The PhenX Toolkit: Standard Measures for Collaborative Research

NIH Symposium: Linking Disease Model Phenotypes to Human Conditions

September 10-11, 2015

Carol M. Hamilton

PhenX: consensus measures for **Phen**otypes and e**X**posures

- PhenX is funded by the National Human Genome Research Institute (NHGRI), Project Scientist, Dr. Erin Ramos with co-funding from the National Institute on Drug Abuse (NIDA)

- NHGRI recognized that including standard measures in genome-wide association studies (GWAS) would have significant impact on biomedical research and released an RFA

- In September 2007, RTI International was awarded a Cooperative Agreement (U01) to select and define high priority measures for GWAS (phase 1)

- In July 2013, RTI International was awarded a Genomics Resource grant (U41) to maintain and expand the Toolkit and extend beyond GWAS (phase 2)

- PhenX uses an established consensus based process, and is driven by the scientific community

- Initially focused on measures for genome-wide association studies, the scope has broadened to translational and clinical research

Why Use Standard Measures?

- Study findings require validation
  - Initial findings need to be replicated, standard measures aid comparisons
- Increased sample size provides greater statistical power
  - For GWAS, to identify moderate associations and more complex interactions
  - For other types of studies, increases statistical confidence in results
- Cross-study analyses increase the impact of individual studies
  - Many diseases and conditions share common risk factors
  - Use of standard (common) measures facilitates cross-study analyses
- What is needed is a common framework (ontology) that supports consistent future development and connects PhenX and other resources, e.g, measures (PROMIS), data repositories, electronic medical records

PhenX Terminology

- **DOMAIN**: Topical area with a unifying theme

- **COLLECTION**: A collection of measures with a shared characteristic, target population or topic. The measures included in a Collection may cut across research Domains

- **MEASURE**: A certain characteristic of, or related to, a study subject

- **PROTOCOL**: Standard procedure recommended by a Working Group to collect and record a PhenX measure
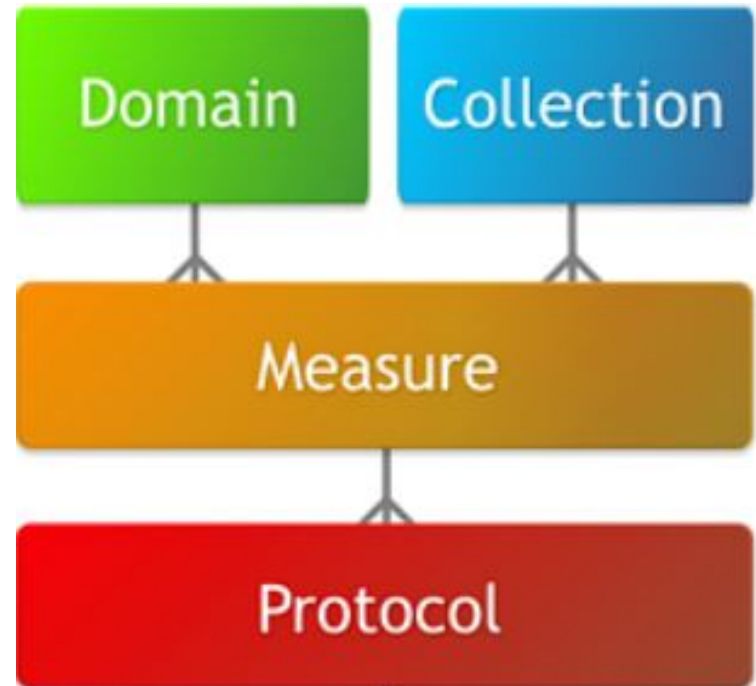
Criteria for Selecting PhenX Measures

- Clearly defined

- Well established

- Broadly applicable

- Validated

- Reproducible

- Specific

- Reliable

- Standard measurement protocols exist

PhenX - Research Domains

- Alcohol, Tobacco, and Other Substances
- Anthropometrics
- Cancer
- Cardiovascular
- Demographics
- Diabetes
- Environmental Exposures
- Gastrointestinal
- Infectious Diseases and Immunity
- Neurology
- Nutrition and Dietary Supplements
- Obesity

- Ocular
- Oral Health
- Physical Activity and Physical Fitness
- Psychiatric
- Psychosocial
- Rare Genetic Conditions
- Reproductive Health
- Respiratory
- Skin, Bone, Muscle, and Joint
- Social Environments
- Speech and Hearing
- Pregnancy and Pediatrics
- TBD

Types of PhenX Measures

PhenX Toolkit

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Smart Query Tool

Search pre-defined search filters listed below
Search by entering your own terms in the box below

Data Collection Mode
- ☑ Interviewer-administered questionnaire
- ☑ Self-administered questionnaire
- ☐ Bioassay
- ☑ Clinical Examination
- ☐ Physical Measurement
- ☐ Medical records abstraction
- ☐ Secondary Data Analysis

Lifestage
- ☐ Infant
- ☐ Toddler
- ☐ Child
- ☐ Adolescent
- ☐ Adult
- ☐ Senior
- ☐ Pregnancy

Time to Complete
- ☐ <=15 minutes
- ☐ >15 minutes

Language
- ☐ English
- ☐ Spanish
- ☐ Other

Enter search term or PhenX ID:

Depression

Show 10 ▼ results per page

Smart Search   Text Search

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Examples of PhenX Measures

- Height and Weight (Anthropometrics)

- Blood pressure (Cardiovascular)

- Stroke (Neurology)

- Ultraviolet light exposure (Environmental Exposures)

- Exposures to violence (Psychosocial)

- Liver function (Gastrointestinal)

- Pain (Type and Intensity) (Gastrointestinal)

Rare Genetic Conditions: New Measures

- Ataxia Rating Scale

- Body Proportions

- Bone Age

- Child Oral Health Pain

- Disability Index

- Disease Progression and Regression

- Disorders of Respiratory Control with Inherent Autonomic Dysregulation

- Echocardiography Phenotypes

- Family Health History

- Growth Charts

- Pediatric Quality of Life

- Scale of Developmental Domains of Early Childhood

- Scoliosis - Physical Assessment

- Scoliosis - Quality of Life

- Sweat Chloride Test

Measures Already in the Toolkit (examples) Applicable to RGC

- Alkaline phosphatase – Paget's Disease

- Audiogram hearing test – Alport Syndrome

- Chest Computer Tomography (CT) - Congenital Pulmonary Lymphangiectasia

- Exercise Capacity/Six-Minute Walk Test - Duchenne Muscular Dystrophy

- Annotation – but potential for inclusion in a "range of phenotypes" ontology

PhenX Supplements - adding depth to the Toolkit

- PhenX Measures for Sickle Cell Disease Research (funded by NHLBI)
  - Ellen Werner, Project Scientist
  - Sickle Cell Disease Research and Scientific Panel (SRSP)
  - Collaborating with H3Africa (Human Heredity and Health in Africa) on a Sickle Cell Disease ontology
- PhenX Measures for Mental Health Research (funded by NIMH)
  - Greg Farber, Project Scientist
  - Mental Health Research Scientific Panel (MHRP)
- PhenX Measures for Tobacco Regulatory Science (funded by TRSP)
  - Kay Wanke, Project Scientist
  - Tobacco Regulatory Research Scientific Panel (TRRP)
- PhenX Measures for Substance Abuse and Addiction (funded by NIDA)
  - Kevin Conway, Project Scientist
  - Substance Abuse and Addiction Scientific Panel (SSP)

Vocabulary Standards
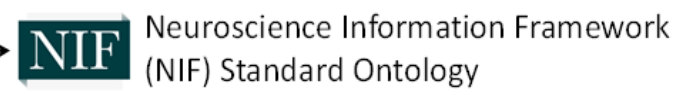
Ontologies

Resources

National Cancer Institute

U.S. National Institutes of Health | www.cancer.gov

caDSR

CDE Browser

CDE Cart   Home   FormBuilder   Help

Admin Tool Curation Tool NCI Metathesaurus NCI Terminology Server Sentinel Tool UML Model Browser   What's new Available Downloads New!

Refresh tree

- caDSR Contexts
  - ABTC (Adult Brain Tumor Consortium)
  - AECC (Albert Einstein Cancer Center)
  - Alliance (Alliance)
  - BOLD (Breast Oncology Local Disease)
  - BRIDG (BRIDG Collaboration)
  - caBIG (NCI cancer Biomedical Informatics Grid)
    - Classifications
      - 10 PROMIS Global Health Questionnaire

Data Element Search

Search for Data Elements   Search preferences   Advanced search
caDSR Contexts
- ● Exact phrase
- ○ All of the words   [   ]   [Name   ▼]
- ○ At least one of the words

Tip: This is an exact match search. To search for partial words or phrases use the * as a wildcard.

- PhenX
  - Anthropometrics
  - ATOS (Alcohol, Tobacco, and Other Substances)
  - Cancer
  - Cardiovascular
  - Demographics
  - Diabetes
  - Environmental Exposures

	Name	Description			Status	ID	Ver
☐	NIH Stroke Scale Evaluation Best Language Score	Best Language	NINDS	caBIG	RELEASED	3210248	1.0
☐	NIH Stroke Scale Evaluation Date	Date of NIHSS	NINDS	caBIG	RELEASED	3201206	1.0
☐	NIH Stroke Scale Evaluation Dysarthria Score	Dysarthria	NINDS	caBIG	RELEASED	3210249	1.0
☐	NIH Stroke Scale Evaluation Limb Ataxia Score	Limb ataxia	NINDS	caBIG	RELEASED	3210246	1.0
☐	NIH Stroke Scale Evaluation Motor Arm Right Score	Motor arm right	NINDS	caBIG	RELEASED	3204336	1.0
	NIH Stroke Scale Evaluation						

- Physical Activity and Physical Fitness
- Psychiatric
- Psychosocial
- Rare Genetic Conditions
- Reproductive Health
- Respiratory
- Sickle Cell Disease Collection
  - Sickle Cell Disease Core Tier 1:
  - Sickle Cell Disease Core Tier 2:
  - Sickle Cell Disease WG 1: Cardiovascular, Pulmonary, and Renal
  - Sickle Cell Disease WG 2: Neurology, Quality of Life, and Health

	Name	Description			Status	ID	Ver
☐	NIH Stroke Scale Level of Consciousness Question Score	LOC questions	NINDS	caBIG	RELEASED	3201209	1.0
☐	NIH Stroke Scale Level of Consciousness Score	Level of consciousness	NINDS	caBIG	RELEASED	3201208	1.0
☐	NIH Stroke Scale Motor Arm Left Score	Motor arm left	NINDS	caBIG	RELEASED	3204316	1.0
☐	NIH Stroke Scale Visual Score	Visual	NINDS	caBIG	RELEASED	3201211	1.0
☐	Vineland Adaptive Behavior Scales Performed Assessment Score Value	What was the vineland adaptive behavior scales value?	NHLBI	DCP,caBIG	RELEASED	3057303	1.0
☐	Vineland Adaptive Behavior Scales Performed Indicator	Were the vineland adaptive behavior scales performed?	NHLBI	DCP,caBIG	RELEASED	3057299	1.0
☐	Vineland Adaptive Behavior Scales Performed Type	What is the vineland adaptive behavior scales performance	NHLBI	DCP,caBIG	RELEASED	3085846	1.0

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NIH › Common Data Element (CDE) Resource Portal

Home | Resource Summaries | Glossary

Home

Summary Table for NIH CDE Initiatives

This table lists summary information for NIH CDE Initiatives. More information on NIH CDE Initiatives: Subject Areas, Detailed Summaries.

Show 50 ▼ entries

Search:

Link to Homepage	Link to CDEs	Brief Summary	Number of Elements	Studies and Publications	CDE Resource Contact
Standardized Asthma Outcomes for Clinical Research	Asthma CDEs	The standardized asthma outcomes for clinical research represent recommendations for core (required in future studies), supplemental (to be used according to study aims), and emerging (requiring validation and standardization) outcomes for 7 domains of asthma clinical research outcome measures. Subject Areas | More...	10 (adults), 25 (children)	--	NHLBI, NIAID
Chronic Low Back Pain CDEs	cLBP	Recommended minimum dataset for research on chronic low back pain. Subject Areas | More...	40	--	NCCAM
Early Detection Research Program	EDRN	CDEs for use in describing samples and data collected as part of cancer biomarker research. Subject Areas | More...	1,600	Publications	NCI
eyeGENE	eyeGENE	As part of eyeGENE, common data elements have been developed for collecting phenotypic data associated with more than 30 inherited ophthalmic diseases. Subject Areas | More...	300+	Studies	NEI
Global Rare Diseases Patient Registry and Data Repository	GRDR	CDEs to facilitate standardized data collection into the GRDR and to assist organizations in establishing rare disease registries that contribute information to GRDR. Subject Areas | More...	70	Publications	ORDR
Quality of Life Outcomes in Neurological Disorders	Neuro-QOL	A core set of quality-of-life questions that address chronic neurologic disorders, plus sets of supplemental questions specific to targeted diseases or subgroups of patients. Subject Areas | More...	500	Publications	NINDS
NIDA Substance Abuse Electronic Health Record Data Elements	NIDA EHR	A set of brief screening and initial assessment tools for substance use disorders (SUDs) for use in general medical settings. Subject Areas | More...	80+	--	NIDA
NIH Toolbox for Assessment of Neurological and Behavioral Function	NIH Toolbox	An integrated set of tools for measuring cognitive, emotional, motor and sensory function. Subject Areas | More...	4 batteries of tests, each with 5-24 tests	Publications	NIH
NINDS Common Data Elements	NINDS CDEs	A core set of data elements for use in NINDS-funded studies, including core and supplementary sets of data elements for use in disease-specific studies. Subject Areas | More...	10,000 unique variables, 550+ instruments	Studies	NINDS
Consensus Measures for Phenotypes and eXposures	PhenX	Standard measures related to complex diseases, phenotypic traits and environmental exposures for inclusion in genome-wide association studies (GWAS) and other large-scale genomic and epidemiologic research efforts. Subject Areas | More...	15,000+ variables, 428 protocols	Publications	NHGRI
Patient Reported Outcomes Measurement Information System	PROMIS	A system of item banks measuring patient-reported health status for various domains of physical, mental, and social health across clinical populations (i.e. not disease-specific). Subject Areas | More...	50 item banks	Publications	NIAMS

Showing 1 to 11 of 11 entries

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New Sickle Cell Disease Research measures available, August 12, 2015 *here*

Research Domains

Featured New Domain

New!
Sickle Cell Disease Research

Tobacco Regulatory Research

Welcome to the PhenX Toolkit

The Toolkit provides *standard* measures related to complex diseases, phenotypic traits and environmental exposures. Use of PhenX measures facilitates combining data from a variety of studies, and makes it easy for investigators to expand a study design beyond the primary research focus. All Toolkit content is available to the public at no cost.

Information about the project is available at www.phenx.org

More »

⊙ Please Read Toolkit Guidance

How to cite use of PhenX measures:

Measures incorporated in this study were selected from the PhenX Toolkit version August 12, 2015, Ver 11.0. More »

How to cite the PhenX Toolkit:

Hamilton, et al. (2011) The PhenX Toolkit: Get the Most From Your Measures. *American Journal of Epidemiology*, **174**(3), 253-60.

PhenX is funded by a Genomic Resource Grant, U41 HG007050, from NHGRI with co-funding from NIDA.

Registration

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Review Measure

Show Tree ☐

MEASURE: Urinary Creatinine Assay for Kidney Function #141600

Definition: A bioassay to measure urine concentration of creatinine, a muscle metabolite that is filtered out of blood by the kidneys.

Purpose: The urinary creatinine measure should be done in conjunction with urinary microablumin to determine ratio of urine albumin to urine creatinine which can predict the risk of nephropathy (National Health and Nutrition Examination Survey and University of Minnesota Laboratory Procedure Manual for Urinary Creatinine, 2008).

Protocols:

Add to My Toolkit   #141601   Urinary Creatinine Assay for Kidney Function »

Essential Measures ?	Related Measures ?	Collections ?
	Blood Pressure (Adult/Primary)	Organ Function
	Personal History of Kidney Failure	Kidney Failure
Current Age	Serum Creatinine Assay for Kidney Funct...	Maternal Complications
Gender	Urinary Microalbumin Assay for Kidney F...	Sickle Cell Disease: Cardiovascular, Pulmonary, and Renal Specialty Collection

Keywords: Centers for Disease Control and Prevention, CDC, National Center for Health Statistics, NCHS, National Health and Nutrition Examination Survey Questionnaire, NHANES, University of Minnesota, Fairview University Medical Center, Nephropathy, diabetic nephropathy, kidney, kidney disease, kidney failure, Cardiovascular disease, Microalbuminaria, Macroalbuminaria, Diabetes

Measure Release Date: May 12, 2010

➕ Add this Measure* to My Toolkit

➕ Add this Measure* and all Essential Measures to My Toolkit

Protocol Overview

Show Tree ☐

Note: Some Protocols contain images. You may click the thumbnails to preview the full image. To print Protocols with full size images, please add those Protocols to your Toolkit and Generate a Report.

URINARY CREATININE ASSAY FOR KIDNEY FUNCTION #141601

Jump to section: ▼   Show Details

Protocol Release Date ⋙

Description of Protocol ⋙

Specific Instructions ⋙

Protocol Text ⋙

Selection Rationale ⋙

Source ⋙

Personnel and Training Required ⋙

Equipment Needs ⋙

Standards ⋙

General References ⋙

Protocol Type ⋙

Derived Variables ⋙

Requirements ⋙

Toolkit Features

- **Browse or Search entire Toolkit**

  - Browse by "Domain", "Measure," or "Collection"

  - Search using "Smart Query Tool"

- **Add measures to "My Toolkit"**

  - Identifies "Essential Measures"

  - Recommends "Related Measures"

  - Registration allows users to save and share multiple Toolkits

- **Download information about selected measures**

  - Custom Reports

  - Custom Data Collection Worksheets (DCW)

  - Data Dictionaries (DD) support data submission to dbGaP

  - REDCap zip instrument files to upload to studies in REDCap

Register Studies

Back to Registered Studies

Name of Funded Study *

Enter PhenX protocols used in your study.
1) start typing the protocol name or ID
2) select the full protocol name and ID from the auto-complete dropdown list
3) click on the "Add" button

Add

Selected PhenX Protocols *

Delete

Study Acronym

Principal Investigator *

Primary Contact Name *

Primary Contact Email *

Number Participants *   Select One

Grant Number *
The grant number you would include in a research publication

REDCap

Research Electronic Data Capture

| Introduction | Software | Consortium Partners | Become a Partner | Video Resources | Citing REDCap | Library | REDCapCon |

REDCap "Instrument ZIP" files

REDCap 6.5.0 and later provides a way to easily add new data collection instruments to a REDCap project by uploading an "instrument ZIP" file. These instrument ZIP files may be downloaded from an external instrument library (e.g., PhenX Toolkit, Medical Data-Models) or from another REDCap project or user, and then uploaded on the Online Designer page in a REDCap project so that they get added as a new data collection instrument. These ZIP files can contain attachment files for "descriptive" fields, which makes it very easy to obtain or share an instrument containing several attachment files.

NOTE: An instrument ZIP file contains only one instrument that gets *added* to a project, whereas a REDCap data dictionary CSV file contains ALL the instruments in a project and would thus *replace all* instruments in the project when uploaded.

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REDCap Instruments ZIP Files

PhenX is collaborating with REDCap to make PhenX protocols available as REDCap instruments zip files that can be uploaded directly to REDCap. More, coming soon. Click on a protocol name below to download the REDCap Zip File. Click here for REDCap "Instrument ZIP" feature.

- Abdominal Aortic Aneurysm
- Acculturation
- Acute Subjective Response to Substances - Current - General
- Acute Subjective Response to Substances - Current - Specific - Alcohol
- Acute Subjective Response to Substances - Current - Specific - Drugs
- Acute Subjective Response to Substances - Current - Specific - Tobacco
- Acute Subjective Responses to Substances - Retrospective - Alcohol
- Acute Subjective Responses to Substances - Retrospective - Tobacco
- Air Contaminants in the Home Environment
- Alcohol - 30-Day Quantity and Frequency
- Alcohol - Age of First Use
- Alcohol - Lifetime Use
- Alcohol - Maximum Drinks in 24 Hours
- Alcohol Breathalyzer
- Alkaline Phosphatase
- Angina
- Annual Family Income
- Anxiety Disorders Screener - Adult
- Anxiety Disorders Screener - Child
- Arm Span
- Arrhythmia (Atrial and Ventricular)

REDCap
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REDCap Shared Library

The REDCap Shared Library is a repository for REDCap data collection instruments and forms that can be downloaded and used by researchers at REDCap partner institutions. Curated instruments have been approved for inclusion by the REDCap Library Oversight Committee (REDLOC) after review for research relevance, accuracy in function and coding (see guidelines), and copyright issues.

You may search below for any available data collection instruments. If you got to this site directly, you will be able to view the shared instruments as they would appear in REDCap or view a PDF version that can be downloaded and/or printed. Otherwise, if you arrived here from the REDCap application, you will have the additional option of importing the form directly into REDCap. If you wish, you may download a list of all library instruments in Excel/CSV format. If you download and utilize an instrument from the REDCap Shared Library, please cite the RSL manuscript. If you have questions or are experiencing issues, please contact redcap@vanderbilt.edu.

Keyword search: PhenX

[Search the library]

Search options:

Minimum downloads: 0
Recent additions: show all ▼

Shared Library
Search

Library Metrics
Consortium Activity

REDLOC
REDLOC Login

Found 1 results matching your search

| Title		Downloads
➤ 🗋 PhenX Toolkit	[External Instrument Library]	

The database of Genotypes and Phenotypes (dbGaP)

- NIH funded genome-wide association studies are required to deposit their data in dbGaP

- Pilot - investigators can search dbGaP and find studies that included measures comparable or related to PhenX measures

- In the future, investigators submitting data to dbGaP will be asked to self-identify PhenX measures
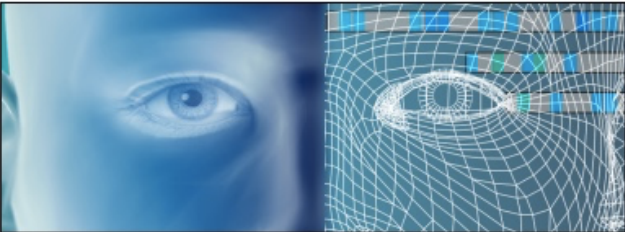
dbGaP

The database of Genotypes and Phenotypes (dbGaP) was developed to archive and distribute the results of studies that have investigated the interaction of genotype and phenotype.

- PhenX has a relatively small number of variables compared to dbGaP, so it is a good starting point for identifying comparable variable, and ways to standardize naming variables

- Standard set of rules for mapping to dbGaP study variables
- Standard set of rules for naming PhenX variables
- No standard set of rules for naming variables in dbGaP studies – thus, mapping requires some manual curation
- Plan for semantic normalization of variables names, potentially to add to dbGaP
- Need standard vocabulary – and ontology
- Ontology should be relevant / portable for use by other resources – and developed collaboratively

dbGaP Advanced Search Builder

Use the builder below to create your search

Edit

Builder

| All Fields ▼ | | ⊖ Show index list |

| Has Document |
| Has PhenX Mapping |
| Has Variable |
| Is Root Study |
| Is Top-Level Study |
| Molecular Data Type |
| Object Type |
| **PhenX** |
| Primary Phenotype in Study |
| Project |
| Study |
| Study Archive |
| Study Design |
| Study Has SRA Components |
| Study ID |
| Study Name |
| Variable |
| Variable Description |
| Variable ID |
| Variable Name |

AND ▼

Search

History

There is

You are here: NCBI > Genetics and Phenotypes (dbGaP)

GETTING STARTED | POPULAR | FEATURED | NCBI INFOR

dbGaP variable search results

Cross-reference table for PhenX measures and variables

PhenX variable	PhenX ID	dbGaP variable	LOINC code	P3G variable*	eMERGE variable	caDSR CDE
Current Age	PXV010101020000	phv00023938.v1 phv00024004.v1	21612-7	Age	Age	2423393
Ethnicity	PXV010501010000	phv00023941.v1 phv00024007.v1	56050-8	Ethnicity	Ethnicity	2200284
Gender	PXV010701010000	phv00023939.v1 phv00024005.v1	46607-8	Gender	Gender	2179640

* P3G DataShaPER doesn't distinguish between "exact" and "similar" mappings to PhenX measures

Annotation Tool – for PhenX Measures

- Some PhenX measures are identified for use in common, complex diseases are also relevant to rare disorders

- With help from Sharon Terry, Genetic Alliance (and PhenX Steering Committee member) – launching a crowdsourcing effort to engage the Rare Genetic Conditions community

PhenX Toolkit

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Contribute to the PhenX Toolkit by providing information about measures you use for specific rare genetic conditions

Purpose: To invite clinicians to share the protocols they use for specific rare genetic conditions and help PhenX investigators annotate PhenX measures.

Please choose a rare genetic condition from the list below.

	Begin typing to autofill	Type rare disease if not listed
Choose a rare genetic condition from the list:	duche ☒	

Duchenne muscular dystrophy

1. Click here to see the full list: begin typing the rare condition name and then select from suggested auto-fill. If your rare genetic condition of interest is not on the list, please enter it in the box to the right.
2. **Click on each PhenX domain name below to browse and mark measures** that you think are useful to study this rare genetic condition. Or enter a keyword to search the PhenX measure using PhenX Smart Query Tool.
3. **Provide a citation** for using this protocol to study this rare genetic condition.
4. **Add comments** about the usefulness of the measure.

Hitting the SUBMIT button in the bottom left corner will allow us to capture the information you have entered.

If you want to be able to return to the form and see your previous work, please provide your email address:

Email: [   ]

## Alcohol, Tobacco and Other Substances

Resources

- www.phenxtoolkit.org
  - Find PhenX measures for inclusion in your study
  - Quick Start guide
  - Tutorial

- www.phenx.org
  - Provides general information about the PhenX project
  - Register to receive periodic updates via e-mail of the PhenX Newsletter and notification of new surveys

- www.genome.gov/gwastudies/
  - A catalog of published Genome-Wide Association Studies
    (Hindorff et al. PNAS 2009)

- http://www.nlm.nih.gov/cde/
  - NIH Common Data Element (CDE) Resource Portal

Acknowledgements

- NHGRI
  - Erin Ramos (Project Scientist)
  - Brenda Iglesias (Program Analyst)
- PhenX Steering Committee
  - Mary Marazita, Co-Chair
  - Cathy McCarty, Co-Chair
- WG Chairs / Members
- NIH Liaisons
- Other Liaisons, HHS, DoD, CDC, FDA, VA
- NIDA lead – Kevin Conway
- TRSP lead – Kay Wanke
- NIMH lead – Greg Farber
- NHLBI lead – Ellen Werner

- RTI Team
  - Carol Hamilton (Principal Investigator)
  - Tabitha Hendershot (Co-Investigator)
  - Amanda Riley (Project Manager)
  - Darigg Brown
  - Wayne Huggins
  - Debbie Maiese
  - Destiney Nettles
  - Helen Pan
  - Mike Phillips
  - Toolkit team
  - Communications team
  - Logistics team
  - Collaborators

Questions?
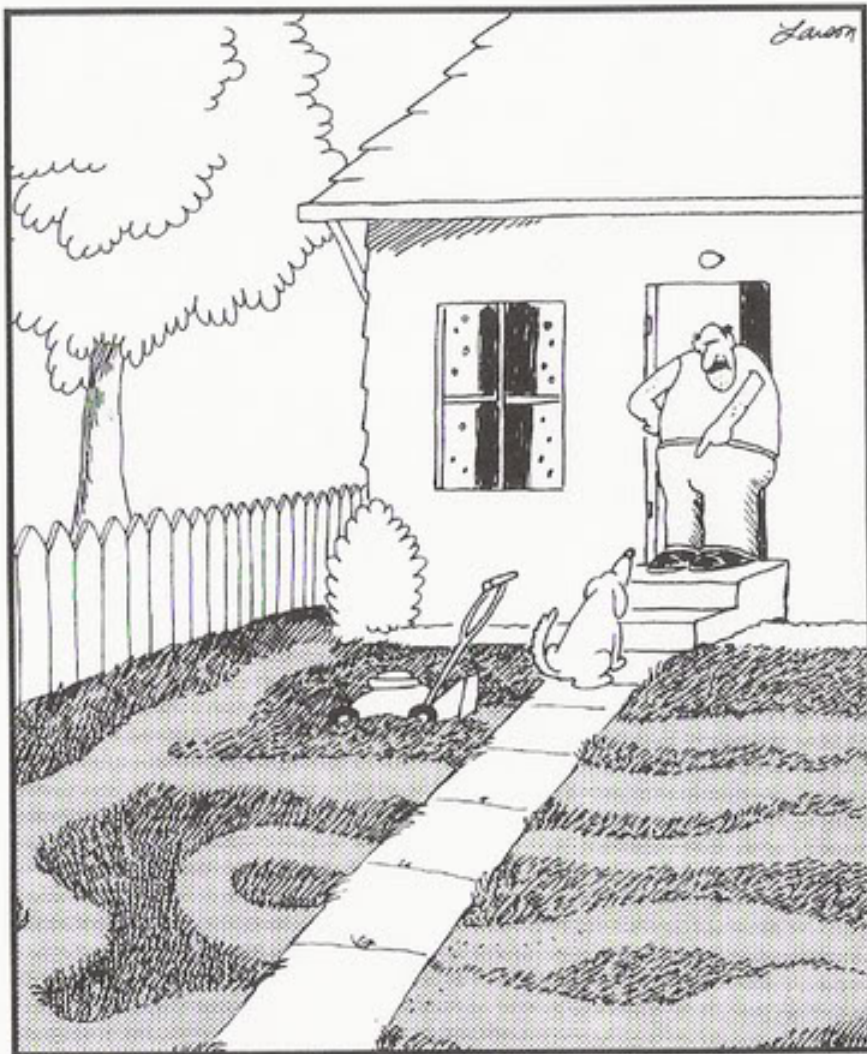
"You call that mowin' the lawn? ... Bad dog! ...
No biscuit! ... Bad dog!"