower SES sometimes but not always linked with deprivation, no clear association between low SES and either threat or deprivation (McLaughlin et al., 2019)
  + Combinations of multiple different types of exposures
    - Drug use best explained by sexual abuse, physical abuse, household mental illness, household substance use and spanking (combined) but not emotional abuse, physical or emotional neglect, mother treated violently, incarcerated household member, parental divorce/separation (Merrick et al., 2017)
    - “moderate/heavy drinking” best explained by sexual abuse, physical abuse, household substance use, spanking (combined) but not emotional abuse, physical or emotional neglect, mother treated violently, incarcerated household member, parental divorce/separation (Merrick et al., 2017)
    - Suicide attempt best explained by sexual abuse, emotional abuse, emotional neglect, household mental illness, incarcerated household member, spanking (combined) but not physical abuse or neglect, mother treated violently, household substance use, parental divorce/separation (Merrick et al., 2017)
    - “Depressed affect” best explained by sexual abuse, physical abuse, emotional neglect, household mental illness or substance use (combined) but not emotional abuse, physical neglect, mother treated violently, incarcerated household member, parental divorce/separation (Merrick et al., 2017)
    - Changes in brain structure depend on type of adverse event exposure (Hong et al., 2021) eg differences in cortical thickness based on exposure to abuse vs exposure to neglect [but two diff samples] (Hong et al., 2021)
    - “While distinguishing among trauma types would have been interesting, 25 different traumas [from LES] were assessed at each timepoint, and statistical models were not powered to account for all of these variables” (Weiss et al., 2023)
  + Other ways to measure / think about modeling risk
    - Factor analysis
      * “groups ACEs by the degree to which they are correlated with one another” (Lacey & Minnis, 2020)
      * “middle ground between the additive, nonaggregated technique (ordinary least squares [OLS] regression) and CR” (Evans et al., 2013)
      * Better predicted heavy drinking and symptoms of depression compared to cumulative score (Lacey & Minnis, 2020)
      * Upsides: interpretability (Evans et al., 2013), explained more variance in outcomes than CR but CR was better at prospective prediction (Evans et al., 2013), allows for weighting of factors (Lacey & Minnis, 2020)
      * Downsides: generalization can be difficult because depends on “distribution of variables in the sample” (Evans et al., 2013), factor scores may be unstable (Evans et al., 2013), predictive power not established yet (Lacey & Minnis, 2020), unclear whether components in given factor have effect based on common mechanism or not (Lacey & Minnis, 2020), ignore single components not associated with any other component (Lacey & Minnis, 2020)
    - LCA
      * “person-centered clustering technique that groups people to show the adversities they tend to report” (Lacey & Minnis, 2020)
      * Assesses whether diff combinations exposure make diff (Lacey & Minnis, 2020)
      * Eg sexual abuse, emotional/physical abuse, household dysfunction (Lacey & Minnis, 2020)
      * Eg household dysfunction, childhood maltreatment (Lacey & Minnis, 2020)
      * Upsides: allows for weighting of components (Lacey & Minnis, 2020)
      * Downside: predictive power not established yet (Lacey & Minnis, 2020)
    - SEM
      * Upsides: “benefit of preserving continuous data and tend to be more invariant across amples than cluster or factor scores because of the explicit inclusion of measurement error estimation in the latent index” (Evans et al., 2013)
      * Downsides: needs large sample size (Evans et al., 2013), testing interactions can be difficult (Evans et al., 2013)
    - \*Cluster analysis – see methods from (Lee et al., 2023)
      * Identify clusters/types of exposures which can use to predict outcomes (Evans et al., 2013)
      * Downsides: generalizability (Evans et al., 2013), vulnerable to overfitting (Evans et al., 2013)
    - Recursive partitioning analytic models (Evans et al., 2013)
  + Stress acceleration: stress causes accelerated neural development esp in circuits related to emotional processing (McLaughlin et al., 2019) from Callaghan 2016a,b
    - White matter “integrity” inc and cortical thickness dec as get older (McLaughlin et al., 2019)
    - Theorizes that amygdala-mPFC connectivity of children who experienced caregiver deprivation should be similar to adolescents rather than similar aged peers (McLaughlin et al., 2019) from Callaghan 2016b
    - Not supported by amygdala-mPFC resting state studies; some evidence based on functional connectivity during emotional processing tasks but not clear on what counts as “more mature development” (McLaughlin et al., 2019)
    - “Stressful family enivronemnts” linked to changes in cingulo-opercular-amygdala resting state functional connectivity and accelerated puberty (A. E. Brieant et al., 2021) from Thijssen et al 2020a and 2020b
    - However other evidence that exposure to stress/adversity dleays rather than accelerates measures of connectivity in some areas (A. E. Brieant et al., 2021)
    - Overall prior work is mixed as to valence of developmental changes in resting state functional connectivity (A. E. Brieant et al., 2021)
  + Mismatch hypothesis aka stress inoculation: mild adversity can be adaptive, see references from (Sun & Cao, 2024)
  + Stress phenotyping framework: integrates effects of stress across many different systems within body as well as interpersonal interactions and relationships (Gilgoff et al., 2024)
  + Stress sensitization: exposure to stress increases response to later stress, related to kindling hypothesis of psychopathology, stress sensitization could potentially predict psychopathology (Harkness et al., 2015)
  + Chronic stress can lead to stress habituation or sensitization (Palamarchuk et al., 2023)
  + Stress inoculation: exposure to some level of stress decreases future responses to stress (Harkness et al., 2015)

# Glucocorticoids

* Glucocorticoid receptor
  + Can be transcriptional activator or repressor (Meijsing, 2015) but more commonly binds enhancers (Clarisse et al., 2024)
  + NR3C1 gene codes for multiple isoforms of glucocorticoid receptors based on post-translational modifications, alternative splicing, and alternative translational initiation; different isoforms have different expression profiles based on tissue type or cell type (Clarisse et al., 2024; Meijsing, 2015)
  + Glucocorticoids enter cell, bind to receptor in cytosol, receptor translocates to nucleus to affect transcription (Meijsing, 2015)
  + Glucocorticoid receptors can affect transcription by directly binding to DNA, typically binds at sites distant from promoter of target genes, about half GR binding sites more than 10kb from transcriptional start site for upregulated genes and often more than 100kb from transcriptional start site for downregulated genes (Meijsing, 2015)
  + GR can also affect transcription of genes such as NFκB via tethered binding (and in case of NFκB specifically epigenetic repression (Palamarchuk et al., 2023)) which is usually repressive, eg coapplication of dexamethasone with TNFα leads to GR binding to about 1000 more regions than dexamethasone alone (Meijsing, 2015)
  + GR can also affect transcription by interacting ie cross-talk with other transcription factors, these interactions could affect genomic site accessibility (Meijsing, 2015)
  + GRs act as transcription factors to increase expression of anti-inflammatory genes and repress transcription of proinflammatory genes eg NFκB (Meijsing, 2015)
  + GR activity impacts memory and learning via cAMP-dependent protein kinase A (Palamarchuk et al., 2023)
  + GR activity impacts fear memory and stress responses via methylation of mitogen-activated protein kinase (Palamarchuk et al., 2023)
  + GR binding is highly cell-type specific and tissue-specific (Clarisse et al., 2024; Meijsing, 2015)
  + GR can affect RNA polymerase II activity, RNA stability, chromatin remodelers, histone modifying enzymes (Meijsing, 2015)
  + GRs expressed in wide variety of cell types throughout body (Jimeno & Rubalcaba, n.d.)
  + GR lower affinity than mineralocorticoid receptors (Jimeno & Rubalcaba, n.d.)
  + Binding of glucocorticoids to GRs in brain causes negative feedback which decreases production of glucocorticoids to return to homeostasis (Jimeno & Rubalcaba, n.d.)
  + More GRs associated with decrease glucocorticoid exposure “stronger physiological responses and greater capacity to adjust this response according to stressor intensity, which may be translated into more resilient and flexible GC phenotypes” (Jimeno & Rubalcaba, n.d.)
  + Dexamethasone exposure affects frequency of GR/chromatin interactions rather than causing novel interactions, affects both activation and repression (Clarisse et al., 2024)
  + GRs highly expressed in PFC and hippocampus, affect stress recovery and information encoding (Palamarchuk et al., 2023)
  + NGFI-A reverses GR expression, DNA methylation, and HPA axis activity by binding GR promoter (Palamarchuk et al., 2023)
  + Decrease BDNF in hippocampus associated with GR desensitization and risk for psychiatric disorders when exposed to stress (Palamarchuk et al., 2023)
  + Polymorphism in GR affects anticipatory cortisol levels (Palamarchuk et al., 2023)
  + Fkbp5 gene close to glucocorticoid-responsive element, polymorphism linked to GR activation and PTSD risk, cortisol responses to stress, risk for depression, GR resistance evidenced by decreased ACTH and plasma cortisol after exposure to dexamethasone in depressed individuals (Palamarchuk et al., 2023)
  + GR activation can lead to glutamate release via re- or post-synaptic mechanisms (Palamarchuk et al., 2023)
  + GR activation can affect calcium retention in mitochondria and subsequent neural toxicity of stress (Palamarchuk et al., 2023)
  + Chronic social stress downregulates NR3C1 expression (Palamarchuk et al., 2023)
* Hypothalamus releases corticotropin-releasing hormone which is part of corticotropin-releasing factor family with urocortin from brainstem, CRH stimulates release of adrenocorticotropic hormone which stimulates release of cortisol from adrenal cortex (Palamarchuk et al., 2023)
* Cortisol follows circadian and ultradian cycles, usually starts increasing about 3-4am and peaks at 8-9am (Lightman & Conway‐Campbell, 2024)
* Main glucocorticoid in humans is cortisol but also have corticosterone (Lightman & Conway‐Campbell, 2024)
* Intracellular glucocorticoid receptors are low affinity, surge of cortisol in the morning can lead to transcription of genes used to prime cells for “metabolic and cognitive demands of the day”, these cortisol oscillations affect attentional bias towards and recognition of emotional faces (Lightman & Conway‐Campbell, 2024)
* Amygdala “sensitive to rapid changes in circulating GC levels”, “Acute stress further changes amygdala electrical properties in a β-adrenergic and GR-dependent manner to facilitate subsequent long-term potentiation induction, contributing to effective memory of emotional and stressful events” (Lightman & Conway‐Campbell, 2024)
* Increased methylation NR3C1 in hippocampus and subsequent decreased gene expression and decreased hippocampal glucocorticoid receptor density, increased anxious and depressed responses following stress linked to childhood maltreatment (Cao et al., 2024)
* More ACEs associated with increased IL-6 and TNFα, IL-6 but not TNFα partially mediated relationship between increased ACEs and increased depressive symptoms (Zagaria et al., 2024)
* Age significantly related to IL-6 levels (Zagaria et al., 2024)
* In both healthy controls and subjects with schizophrenia history of ACEs associated with higher levels of IL-6 and TNFα (Misiak et al., 2024)
* Higher levels of IL-5, IL13, IL-17, TNFα, IFNγ, CRP in subjects with schizophrenia compared to controls but not interaction between effect of history of ACEs and shiczohprenia vs controls on these levels (Misiak et al., 2024)
* At baseline no diff in gene exp between human induced pluripotent stem cell-derived glutamatergic neurons from combat veterans with PTSD and without PTSD but when exposed to hydrocortisone 402 genes responded differentially in PTSD vs non-PTSD cells, these genes were enriched in dlPFC and OFC postmortem tissue (Seah et al., 2022)
* Offspring of rats with low corticosterone responses themselves had low corticosterone responses to stress, decreased size in multiple hippocampal regions, increased mineralocorticoid/glucocorticoid receptor ratios in hippocampal areas, fewer but longer bouts of REM sleep, and in males but not females fear extinction deficits and increased susceptibility to fear relapse compared to controls; high corticosterone responders also had smaller hippocampal regions but no change in fear extinction compared to controls (Monari et al., 2024)
* Over year following cancer diagnosis of child mothers with less childhood trauma had larger increases in cortisol and steeper reductions in perceived stress compared to mothers with more childhood trauma (Marsland et al., 2024)
* Increased cortisol in adolescents if higher SES compared to lower SES, increased cortisol awakening response in adolescents if high or low but not medium SES, both genetic and environmental factors influenced awakening cortisol levels (Cantave et al., 2023)
* Timing and type of adversity influence cortisol responses
  + Minor adolescent adversity exposure linked with increased average daily cortisol, major childhood adversity exposure associated with less steep changes in cortisol, type of adversity also mattered because major physical abuse linked to increased waking cortisol, sexual abuse linked to increased cortisol awakening response, and both major sexual abuse and major neglect linked to decreased waking cortisol and less steep changes in cortisol (Kessler et al., 2023)
  + See also (Kuhlman, 2024)
* Lower glucocorticoid mRNA expression and increased cortisol levels in adolescent girls exposed to both higher chronic interpersonal stress and a major life event but not only one or other compared to controls (Marin et al., 2007)
* Polygenic score created based on gene changes in hippocampus of female macaques following chronic betamethasone administration moderated relationship between exposure to early life adversity and adult psychotic disorder diagnosis (Arcego et al., 2024)
* If MDD and female then lower baseline cortisol and decreased cortisol response to stress compared to controls; if remitted MDD and female then no difference in cortisol response to stress but still lower baseline cortisol compared to controls; if MDD and male then increased baseline cortisol compared to controls but no difference in cortisol response to stress and no differences in cortisol if remitted MDD and male (Zorn et al., 2017)
* If anxiety and female then no difference in baseline cortisol but decreased cortisol response to stress, no diff in cortisol if anxiety and male; if specifically social anxiety disorder and male but not female then no change in cortisol response to stress but increased baseline cortisol level (Zorn et al., 2017)
* Decreased baseline cortisol if schizophrenia and male or female but decreased cortisol response to stress if schizophrenia and male but not female (Zorn et al., 2017)
* Repetitive stress exposure risk factor for psychological disorders such as anxiety, MDD, schizophrenia (Zorn et al., 2017)
* Change in cortisol in response to stress are adaptive if transient but if chronic or sustained can lead to allostatic overload and be harmful if chronic or sustained (Zorn et al., 2017) and if chronic or sustained then can lead to allostatic overload and eventually allostatic failure which is harmful/maladaptive (Palamarchuk et al., 2023)
* No sig diff in cortisol based on age for men or for women (Zorn et al., 2017)
* No sig diff in baseline cortisol for men or women (Zorn et al., 2017)
* Lower SES linked with increased chronic stress but mixed evidence for whether leads to decreased, increased, or no change in cortisol levels across multiple types of cortisol measures; could be due to differences in duration of socioeconomic disadvantage ie initiual upregulation followed by longer-term downregulation of HPA axis activity (Merz et al., 2024)
* Discrimination and systemic racism may have effects on HPA axis activity distinct from socioeconomic disadvantage even though both linked (Merz et al., 2024)
* Different effects of socioeconomic disadvantage for males and females potentially due to interactions between HPA axis and testosterone and estrogen (Merz et al., 2024)
* Chronic exposure to given type of stress can lead to habituation ie decreased glucocorticoid responses but can also cause sensitization ie increased glucocorticoid responses if exposed to novel type of stress (Palamarchuk et al., 2023)
* Increased glucocorticoid responses ie hypercortisolemia linked with anxiety and depression (Palamarchuk et al., 2023)

# ABCD (and not adversity)

## General

* + Youths 9-10 years old at baseline (Barch et al., 2018)
  + Longituindal: will span 10 years (Barch et al., 2018), can investigate differences both between subjects and within subjects over time (Saragosa-Harris et al., 2022)
  + Originally developed to study onset of substance use in adolescence but quickly expanded to address other questions as well (Karcher & Barch, 2021)
  + Some measures chosen based on PhenX initiative to attempt to use measures “recommended as common data elements”, see p 56 for ref on PhenX (Barch et al., 2018)
  + Demographics for baseline, year 1 follow-up, and year 2 follow-up in table 1 from (Gonzalez et al., 2021)
  + Info on development of and reliability/validity references for ASEBA scales ie CBCL and BPM available on p 5 from (Barch et al., 2021)
  + Relevant demographic measures assessed each year (table 2 from (Barch et al., 2018) and table 1 from (Barch et al., 2021)), baseline demographics available supp fig 3 from (Barch et al., 2021)
    - ABCD has variable for combined race/ethnicity that groups into white/non-hipanic, black/non-hispanic, Hispanic, Asian, multiracial/multiethnic (Karcher et al., 2022)
    - Parent: home address from Residential History Questionnaire, can be used to calculate ADI based on census tract (Barch et al., 2021)
    - Parent: Parent about youth, self, family from PhenX (Barch et al., 2018)
    - Parent: Parent/guardian age, birth sex, gender, race, ethnicity, education, occupation, current income from PhenX (Barch et al., 2018)
    - Parent: Family income from PhenX (Barch et al., 2018), “family income at baseline was assessed using the income-to-needs calculated by dividing the reported total household income by the federal poverty line for a given household size” (Barch et al., 2021) with similar method used by (Barnhart et al., 2022) , more likely to be missing this information if lower caregiver education or if Black or Hispanic (Barch et al., 2021)
    - Parent: Parent-Reported Financial Adversity Questionnarie (Barch et al., 2021)
    - Parent: Household composition from Household Roster Questionnaire from General Social Survey and PhenX (Barch et al., 2018)
    - Parent: Economic insecurity from Best Practices in Conceptualizing and Measuring Social Class in Psychological Research (Barch et al., 2018)
    - Parent: School performance, repeating a grade, detentions/suspesions, drop in grades, special services from Introudction to KSADS (Barch et al., 2018)
    - Youth: sexual orientation, gender identity from Introduction to KSADS (Barch et al., 2018)
    - Youth: repeating a grade, detentions/suspesions, drop in grades from Introduction to KSADs
    - Youth: friendships: from questions on number of same and different gender friends (Barch et al., 2018)
  + Residential data: originally collected at baseline, protocols updated in April 2023 to have prospective and retrospective addresses (Badilla et al., 2024)
  + Relevant physical health measures (table 3 from (Barch et al., 2018))
    - Parent: youth current medications from Medication Inventory from PhenX (Barch et al., 2018)
    - Parent: youth brain injury/concussion from Modified Ohio State University TBI Screen Short Version (Barch et al., 2018)
  + Relevant baseline mental health history measures (table 4 from (Barch et al., 2018) and table 2 from (Barch et al., 2021))
    - Parent: youth categorical and dimensional psychopathology, suicidality/homicidality, adaptive function from KSADS administered each year (Barch et al., 2018) (Barch et al., 2021)
    - Parent: youth mania symptoms from Praent General Behavior Inventory 10 from Mania Scale assessed at baseline, year 1, year 2, year 4, year 4 but not year 3 (Barch et al., 2018) (Barch et al., 2021)
    - Parent: family history of mental health and substance abuse services from Introduction to KSADS assessed only at baseline (Barch et al., 2018)
    - Youth: categorical psychopathology, suicide from KSADS assessed at baseline and years 1, 2, 3, 4, and 5 (Barch et al., 2018)
    - Youth: psychosis from Pediatric Psychosis Questionnaire Brief Version assessed at baseline and years 1, 2, 3, 4, and 5 (Barch et al., 2018)
    - Youth: impulsivity from Modified UPPS-P for Children from PhenX (Barch et al., 2018)
    - Youth: about self Brief Problem Monitor assessed at years 1, 3, 5 (Barch et al., 2021)
    - Youth: about self NIH Toolbox Positive Affect Items assessed at years 1, 3, 5 (Barch et al., 2021)
    - Youth: about self 7-Up Mania Scale (Barch et al., 2021)
    - Youth: about self Behvairoal Inhibitiona and Behvaioral Activation Scale (Barch et al., 2021)
    - Youth: about self 10-Item Delinquency Scale assessed at years 1, 2, 3, and 4 (Barch et al., 2021)
    - Youth: about self Life Events Scale assessed at eyars 1, 2, 3, 4 and 5 (Barch et al., 2021)
    - Youth: about self Emotion Regulation Questionnaire assessed at years 3, 4, 5 (Barch et al., 2021)
    - Youth: about self Peer Experiences Questionnarie assessed at years 2, 3, 4, 5 (Barch et al., 2021)
    - Youth: about self Cyberbullying Questionnaire assessed at years 2, 3, 4, 5 (Barch et al., 2021)
    - Parent: self/family dimensional psychopathology, adaptive function from Achenback Adult Self Report Questionnaire (Barch et al., 2018)
    - Parent: self/family history of psychopathology from Modification fothe Family History Assessment from ASEBA (Barch et al., 2018)
    - Parent: Adult Self Report assessed at baseline, year 2, year 4 (Barch et al., 2021)
    - Parent: Adult Behavior Checklist assessed at year 2 and year 4 (Barch et al., 2021)
    - Parent: about self Perceived Stress Scale assessed at year 3 (Barch et al., 2021)
    - Parent: Child Behavior Checklist assessed each year (Barch et al., 2021)
    - Parent: about youth Short Social Responsiveness Scale assessed at year 1 and year 5 (Barch et al., 2021)
    - Parent about youth: Life Events Scale assessed at years 1, 2, 3, 4, and 5 (Barch et al., 2021)
    - Parent about youth: Early Adolescent Temperament Questionnaire assessed at year 2 (Barch et al., 2021)
    - Parent about youth: Difficulty in Emotion Regulation Scale assessed at years 3, 4, 5 (Barch et al., 2021)
    - Teacher: youth dimensional psychopathology, adaptive function from Achenbach Brief Problem Monitor (Barch et al., 2018)
  + Relevant cultural measures (Gonzalez et al., 2021)
    - Vancouver Index of Acculturation: “adherence to American and Heritage cultures on separate subscales…not developed for a specific racial/ethnic group”, Heritage culture self-described in open-ended item at baseline and then put into drop-down menu of choices in future assessments, administered only if identified culture other than only ‘American’ (Gonzalez et al., 2021)
    - Native-American Acculturation Scale: administered only if self-described as American Indian or Alaska Native, scale asks about “Native American cultural engagement” (Gonzalez et al., 2021)
    - Multi-Group Ethnic Identity Measure Revised: ethic identity defined as “quality of a person’s affiliation with their own ethnic group”, ethnic group selected from 14 options (Gonzalez et al., 2021)
    - Mexican-American Cultural Values Scale: “originally developed to assess cultural values often associated with Mexican-American families, but is useful for measuring family values across many cultural traditions” (Gonzalez et al., 2021)
    - Perceived Discrimination Scale: asks about “racial/ethnic discrimination; discrimination due to country of origin; discrimination due to gender identity; discrimination due to body type/weight” (Gonzalez et al., 2021)
    - School attendance and grades, data collected beginning in year 2 follow-up (Gonzalez et al., 2021)
    - Neighborhood safety from PhenX Neighborhood Safety, only three items (Gonzalez et al., 2021)
    - Collective Efficacy – Community Cohesion and Informal Social Control from PhenX: “collectivity efficacy refers to the level of social cohesion in a neighborhood and willingness of neighbors to work together toward common gaosl and social good” (Gonzalez et al., 2021)
    - Family Environment Scale Conflict subscale (Gonzalez et al., 2021)
    - Child Report of Behavior Inventory parental acceptance items (Gonzalez et al., 2021)
    - Parental Monitoring scale (Gonzalez et al., 2021)
    - SDQ Prosocial Behavior Scale (Gonzalez et al., 2021)
    - Peer Behavior Profile subscales of peer involvement and delinquent peer involvement (Gonzalez et al., 2021)
    - Peer network health assessed based on modification from Adolescent Social Network Assessment, only five items (Gonzalez et al., 2021)
    - Wills Problem Solving Scale (Gonzalez et al., 2021)
    - For test-retest reliability of above measures see table 8 in (Gonzalez et al., 2021)
  + Recruitment
    - Attempted to recruit sample similar to overall US demographics based on American Community Survey and enrollment data for 3rd and 4th graders from National Center for Education Statistics (Garavan et al., 2018), to do this oversampled some schools eg schools with relatively high number of African American students (Garavan et al., 2018) , schools for given site randomly divided into four replicates so could use some replicates to adjust recruitment over two year time period to try to make sample characteristics match US (Garavan et al., 2018)
    - Small portion ie 10% sample recruited through other methods than through schools e.g. mailing lists, affiliates of current participatns allowed to self-select for enrollment, snowballing referrals ie compensation for referring others, twin registry, recruitment during summer eg through YMCA programs (Garavan et al., 2018)
    - Modified version probability sampling based on sites which had the necessary neuroimaging equipment and expertise which tended to be in urban areas so possible that rural youth are under-represented (Garavan et al., 2018)
    - Recruited through schools (Garavan et al., 2018)
    - Recruited based on urbanicity, SES, race/ethnicity, gender, age (Garavan et al., 2018), other demographics not explicitly considered in recruitment strategy may not be representative of the US (Garavan et al., 2018)
    - Subset of participants recruited because twins (Garavan et al., 2018)
  + Discrimination reported most commonly for weight but also for race/ethnicity, experiences of discrimination differ based on race/ethnicity (Gonzalez et al., 2021)
  + Most youths have grades between B+ and A- with minimal unexcused school absences (Gonzalez et al., 2021)
  + KSADS reliability and validity references in p 60 from (Barch et al., 2018)
  + Population weighting
    - Goal: “control for specific sources of selection bias and restore unbiasedness to descriptive and analytic estimates of the population characteristics and relationships” (Dick et al., 2021)
    - Available for ABCD data, see Heeringa and Berglund 2020 and see for R script (Dick et al., 2021)

## Psychopathology

* + Can predict ADHD symptoms based on MRI measures of during behavioral tasks (Owens, Allgaier, et al., 2021)
  + BPM
    - Depressed mood and worthlessness strongly predicted each other reciprocally from 6 months to 12 months and from 12 months to 18 months (Funkhouser et al., 2021)
    - Threats of violence strongly predicted irritability from 6 months to 12 months but only weakly predicted from 12 months to 18 months (Funkhouser et al., 2021)
    - Strongest bridge symptoms between internalizing and externalizing symptoms are depressed mood, worry, threats of violence, destructiveness, disobedience (Funkhouser et al., 2021)
    - Symptoms network from 6 months to 12 months and from 12 months to 18 months only moderately correlated ie about 0.6 to 0.8 (Funkhouser et al., 2021)
  + Overall low incidence of PTSD based on KSADS (Thompson et al., 2022)
  + CBCL (note used p=0.01 cutoff, see table 4, supp table 4, supp table 5 and figs 2, 3, supp fig p 6-17) (Barch et al., 2021)
    - Four components of internalizing symptoms identified based on item-level analysis as stable over time: somatic problems, withdrawal, depression, anxiety (Brislin et al., 2022)
    - Decreased inhibition and attentional shifting associate dwith increased withdrawal and anxiety stable components of internalizing (Brislin et al., 2022)
    - Decreased inhibition at baseline predicted increased withdrawal at year 2 where inhibition and withdrawal are stable comopnents of internalizing (Brislin et al., 2022)
    - Decreased shifting at baseline predicted decreased anxiety at year 2 where anxiety is a stable component of internalizing (Brislin et al., 2022)
    - Accounting for variance from general psychopathology p factor increased internalizing for females vs males and decreased internalizing for african American vs white (Brislin et al., 2022)
    - Accounting for variance from general psychopathology p factor increased exeternalizing for males vs females and increased externalizing for African American vs white and increased externalizing for subjects with unmarried parents (Brislin et al., 2022)
    - For findings on race/ethnicity “we would still caution any strong interpretations of these data, as we were not able to address a range of other potentially contexturalizing facores, such as cultural differences in reporting of mental health related symptoms, or experiences of discrimination or other forms of systemic racism” (Barch et al., 2021)
    - Externalizing but not internalizing change over from baseline to year 1 follow-up to year 2 follow-up (A. Brieant et al., 2022)
    - Externalizing ysmptoms decreased for males but not females over from baseline to year 1 to year 2 (A. Brieant et al., 2022)
    - No change in internalizing symptoms over from baseline to year 1 to year 2
    - Five trajectories based on internalizing and externalizing from baseline to year 1 to year 2: low externalizing and moderate internalizing both increasing over time, low externalizing and internalizing and decreasing over time, moderate interanlizzing and externalizing and both increasing over time, high internalizing and moderate externalizing both decreasing over time, moderate internalizing and high externalizing both decreasing over time (A. Brieant et al., 2022)
    - Increased externalizing and total problems for males vs females (Barch et al., 2021)
    - Decrease in externalizing and total problems for both males and females over time but steeper decrease for males vs females (Barch et al., 2021)
    - Decreased externalizing and total problems fro Hispanic, non-Hispanic Black, and Asian youths compared to non-Hispanic White [accounting fro SES] (Barch et al., 2021)
    - Decreased internalizing problems fro non-Hisapnic Black and Asian compare dto non-Hispanic Whtie (Barch et al., 2021)
    - Increased internalizing problems for Native American/Alaska Ntaive youth vs non-Hispanic Asian/white/black and hispanic youth (Barch et al., 2021)
    - Decreased internalizing problems over time for non-Hispanic Black youth (Barch et al., 2021)
    - Increased internalizing problems over time for Native American/Alaska Native youth over time (Barch et al., 2021)
    - Decreased total problems and change in total problems over time if increased caregiver education (Barch et al., 2021)
    - Increated total, externalizing, internalizing if increased financial adversity (Barch et al., 2021)
    - Increased internalizing problems over time if reported financial adveristy (Barch et al., 2021)
    - Financial adversity ie ADI did not affect caregiver mental health (Barch et al., 2021)
    - If female then more likely moderate internalizing and low externalizing both increasing compared to low internalizing and low externalizing both decreasing from baseline to year 1 to year 2 (A. Brieant et al., 2022)
    - If meale then more likely moderate externalizing and low internalizing both increasing from baselie to year 1 to year 2
    - Correlations for internalizing and externalizing for each year in table 1 from (A. Brieant et al., 2022)
    - At baseline in ABCD if less neighborhood poverty [but not if more neighborhood poverty] then relationship between neigborhood poverty and externalizing ysmpoms buffered by parental support (Maxwell et al., 2022)
    - AT baseline in ABCD decreased feelings of safety but not increased ‘objective crime rates’ associated with increased externalizing symptoms (Maxwell et al., 2022)
    - Factor analysis based on CBCL using ABCD data frome baseline, year 1, and year 2 found externalizing, internalizing, somatic, neurodevelopmental measures decreased over time, “more interindividual variability in the intercepts than the slopes, with minimal variability in the sloeps of the factor scores over time” (Romer et al., 2023)
    - Age (p=0.01) (Barch et al., 2021)
      * Sig dec depression, adhd, oppositional but not anxiety or conduct over time (Barch et al., 2021)
    - Sex (p=0.01) (Barch et al., 2021)
      * Sig diff depression, adhd, oppositional, conduct but not anxiety (Barch et al., 2021)
      * Sig ixn sex vs time for depression, anxiety, oppositional, conduct but not adhd (Barch et al., 2021)
    - Race/ethnicity (p=0.01) (Barch et al., 2021)
      * Dec depression, anxiety, oppositional but not adhd, conduct for non-hispanic black vs white (Barch et al., 2021)
      * Dec oppositional, conduct but not depression, anxiety, adhd for Hispanic vs white (Barch et al., 2021)
      * Dec depression, anxiety, adhd, oppositional but not conduct for Asian vs white (Barch et al., 2021)
      * Dec conduct but not depression, anxiety, adhd, oppositional for native American/Alaska native vs white (Barch et al., 2021)
      * Dec conduct but not depression, anxiety, adhd, oppositional for multiracial vs white (Barch et al., 2021)
      * No diff ‘additional races’ vs white (Barch et al., 2021)
      * Dec epip 2022ression and adhd but not anxiety, oppositional, conduct
      * over time for non-hispanic black
      * Dec depression but not anxiety, adhd, conduct, oppositional for native american/Alaska native (Barch et al., 2021)
    - Caregiver education (p=0.01) (Barch et al., 2021)
      * Dec conduct but not depression, anxiety, adhd, oppositional for inc caregiver education (Barch et al., 2021)
    - Finances (p=0.01) (Barch et al., 2021)
      * Dec depression, anxiety, adhd, oppositional, condct for inc income-to-needs or financial adversity (Barch et al., 2021)
      * Dec conduct but not depression, anxiety, adhd, oppositional for ADI (Barch et al., 2021)
      * Dec anxiety over time for increased financial adversity (Barch et al., 2021)
      * Lower income to needs ratio ie more socioeconomically disadvantaged link to with increase internalizing symptoms at baseline and year 1 follow-up visit (Ip et al., 2022)
  + Changes in psychopathology based on other samples
    - Increases in depression from ‘school age to adolescence’ with larger increase for females than males (Barch et al., 2021)
    - Mixed evidence for changes in internalizing and mixed evidence for changes in externalizing ‘across adolescence’ (A. Brieant et al., 2022)
    - Some prior work found decreases in anxiety from ‘school age to adolescence’ but mixed evidence (Barch et al., 2021)
    - Decreases in rule-breaking, attention, and aggressiveness problems from ‘middle childhood to adolescence’ (Barch et al., 2021)
    - Increased depression in females compared to males (Barch et al., 2021), increased internalizing in females compared to males (A. Brieant et al., 2022)
    - “less evidence of sex differences in childhood/adolescence” for anxiety
    - Increased externalizing problems for males compared to females (Barch et al., 2021) (A. Brieant et al., 2022)
    - No change in exernalizing symptoms for females over years 10-13 but increase for males (A. Brieant et al., 2022)
    - Increase in internalizing symptoms over ages 10-13 for both males and females (A. Brieant et al., 2022)
    - Mixed evidence for differences in externalizing, anxiety, depression based on race/ethnicity and many studies ignore important sociocultural contextual factors eg discrimination, for specifics see p 7 (Barch et al., 2021)
    - Increased externalizing, anxiety, depression if lower SES (Barch et al., 2021)
    - Increased internalizing and externalizing associated with lower SES (Barnhart et al., 2022)
    - “low SES in early childhood predicts higher levels of later externalizing and internalizing behaviors” (Barnhart et al., 2022)
    - In abcd at baseline, year 1 and year 2 overall psychopathology ie p factor and most other psychopathology factors identified linked with decreased cortical volume, subcortical volume, and surface area but no change in cortical thickness (Romer et al., 2023)
    - In abcd no diff in slopes for psychopathology factors from baseline to eyar 1 to year 2 identified based on factor analysis from abcd except for internalizing, for internalizing if decreased mean cortical thickness at baseline then tend to have greater decrease in internalizing over time (Romer et al., 2023)

## Brain changes

* Structural
  + Increased overall psychopathology based on KSADS associated with decreased global surface area and volume but no change in cortical thickness at baseline, also true generally across specific regions at baseline (Mewton et al., 2022)
  + Increased neighborhood poverty as measured with ADI linked with decreased left but not right amygdala volume at baseline (Maxwell et al., 2022)
  + Increased neighborhood poverty as measured with ADI linked with decreased intracranial volume (mediator) and decreased feelings of safety (mediator) which is linked with increased externalizing symptoms at baseline (Maxwell et al., 2022)
  + Increased neighborhood poverty as measured with ADI related to decreased cognition and decreased DLPFC, DMPFC, SFG, and hippocampal volume but can’t say if brain changes are mediator because only at baseline (Taylor et al., 2020)
  + Increased household income related to increased cognition and increased hippocampal and prefrontal volume but can’t say if brain changes are mediator because only as baseline (Taylor et al., 2020)
  + Increased material hardship related to decreased grey matter volume in caudal anterior cingulate cortex and caudal middle frontal gyrus at baseline (Dumornay et al., 2023)
  + Increased parental employment related to increased amygdala grey matter volume at baseline (Dumornay et al., 2023)
  + Increased family income related to increased grey matter volume in many areas including frontal areas but no difference in hippocampus or amygdala at baseline (Dumornay et al., 2023)
  + Parental education related to changes in pars opercularis, rostral middle frontal gyrus, and insula at baseline (Dumornay et al., 2023)
  + Neighborhood disadvantage related to changes in gray matter volume of pars triangularis and insula at baseline (Dumornay et al., 2023)
  + No diff in gray matter volume based on family conflict or parental employment at baseline (Dumornay et al., 2023)
  + “accounting for the differences in childhood adversity attenuated the magnitude of some race-related differences in grey matter volume” at baseline (Dumornay et al., 2023)
  + Decreased log income to needs ratio linked with decreased hippocampal volume and increased internalizing especially in areas with high cost of living but relationship was attenuated if high cost of living state also provided ‘more generous’ cash benefits (Weissman et al., 2023)
* Functional
  + More negative coupling between bilateral amygdala and medial OFC to frontoparietal network if more socioeconomically disadvantaged (Ip et al., 2022)
  + Increased neighborhood deprivation linked with increased internalizing symptoms only if more positive rather than more negative amygdala-mOFC coupling (Ip et al., 2022)

## Genetics

* Polygenic risk score (PRS)
  + PRS “can be estimated by summing the log odds ratio of individual SNPs multiplied by the number of risk alleles present at the corresponding loci” (Guloksuz et al., 2019)
  + PRS for specific things may be associated with general psychopathology factor (p-factor): p-factor associated with PRS for disinhibition, number of sexual partners, smoking regularly, depression, neuroticism, PTSD, insomnia, ADHD, ASD, chronic multisite pain, chronic back pain, educational attainment, BMI (Waszczuk et al., 2023)
  + “while some polygenetic vulnerability is broad and transdiagnostic, a significant proportion of polygenetic risk is specific to narrower psychiatric constructs, underscoring the added benefit of fine-grained modeling of psychopathology” (Waszczuk et al., 2023)
* Interaction between effects of cumulative exposure to adverse events and neurodevelopment on risk for psychopathology: “for the 22.42% of the participants who were least exposed to adversity, the functional neurodevelopmental alterations link to genetic risk exerted a protective [decreased] role against psychopathology, whereas the alterations linked to lifestyle buffers predicted a slightly increased risk of psychopathology…for the 2.04% of the sample who were most exposed to adversity, the lifestyle-connected maturational alterations [protective] predicted reduced psychological vulnerability, whereas the genetic risk-connected alterations predicted increased vulnerability” (Petrican et al., 2023)
* Models of cognition more parsimonious using only exposome factors vs exposome factors and personalized functional network topography [“individually-defined networks that capture each brain’s unique pattern of functional topography”] because adding topography greatly increases number of variables (A. S. Keller et al., 2023)

# Methods

## ABCD

* ABCD study should not be considered representative of the US (Compton et al., 2019) (Garavan et al., 2018)
* Script to impute missing demographic data, see p 8 and supplement from (Barch et al., 2021)
* Consider using cutoff of p=0.01 as in (Barch et al., 2021)
* Use flowcharts to “illustrate changes, such as your sample size, at each quality control stage” e.g. with DiagrammeR in R (Saragosa-Harris et al., 2022)
* Site significantly affected externalizing scores measured with CBCL (Teeuw et al., 2023)
* See (Fan et al., 2023) for info on genetic information collection, genotyping etc
* Examples of using LASSO to identify relevant environmental variables (Thapaliya et al., 2021) (Thapaliya et al., 2024)
* Problems with specific scales
  + Issues with DSM diagnostic categories from KSADS-COMP, see p 4 from (Barch et al., 2021)
  + Issues with Self-Reported Delinquency Scale, see p 5 from (Barch et al., 2021)
* Potential cohort effects (Saragosa-Harris et al., 2022)
  + Covid pandemic: “researchers should be aware that data collected from 2020 to 2022 may have been collected differently than in previous sessions and will be collected differently in the future” (Saragosa-Harris et al., 2022), other samples found increased internalizing symptoms during the Covid pandemic (Saragosa-Harris et al., 2022), may also influence discrimination/racism experienced (Saragosa-Harris et al., 2022)
  + BLM (Saragosa-Harris et al., 2022)
* Reporting concordance, parent/caregiver vs youth
  + Concordance between caregiver and youth reports of social victimization between 18 and 50%, highest for ‘witnessing violence’ and ‘conventional crime’ (Tang et al., 2023)
  + Higher rates of concordance between youth and caregiver overall linked with increased externalizing and internalizing symptoms (Tang et al., 2023)
  + Concordance between youth and caregiver differed based on race (Tang et al., 2023)
  + Reports from youth and caregivers about youth begin to diverge around early adolescence (Barch et al., 2018)
  + May be more divergence in reports for internalizing compared to externalizing (Barch et al., 2018)
  + Parental psychopathology can affect reports of youth psychopathology (Barch et al., 2018)
  + “youth report may have predictive utility over and above parent report in at least some domains” (Barch et al., 2018)
* Modeling
  + Be sure variables are in appropriate format (Saragosa-Harris et al., 2022)
  + Scale continuous predictors as in (Barch et al., 2021)
  + Nested structure: consider “three-level models with random effects for family and site”, “nesting time within individuals (within families and sites)”, need to account for scanner if using MRI data (Saragosa-Harris et al., 2022)
  + Outliers: identify how will address beforehand (Saragosa-Harris et al., 2022)
  + Overfitting: “inclusion of covariates should be linked directly to hypotheses and supported by a clear theoretical justification for each covariate” (Saragosa-Harris et al., 2022)
  + “Including covariates like “race/ethnicity” does not simply “control” for the effects such factors may have on a child’s development and the nuance of their unique experience (e.g., such variables do not account for experiences of racism)” (Saragosa-Harris et al., 2022)
* Effect size: “standardized index of the strength or magnitude of an association between two variables or the size of difference between two groups” (Owens, Potter, et al., 2021)
  + Phenomenon with relatively small effect sizes can compound over time leading to cumulative effect (Owens, Potter, et al., 2021)
  + Correlations greater for subscales within instrument vs across instruments, greater for diff scales from same reporter vs across reporters (Owens, Potter, et al., 2021)
  + Across 161 constructs from all tasks and questionnaires administered in ABCD Study at baseline accounting for sex, age, race, parental income, parental education, parental marital status, and scanner site but not family i.e. “real-world” and using FDR and restricted only to analyses of relationships between scales from distinct instruments “median in-sample effect size was .05, and values at the first and third quartiles were .03 and .09”, with .18 as 90th percentile (Owens, Potter, et al., 2021)
  + “a ‘below average’ effect size is around .03, an ‘average’ effect size is one of around .05, an ‘above average’ effect size is one of around .09, and an ‘extremely above average’ effect size is one around .18 and above” (Owens, Potter, et al., 2021)
  + Relationship between traumatic experiences and total psychological problems is extremely above average at .20 (Owens, Potter, et al., 2021)
  + Report effect size with R2 i.e. percentage of variance explained or with Cohen’s d i.e. “difference attributed to a variable” (Saragosa-Harris et al., 2022)
  + Report effect size with R2 i.e. percentage of variance explained or with Cohen’s d i.e. “difference attributed to a variable” (Saragosa-Harris et al., 2022)

## Making PRS (Choi et al., 2020)

* Requires base data (eg from GWAS) and target data (sample for which want to make PRS)
* PRS predictive power lower than SNP heritability but will increase as sample size of GWAS increases
* Quality control for base data (eg GWAS)
  + SNP heritability ie h2SNP > 0.05 (can estimate from summary stats with software if not provided)
  + Identify effect allele
* Quality control for target data: must have 100 or more subjects
* Quality control for both base and target data
  + Make sure base and target data “have genomic positions assigned on the same genome build”
  + Genotyping rate >0.99
  + Sample missingness < 0.02
  + Hardy-Weinberg Equilibrium P > 1x10-6
  + Heterozygosity 3 or fewer standard deviations from the mean
  + Minor allele frequency (MAF) >1% or if target data has fewer than 1000 subjects MAF >5%
  + Imputation info score >0.8
  + Remove ambiguous SNPs which can result from using different genotyping chips for base and target data which may have used different chromosome strands
  + Strand-flip SNPs with mismatching alleles in base and target data
  + Make sure no duplicated SNPs in base or target data
  + Remove SNPs from sex chromosomes (unless explicitly studying)
* Newer PRS methods perform some form of shrinkage and/or regularization
* Clumping and thresholding: older technique for handling LD where clumping “does not merely thin SNPs by LD at random (like pruning) but preferentially selects SNPs most associated with the trait under study, and retains multiple SNPs in the same genomic region if there are multiple independent effects there: clumping does not simply retain only the most-asociated SNP in a region”, however threshold chose arbitrarily so not great method, instead newer methods use LD modeling (which still necessitates estimating LD between SNPs)
* PRS will be in same units as GWAS effect sizes eg if height GWAS in centimeters then associated PRS will be in centimeters, PRS can be standardized, may be log transformed
* PRS for binary phenotype uses log odds ratios as effect sizes for weighing, “PRS values are computed in relation to a hypothetical individual with the non-effect allele at every SNP, and, thus, they provide only a relative (compared to other idnividuals) estimate of risk (or trait effect) rather than an absolute estimate”
* “the non-random mating of individuals in a population, caused chiefly by the tendency for individuals to find a partner born in a nearby geographic location, generates structure in genetic variation across a population. Since environmental risk factors also tend to be geographically structured, this creates the potential for associations between many genetic variants and the tested trait that are confounded by, for example, location” so to account for this need to use genetic principal components
* “we recommend reporting results with and without important covariates when testing binary outcomes; confounders, such as genetic PCs, should be included as usual”
* Instead of Nagelkerke R2 use Lee R2
* Use quantile plots with PRS quantiles on x axis and outcome on y axis to display results, should look linear for linear regression or S-shaped for logistic, if logistic then S shape is normal and tail isn’t interesting
* “if the results are shown to be robust to confounding (see Population genetic structure and the generalizability of PRSs), then the effect size is not important if the aim is only to establish whether an association exists, which may provide etiological insight.”
* Check PRS distribution – should be approximately normally distributed
* Perform out of sample predictions to avoid overfitting ie use training, test, and validation sets

## To potentially investigate more

* \*cumulative consensus distribution (Hong et al., 2021)
* “multivariate predictive modeling method” Brain Basis Set (Weigard et al., 2021) from Sripada et al 2019
* Network Based Statistic (Sisk et al., 2021)
* Used ICA, machine learning on 40 environmental variables to make “Brain-Environment Resilience Index (BERI) by 1. using machine learning to predict the socioeconomic component from brain macro-structural measures and 2. defining BERI as the difference between the predicted and the observed socioeconomic component” (Modabbernia & Frangou, 2022)
* Zero-inflated negative binomial regression (Webster, 2022)
* Similarity network fusion (Hong et al., 2021)
* Cross-lagged panel network modeling (Funkhouser et al., 2021) (Wallace, 2023)

## Adversity

* Should account for effects of discrimination (Karcher et al., 2022)
* “we recommend that researchers guide their variable selection based on frameworks that place environmental features in context with other variables, and/or provide a concrete operationalization of the constructs in the dataset…using data-driven, AI, and machine-learning methods without appropriate ethical frameworks may risk perpetuating existing disparities” (Cardenas-Iniguez et al., 2024)
* Retrospective report of maltreatment as a child from adults found increased likelihood of internalizing and externalizing if subjective measure of maltreatment but not if objective i.e. court records (Danese & Widom, 2020)
* Duration of exposure can affect response (Nelson et al., 2020)
* Exposure to adverse life events may depend on subjects behavior (Evans et al., 2013)
* Dichotomizing variables can obscure nonlinear relationships (Evans et al., 2013)
* Definition of “high risk” should be based on “nationally representative data on risk factor exposure” rather than using 1 SD above mean or upper quartile (Evans et al., 2013)
* Important to separate influence of exposure to adverse event and response to that event (Nelson et al., 2020)
* Exposure to different types of adversity can impact youth with different intensities and/or lead to different responses (Nelson et al., 2020)
* Moderate stress exposure may buffer responses to later stress exposure but chronic stress more likely lead to increased psychopathology and detrimental effects on frontolimbic regions (Gee & Casey, 2015)
* Not responding to questions on ACE exposures linked to both “riskier” behavior eg smoking and “healthier” behavior eg lifetime HIV testing (Grigsby et al., 2024)
* Co-occurrence of different types of adversity
  + “Multiple dimensions of adversity must be measured and entered simultaneously into the same statistical model” rather than studying only children exposed to one type at a time (McLaughlin et al., 2019)
  + If don’t control for co-occurring adversity then “likelihood of spurious associations is high” (McLaughlin et al., 2019)
  + “This co-occurrence creates challenges for interpreting the results of studies that measure only a single type of adversity but is not sufficiently great to introduce problems of multicollinearity when trying to tease apart distinct associations between particular experiences and neurodevelopmental outcomes” (McLaughlin et al., 2019) from McLaughlin 2012
* Timing
  + Timing of adversity could affect outcomes based on critical periods but don’t have specific ages for cog, emotional, social critical periods (McLaughlin et al., 2019)
  + Timing of exposure can affect response (Nelson et al., 2020)
  + Adolescence as key developmental period (Webster, 2022) and sensitive period so maybe more susceptible to effects of stress (Gee & Casey, 2015) (Karcher et al., 2022) (A. E. Brieant et al., 2021)
  + Differences in effects of fear extinction in adolescence in animals and human vs childhood or adult (Gee & Casey, 2015)

## General methods tidbits

* Dimensional reduction
  + PCA
    - “PCA can see structure that does not exist and miss structure that exists” (Dyer & Kording, 2023)
    - “first principal component is defined as the direction of unit length that captures the maximum variance in the data, and the second principal component is the direction, orthogonal to the first, that captures the maximum remaining variance” (Dyer & Kording, 2023)
    - “diverse datasets can yield similar principal components, complicating the attribution of specific meanings or origins to these components” (Dyer & Kording, 2023)
  + ICA: “introduces the concept that natural data can often be represented as a combination of elements from an overcomplete dictionary, leading to representations that are both efficient and interpretable due to their parsimony” (Dyer & Kording, 2023)
* Odds and risk
  + Risk: “chance of the outcome of interest / all possible outcomes” (Ranganathan et al., 2015)
  + Odds: “probability of occurrence of an event / probability of the event nor occurring” (Ranganathan et al., 2015)
  + Relative risk: aka risk ratio, “ratio of risk of an event in one group (e.g., exposed group) versus the risk of the event in the other group (e.g., nonexposed group)”, 1 = no diff between groups, > 1 = increased risk, < 1 = decreased risk, not used in multiple logistic regression (Ranganathan et al., 2015)
  + Odds ratio: “ratio of odds of an event in one group versus the odds of the event in the other group”, 1 = no diff between odds, > 1 = increased odds, < 1 = decreased odds, used in multiple logistic regression (Ranganathan et al., 2015)
  + If probability of event is low i.e. about 10% or less then odds and risk are closer i.e. if event is rare then odds about same as risk (Ranganathan et al., 2015)
  + Odds ratio more different from 1 than risk ratio (Ranganathan et al., 2015)
  + Square root of marginal pseudo R2 is the same as Pearson’s correlation (Owens, Potter, et al., 2021)

## Reporting on race, ethnicity, and culture

* Conceptual considerations and interpretation
  + Generalization of theories created based on Western/white communities (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Representativeness of sample (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Interpret carefully and in context of historical and present-day systemic oppression (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Reliability and validity of measures for diverse populations (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + “categories are subject to political and historical context, as demonstrated by the changes in these labels over time…may contribute to the ongoing erasure, invisibility, and lack of recognition of various important populations, such as those that identify as American Indian and Alaska Native, Native Hawaiian or Other Pacific Islander, Middle Eastern or North African, or individuals that identify as multiracial” (Saragosa-Harris et al., 2022)
  + “upon identifying a relation between SES and a brain metric-or when studying executive functioning among minoritized youth- culturally- and contextually-informed alternative explanations to the deficit framework should be considered” (Saragosa-Harris et al., 2022)
  + “in the United States many people feel that Hispanic is their racial identity, or part of their racial identity” (Karcher et al., 2022)
* Reporting and writing
  + State definitions clearly (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + See APA guidelines for bias-free writing (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Positionality statement (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Talk about any oversampling (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Missingness based on culture/race/ethnicity (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Race/ethnicity not just ‘controlled for’ but need to report variance accounted for by these variables (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)
  + Citations for diverse authors (*JARS–Race, Ethnicity, and Culture: Table 1*, 2023)

# Good figures

* Diagrams of different factors that influence effects of exposure to adversity: figs 1 and 2 from (Nelson et al., 2020)
* Social determinants of health diagram (Metzler et al., 2017)
* Diagram of threat vs deprivation dimensions and examples: fig 1 (McLaughlin et al., 2014)
* Sensitive periods in life based on hormones and brain changes, adolescence as important period: fig 1 (Gee & Casey, 2015)
* Original diagram on effects of ACEs: fig 2 (Felitti et al., 1998)
* PRS figures (Choi et al., 2020)
* Cortisol changes in different psych disorders (Zorn et al., 2017)
* Glucocorticoid activity: (Clarisse et al., 2024; Meijsing, 2015; Palamarchuk et al., 2023)

# To read (low priority)

* General reviews
  + Adolescence as an important developmental stage: (Crone & Dahl, 2012)
  + Mental disorder prevalence: (Silva et al., 2020)
* Stress → brain changes and psychopathology
  + (Patel & Pelham, 2023)
  + (Xu et al., 2023)
  + (Albertina et al., 2022)
  + (Huffman et al., 2023)
  + (Belleau et al., 2023)
  + (Luby et al., 2019)
  + (Fassett-Carman et al., 2023)
  + (Farkas & Jacquet, 2023)
  + (Deng & He, 2023)
  + (Yu et al., 2019)
  + (Nkrumah et al., 2024)
  + (Xia et al., 2024)
  + (Borchers et al., 2024)
  + (Miller et al., 2022)
* Stress and psychopathology
  + (Ayawvi et al., 2023)
  + (Raghunathan et al., 2024)
  + (Vasupanrajit et al., 2024)
  + (Hinnant et al., 2015)
* Stress and genetics
  + (Gautier et al., 2024)
  + (Brody et al., 2013)
  + (Brody et al., 2013)
  + (Meaney, 2001)
* Stress → brain changes
  + (Gandy et al., 2024)
  + (Hall et al., 2015)
  + (McEwen et al., 2016)
  + (Lupien et al., 2009)
* Stress and genetics → brain changes in ABCD
  + (Petrican & Fornito, 2023)
* Stress and genetics → psychopathology
  + (McKenna et al., 2021)
  + (Starr et al., 2019)
* Brain changes, psychopathology and ABCD
  + (Holt-Gosselin et al., 2024)
* Psychopathology and ABCD
  + (Wen et al., 2023)
  + (D. A. Clark et al., 2021)
  + (Vijayakumar et al., 2023)
  + (Demidenko et al., 2022)
  + (Sanchez et al., 2023)
  + (Wallace, 2023)
  + (Marshall et al., 2021)
  + (Raney et al., 2023)
  + (Owens et al., 2022)
  + (Mendoza et al., 2024)
  + (Xia et al., 2024)
  + (De Lacy & Ramshaw, 2023)
* Genetics and brain changes and ABCD
  + (Pine et al., 2024)
* Psychopathology
  + (Hatoum et al., 2018)
  + (Marx et al., 2023)
* Genetics and psychopathology and ABCD
  + (Ohi et al., 2021)
* Stress and genetic changes
  + (Condon et al., 2024)
  + (Merz et al., 2024)
* Glucocorticoids
  + (Barsegyan et al., 2010)
  + (Wingenfeld et al., 2011)
  + (Parade et al., 2021)
  + (Zannas & Binder, 2014)
* Gender, SGM, and ABCD
  + (Gordon et al., 2024)
  + (Torgerson et al., 2024)
* ABCD
  + (Fan et al., 2021)
  + (D. B. Clark et al., 2018)
  + (Uban et al., 2018)
  + (Lisdahl et al., 2018)
  + (Luciana et al., 2018)
  + (Feldstein Ewing et al., 2018)
  + (Auchter et al., 2018)
  + (Charness, 2018)
  + (Hoffman et al., 2018)
  + (Bagot et al., 2018)
  + (Heeringa & Berglund, 2020)
  + (Iacono et al., 2018)
  + (Zucker et al., 2018)
  + (Casey et al., 2018)
  + (Hamilton et al., 2011)
* Genetics
  + (Freis et al., 2022)
  + (Dash et al., 2023)
  + (Petrican et al., 2022)
  + (Jalili et al., 2024)
  + (LaBianca et al., 2023)
  + (Xie et al., 2023)
  + (Uhart et al., 2004)
  + (Bourque et al., 2024)
* Stress
  + (Radley & Herman, 2023)
  + (Weiss et al., 2015)
* Exposome
* Brain changes and psychopathology
  + (Buthmann et al., 2023)
  + (Etami et al., 2023)
  + (Zhu et al., 2023)
* Methods
  + (Cecchetti & Handjaras, 2022)
  + (Achenbach et al., 2008)
  + (Aloe & Thompson, 2013)
  + (Bates et al., 2015)
  + (Luo et al., 2021)
  + (Early Intervention Foundation, n.d.)
  + (McPhetres, 2020)
  + (Wamser-Nanney & Campbell, 2021)
  + (Mengelkoch et al., 2024)
  + (Elsenburg et al., 2024)
  + (Cardenas-Iniguez & Gonzalez, 2024)
* Other

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