



# Community tools for data harmonization and genetic variant interpretation

Erin M. Ramos, PhD MPH

Division of Genomic Medicine, NHGRI

9.28.17



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National Human Genome Research Institute

*Advancing human health through genomics research*

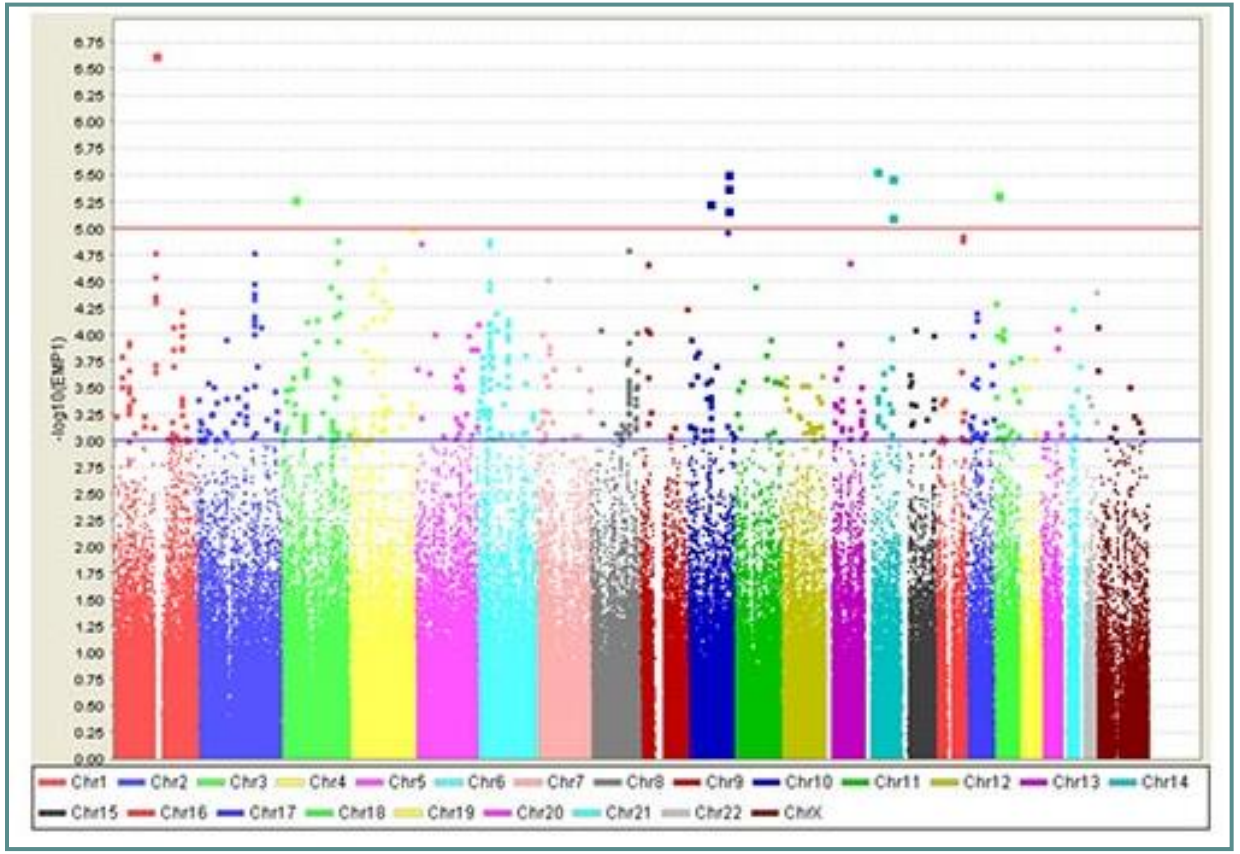
# NHGRI's Strategic Plan


*"A complete understanding of disease also requires…high-quality phenotypic data. Obtaining phenotypic data that are both thorough and accurate enough to be analyzed in conjunction with genomic and environmental data requires meticulous application of phenotyping methods, improved definitions of phenotypes, new technologies,* ***and the consistent use of data standards (http://www.phenx.org****)."*

Green and Guyer, 2011

# 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 and replication limited by lack of standardized measures

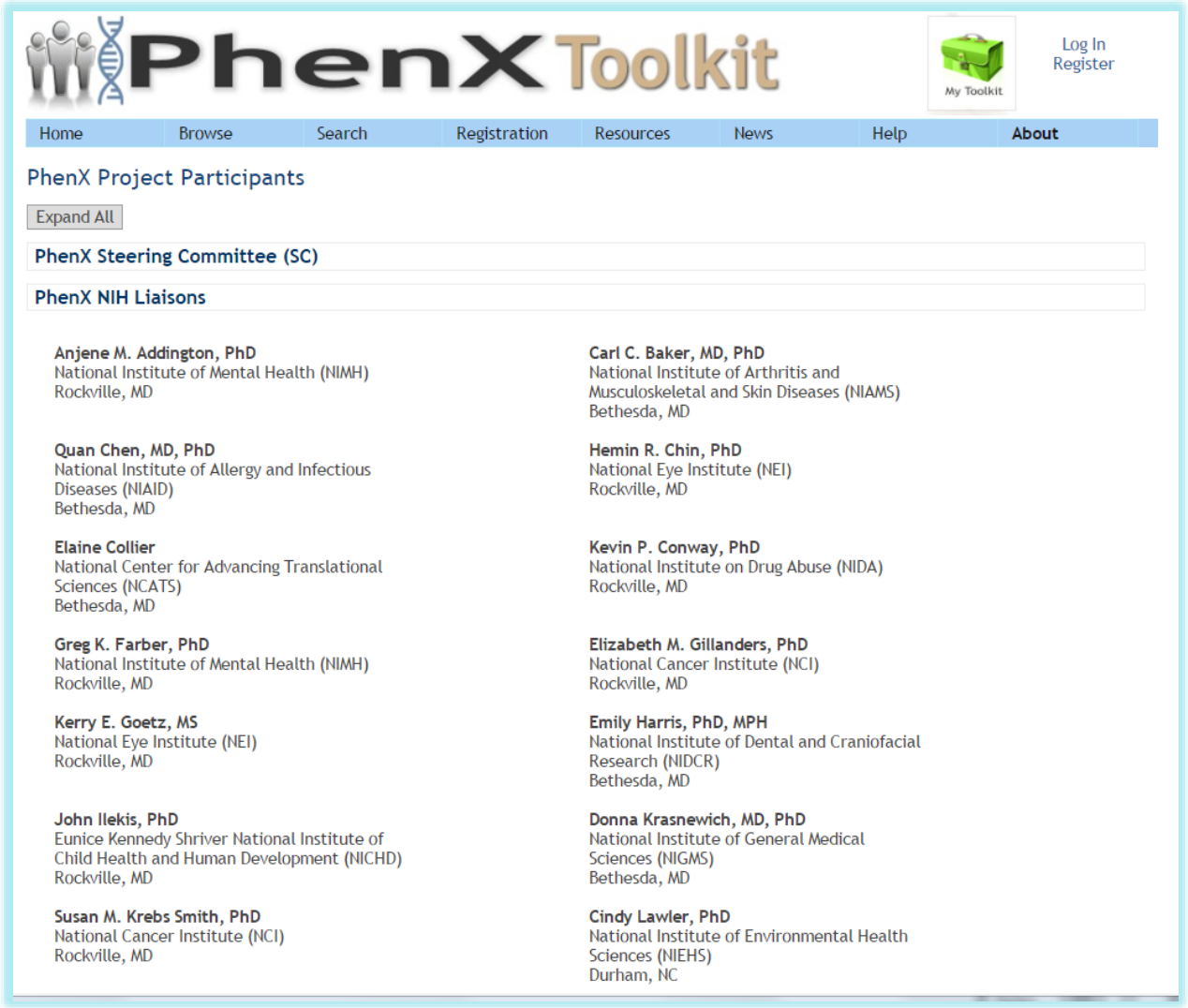
# The PhenX Project

- **Goal:** Create online resource of standard (common) phenotypic & environmental exposure measures
- PI: Carol Hamilton, RTI International
- 500+ measures (< 620 protocols) addressing 24 domains
- Protocols, data element dictionaries, data collections worksheets


(www.phenxtoolkit.org)

# Trans-NIH Effort

- **NHGRI:** National Human Genome Research Institute
- **NIDA:** National Institute of Drug Abuse
- **NIMH:** National Institute of Mental Health
- **NHLBI:** National Heart, Lung, and Blood Institute
- **OBSSR:** Office of Behavioral and Social Sciences Research
- **TRSP:** NIH Office of Disease Prevention, Tobacco Regulatory Science Program



# PhenX Definitions

- **DOMAIN**: Topical area with unifying theme (organ system, complex disease)

  Substance Use

- **MEASURE**: Certain characteristic of, or relating to, a study subject

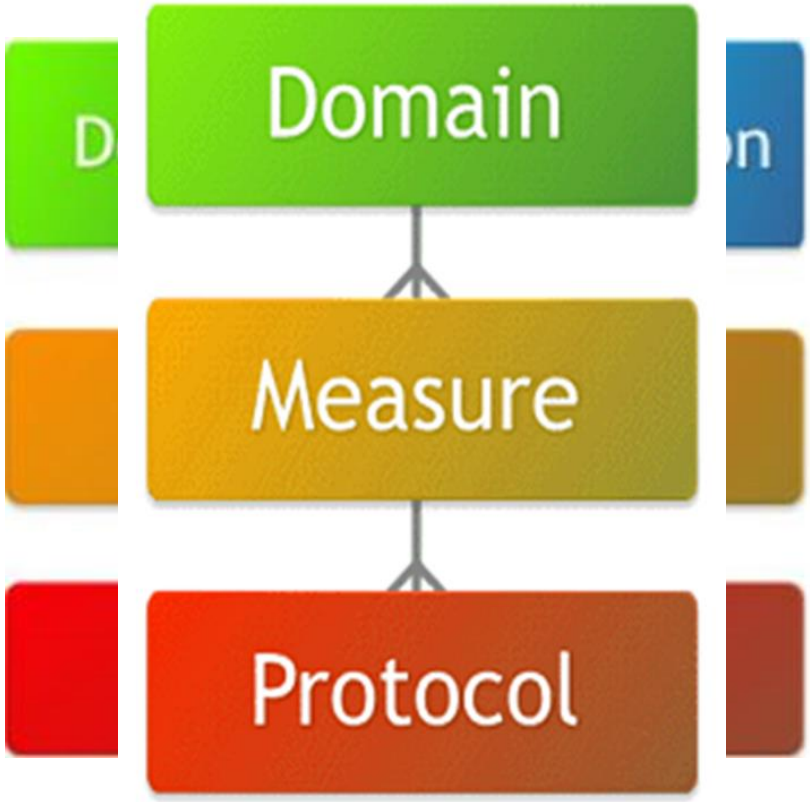
  Nicotine Dependence

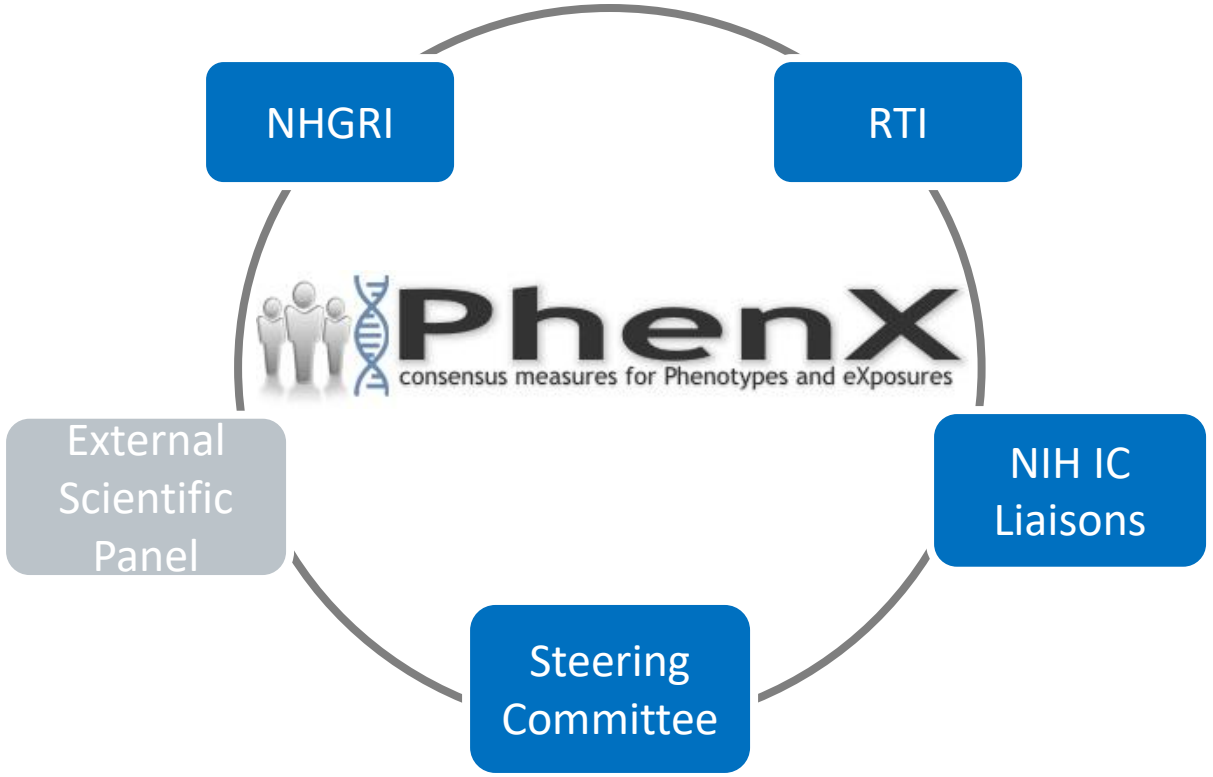
- **PROTOCOL:** Standard procedure recommended for collecting and recording a PhenX measure

  Fagerstrom Test

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

  Mental Health Research



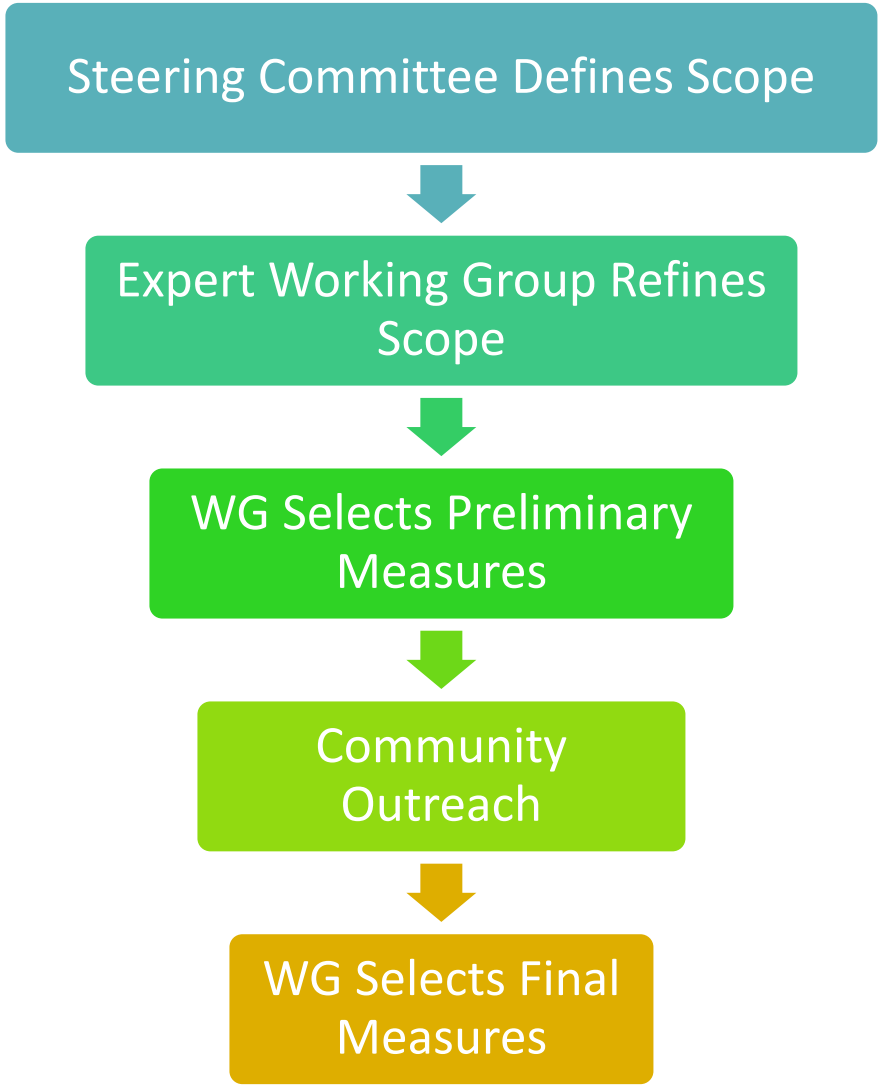



## Steering Committee

Lindsay Farrer
Elaine Faustman
Jonathan Haines
Tabitha Hendershot
Dan Masys
Cathy McCarty
Erin Ramos
Sharon Terry
Rosalind Wright
Mary Marazita

| | | | | |
|---|---|---|---|---|
| Rare Genetic Conditions | Alcohol, Tobacco, Other Substances | Anthropometrics | Cancer | Pregnancy |
| Obesity | Cardiovascular | Demographics | Diabetes | Geriatrics |
| Environmental Exposures | Gastrointestinal | Infectious Disease & Immunity | Neurology | Nutrition/Dietary Supplements |
| Ocular | Oral Health | Physical Activity & Fitness | Psychiatric | Psychosocial |
| Reproductive Health | Respiratory | Skin, Bone, Muscle & Joint | Social Environments | Speech and Hearing |

# Selecting PhenX Measures




## Criteria for measures selection:

- Well-established
- Low burden to participant & investigator
- Reproducible
- Open-source software
- Useful to investigators who are *not* domain experts

## Data collection mode

- Interviewer- or self-administered
- Bioassays
- Clinical exam, physical measurement
- GIS, Census data

# Pregnancy Measures

## Working Group

Siobhan Dolan, MD MPH (Chair)
Albert Einstein College of Medicine

Patrick Catalano, MD
Case Western Reserve University

Ann Kinga Malinowski, MD
Mt. Sinai Hospital

Mark Klebanoff, MD MPH
Nationwide Children's Hospital

Hyagriv Simhan, MD MS
McGee Research Insitute

Cande Ananth, PhD
Columbia University

Erin Hines, PhD
US EPA

Russ Kirby, PhD
U of South Florida

John Mulvihill, MD
NHGRI

Rosalind Wright, MD
Icahn School of Medicine

Lisa Kilpatrick
RTI International

Mike Phillips, MS
RTI International


- Considered input from the pregnancy experts and the broader research community
- Recommend 15 protocols
- Complement the existing PhenX domains, including reproductive health, anthropometrics, demographics, and substance use.

# Pregnancy Measures


Add to My Toolkit #240100 Adequacy of Prenatal Care »

Add to My Toolkit #240200 Concentrations of Flame Retardants »

Add to My Toolkit #240300 Concentrations of Phenols and Parabens »

Add to My Toolkit #240400 Concentrations of Polychlorinated Biphenyls

Add to My Toolkit #240500 Concentrations of Trace Metals »

Add to My Toolkit #240600 Current Pregnancy Status »

Add to My Toolkit #240700 Difficulties in Pregnancy »

Add to My Toolkit #240800 Family History of Pregnancy Complications »

Add to My Toolkit #241500 Fetal Growth Assessment - Percentiles for U.S. Populations »

Add to My Toolkit #240900 Gestational Age »

Add to My Toolkit #241000 Gestational Diabetes »

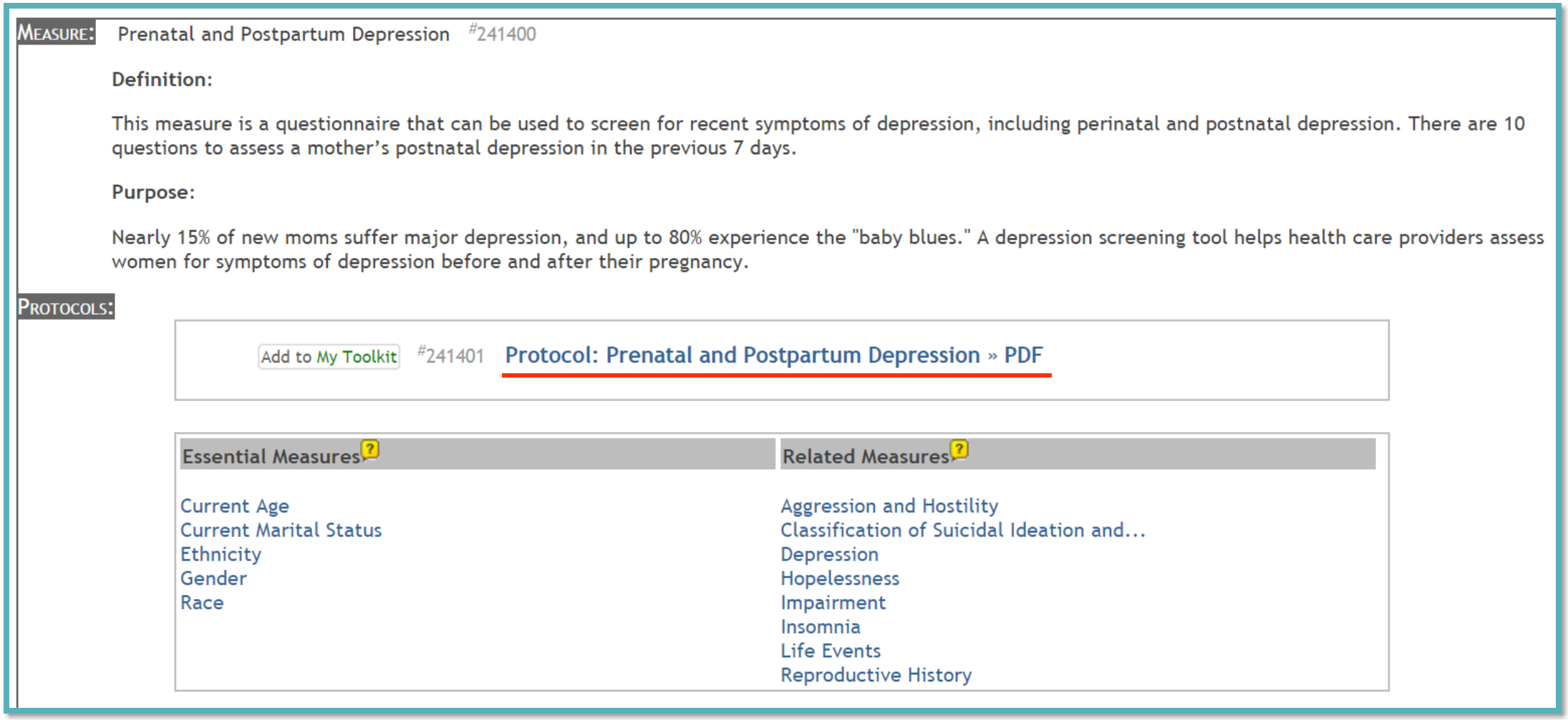
Add to My Toolkit #241100 Health and Wellness Before, During, and After Pregnancy »

Add to My Toolkit #241200 Mode of Conception »

Add to My Toolkit #241300 Mode of Delivery »

Add to My Toolkit #241400 Prenatal and Postpartum Depression »

# Prenatal and Postpartum Depression



MEASURE: Prenatal and Postpartum Depression #241400

**Definition:**

This measure is a questionnaire that can be used to screen for recent symptoms of depression, including perinatal and postnatal depression. There are 10 questions to assess a mother's postnatal depression in the previous 7 days.

**Purpose:**

Nearly 15% of new moms suffer major depression, and up to 80% experience the "baby blues." A depression screening tool helps health care providers assess women for symptoms of depression before and after their pregnancy.

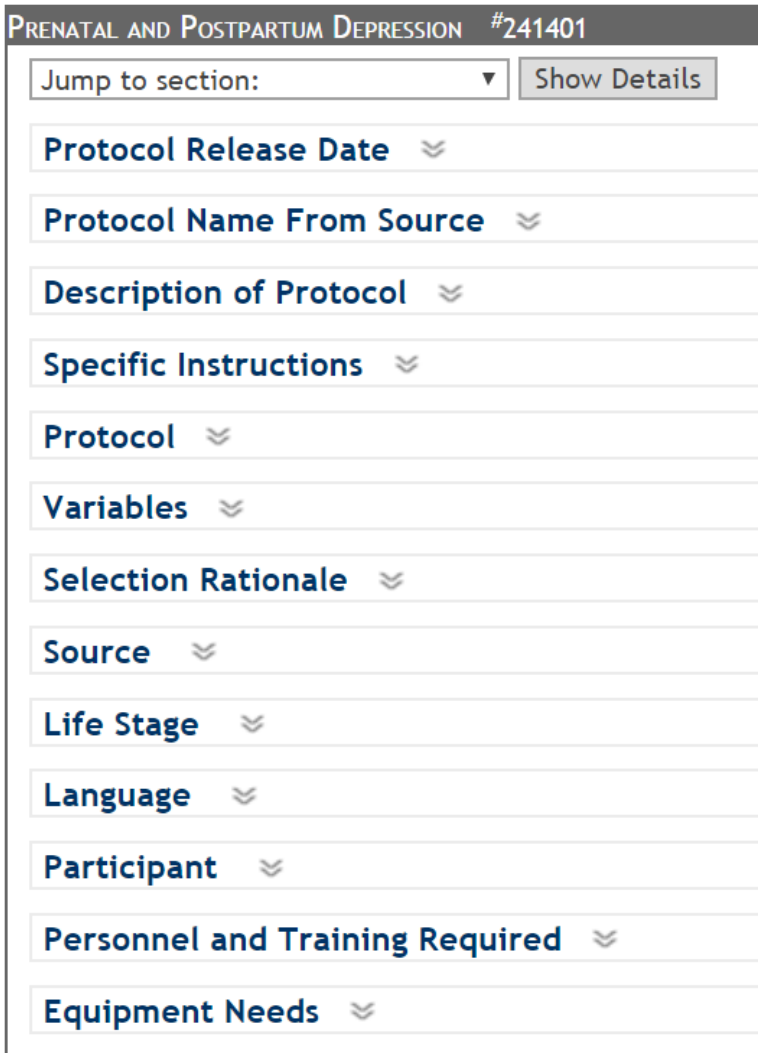
PROTOCOLS:

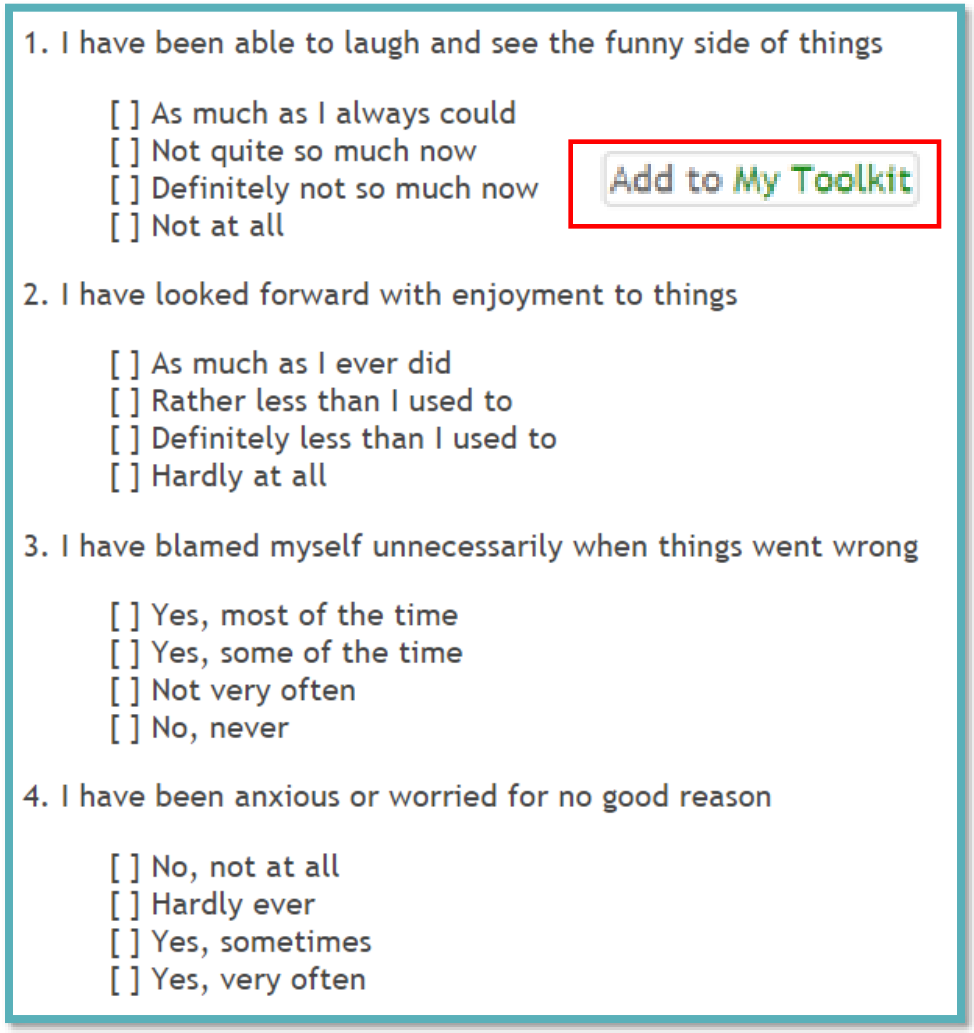
Add to My Toolkit #241401 Protocol: Prenatal and Postpartum Depression » PDF

| Essential Measures | Related Measures |
|---|---|
| Current Age | Aggression and Hostility |
| Current Marital Status | Classification of Suicidal Ideation and... |
| Ethnicity | Depression |
| Gender | Hopelessness |
| Race | Impairment |
| | Insomnia |
| | Life Events |
| | Reproductive History |

Source: Cox, J. et al (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786.

# Prenatal and Postpartum Depression




Source: Cox, J. et al (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786.

# Prenatal and Postpartum Depression

Download Report | Download Data Collection Worksheet | Download Data Dictionary | Download REDCap Instrument Zip

**USERS WHO CHOSE THIS MEASURE ALSO CHOSE:**

- Add to My Toolkit Mode of Conception (Pregnancy)
- Add to My Toolkit Gestational Diabetes (Pregnancy)
- Add to My Toolkit Health and Wellness Before, During, and After Pregnancy (Pregnancy)
- Add to My Toolkit Gestational Age (Pregnancy)

Empty My Toolkit

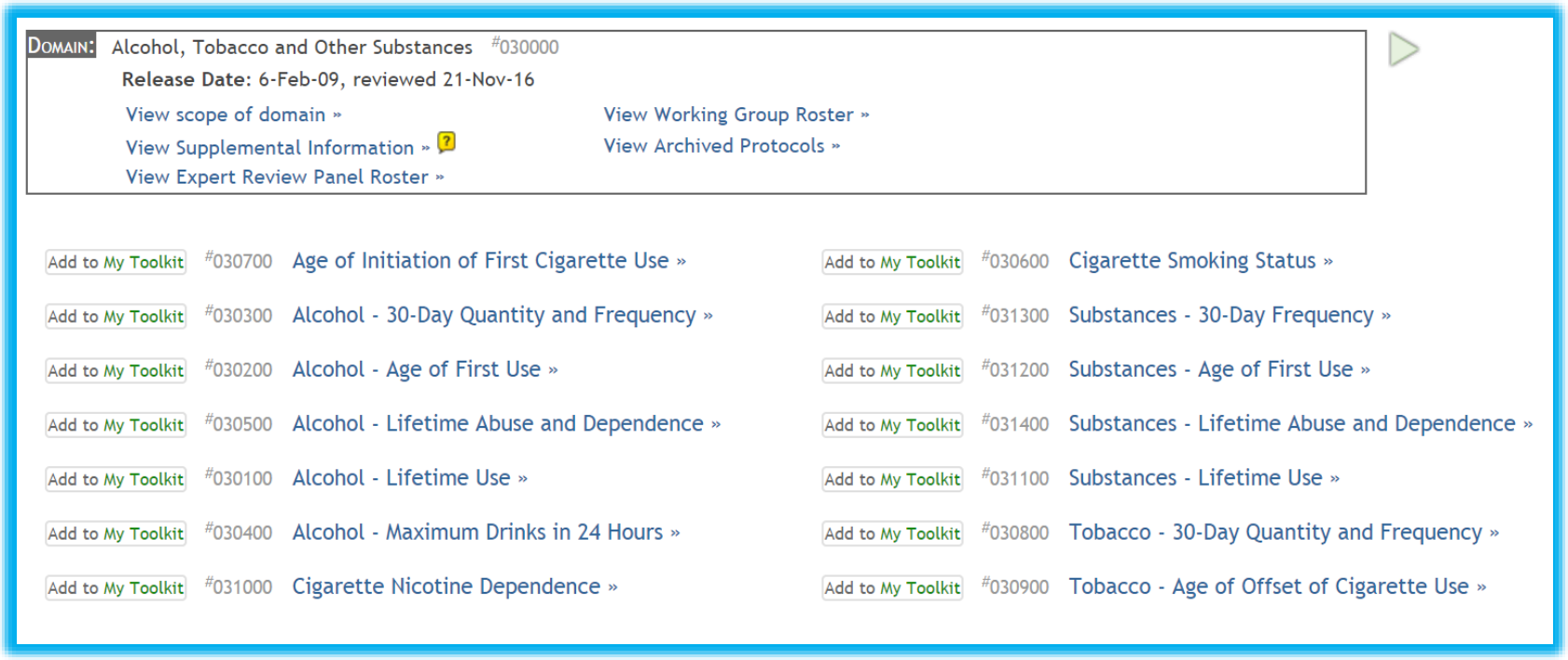
| Measure | Protocol | Requirements | Essential Measures |
|---|---|---|---|
| Prenatal and Postpartum Depression<br>*Remove* \| *Related Measures* | Prenatal and Postpartum Depression *Remove* | | ⚠ Essential Measures are not in the cart<br>Review additional Essential Measures:<br>☐ Current Age<br>☐ Current Marital Status<br>☐ Ethnicity<br>☐ Gender<br>☐ Race |

⚠ Essential Measures are needed to interpret your data. Add all Essential Measures to your Toolkit »

Share this Toolkit »

Measures: 1 Protocols: 1

# Substance Use Measures



DOMAIN: Alcohol, Tobacco and Other Substances #030000

**Release Date:** 6-Feb-09, reviewed 21-Nov-16

View scope of domain »
View Supplemental Information »
View Expert Review Panel Roster »
View Working Group Roster »
View Archived Protocols »

| | | | | | |
|---|---|---|---|---|---|
| Add to My Toolkit | #030700 | Age of Initiation of First Cigarette Use » | Add to My Toolkit | #030600 | Cigarette Smoking Status » |
| Add to My Toolkit | #030300 | Alcohol - 30-Day Quantity and Frequency » | Add to My Toolkit | #031300 | Substances - 30-Day Frequency » |
| Add to My Toolkit | #030200 | Alcohol - Age of First Use » | Add to My Toolkit | #031200 | Substances - Age of First Use » |
| Add to My Toolkit | #030500 | Alcohol - Lifetime Abuse and Dependence » | Add to My Toolkit | #031400 | Substances - Lifetime Abuse and Dependence » |
| Add to My Toolkit | #030100 | Alcohol - Lifetime Use » | Add to My Toolkit | #031100 | Substances - Lifetime Use » |
| Add to My Toolkit | #030400 | Alcohol - Maximum Drinks in 24 Hours » | Add to My Toolkit | #030800 | Tobacco - 30-Day Quantity and Frequency » |
| Add to My Toolkit | #031000 | Cigarette Nicotine Dependence » | Add to My Toolkit | #030900 | Tobacco - Age of Offset of Cigarette Use » |

Tobacco Regulatory Research

- Collaborative data consensus effort from the NIH Tobacco Regulatory Science Program and the FDA Center for Tobacco Products (CTP)

- Social/Cognitive — Interpersonal factors influencing product use (stress, motivation to quit)
- Biobehavioral — Product use, exposure, and health outcomes (use patterns, biomarkers)
- Agent — Assessing tobacco product (toxicology, warning labels, brands)
- Vector — Industry and retailer activity (packaging, price, advertising)

(Project lead = Kay Wanke, TRSP)

# Social Environment Measures

**Domain:** Social Environments #210000

**Release Date:** 8-Oct-10, reviewed 31-May-16

View scope of domain »
View Supplemental Information »
View Expert Review Panel Roster »
View Working Group Roster »
View Archived Protocols »

| | | | | | |
|---|---|---|---|---|---|
| Add to My Toolkit | #210200 | Child-Reported Parental Education Attainment » | Add to My Toolkit | #211500 | Life Events » |
| Add to My Toolkit | #210100 | Childhood Maltreatment » | Add to My Toolkit | #210800 | Neighborhood Collective Efficacy - Community |
| Add to My Toolkit | #210300 | Discrimination » | Add to My Toolkit | #211300 | Neighborhood Concentrated Disadvantage » |
| Add to My Toolkit | #210400 | Family Conflict » | Add to My Toolkit | #210900 | Neighborhood Safety » |
| Add to My Toolkit | #210500 | Family Control and Organization » | Add to My Toolkit | #211400 | Race/Ethnic Residential Segregation » |
| Add to My Toolkit | #210600 | Family Interpersonal Relationships » | Add to My Toolkit | #211000 | School Social Environment » |
| Add to My Toolkit | #210700 | Healthy Food Environments » | Add to My Toolkit | #211100 | Social Networks » |
| Add to My Toolkit | #211200 | Job Strain » | | | |

# Integration by Large Research Programs

GuLF STUDY

Adolescent Brain Cognitive Development

*Teen Brains. Today's Science. Brighter Future.*

ECHO

Environmental Influences on Child Health Outcomes

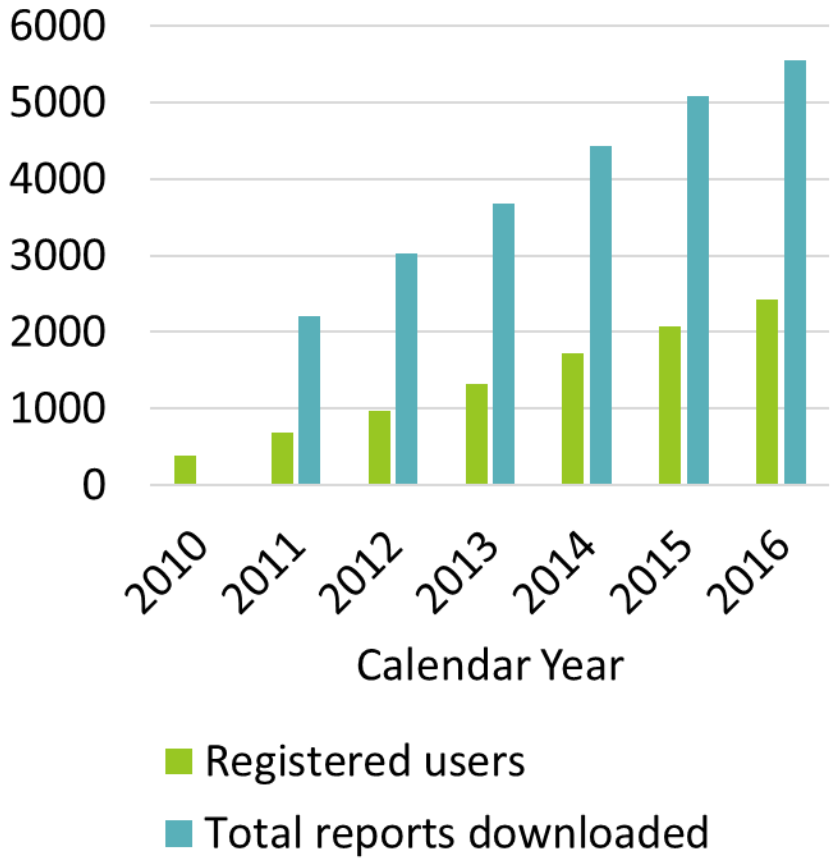
PATH

Population Assessment of Tobacco and Health

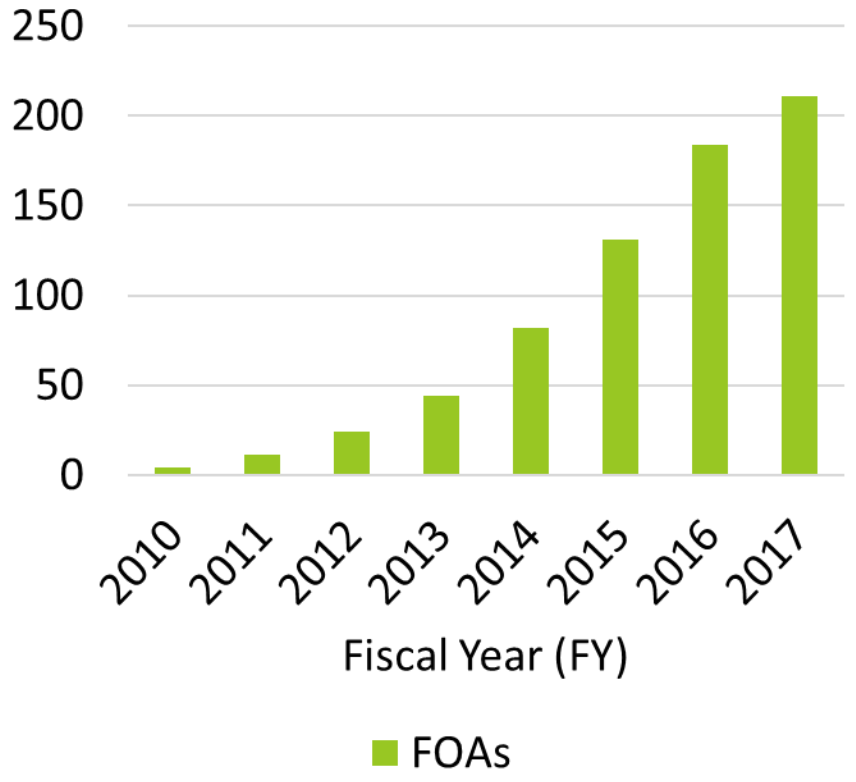
*A collaboration between the NIH and FDA*

# PhenX Toolkit Use

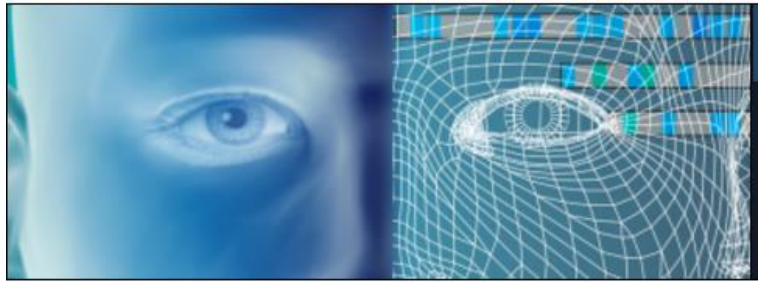
PhenX Users, Cumulative (2010-2016)




FOAs Citing PhenX, Cumulative (FY2010-2017)




**Number of Visits: 1,192,834**



# dbGaP

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

| PhenX Variable ID | PhenX Variable Name | Measure Name | Mapping level | dbGAP Study | dbGAP Variable |
|---|---|---|---|---|---|
| PX030301010000 | PX030301_Alcohol_30Day_Frequency | Alcohol - 30-Day Quantity and Frequency | comparable | NHLBI Cleveland Family Study (CFS) Candidate Gene Association Resource (CARe) | phv00129665 |
| PX030301010000 | PX030301_Alcohol_30Day_Frequency | Alcohol - 30-Day Quantity and Frequency | comparable | NEIGHBOR Consortium Glaucoma GWAS | phv00072936 |
| PX030301010000 | PX030301_Alcohol_30Day_Frequency | Alcohol - 30-Day Quantity and Frequency | comparable | Genetic Multiple Sclerosis Associations - GeneMSA | phv00090478 |
| PX030301010000 | PX030301_Alcohol_30Day_Frequency | Alcohol - 30-Day Quantity and Frequency | comparable | The Vaginal Microbiome: Disease, Genetics and the Environment | phv00081806 |
| PX030301010000 | PX030301_Alcohol_30Day_Frequency | Alcohol - 30-Day Quantity and Frequency | comparable | GenADA/LONG/Imaging (Genetic Alzheimer's Disease Associations) | phv00090481 |
| PX030301020000 | PX030301_Alcohol_30Day_Quantity | Alcohol - 30-Day Quantity and Frequency | comparable | The Vaginal Microbiome: Disease, Genetics and the Environment | phv00129666 |

# Acknowledgements


- NHGRI
  - Margaret Ginoza
  - Teri Manolio
- PhenX Steering Committee
  - Mary Marazita, Co-Chair
  - Cathy McCarty, Co-Chair
- WG Chairs & BMembers
- NIH Liaisons
- OBSSR lead – Bill Riley/Erica Spotts
- NIDA lead – Kevin Conway
- TRSP lead – Kay Wanke
- NIMH lead – Greg Farber
- NHLBI lead – Ellen Werner
- NCBI's dbGaP Team
- RTI Team
  - Carol Hamilton (Principal Investigator)
  - Tabitha Hendershot (Co-Investigator)
  - Amanda Riley (Project Manager)
  - Darigg Brown
  - Wayne Huggins
  - Debbie Maiese
  - Lisa Jackson
  - Helen Pan
  - Mike Phillips
  - Toolkit team
  - Communications team
  - Logistics team




# Community tools for data harmonization and genetic variant interpretation

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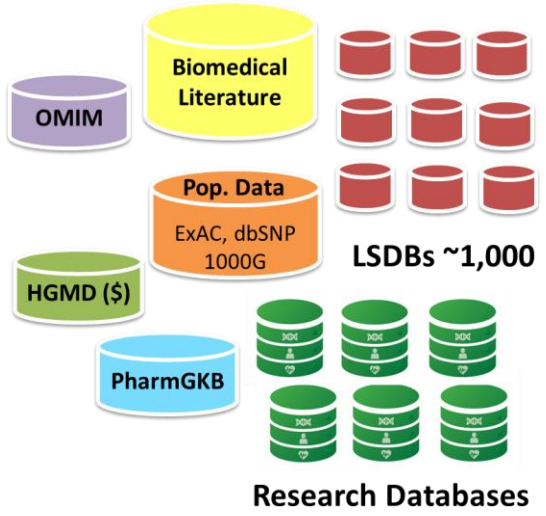
National Human Genome Research Institute

*Advancing human health through genomics research*

# The Problem

- Ability to detect DNA variants has greatly surpassed our ability to interpret their clinical impact
- >19,000 genes and > 88 million known variable sites in the human genome




**Largely without standard assertions**

**Clinical Testing Lab Databases**

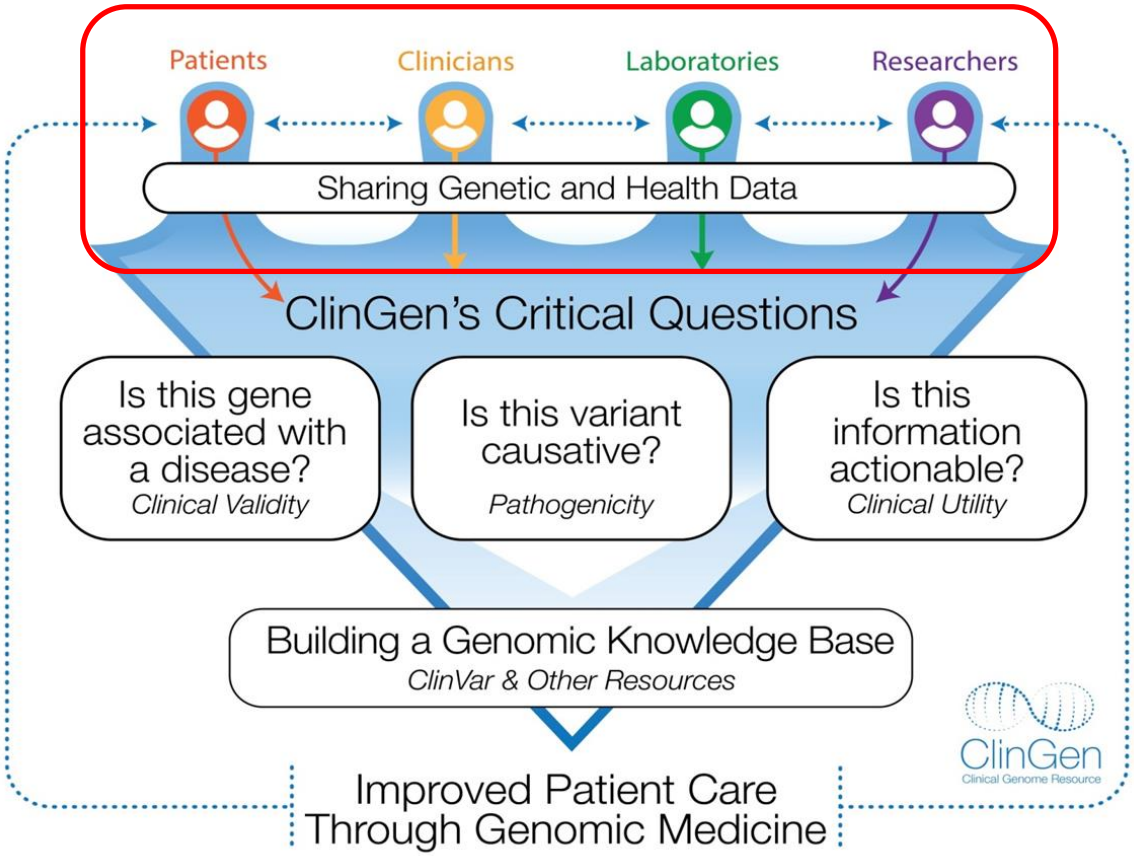
**Largely absent from public domain**

# Improving our knowledge of the clinical impact of genomic variation requires a massive effort in data sharing and collaborative curation

# The Clinical Genome Resource

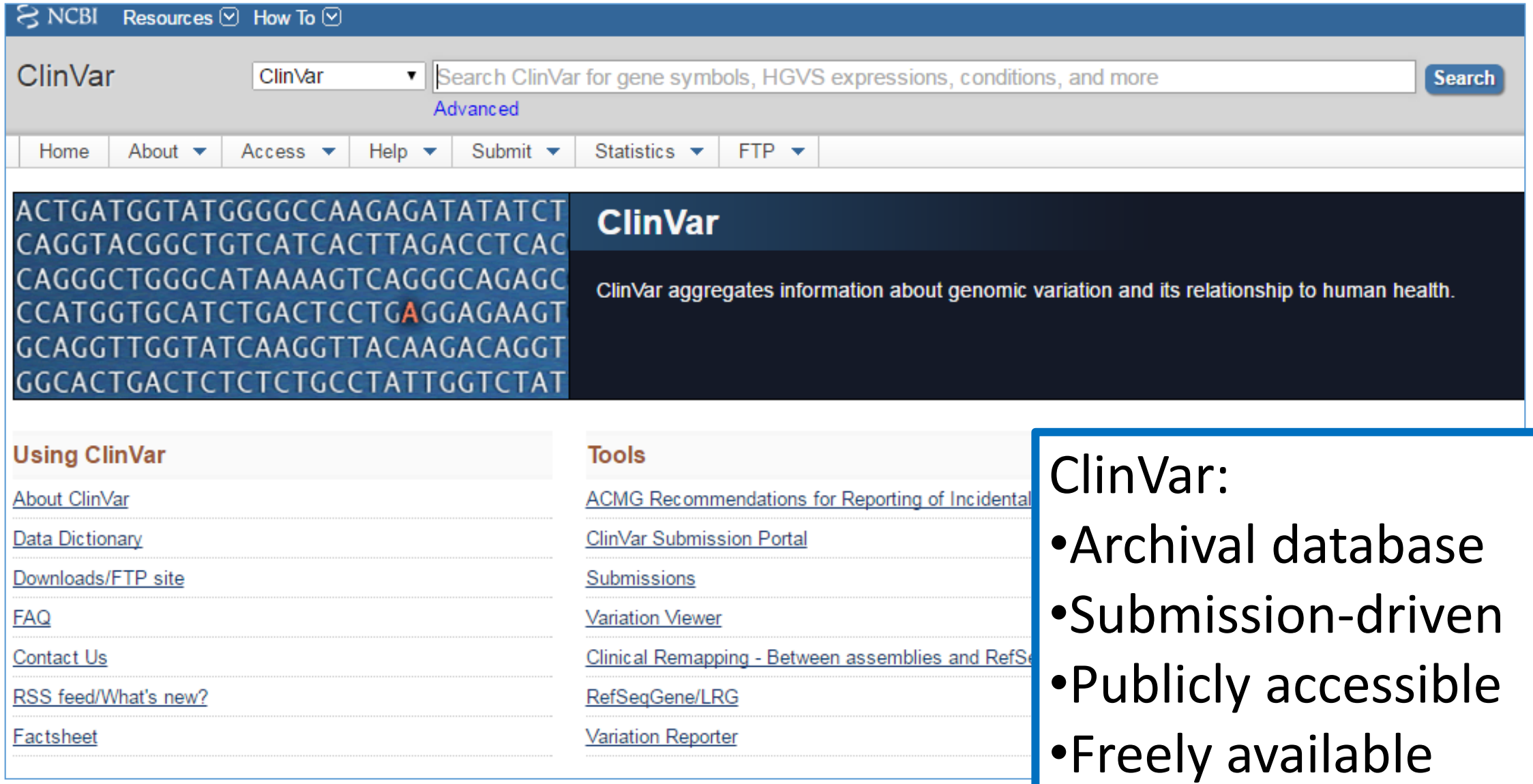
- **ClinGen** is creating standard curation approaches and a central resource of clinically relevant genes and variants for use in medicine and research

- **NIH-funded program launched Sept. 2013**
  - NHGRI, NCI, NICHD, *All of Us*
  - 3 Genomic Resource Grants (U41) & NCBI's ClinVar
  - > 570 researchers & clinicians from 230 institutions




THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL · Stanford MEDICINE · National Center for Biotechnology Information NCBI · ACMG American College of Medical Genetics and Genomics Translating Genes Into Health® · BCM Baylor College of Medicine · GEISINGER HEALTH SYSTEM · PARTNERS HEALTHCARE · KAISER PERMANENTE®

# ClinVar




ClinVar:

- Archival database
- Submission-driven
- Publicly accessible
- Freely available

www.ncbi.nlm.nih.gov/clinvar/

# Example ClinVar Record

**NM_021007.2(SCN2A):c.788C>T (p.Ala263Val)**

Variation ID: 29888

Review status: ★★☆☆ criteria provided, multiple submitters, no conflicts

## Interpretation

Go to:

Clinical significance: Pathogenic

Last evaluated: Jun 5, 2017

Number of submission(s): 4

Condition(s):

- Benign familial neonatal-infantile seizures [MedGen - Orphanet - OMIM]
- Early infantile epileptic encephalopathy 11 [MedGen - OMIM]
- Epileptic encephalopathy [MedGen - Human Phenotype Ontology]

See supporting ClinVar records

## Allele(s)

Go to:

**NM_021007.2(SCN2A):c.788C>T (p.Ala263Val)**

Allele ID: 38843

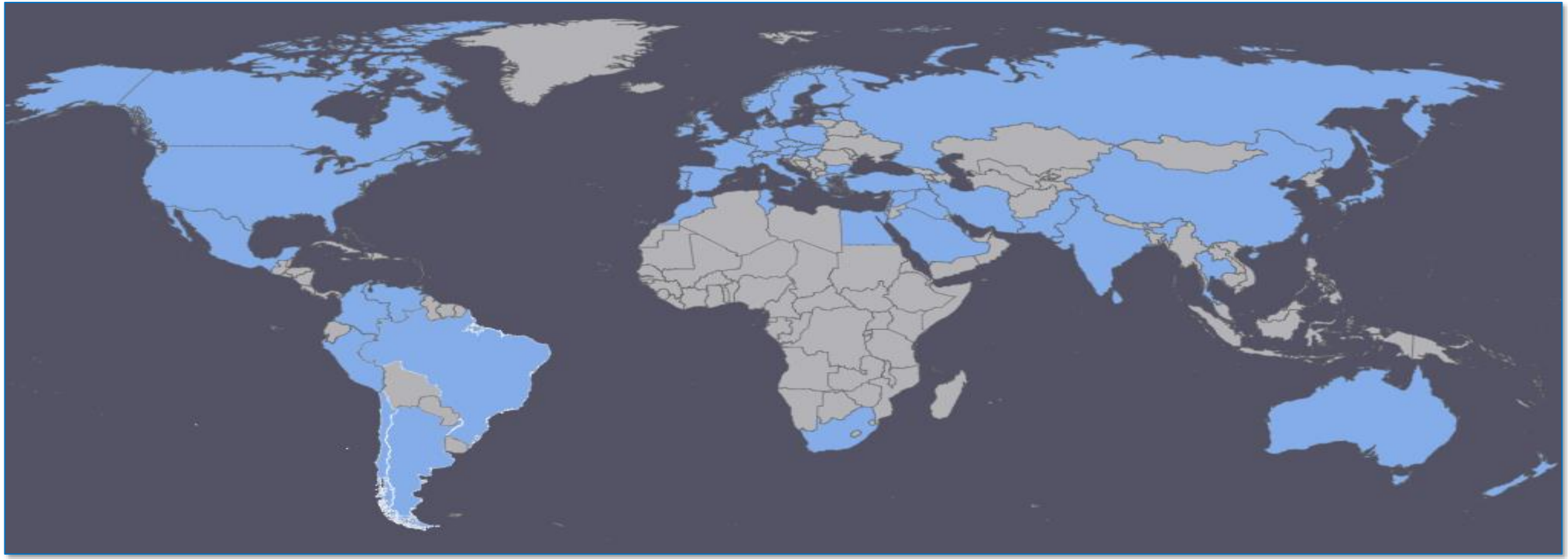
Variant type: single nucleotide variant

Cytogenetic location: 2q24.3

# Example ClinVar Record

| Clinical significance (Last evaluated) | Review status (Assertion method) | Collection method | Condition(s) (Mode of inheritance) | Origin | Citations | Submitter - Study name |
|---|---|---|---|---|---|---|
| Pathogenic (Aug 6, 2013) | criteria provided, single submitter • ACMG Guidelines, 2007 | clinical testing | Benign familial neonatal-infantile seizures (Autosomal dominant inheritance) [MedGen \| Orphanet \| OMIM] | germline | | Genetic Services Laboratory, University of Chicago |
| Pathogenic (Jun 5, 2017) | criteria provided, single submitter • GeneDx Variant Classification (06012015) | clinical testing | not provided [MedGen] | germline | | GeneDx |
| Pathogenic (Nov 16, 2016) | criteria provided, single submitter • ACMG Guidelines, 2015 • ACMG Guidelines, 2015 | clinical testing | Epileptic encephalopathy [MedGen \| Human Phenotype Ontology] | de novo | | Neurogenetics Laboratory - MEYER,AOU Meyer |

# 801 ClinVar Submitters from 60 Countries



NCBI ClinVar

August 2017

- Submission from clinical testing labs, healthcare providers, patient registries, researchers, locus-specific databases, expert panels and professional societies
- 328,851 unique variants

# ClinGen Curation Standards

- **Gene-Disease Validity**
  - **Can variation in this gene cause disease?**
- Dosage Sensitivity
  - Is haploinsufficiency or triplosensitivity an established disease mechanism for this gene?
- Variant Pathogenicity
  - Which changes in this gene cause disease?
- Clinical Actionability
  - Are there actions that could be taken to improve outcomes for patients with this genetic risk?

## Evaluating the Clinical Validity of Gene-Disease Associations: An Evidence-Based Framework Developed by the Clinical Genome Resource

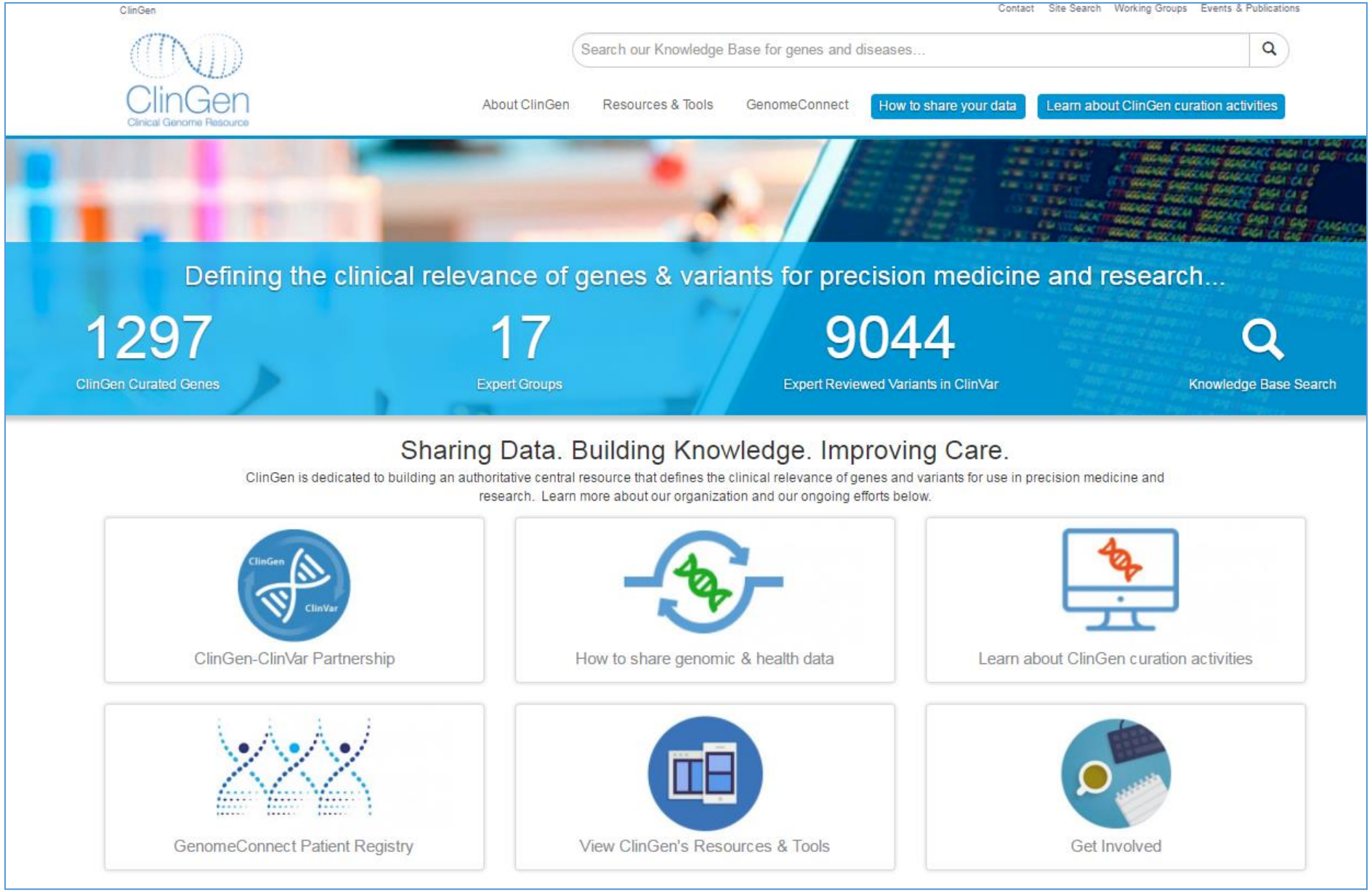
Marina DiStefano,[4] Selina S. Dwight,[8] Jenny Goldstein,[1] Rajarshi Ghosh,[9] Bryce A. Seifert,[1] Tam P. Sneddon,[8] Matt W. Wright,[8] Laura V. Milko,[1] J. Michael Cherry,[8] Monica A. Giovanni,[3] Michael F. Murray,[3] Julianne M. O'Daniel,[1] Erin M. Ramos,[10] Avni B. Santani,[11,12] Alan F. Scott,[13] Sharon E. Plon,[9] Heidi L. Rehm,[4,5,6,7] Christa L. Martin,[2,3,*] and Jonathan S. Berg[1,*]

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Case-Level Data[1] | Evidence Type | | Case Information | | | Suggested Points/Case: Default | Suggested Points/Case: Range | Points Given | Max Score |
| | Variant Evidence | Autosomal Dominant OR X-Linked Disorder[2] | Variant is *de novo*[3] | | | 2 | 0-3 | | 12 |
| | | | Proband with predicted or proven null variant[4] | | | 1.5 | 0-2 | | 10 |
| | | | Proband with other variant type with some evidence of gene impact[5] | | | 0.5 | 0-1.5 | | 7 |
| | | Autosomal Recessive | Two variants in *trans* and at least one *de novo*[3] or a predicted/proven null variant[4] | | | 2 | 0-3 | | 12 |
| | | | Two variants (not predicted/proven null) with some evidence of gene impact[5] in *trans* | | | 1 | 0-1.5 | | |
| | Segregation Evidence | | Evidence of segregation in one or more families[6] | LOD Score Examples | 3 | 5 | 0-7 | | 7 |
| | | | | | 2 | 4 | | | |
| | | | | | 1.5 | 3 | | | |
| | | | | | 1 | 1.5 | | | |
| Case-Control Data[7] | Case-Control Study Type[8] | | Case-Control Quality Criteria[9] | | | Suggested Points/Study | | Points Given | Max Score |
| | Single Variant Analysis[8a] | | • Variant Detection Methodology[9a]<br>• Power[9b] | | | 0-6 | | | 12 |
| | Aggregate Variant Analysis[8b] | | • Bias and Confounding Factors[9c]<br>• Statistical Significance[9d] | | | 0-6 | | | |
| TOTAL ALLOWABLE POINTS for Genetic Evidence | | | | | | | | | 12 |

# Gene-Disease Validty

## Clinical Validity Classification Summaries

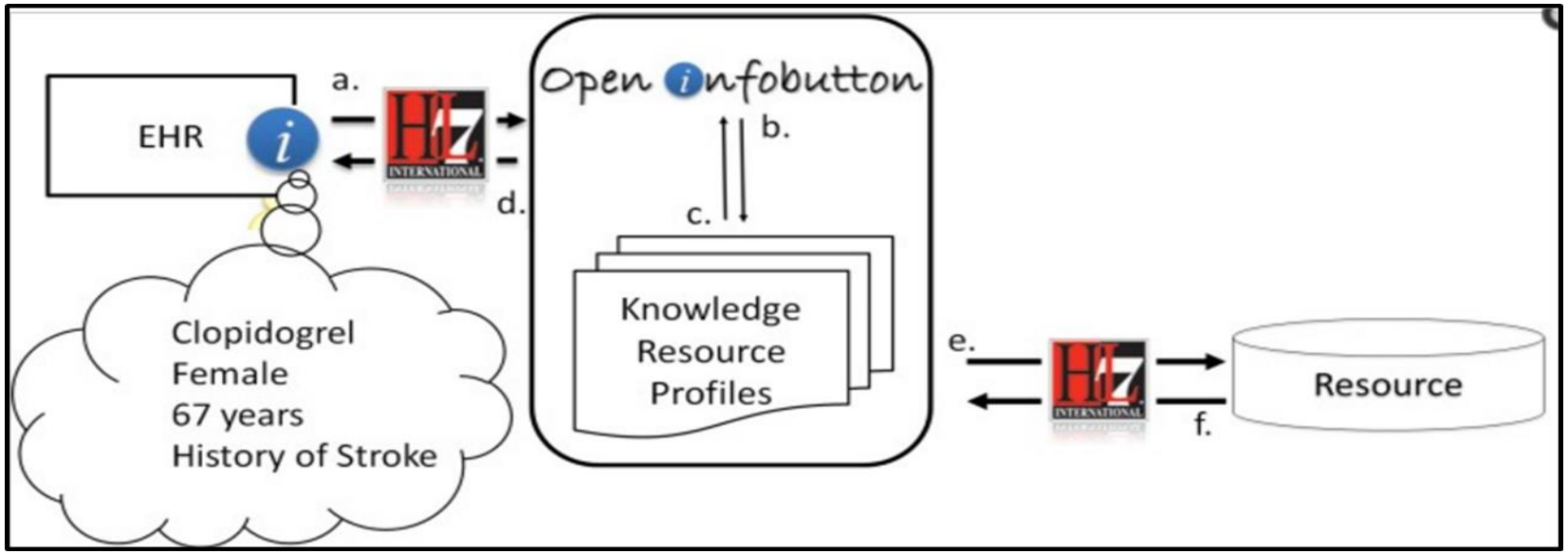
| HGNC Gene Symbol | Disease curated | Orphanet ID | OMIM ID | Clinical Validity Classification |
|---|---|---|---|---|
| | Hypertrophic cardiomyopathy | ORPHA217569 | 608751 | Definitive - 10/04/2016 |
| *ACTA2* | Familial thoracic aortic aneurysm and aortic dissection | ORPHA91387 | 102620 | Definitive - 09/27/2016 |
| *ADCY1* | Nonsyndromic sensorineural hearing loss | ORPHA90636 | 610154 | Limited - 05/10/2017 |
| *ADGRV1* | Usher syndrome type 2 | ORPHA231178 | 605472 | Definitive - 02/15/2017 |
| *AGTR2* | X-linked non-syndromic intellectual disability | ORPHA777 | N/A | Contradictory (disputed) - 11/16/2016 |
| *AKAP9* | Long QT syndrome | ORPHA101016 | 611820 | Limited - 12/15/2016 |
| *ALMS1* | Alstrom syndrome | ORPHA64 | 203800 | Definitive - 02/10/2017 |
| *ARSD* | Chondrodysplasia punctata | N/A | N/A | No Reported Evidence - 11/15/2016 |
| *ATF6* | Achromatopsia | ORPHA49382 | 616517 | Strong - 11/16/2016 |
| *AXIN2* | Hereditary colorectal cancer | ORPHA:443909 | 604025 | Moderate - 06/08/2017 |
| *BAG3* | Myofibrillar Myopathy | ORPHA593 | 612954 | Definitive - 12/18/2016 |
| *BAP1* | Hereditary pheochromocytoma-paraganglioma | 29072 | 603089 | Limited - 07/22/2017 |
| *BARD1* | Colorectal cancer | ORPHA443909 | 601593 | Limited - 06/08/2017 |




(www.clinicalgenome.org)

# EHR HL7 Readiness

- HL7 Compliance
  - Bring all ClinGen resources into HL7 compliance
  - Work with one resource, GTR, to move it to HL7 compliance
- Create a library of indexed clinical genomic resources using OpenInfobutton's Librarian Infobutton Tailoring Environment




**Courtesy of Marc Williams**

(J Appl Clin Inform, 2016)

# Get Involved!

- Incorporate ClinVar into your daily practice and provide feedback on it's utility
- Submit data to ClinVar
- Support laboratories that make their data publicly available
- Join the monthly ClinVar Community Call
- Nominate topics for Clinical Actionability or Gene-Disease Validity curation
- Volunteer as a ClinGen curator
- Apply to be an Expert Panel in ClinVar
- Participate in continuing education activities involving variant reassessment

**www.clinicalgenome.org/about/get-involved/**

Contact us:

**clingen@clinicalgenome.org**

@ClinGenResource

## ClinGen Steering Committee

**Jonathan Berg,** UNC
**Carlos Bustamante,** Stanford
**James Evans,** UNC
**Andy Faucett**, Geisinger
**Katrina Goddard**, Kaiser Permanente
**David Ledbetter,** Geisinger
**Christa Lese Martin,** Geisinger
**Aleks Milosavljevic**, Baylor
**Kelly Ormond,** Stanford
**Sharon Plon,** Baylor
**Heidi Rehm,** Harvard
**Michael Watson,** ACMG
**Kirk Wilhelmsen**, UNC
**Marc Williams**, Geisinger
**Brandi Kattman,** NCBI
**Lisa Brooks**, NHGRI
**Andy Freedman**, NCI
**Danuta Krotoski**, NICHD
**Melissa Landrum,** NCBI
**Erin Ramos**, NHGRI

### Program Coordinators

Danielle Azzariti, Erin Currey, Robert Fullem, Miranda Hallquist, Jenny Goldstein, Kristy Lee, Lisa Kurtz, Laura Milko, Jules Savatt, Meredith Weaver

## ClinGen Working Groups (WG) and WG Chairs

**Clinical Domain Oversight Committee**

Jonathan Berg, Sharon Plon, Heidi Rehm

**Hereditary Cancer** : Ken Offit, Sharon Plon

**Somatic Cancer**: Shashi Kulkarni, Subha Madhavan

**Cardiovascular**: Birgit Funke, Ray Hershberger

**Inborn Errors of Metabolism:** Rong Mao, Robert Steiner, Bill Craigen

**Pediatric Neurology:** Michael Friez, Heather Mefford, Scott Myers

**Hearing Loss:** Sami Amr, Ahmad Abou Tayoun, Heidi Rehm

**Actionability WG**

Jim Evans, Katrina Goddard

**Biocurators WG**

Jenny Goldstein

**Consent and Disclosure Recommendations WG**

Andy Faucett, Kelly Ormond

**Data Model WG**

Larry Babb, Chris Bizon

**Dosage Sensitivity WG**

Erica Andersen, Erik Thorland

**Education, WG**

Danielle Azzariti, Erin Rooney Riggs

**Electronic Health Record WG**

Marc Williams

**Gene Curation WG**

Jonathan Berg, Christa Martin

**Genomic Variant WG**

Christa Martin, Sharon Plon, Heidi Rehm

**Informatics WG**

Carlos Bustamante

**Sequence Variant Interpretation WG**

Leslie Biesecker, Steven Harrison

**Structural Variant WG**

Swaroop Aradhya, Daniel Pineda-Alvarez

# THANK YOU!

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NIH National Human Genome Research Institute

*Advancing human health through genomics research*

PhenX

consensus measures for Phenotypes and eXposures

ClinGen

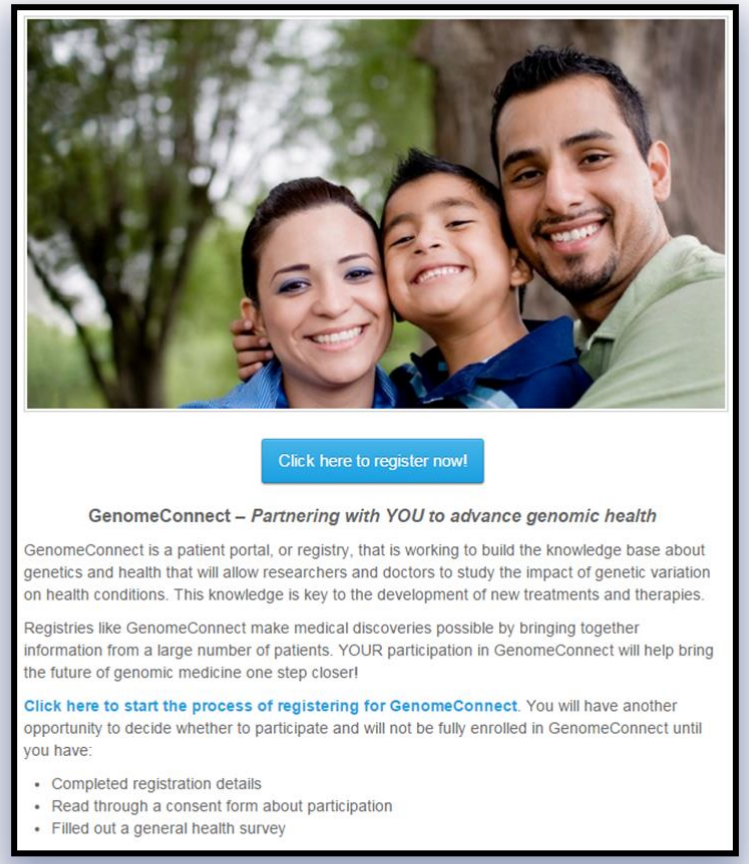
Clinical Genome Resource

# EXTRA SLIDES

# Patients and Patient Advocacy Groups

**A web-based patient registry that aims to:**

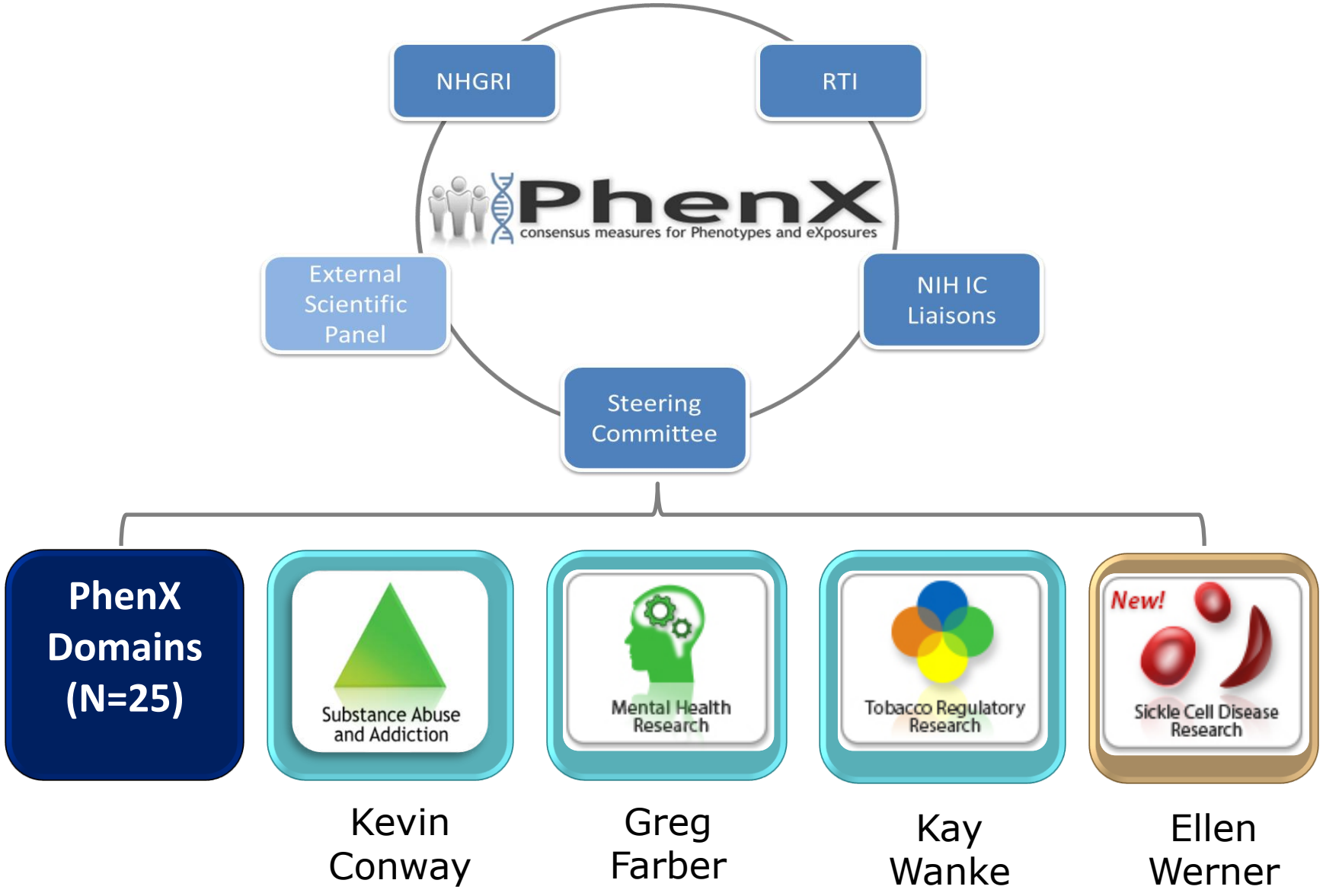
- Provide a mechanism for patients to securely share their genetic and health information
- Support patients as a valuable partner in advancing genomic medicine
- Enable patients to connect with other individuals, genetic testing laboratories healthcare providers, and researchers




**www.genomeconnect.org**

(Slide modified from Juliann Savatt, MS, LGC, Geisinger)

# NIH Collaborations: PhenX Evolution



# 2017-2020 Goals

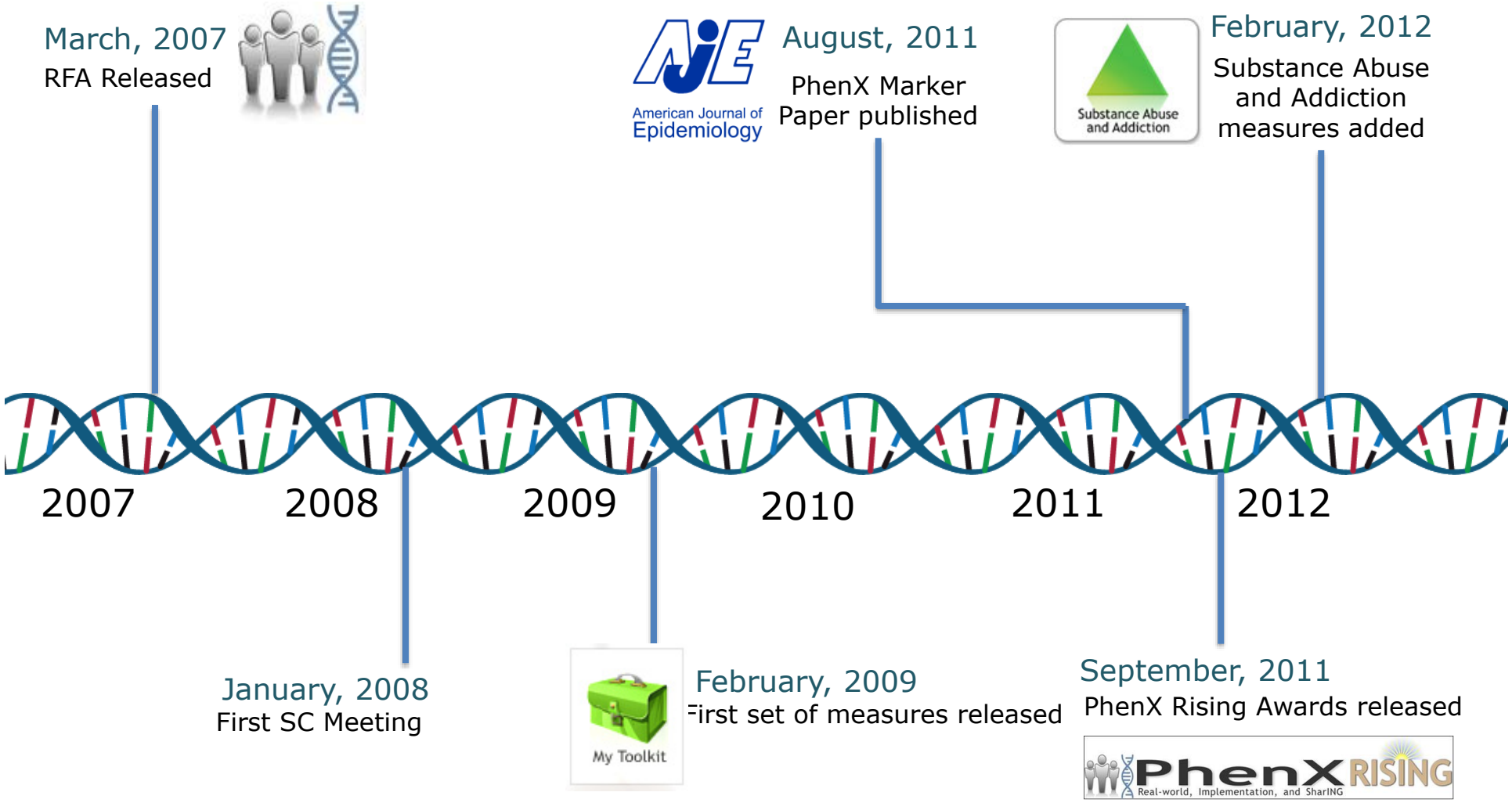
- **Expand PhenX Toolkit research domains**
  - Cancer, Environmental Exposures, Pediatrics, Social Determinants of Health
- **Link PhenX measures to established ontologies**
- **Provide new tools that investigators need**
  - Updated interface
  - Novel tools for comparing measures and variables.

# Social Determinants of Health

- Possible Area of Expansion
  - Some coverage by existing measures, but several gaps identified

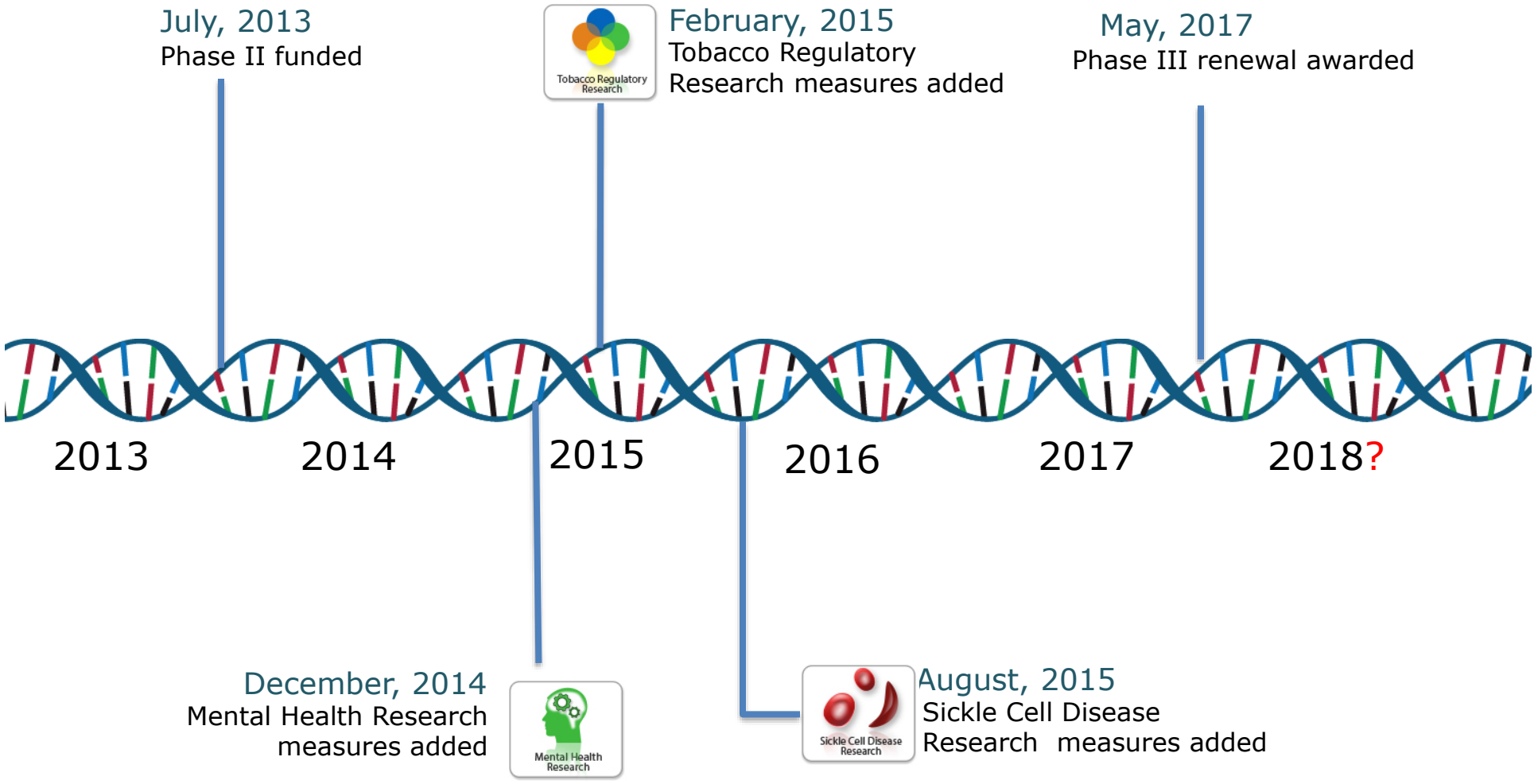
- Topic areas include
  - Economic Stability
  - Education
  - Social and Community Context
  - Neighborhood and Built Environment
  - Health and Health Care
  - Protective Factors
  - Risk Factors
  - Outcomes

# 10th Anniversary: Key Accomplishments




Slide created by Margaret Ginoza

# 10th Anniversary: Key Accomplishments

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Margaret Ginoza