# Unharmonized TOPMed study phenotypes on dbGaP

Leslie Emery

Research scientist, TOPMed DCC

## What is phenotype harmonization?

- Individual TOPMed studies collected and stored phenotype data in heterogeneous ways
- Harmonization is the process by which source phenotypes from multiple TOPMed studies are transformed so that they can be used together
  - Source phenotypes / unharmonized phenotypes
  - Harmonized phenotypes

## Where can I get TOPMed phenotype data?

- Get DCC harmonized phenotypes from the Exchange Area
- 2. Get (harmonized or unharmonized) phenotypes directly from the studies (transfer via EA)
- 3. Get unharmonized phenotypes from dbGaP

<sup>\*</sup> All three methods for obtaining data require dbGaP application and DAC approval

## Where can I get TOPMed phenotype data?

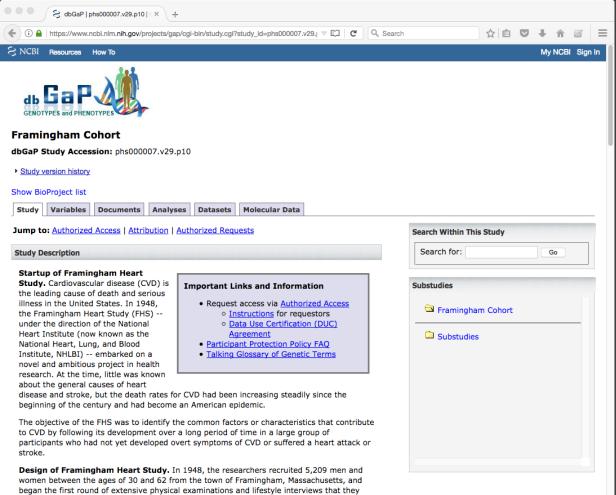
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## The Structure of TOPMed data on dbGaP

### TOPMed studies on dbGaP

- Most TOPMed studies already had data from previous projects in dbGaP
- Each dbGaP study is assigned a unique accession number (phs)
  - e.g. Framingham Heart Study (FHS) is phs 7 (link)



Design of Framingham Heart Study. In 1948, the researchers recruited 5,209 men and women between the ages of 30 and 62 from the town of Framingham, Massachusetts, and began the first round of extensive physical examinations and lifestyle interviews that they would later analyze for common patterns related to CVD development. Since 1948, the subjects have returned to the study every two years for an examination consisting of a detailed medical history, physical examination, and laboratory tests, and in 1971, the study enrolled a second-generation cohort -- 5,124 of the original participants' adult children and their spouses -- to participate in similar examinations. The second examination of the Offspring cohort occurred eight years after the first examination, and subsequent examinations have occurred approximately every four years thereafter. In April 2002 the Study entered a new phase: the enrollment of a third generation of participants, the grandchildren of the original cohort. The first examination of the Third Generation Study was completed in July 2005 and involved 4,095 participants. Thus, the FHS has evolved into a prospective, community-based, three generation family study. The FHS is a joint project of the National Heart. Lung and Blood Institute and Boston University.

Research Areas in the Framingham Heart Study. Over the years, careful monitoring of the FHS population has led to the identification of the major CVD risk factors -- high blood pressure, high blood cholesterol, smoking, obesity, diabetes, and physical inactivity -- as well as a great deal of valuable information on the effects of related factors such as blood triglyceride and HDL cholesterol levels, age, gender, and psychosocial issues. Risk factors have been identified for the major components of CVD, including coronary heart disease, stroke, intermittent claudication, and heart failure. It is also clear from research in the FHS and other studies that substantial subclinical vascular disease occurs in the blood vessels, heart and brain that precedes clinical CVD. With recent advances in technology, the FHS has

## Child vs. parent accessions

- A parent accession (phs) usually holds all of the phenotype data
- A child accession (phs) usually holds all of the genotype data

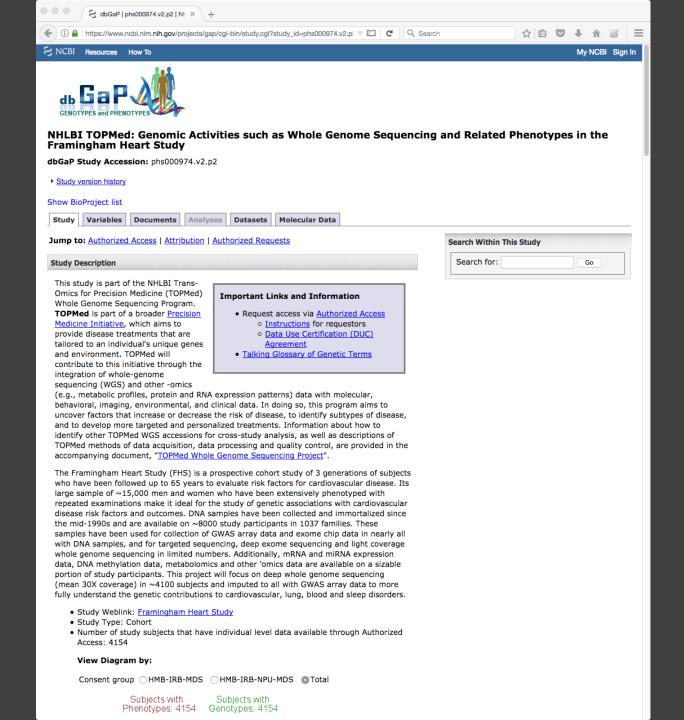
The Framingham Cohort is utilized in the following dbGaP substudies. To view genotypes, analysis, expression data, other molecular data, and derived variables collected in these substudies, please click on the following substudies below or in the "Substudies" box located on the right hand side of this top-level study page phs000007 Framingham Cohort.

- phs000342 Framingham SHARe
- phs000282 Framingham CARe
- phs000363 Framingham SABRe
- phs000307 Framingham Medical Resequencing
- phs000401 Framingham ESP Heart-GO
- phs000651 Framingham CHARGE-S
- phs000724 Framingham DNA Methylation

The unflagging commitment of the research participants in the NHLBI FHS has made more than a half century of research success possible. For decades, the FHS has made its data and DNA widely available to qualified investigators throughout the world through the Limited Access Datasets and the FHS DNA Committee, and the SHARe database will continue that tradition by allowing access to qualified investigators who agree to the requirements of data access. With the SHARe database, we continue with an ambitious research agenda and look forward to new discoveries in the decades to come.

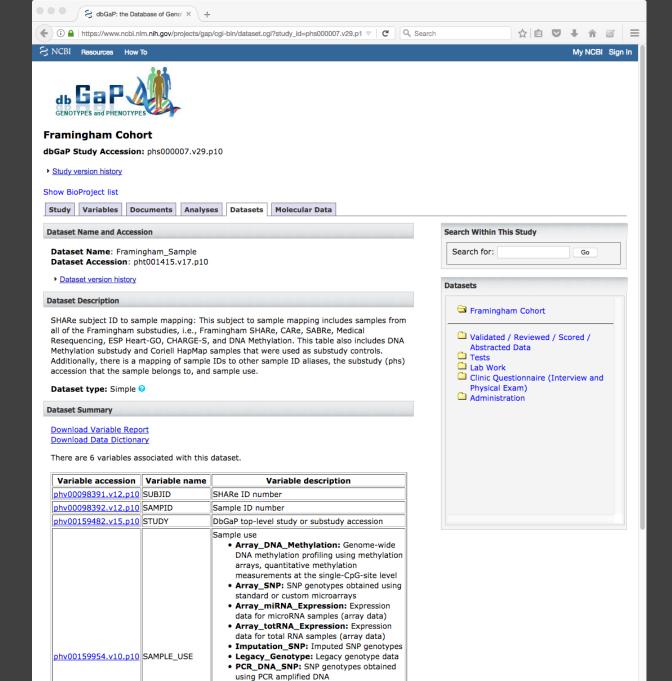
## **TOPMed accessions**

- A TOPMed accession is the phs that will hold TOPMed sequence data
  - Currently a separate parent accession
  - Will eventually be made into a child linked to the original parent accession
- A few studies without previous parent accessions only have a TOPMed accession
  - Sequence data and phenotype data are both in the TOPMed accession
  - e.g. CRA, Amish
- View a table of each study's TOPMed accession on the TOPMed website
  - e.g. FHS TOPMed accession is phs 974 (link)



## dbGaP phenotype variables

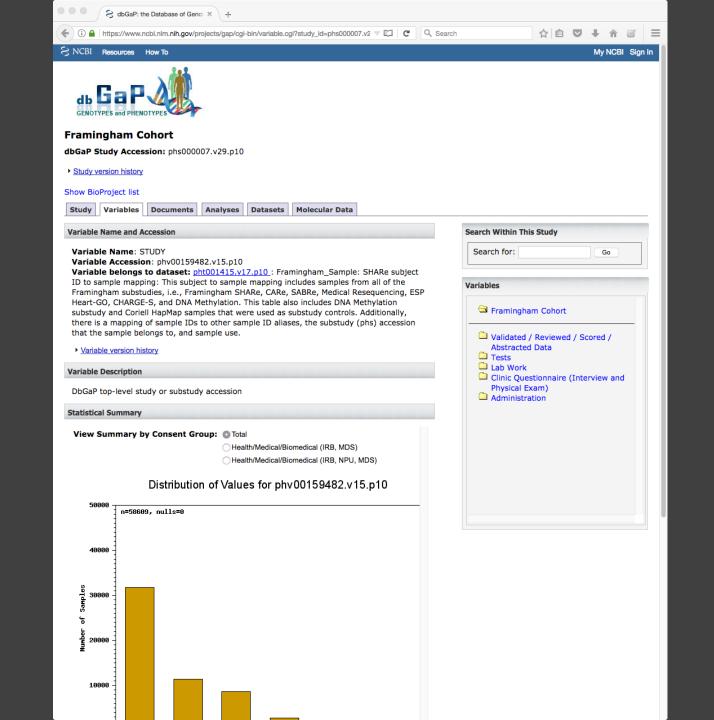
- Phenotype data is organized into datasets, which have a dataset accession (pht) (link)
- Each phenotype variable is assigned a variable accession (phv) (link)



· Seq\_DNA\_SNP: SNP genotypes derived

 Seq\_DNA\_SNP\_CNV: SNP and CNV genotypes derived from sequence data

from sequence data



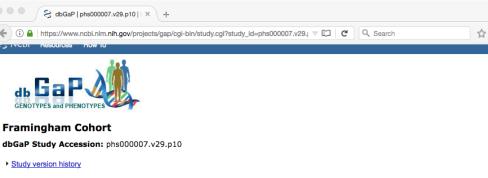
## Searching phenotype data in TOPMed studies on dbGaP

## Methods for searching dbGaP variables

- Search box on study page
- Advanced search methods
  - Entrez Search (link)
  - Faceted Search (link)

## Searching from the dbGaP study page

- You can search for variables from the withinstudy search box
- Other dbGaP search tools are more flexible



#### Show BioProject list

#### **Study Description**

Startup of Framingham Heart
Study. Cardiovascular disease (CVD) is
the leading cause of death and serious
illness in the United States. In 1948,
the Framingham Heart Study (FHS) -under the direction of the National
Heart Institute (now known as the
National Heart, Lung, and Blood
Institute, NHLBI) -- embarked on a
novel and ambitious project in health

research. At the time, little was known about the general causes of heart

#### **Important Links and Information**

- Request access via <u>Authorized Access</u>
  - o <u>Instructions</u> for requestors
  - o Data Use Certification (DUC)
  - Agreement
- Participant Protection Policy FAQ
- Talking Glossary of Genetic Terms

disease and stroke, but the death rates for CVD had been increasing steadily since the beginning of the century and had become an American epidemic.

The objective of the FHS was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke.

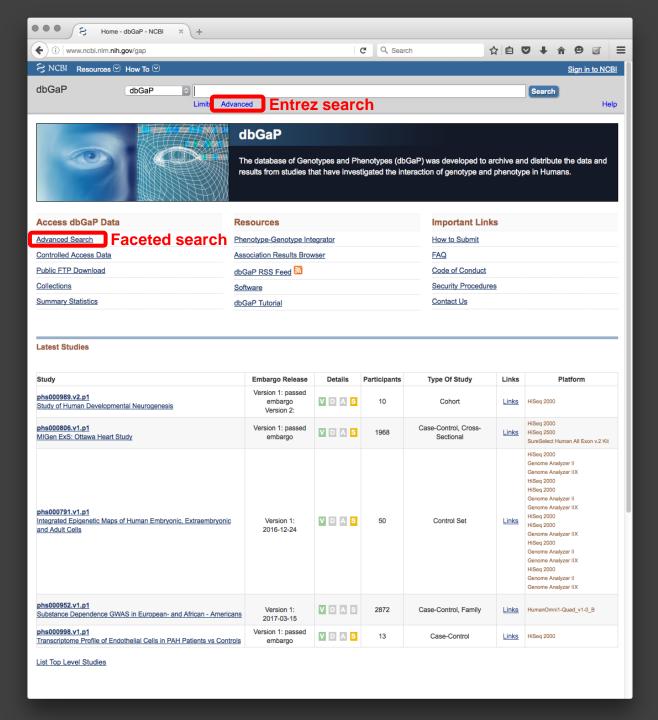
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Search for: bmi	Go
ubstudies	
Framingham Cohort	
Substudies	

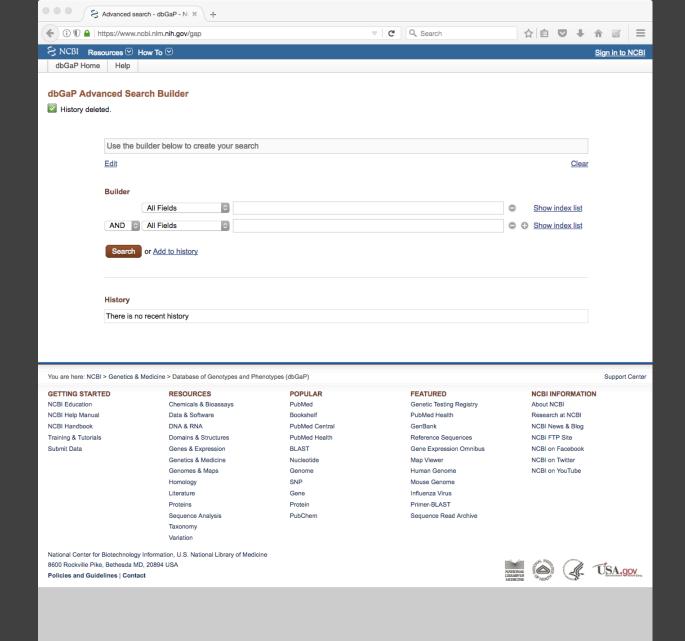
# There are two dbGaP advanced search options

Entrez
 Faceted



## Entrez searching (link)

- Use the Advanced search builder or type search field qualifiers into the search bar
- Use the "Belongs To" field qualifier to search for variables within studies
- Searches are automatically saved to your search history if you are logged in to a My NCBI account
- Once you have search results, click on the "Variables" tab to see results for phenotype variables

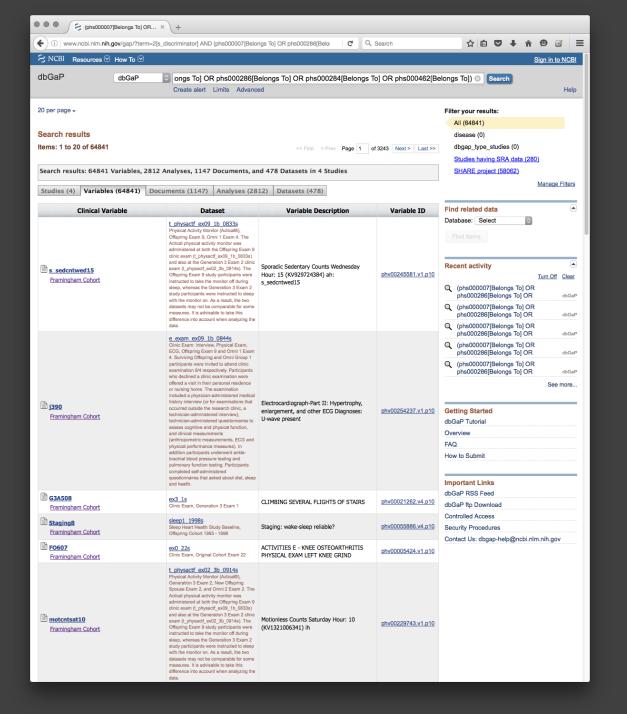


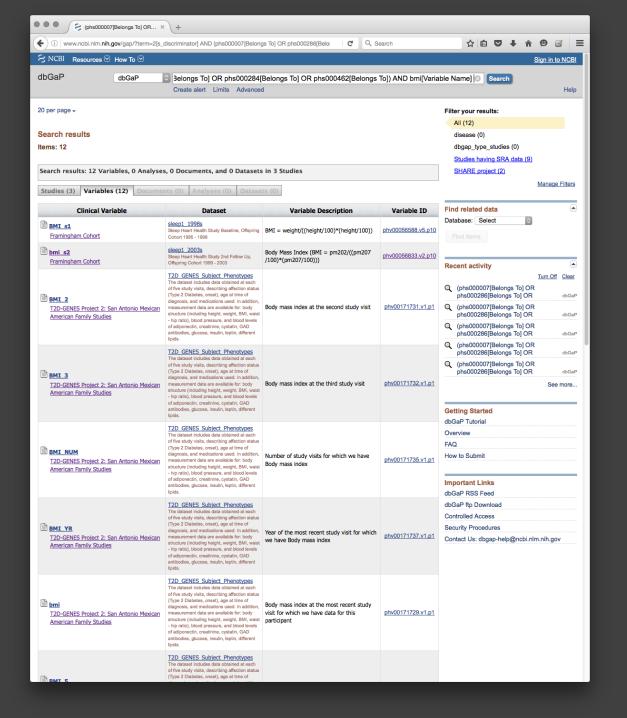
## Entrez search examples

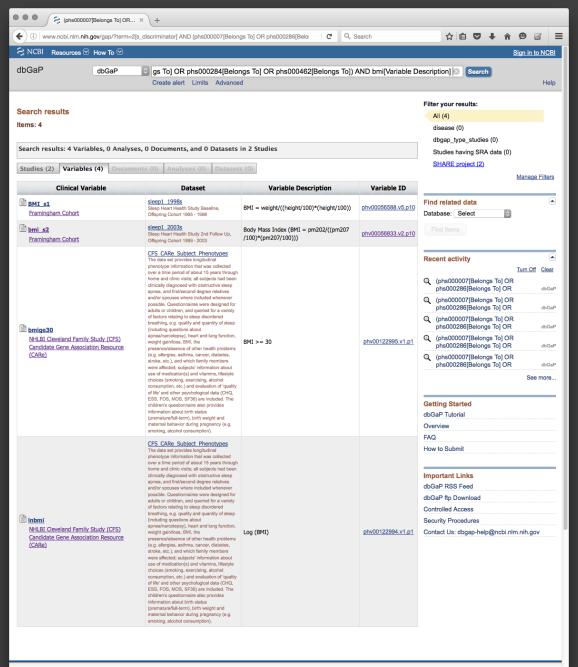
- Search within several TOPMed studies:
  - (phs000007[Belongs To] OR phs000286[Belongs To] OR phs000284[Belongs To] OR phs000462[Belongs To])
- Search for variables within those studies

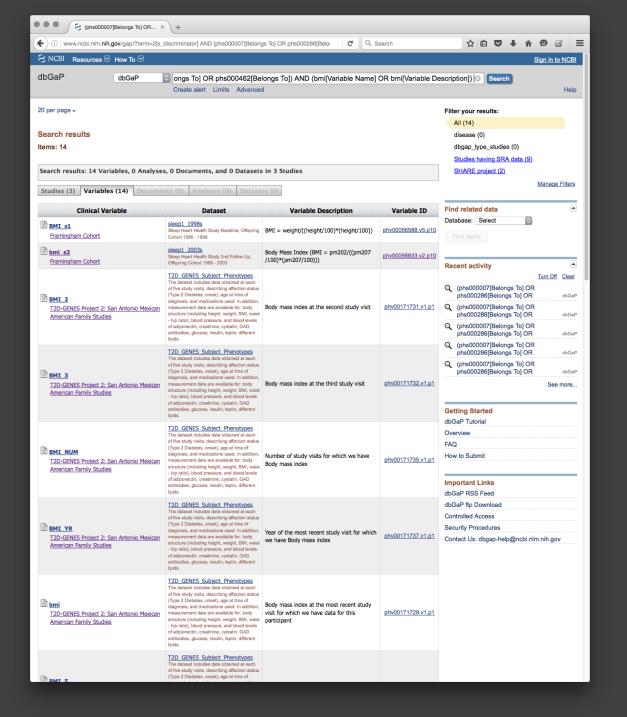
(add these to the end of the above search string)

- Search within variable names
  - AND bmi[Variable Name]
- Search within variable descriptions
  - AND bmi[Variable Description]
- Search within variable name OR variable description
  - AND (bmi[Variable Name] OR bmi[Variable Description])



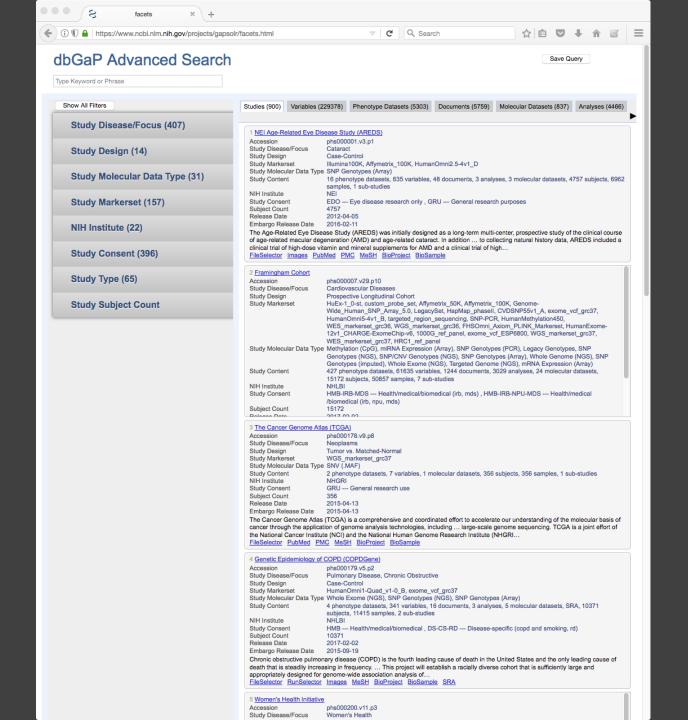




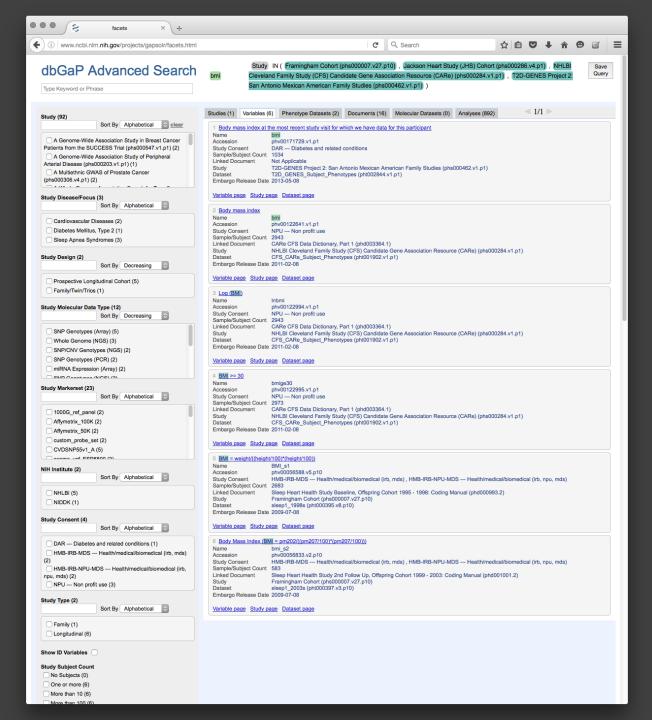


## Faceted searching (link)

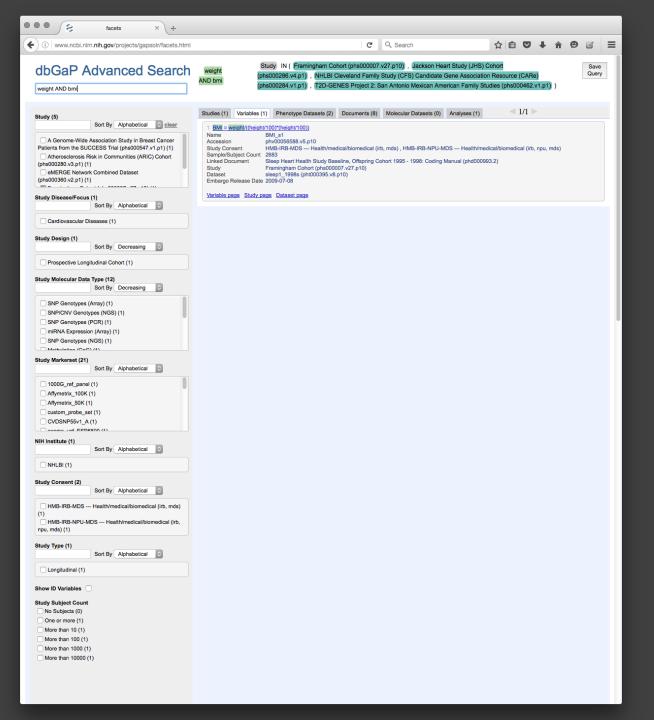
- Go to the Variables tab
- Put the phs number into the "Study" box
  - Only digits are required
  - Zero padding may be necessary e.g. for 000007
- Check the box for the study when it comes up
- The study name gets added to the search construction at top of page



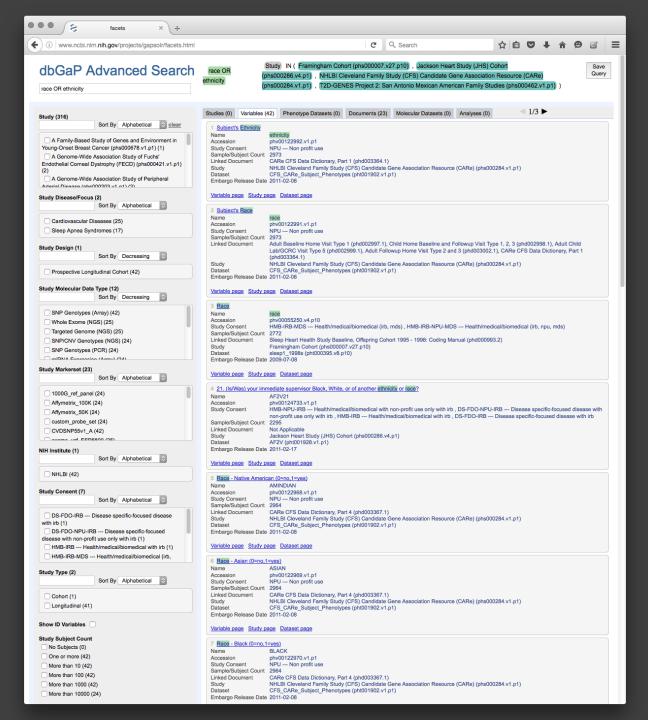
Search for "bmi" within variable names and descriptions for several studies



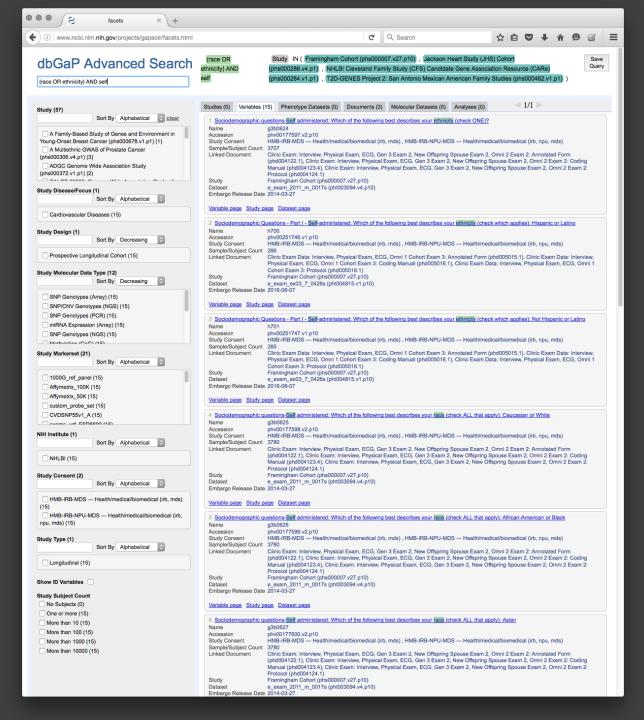
Search for "bmi" and "weight" within variable names and descriptions for several studies



Search for "race" or "ethnicity" within variable names and descriptions for several studies

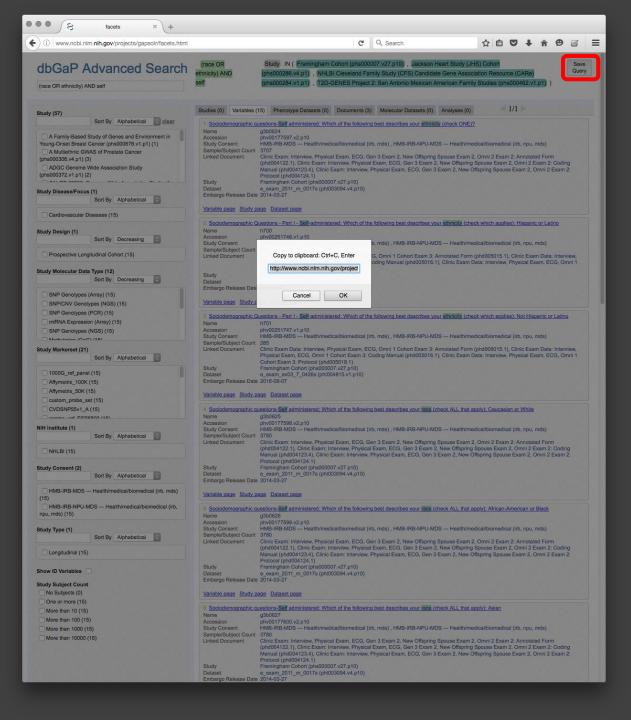


Search for ("race" OR "ethnicity") AND "self" within variable names and descriptions for several studies



# Copy a link to the search to use again later by clicking "Save Query" button

\* Doesn't work in Safari



## Comparison of search tools

#### Entrez advanced search

- Updates when hitting "Search"
- Easily re-use a search string to search within multiple studies
- Save searches in account history
- Searching within variables is more difficult
- Specify whether to search within variable names and/or descriptions
- Must click on Variables tab after every search

#### Facets advanced search

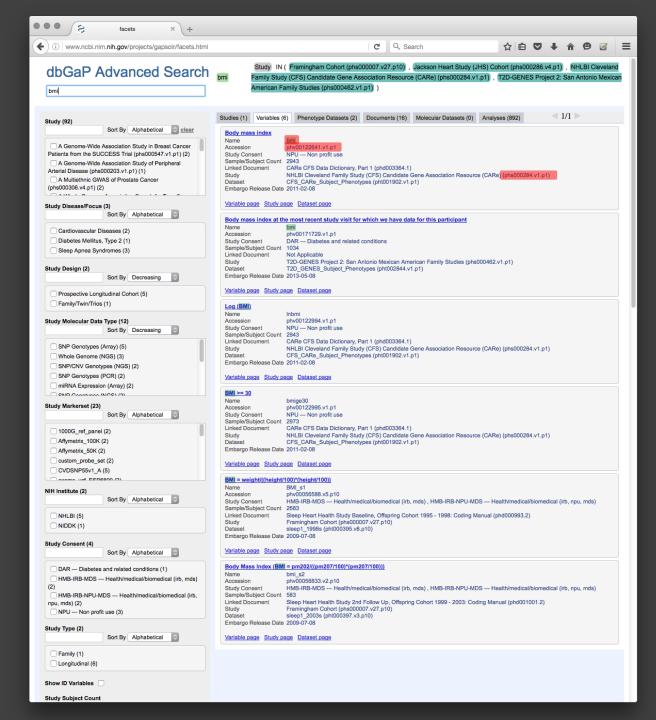
- Live updating
- Manually select each study to search within
- Save a link to the search for later
- Easily search within variables

- Searches within variable names and descriptions
- Stays in the Variables tab after search modifications

## Saving phenotype variables for later reference

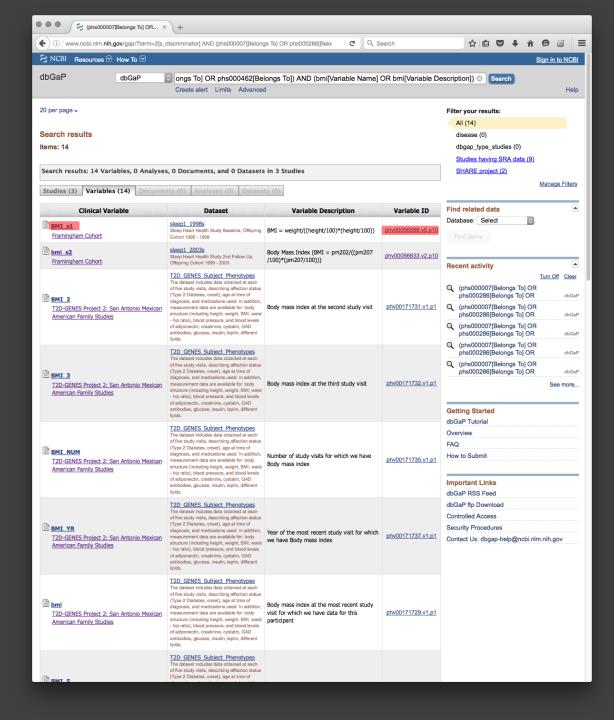
- Variable accession number (phv) with version
- Study accession number (phs) with version
- Variable name

Variable information on faceted search results page

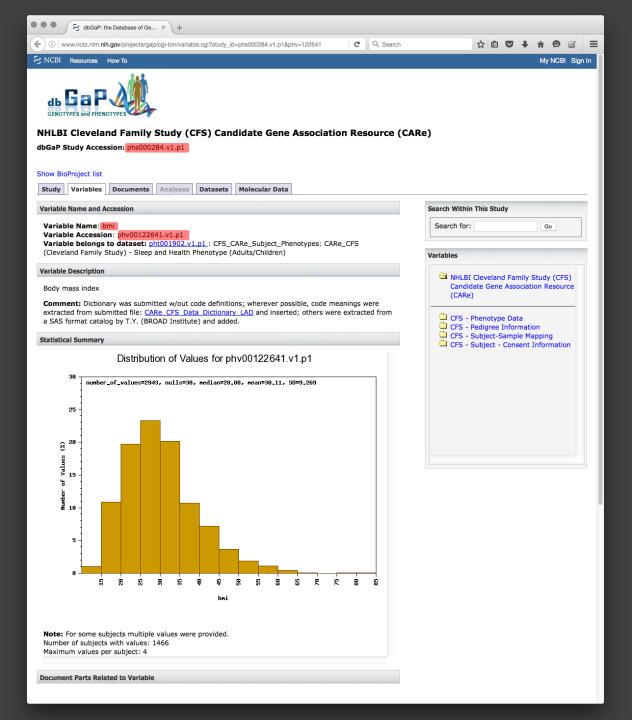


# Variable information on Entrez search results page

\* You'll have to click through to the variable detail page to find the study phs number



Variable information on variable detail page



## Links

- dbGaP demos <a href="http://www.ncbi.nlm.nih.gov/projects/gap/tutorial/dbGaP\_demo\_1.htm">http://www.ncbi.nlm.nih.gov/projects/gap/tutorial/dbGaP\_demo\_1.htm</a>
- NCBI Handbook: dbGaP <a href="http://www.ncbi.nlm.nih.gov/books/NBK154410/">http://www.ncbi.nlm.nih.gov/books/NBK154410/</a>
- NCBI Entrez information <a href="http://www.ncbi.nlm.nih.gov/Class/MLACourse/Original8Hour/Entrez/">http://www.ncbi.nlm.nih.gov/Class/MLACourse/Original8Hour/Entrez/</a>
  - Especially the section "Three Levels of Search Complexity"
- Faceted search demo webinar video https://www.youtube.com/watch?v=ePQ9p2SL\_wM
- Entrez search help http://www.ncbi.nlm.nih.gov/books/NBK3837/

#### Publications:

Mailman et al. 2007. The NCBI dbGaP database of genotypes and phenotypes. Nature Genetics. 39(10): 1181 - 1186.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2031016/

Tryka et al. 2014. NCBI's Database of Genotypes and Phenotypes: dbGaP. Nucleic Acids Research. 42: D975 – D979.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3965052/