PhenX Pediatric Development Working Group

Child Behavior

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The challenge

- Child behavior encompasses a broad set of outcomes
- Heterogeneity of presentation across individuals poses challenges when categorizing
Behavioral outcomes

1. ADHD
2. ASD
3. Externalizing behaviors
   a. Aggression
   b. Conduct problems
   c. Hyperactivity
4. Internalizing behaviors
   a. Depression
   b. Anxiety
5. Attention
6. Other behavioral/mental health outcomes/disorders:
   a. Bipolar disorder
   b. Psychosis
   c. Oppositional defiance disorder
   d. Conduct disorder
   e. Obsessive compulsive disorder
   f. Suicidality
5. Executive function
Behavioral outcomes

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Executive function
Attention deficit hyperactivity disorder (ADHD)
ADHD: Definition

- Persistent pattern of inattention and/or hyperactivity–impulsivity that interferes with functioning or development
ADHD: Concepts

• Diagnosis
  – (in the U.S.) may be made by a pediatrician or psychologist using DSM-5 criteria
    • Present before 12 years
    • Present in 2+ settings
    • Symptoms interfere with social, school, or work functioning
    • Symptoms not explained by another mental disorder (e.g., mood disorder)
  – 3 symptom-based presentations: predominantly inattentive, predominantly hyperactive-impulsive, combined
  – Uses parent and teacher report of symptoms via behavioral rating scales (Conners, BASC, CBCL, TRF, etc.)
    • Can also use more objective measures, such as observation or performance-based tasks (e.g., CPT), though these are less common
ADHD: Considerations

• Presents as heterogeneous disorder
  – Symptom presentation and severity vary
• Response to treatment variable
• Symptoms often persist into adulthood
• Etiology multifactorial, high genetic heritability
• Often co-morbid with other conditions
  – depression and anxiety
  – oppositional defiance disorder
  – learning disabilities
  – motor difficulties
ADHD – Considerations

• Challenges of diagnosis
  – May not account for heterogeneity presentation/severity of traits
  – ADHD diagnostic criteria have change over time (with successive DSMs)
  – May be variable across providers
    • May be influenced by factors that impact access to care (SES etc.)
    • Fine line between ADHD and “high functioning” ASD

• An individual may exhibit some or all symptoms but may not receive the diagnosis

• There are advantages to examining ADHD symptomatology (vs. diagnosis)
ADHD – existing measures in toolbox

• Measure #1 “Attention-Deficit/Hyperactivity Disorder Symptoms”
  – Protocol #121502 “Attention-Deficit Hyperactivity Disorder Symptoms – Child”

• Strengths and Weaknesses of Attention-Deficit/Hyperactivity Disorder Symptoms and Normal Behavior Scale (SWAN)
  – Questions on the SWAN directly reflect DSM criteria
  – Reports on child or adolescent under 18 years
  – 18 questions: Direct correspondence to 9 inattentive and 9 impulsive-hyperactive categories (6+ need to be present for each subtype for dx)
  – Likert scale: [ ] far below [ ] below [ ] slightly below [ ] average [ ] slightly above [ ] above [ ] far above
Competing Measures

- There are other protocols that also measure ADHD symptomatology
  - E.g., Conners Rating Scale, Conners ADHD/DSM-IV Scale
- Note under PhenX: “SWAN was vetted against similar protocols and selected because it is a validated, parent- or teacher-reported instrument that is relatively low burden for investigators and respondents”
- Question for this WG: do we want to accept protocol recommendations from this prior WG or suggest additional protocols?
  - SWAN and Conners, for example, are very similar but Conners is more well recognized in some fields
  - There may be access considerations (e.g., SWAN is free, Conners needs to be purchased via publisher)
Missing elements

• ADHD Diagnosis and Treatment
  – Parent report
  – Pediatric medical record
  – Structured Clinical Interview for DSM-5 Disorders-Clinician Version (SCID-5-CV)
    • Adolescents and adults
    • Add for child?
Filling in the Gaps

• Recommendation #1: ADHD Diagnosis Measure
  – Protocol #1 Parent (or guardian) report of ADHD diagnosis: “Has a physician or other health professional ever told you that your child had attention deficit hyperactivity (ADHD) or attention deficit disorder (ADD)”?
    • Vulnerable to under or over-reporting
    • Age of child at diagnosis can be specified in a follow up question
    • May want to ask about which health professional reported diagnosis (e.g., pediatrician, psychiatrist, psychologist, other)
    • Ask about whether the child still has the diagnosis

  – Protocol #2 Medical record abstraction of ADHD diagnosis
    • Pediatric medical record, other records
Filling in the Gaps

- Recommendation #2: ADHD Treatment
  - Protocol #1 Parent (or guardian) report of ADHD medication prescription and use: “Has a physician or other health professional ever prescribed medication for ADHD for your child (e.g., stimulant, non-stimulant ADHD medication)?
    - Vulnerable to under or over-reporting
    - Age of child at prescription can be specified in a follow up question
    - May want to ask about which health professional prescribed the medication (e.g., pediatrician, psychiatrist, psychologist, other)
    - Ask about whether the child is still receiving treatment
    - What about non-prescription treatments?
      - Herbal supplements, behavioral therapy
  - Protocol #2 Medical record abstraction of ADHD treatment
    - Pediatric medical record, other records
Recommendations to the WG

• Recommendation #1: ADHD symptomatology
  – We could stay with protocol recommended by other WG (SWAN) or propose others (e.g., Conners)

• Recommendation #2: Add ADHD diagnosis
  – Parent report
  – Medical record review
  – Structured interview (child SCID)

• Recommendation #3: Add ADHD treatment
  – Parent report
  – Medical record review
Additional notes

• Related traits
  – There are measures/protocols for a number of ADHD-related symptoms
    • Attention (selective, sustained)
    • Impulsivity/hyperactivity
    • Executive function
  – Will discuss measures/protocols under the Child Behavior scope construct presentation
Autism Spectrum Disorders (ASD)
ASD: Definition

• Developmental disorder(s) that affects social interaction, speech and non-verbal communication, and restricted/repetitive behaviors
ASD: Concepts

- ASD diagnosis
  - DSM-V Criteria
    - Deficits in social communication and interaction
    - Restricted, repetitive patterns of behavior, interests, or activities
    - Symptoms present early in development
    - Significant impairment in social, occupational, or other important areas of current functioning
    - Not better explained by ID or global dev delay
  - Three severity levels
    - 1: “requiring support” to 3:”requiring very substantial support”
    - Across levels of social communication and RRB
  - Screening at well-child visits with pediatrician (e.g., MCHAT)
  - Follow up evaluation by professional (psychologist, dev ped)
    - typically based on observation (e.g., ADOS) and parent report (e.g., ADI-R)
ASD: Considerations

• Presents as an extremely heterogeneous disorder with variable symptom presentation and severity
• Symptoms often persist into adulthood
• Etiology multifactorial, high genetic heritability
• Often co-morbid with a number of other conditions
  – E.g., ADHD, Anxiety Disorder, sensory processing challenges
• US Prevalence (CDC): 1 in 59 (1.69%)
• Male:female = ~3/4:1
ASD – existing measures in toolbox

• Measure #1 “Symptoms of Autism Spectrum Disorders”
  – Protocol #120903 “Symptoms of Autism Spectrum Disorders - Child”
    • Childhood Autism Spectrum Test (CAST)
      – 37 item questionnaire administered to parent
      – child age 3-11 years
      – based on core features (social impairments, communication impairments, and repetitive or stereotyped behaviors)
• Pros: Not proprietary, brief
• Cons: No indication of frequency of behaviors, time frame
  – could limit the sensitivity of this existing protocol
ASD – existing measures in toolbox

• Measure #1 “Symptoms of Autism Spectrum Disorders”
  – Protocol #120902 “Symptoms of Autism Spectrum Disorders - Adolescent”
  • Autism Spectrum Quotient (AQ)
    – 50 item questionnaire administered to parent
    – child age 12-15 years
    – Example of questions
      1. S/he prefers to do things with others rather than on her/his own.
         [ ] Definitely Agree [ ] Slightly Agree [ ] Slightly Disagree [ ] Definitely Disagree

      2. S/he prefers to do things the same way over and over again.
         [ ] Definitely Agree [ ] Slightly Agree [ ] Slightly Disagree [ ] Definitely Disagree
Missing elements

• Better characterization of ASD symptomatology
• ASD Diagnosis
Filling in the Gaps

- Recommendation #1: Symptoms of ASD Measure
  - Social Responsiveness Scale, Version 2 (SRS-2)
    - 65-item scale (parent, teacher, self-report)
    - Children age 4-18
    - Frequency of behaviors in the previous 6 months
      - 1=not true, 2=sometimes true, 3=often true, and 4=almost always true
    - Well validated for use in *general population* samples with broad distribution of scores in general population samples (Constantino 2003)
    - T-scores for Total SRS, Social Communication Index (SCI), Restricted and Repetitive Behaviors (RRB)
    - 5 subscales:
      - Social awareness, social cognition, social communication, social motivation and autistic mannerisms
  - Pros: More sensitive
  - Cons: Longer, proprietary
Filling in the Gaps

• Recommendation #2: Add ASD Diagnosis Measure
  – Protocol #1 Parent (or guardian) report of ASD diagnosis: “Has a physician or other health professional ever told you that your child has an autism spectrum disorder (ASD)”?
    • Vulnerable to under or over-reporting
    • Age of child at diagnosis can be specified in a follow up question
    • May want to ask about which health professional reported diagnosis (e.g., pediatrician, psychiatrist, psychologist, other)
  – Protocol #2 Medical record abstraction of ASD diagnosis
    • Pediatric medical record, other records
  – Protocol #3 ASD diagnostic tests
    • ADOS, ADI-R
Recommendations to the WG

- Recommendation #1: Modify ASD symptomatology measure
  - SRS-2

- Recommendation #2: Add ASD diagnosis
  - Parent report
  - Medical record
  - Diagnostic measures
Child Behavior:
- Externalizing behaviors
  - including attention problems
- Executive function
Externalizing behaviors: Definition

• Behavior problems manifesting in outward “acting out” behavior; negatively acting on the external environment.

• Behaviors include:
  – Aggression (act in a hostile manner that may appear threatening to others)
  – Conduct problems (engage in anti-social rule-breaking behavior)
  – Hyperactivity/impulsivity (overly active or acting without thinking)
Externalizing behaviors: concepts & considerations

- Often comorbid with, or a consequence of, a developmental disorder (e.g., ADHD, ASD) or other behavior problem
- Tends to be more common among males than females
- Predictor of conduct disorder and criminality
Externalizing behaviors – existing measures in toolbox

• Measure #1 “Internalizing, Externalizing, and Substance Use Disorders Screener”
  – Protocol #580101 “Internalizing, Externalizing, and Substance Use Disorders Screener”
• Global Appraisal of Individual Needs-Short Screener (GAIN-SS) (Whiteside and Lynam, 2001)
  – 20 item screener, used to identify behavioral health disorders, including internalizing psychiatric disorders, externalizing psychiatric disorders, and substance use disorders
  – Adolescents (13-17) and adults (18+)
  – contains a five-item internal disorder screener, a five-item external disorder screener, and a five-item substance use disorder screener
  – measures the recency of the problem (e.g., in the past month, 2-12 months ago, more than one year ago, or never)
Externalizing behaviors – existing measures in toolbox

- **Measure #2 “Disinhibiting Behaviors - Impulsivity”**
  - Protocol #180402 “Disinhibiting Behaviors - Impulsivity - Child”
- **UPPS Impulsive Behavior Scale for Children (Whiteside and Lynam, 2001)**
  - assessment with five subscales (urgency, premeditation, perseverance, sensation seeking, and positive urgency) that are used to measure five distinct dimensions of impulsive behavior
  - ages 11-13
  - 40 self-administered questions
  - Example of questions
    1. If I feel like doing something, I tend to do it, even if it's bad
       [ ] Not at all like me [ ] Not like me [ ] Somewhat like me [ ] Very much like me
    2. I like new, thrilling things to happen
       [ ] Not at all like me [ ] Not like me [ ] Somewhat like me [ ] Very much like me
Externalizing behaviors – existing measures in toolbox

• Measure #3 “Disruptive Behavior”
  – Protocol #540201 “Disruptive Behavior”
    • Disruptive Behavior Disorders Rating Scale (DBDRS)
      – Proxy administered (parent or teacher)
      – based on Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD)
      – age 4-14 years (preschool – grade 8)
      – ADHD-related items have been excluded from this protocol. Please refer to the Attention-Deficit/Hyperactivity Disorder Symptoms measures in the Psychiatric domain in the Toolkit
Externalizing behaviors – existing measures in toolbox

• Measure #4 “Broad Psychopathology”
  – Protocol #610202 “Broad Psychopathology – Child”
  • Strengths and Difficulties Questionnaire (SDQ)
    – Proxy administered (parent or teacher, self for 11-17)
    – Screen children for positive and negative attributes
    – 25 questions (likert-scale)
    – Ages 3-10 and 11-17 years
    – Assess emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior
Externalizing behaviors – existing measures in toolbox

- **Measure #5 “Aggression and Hostility”**
  - Protocol #640701
  - **Buss-Perry Aggression Questionnaire (BPAQ)**
    - 29 self-administered items rated on a 5-point Likert scale
    - four subscales: Physical Aggression, Verbal Aggression, Anger, and Hostility
    - Ages 12+
Externalizing behaviors – existing measures in toolbox

- Measure #6 “Lack of Prosocial Emotions”
  - Protocol # 121602: Preschool Parent Report
    - Inventory of Callous-Unemotional Traits (ICU)
    - Preschool age
    - 23 items, 3 subscales (callousness, uncaring, unemotional), Likert scale (4)
  - Protocol # 121603: Preschool Teacher-report Version
  - Protocol # 121604: Children Self-report Version
    - Age 10-18
  - Protocol # 121605: Children Teacher-report Version
    - Age 10-18
Externalizing behaviors – existing measures in toolbox

• Measure #7 “Inhibitory Control (Stop Signal Paradigm)”
  – Protocol #530402
  • STOP-IT (Verbruggen et al. 2008)
    – Computer administered stop-signal task: participants react as quickly as possible to a visual stimulus unless it is followed by an auditory stop signal presented after a variable delay
    – Age 7+
    – Measures inhibitory control, a component of impulsivity and poor response inhibition
Externalizing behaviors – existing measures in toolbox

- Measure #8 “Sustained and Selective Attention”
  - Protocol #821201
  - Conners Continuous Performance Test 3rd Ed. (CPT 3)
    - Computer administered
    - Assesses inattentiveness, impulsivity, sustained attention and vigilance
    - Age 8+
Missing elements

• PhenX toolkit already includes a lot around behavior!

• A couple of gaps:
  – Aggression <12 years
  – Impulse control <7 years
Filling in the Gaps

- Recommendation #1: Behavioral Inventory for children
- Protocol
  - Behavioral Scale for Children, 3rd Ed. (BASC-3)
    - 105-165 items (parent and teacher 10-20’, self-report 30’)
    - Children ages 2-5, 6-11, 12-21
    - Comprehensive, includes externalizing & internalizing behaviors
    - Other subscales: adaptability, aggression, anxiety, attention problems, atypicality, conduct problems, depression, functional communication, hyperactivity, leadership, learning problems, social skills, somatization, study skills, withdrawal

- This could replace some of the existing measures in the toolkit (e.g., SDQ)
Filling in the Gaps

• Recommendation #2: Continuous Performance Test for children <7

• Protocol
  – Conners Kiddie Continuous Performance Test Second Ed. (K-CPT 2)
    • Children ages 4-7
    • Administration time: 7.5 minutes