New Content and Tools in the PhenX Toolkit

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PhenX Toolkit
consensus measures for Phenotypes and eXposures
https://www.phenxtoolkit.org

What Is PhenX?

PhenX is a consensus-based process to identify measurement protocols of **Phen**otypes and e**X**posures for biomedical research studies. Working Groups (WGs) of subject-matter experts lead the consensus process and recommend measurement protocols for each research domain based on the scope presented by the PhenX Steering Committee (SC). The scientific community also has an opportunity to review the measurement protocols before they are finalized. The result is a domain of 15 well-established measurement protocols that are made available to researchers via the PhenX Toolkit (**https://www.phenxtoolkit.org/**), a web-based catalog.

PhenX is funded by the National Human Genome Research Institute (NHGRI) as a genomic resource grant (U41), with co-funding from the National Institute on Drug Abuse (NIDA) and the Office of Behavioral and Social Science Research (OBSSR). The PhenX Toolkit content has also been enhanced with depth in several areas, including the following:

- Substance Abuse and Addiction (funded by NIDA),
- Mental Health Research (funded by the National Institute of Mental Health [NIMH]),
- Tobacco Regulatory Science (funded by the National Institutes of Health's [NIH's] Office of Disease Prevention [ODP] and Tobacco Regulatory Science Program and the U.S. Food and Drug Administration [FDA]), and
- Sickle Cell Disease and Hemophilia Inhibitors (funded by the National Heart, Lung, and Blood Institute [NHLBI]).

More information about the PhenX project is available at the PhenX website (**https://www.phenx.org**).

There are several advantages to using PhenX measurement protocols, including

- access to established and widely used protocols,
- standardized measurement protocols to facilitate cross-study analyses;
- expansion of original research scope with measurement protocols from other fields of research,
- combination of data with other studies that use the same measurement protocols to increase statistical power to detect subtle gene associations with health outcomes, and
- one-stop shopping for a wide range of phenotypes rather than literature searches.

The PhenX Toolkit

The PhenX Toolkit (**https://www.phenxtoolkit.org/**) includes more than 700 measurement protocols across 25 research domains (**Table 1**) with more in-depth collections of measurement protocols for substance abuse and addiction, mental health, sickle cell disease, and tobacco regulatory research (**Figure 1**). The PhenX Toolkit has been recommended in more than 200 NIH funding opportunity announcements.

For each measurement protocol, the Toolkit provides

- description of the protocol,
- rationale for the protocol's inclusion,
- detailed protocol(s) for collecting the data,
- information for administering the protocol, and
- other supporting documentation.

Toolkit users can search for measures using keywords, download individual measurement protocols, identify essential and related measurement protocols, and access data collection worksheets, data dictionaries, and common data elements (CDEs) for each measurement protocol. Registered users can also save groups of measurement protocols to their personal toolkit, share measurement protocols, provide comments during community outreach, and receive updates about Toolkit changes.

Table 1. PhenX Research Domains

- Alcohol, Tobacco and Other Substances
- Anthropometrics
- Cancer
- Cancer Outcomes and Survivorship*
- Cardiovascular
- Demographics
- Diabetes
- Environmental Exposures
- Gastrointestinal
- Genomic Medicine Implementation*
- Geriatrics
- Infectious Diseases and Immunity
- Neurology
- Nutrition and Dietary Supplements
- Obesity
- Ocular
- Oral Health
- Pediatric Development*
- Physical Activity and Physical Fitness
- Pregnancy
- Psychiatric
- Psychosocial
- Rare Genetic Conditions
- Reproductive Health
- Respiratory
- Skin, Bone, Muscle and Joint
- Social Determinants of Health*
- Social Environments
- Speech, Language and Hearing

* Under development

Figure 1. PhenX Toolkit Home Page

Updates from Research Domains

Speech, Language and Hearing

The Speech and Hearing Expert Review Panel (ERP) reviewed and updated this domain to improve the precision and consistency of speech, language, and hearing disorder phenotypes. The ERP was led by Dr. Cynthia Morton of Brigham and Women's Hospital and Harvard Medical School. This ERP convened repeatedly from August 2018 through February 2019 to update the 28 protocols to reflect the latest science and technology. The ERP recommendations include six new protocols, five updated protocols (from the same source), and one retired protocol. New additions include two voice-related, three hearing-related, and two speech-related protocols. Changes reflect new phone/tablet applications (apps) for hearing and language and for clinical evaluations of voice. The ERP decided to update the domain name to Speech, Language and Hearing to reflect the inclusion of nine language-related protocols. The measurement protocols in the Speech, Language and Hearing domain can facilitate assessment of speech, language, and hearing in clinical and population research.

Pediatric Development

The Pediatric Development WG was led by Dr. Michelle Bosquet Enlow of Harvard University and Boston Children's Hospital. The WG met in the Washington, DC, area in November 2018 and will soon present 18 new measurement protocols (**Table 2**) to the PhenX SC for approval. Approved protocols will be released in the PhenX Toolkit in fall 2019. These protocols will cover many aspects of pediatric development, including physical, psychological, and psychosocial measures. Measurement protocols covering the full spectrum of childhood, from Neonatal Abstinence Syndrome (NAS) and Neonatal Opioid Withdrawal Syndrome (NOWS) to Academic

Performance and Achievement, are among the additions. Other new measurement protocols assess parenting style, quality of the home environment, household composition, and child care quality. These new protocols will complement the many existing pediatric protocols in the PhenX Toolkit.

Table 2. Pediatric Development Measurement Protocols

Measurement Protocols	
Academic Performance and Achievement - Grades 4 to 6	• Child Report • Parent Report
Bullying	
Child Care Quality - Formal and Informal	• Younger • Older - Educational Setting
Child's Lifetime Household Composition	
Household Chaos and Unpredictability	
Interviewer-Administered Pediatric Psychiatric Assessment	
Neonatal Abstinence Syndrome (NAS) and Neonatal Opioid Withdrawal Syndrome (NOWS)	
Parenting Style	• Child Report • Parent Report
Peer Relationships	• Proxy Report • Self-Report
Psychological Resilience	• Child
Psychological Symptomology of Children	• Ages 1 to 5 • Ages 6 to 11
Psychological Symptomology of Parents/Caregivers	
Quality of the Child's Home Environment	
Supplemental Information	
Child's Living Environment	
Youth Alcohol Screener	

Social Determinants of Health (SDOH)

With supplemental funding from the National Institute of Minority Health Disparities (NIMHD), the goal of SDOH is to provide standard measures to help improve understanding of the causes of health inequities and effective interventions to reduce disparities. Key elements of influence in health disparities research include biological, behavioral, physical/built environment, sociocultural environment, and health care system. The SDOH WG met in person on February 20, 2019, and has been responsible for proposing new measures and associated protocols for this new SDOH domain. The SDOH WG is co-chaired by Drs. Barbara Entwisle from the University of North Carolina at Chapel Hill and Alicia Fernandez from the University of California, San Francisco. Community outreach for selected measures for the Toolkit will be in late fall 2019.

Hemophilia Inhibitor Research Collection

The Hemophilia Inhibitor Research Collection, funded by NHLBI, was released in the Toolkit on May 7, 2019. The collection includes 38 measurement protocols to determine levels of Factors VIII and IX, quantify inhibitors to Factors VIII and IX, measure the biological response to therapeutics, and capture key outcomes. The Hemophilia Inhibitor Research WG, co-chaired by Drs. Barbara Konkle of Bloodworks Northwest and Steven Pipe of the University of Michigan, recommended the measures for inclusion in the Toolkit, and the PhenX SC approved this recommendation.
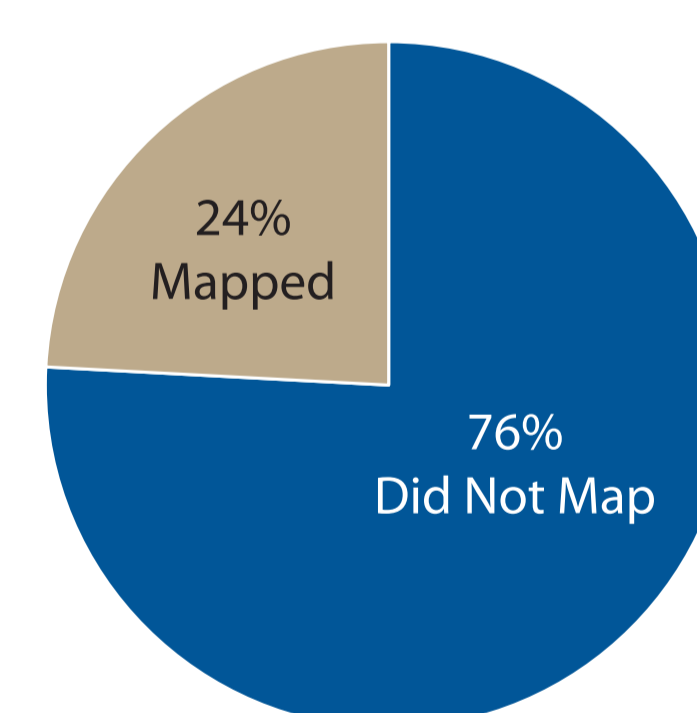
Bioinformatics and Toolkit Enhancement Updates

Observational Medical Outcomes Partnership (OMOP)

With supplemental funding from NHGRI, the PhenX team launched a pilot study to determine the feasibility and workload of mapping PhenX variables to CDEs within the OMOP common data model (CDM). The approach focused on using PhenX variables and protocols from five domains—Cardiovascular, Gastrointestinal, Pregnancy, Psychiatric, and Speech, Language and Hearing—in this initial mapping effort. Because all PhenX variables and protocols have Logical Observation Identifiers Names and Codes (LOINC) PhenX codes within the OMOP CDM, we mapped the existing LOINC PhenX codes to other vocabularies contained in the OMOP CDM. Using programmatic mapping, initial results included 2,093 PhenX LOINC codes and 9,972 mappings; a preliminary review of the results identified 24% as real mappings. Next steps include a secondary review and verification of the final mapping results.
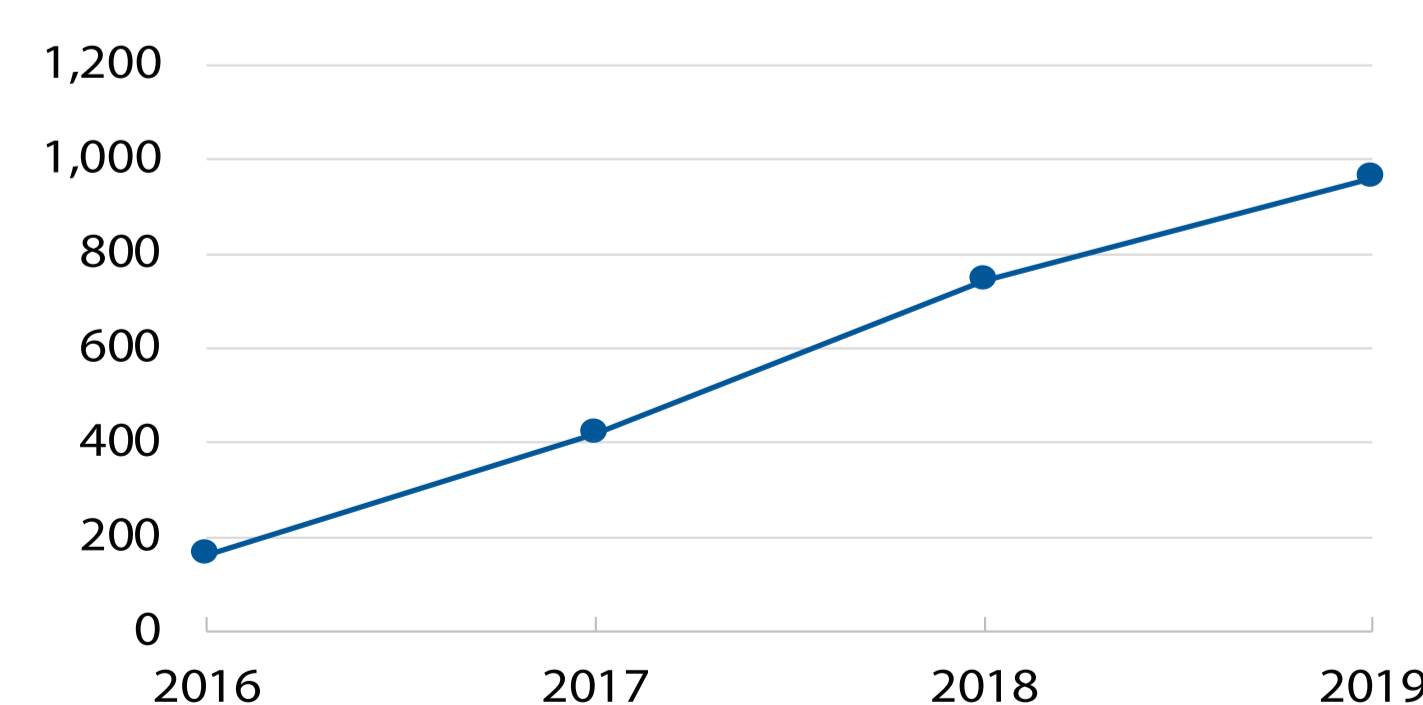
Preliminary PhenX-OMOP Mappings

- 24% Mapped
- 76% Did Not Map

PhenX Links to Other Semantic Resources

PhenX includes links to relevant ontologies such as Human Phenotype Ontology (HPO), controlled vocabulary and CDEs and standards such as the cancer Data Standards Repository (caDSR), and the National Library of Medicine (NLM) Unified Medical Language System (UMLS) as part of LOINC. These links are available in the protocol "Details."

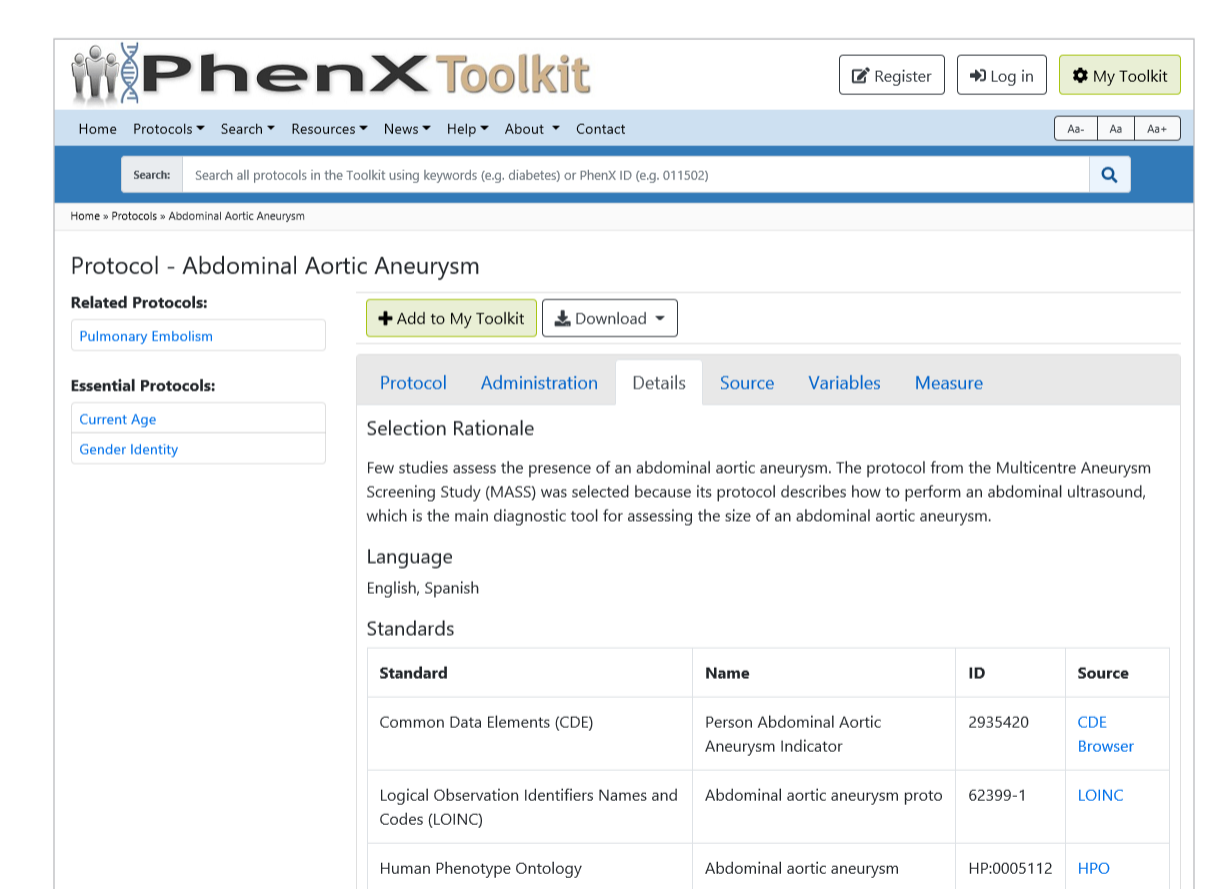## How the Research Community Is Using the PhenX Toolkit

PhenX variables are included in the NIH CDE Repository and the National Cancer Institute cancer Data Standards Registry and Repository (caDSR) Form Builder, and the NLM UMLS as part of LOINC. To date, 270 PhenX protocols have been cited in 105 publications, available in the PhenX "Studies Using PhenX" feature; 388 protocols have been used 952 times at 134 Research Electronic Data Capture (REDCap) institutes, including 39 institutes from seven continents.

Use of PhenX Protocols in REDCap

How to Cite Use of PhenX Measurement Protocols

When incorporating PhenX measurement protocols in a research study, please cite the version of the Toolkit that was used when the measurement protocols were selected. Because Toolkit content is occasionally updated, citing the version helps facilitate cross-study comparisons that used the same PhenX measures. The following example shows how PhenX should be cited:

Measurement protocols incorporated in this study were selected from the PhenX Toolkit version June 4, 2019, Ver 26.0.

How to Add a Reference for the PhenX Toolkit

Hamilton, C. M., Strader, L. C., Pratt, J. G., Maiese, D., Hendershot, T., Kwok, R. K., . . . Haines, J. (2011). The PhenX Toolkit: Get the most from your measures. *American Journal of Epidemiology, 174*(3), 253–260.

How to Get Involved

If you would like to receive e-mail notifications and updates about the PhenX Toolkit, please send your name and e-mail address to **contact@phenxtoolkit.org**.

National Human Genome Research Institute

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