The PhenX Toolkit

Erin M. Ramos, PhD MPH

Deputy Director, Division of Genomic Medicine
February 22, 2021

NHGRI PhenX Team: Jyoti Dayal, Madison Goldrich
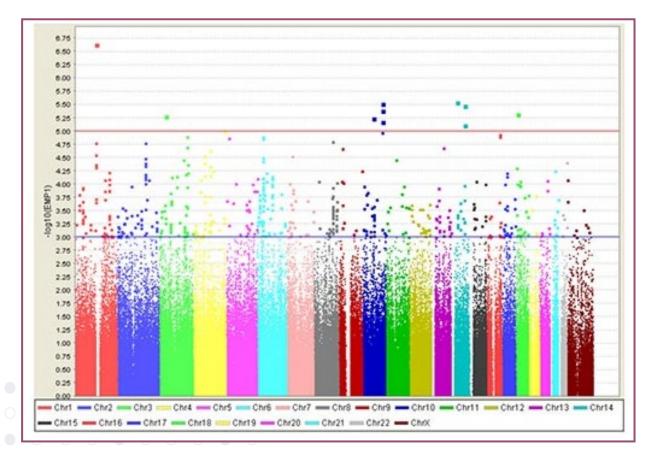
National Human Genome
Research Institute

The **Forefront**
of **Genomics**®

Standard Measures Needed – c2006

Type 2 Diabetes GWAS (>380K SNPs)

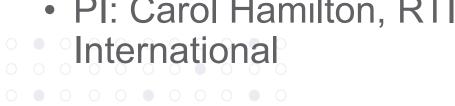(www.broad.mit.edu/diabetes/scandinavs/type2.html)

- To detect loci with moderate effect size and G x G; G x E interactions, **large sample sizes needed**.

- Standard (common) measures facilitates **replication of study findings**.

- Potential for **cross-study analysis** increases with common measures

NIH NHGRI PhenX consensus measures for Phenotypes and eXposures

The PhenX Toolkit

- Catalog of recommended measurement protocols

- Facilitate cross-study analysis, increasing impact of individual studies

- Funding: NHGRI + **7** NIH ICs

- PI: Carol Hamilton, RTI International

www.phenxtoolkit.org

Content

- 863 Protocols from 28 Research Domains

- Domain Examples:
  - Demographics, Substance Use, Physical Activity
  - Reproductive Health, Pregnancy, Pediatric Development, Geriatrics
  - Diabetes, Cardiovascular, Oral Health

- Special Collections:

| Substance Abuse and Addiction | Tobacco Regulatory Research | Mental Health Research | Blood Sciences Research | Social Determinants of Health | COVID-19 Research |

Building Consensus

Steering Committee

NIH Institutes and Centers

Expert Working Groups

Outreach

Expert Review Panels

Criteria for Protocol Selection
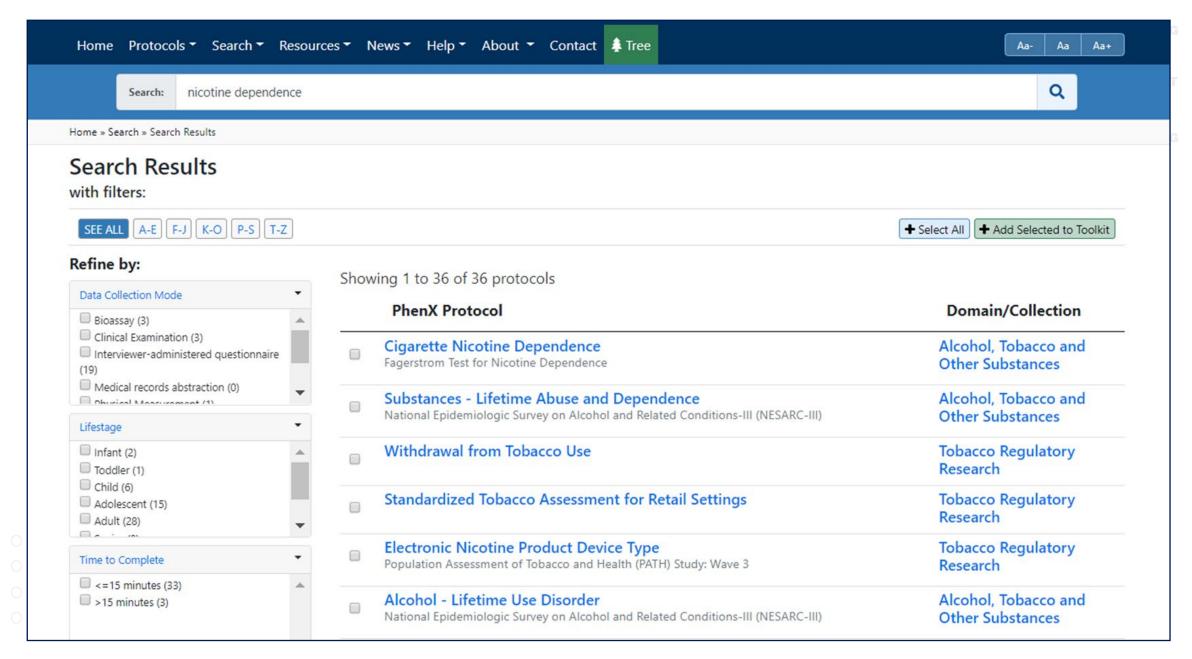
Standard protocol exists

Broadly applicable

Low burden
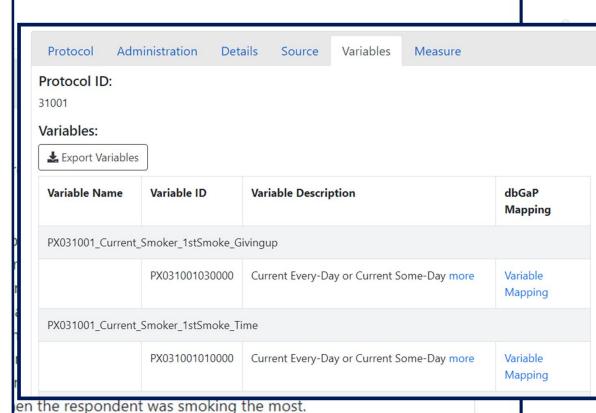
Valid & reproducible

Open source

Current Every-Day or Current Some-Day Smokers: *Instructions to interviewer: The following six questions are asked twice: once with the lead-in statement about current usage and, if appropriate, a second time with the lead-in statement about the period of maximum usage. a. Currently,... (ask 6 questions) b. Was there a 6-month period when you smoked more than you do now? (If "Yes," then continue to ask 6 questions again. If "No," stop.)*

1. How soon after you wake up do/did you smoke your first cigarette?

   1 [ ] Within 5 minutes [3 points]

   2 [ ] 6-30 minutes [2 points]

   3 [ ] 31-60 minutes [1 point]

   4 [ ] After 60 minutes [0 points] 2. Do/Did you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in a cinema, etc.?

   1 [ ] Yes [1 point]

   2 [ ] No [0 points]

3. Which cigarette would you hate most to give up?

   1 [ ] The first one in the morning [1 point]

   2 [ ] All others [0 points]

4. How many cigarettes per day do/did you smoke?

   1 [ ] 10 or less [0 points]

   2 [ ] 11-20 [1 point]

   3 [ ] 21-30 [2 points]

   4 [ ] 31 or more [3 points]

5. Do/did you smoke more frequently during the first hours after waking than during the rest of the day?
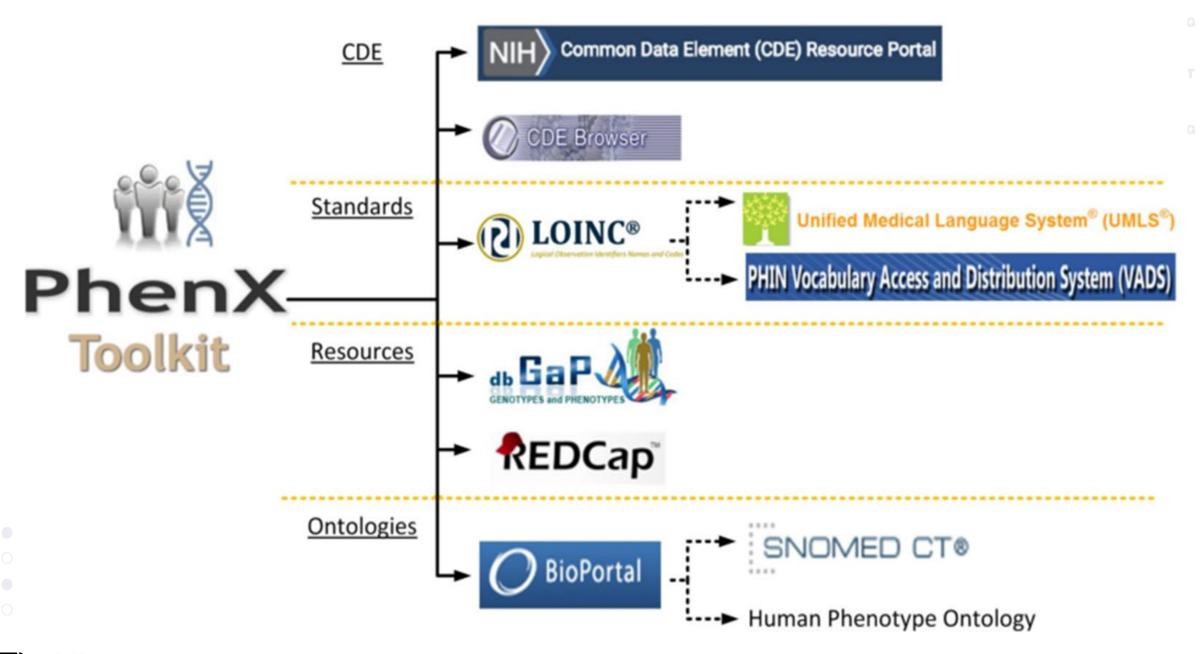
   1 [ ] Yes [1 point]

   2 [ ] No [0 points]

Protocol   Administration   Details   Source   Variables   Measure

Protocol ID:

31001

Variables:

⬇ Export Variables

Variable Name	Variable ID	Variable Description	dbGaP Mapping
PX031001_Current_Smoker_1stSmoke_Givingup			
	PX031001030000	Current Every-Day or Current Some-Day more	Variable Mapping
PX031001_Current_Smoker_1stSmoke_Time			
	PX031001010000	Current Every-Day or Current Some-Day more	Variable Mapping

...en the respondent was smoking the most.

...ded to be used for other tobacco products and could be difficult ...day is a key variable.

Linking PhenX and dbGaP Variables for Data Harmonization and Cross-Study Analysis

- PhenX links for **13,655** dbGaP variables, accessible at:
  - dbGaP - a CDE facet browser and a search filter
  - PhenX Toolkit –a search tool and links at variable page

Mapped dbGaP Studies

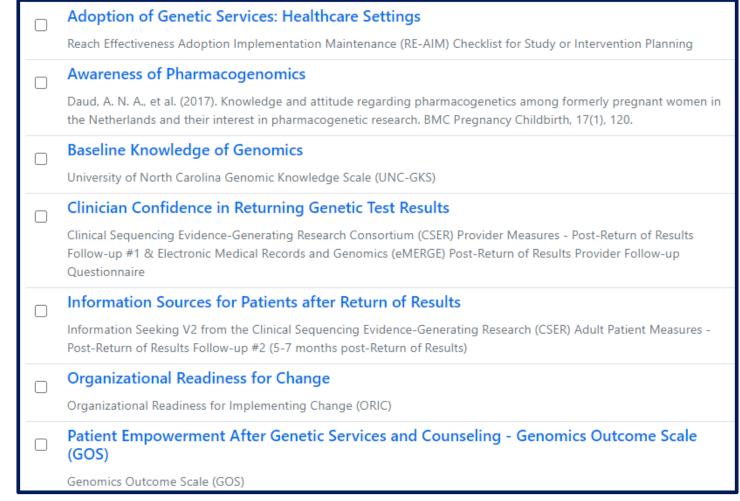| PhenX Variable ID	PhenX Variable Name	Protocol Name	Mapping level	dbGaP Study	dbGaP Variable
PX030301010000	PX030301_Alcohol_30Day_Frequency	Alcohol - 30-Day Quantity and Frequency	comparable	GenADA/LONG/Imaging (Genetic Alzheimer's Disease Associations)	phv00081806
PX030301010000	PX030301_Alcohol_30Day_Frequency	Alcohol - 30-Day Quantity and Frequency	comparable	Genetic Multiple Sclerosis Associations - GeneMSA	phv00072936
PX030301010000	PX030301_Alcohol_30Day_Frequency	Alcohol - 30-Day Quantity and Frequency	comparable	NEIGHBOR Consortium Glaucoma GWAS	phv00129665
PX030301010000	PX030301_Alcohol_30Day_Frequency	Alcohol - 30-Day Quantity and Frequency	comparable	The Vaginal Microbiome: Disease, Genetics and the Environment	phv00090478
PX030301010000	PX030301_Alcohol_30Day_Frequency	Alcohol - 30-Day Quantity and Frequency	comparable	The Vaginal Microbiome: Disease, Genetics and the Environment	phv00090481
PX030301010100	PX030301_Alcohol_30Day_Frequency_Coded	Alcohol - 30-Day Quantity and Frequency	comparable	GWAS on Cataract and HDL in the PMRP	phv00181344

Genomic Medicine Implementation

Scope:

- Understanding of baseline genetic information and their implications

- Impact of genomic interventions on patients, families, and providers

- Assessment of organizational characteristics and readiness to adopt genetic services

☐ **Adoption of Genetic Services: Healthcare Settings**

Reach Effectiveness Adoption Implementation Maintenance (RE-AIM) Checklist for Study or Intervention Planning

☐ **Awareness of Pharmacogenomics**

Daud, A. N. A., et al. (2017). Knowledge and attitude regarding pharmacogenetics among formerly pregnant women in the Netherlands and their interest in pharmacogenetic research. BMC Pregnancy Childbirth, 17(1), 120.

☐ **Baseline Knowledge of Genomics**

University of North Carolina Genomic Knowledge Scale (UNC-GKS)

☐ **Clinician Confidence in Returning Genetic Test Results**

Clinical Sequencing Evidence-Generating Research Consortium (CSER) Provider Measures - Post-Return of Results Follow-up #1 & Electronic Medical Records and Genomics (eMERGE) Post-Return of Results Provider Follow-up Questionnaire

☐ **Information Sources for Patients after Return of Results**

Information Seeking V2 from the Clinical Sequencing Evidence-Generating Research (CSER) Adult Patient Measures - Post-Return of Results Follow-up #2 (5-7 months post-Return of Results)

☐ **Organizational Readiness for Change**

Organizational Readiness for Implementing Change (ORIC)

☐ **Patient Empowerment After Genetic Services and Counseling - Genomics Outcome Scale (GOS)**

Genomics Outcome Scale (GOS)

NIH
NHGRI

PhenX
consensus measures for Phenotypes and eXposures

Social Determinants of Health

PhenX Social Determinants of Health Assessments Collection

An open-access resource for standard social determinants of health measures.

National Institute on Minority Health and Health Disparities

RAPID ACCELERATION OF DIAGNOSTICS (RADX)

- Individual
  - Discrimination, Food Insecurity, Spirituality
- Structural
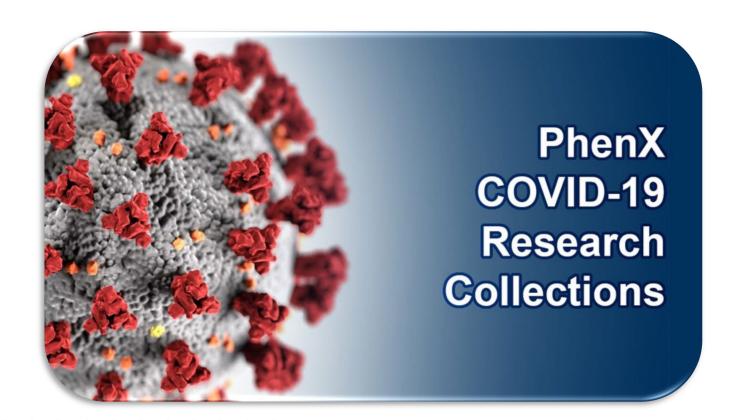 - Concentrated poverty, Social vulnerability

- Aims to understand factors that have led to disproportionate burden of the COVID19 pandemic on the underserved and/or vulnerable populations

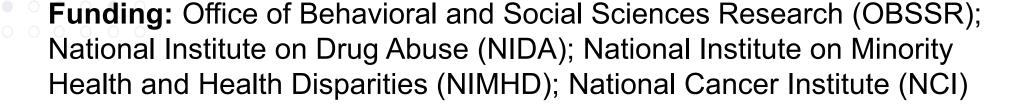**Co-chairs: Barbara Entwisle, PhD & Alicia Fernandez, MD**

COVID-19 Research Collection

- Behaviors and Risks
- History, Treatment and Outcome
- Information Resources
- Psychosocial and Mental Health
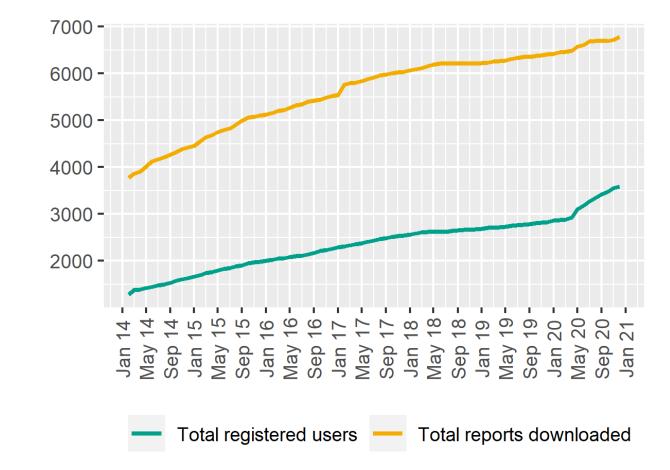- Race, Ethnicity and Demographics
- Socioeconomic

Toolkit Use & Statistics

394 NIH Funding Opportunity Announcements Reference PhenX

1.6M page visits & nearly **7,000** report downloads

Top 10 Protocols

1. Ethnicity and Race
2. Current Employment Status
3. Current Age
4. Educational Attainment - Individual
5. Annual Family Income
6. Gender Identity
7. Access to Health Services
8. Food Insecurity
9. Health Literacy
10. English Proficiency

Legend: Total registered users — Total reports downloaded

Acknowledgements

- Carol Hamilton, PI
- Tabitha Hendershot, Co-I
- Amanda Riley
- Deborah Maiese
- Lisa Cox
- Lauren Gridley
- Wayne Huggins
- Stephen Hwang
- Cataia Ives
- Michelle Krzyzanowski
- Mark Nelms
- Helen Pan
- Michael Phillips
- Pat West

Steering Committee

- Mary Marazita, co-Chair
- Catherine McCarty, co-Chair
- Marylyn Ritchie
- Lindsay Farrer
- Sharon Terry
- Elaine Faustman
- Marsha Treadwell
- Jonathan Haines
- Rosalind Wright

NHGRI

- Jyoti Dayal
- Madison Goldrich
- Teri Manolio

https://www.phenxtoolkit.org/about/teams

15