Calculating Risk using Open Mendel

Presented on behalf of the Open Mendel Project Team
by Janet Sinsheimer PhD

David Geffen School of Medicine at UCLA

Pre-Workshop Preparation?

- Installed Julia and Open Mendel including MendelGeneticCounseling?

- If not, pair up with another who didn't have a chance

- On <u>one computer</u> go to: https://github.com/OpenMendel

- Or google:

- Github OpenMendel

OpenMendel · GitHub

https://github.com › OpenMendel ▾

OpenMendel has 22 repositories available.

Click on **GeneticCounseling_ASHG2019**

- Go to the bottom of the webpage and click on

launch binder

To Run the Tutorial

- **<u>If you have installed Open Mendel:</u>**
  - Launch Julia 1.2 by clicking on the app
  - Type "using IJulia"
  - Type "notebook()"
  - Go to the resulting webpage and drill down to the directory with the jupyter notebooks for this tutorial
  - Click MendelGeneticCounselingTutorial.ipynb

- **<u>Or when Binder has Launched</u>**
  - Click MendelGeneticCounselingTutorial.ipynb
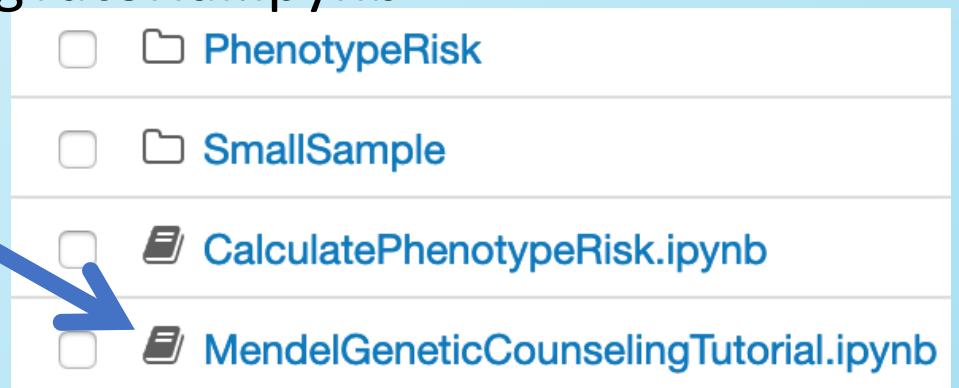
While Binder launches – A little Background on the Open Mendel Project

- Goal: Interactive, interpretable statistical genetics software that scales to big data and aids in reproducible research.

- Started in 2016 by Profs. Kenneth Lange, Janet Sinsheimer, Eric Sobel, Jin Zhou and Hua Zhou
  - Major contributors: students, postdoctoral scholars and faculty at Jilin U., NC State, Seoul National U., U. Arizona, UCLA, UCSF, U. Wisconsin.

- Written in Julia - new computing language that "walks like python, runs like C". (https://opensourceforu.com/2016/10/julia-language/). Solves the two language problem, i.e. easily scales to big data.

- Open Mendel team want suggestions for improvements/ additions and more collaborators.

- See: H.Zhou et al. (2019) OpenMendel: a cooperative programming project for statistical genetics. *Human Genetics*.

Today's Tutorial Features MendelGeneticCounseling.jl

- See Open Mendel github site for tutorials of other modules.

- Today: How to calculate genetic risks for individuals using their family histories and covariate information via a likelihood approach to form conditional probabilities.

- MendelGeneticCounselingTutorial.ipynb, has more details and background material.
  - The version you are running is beta and should be used for research purposes only.

General Idea for Today's Tutorial:

- Assumes a single family of interest with a underlying and possibly unmeasured trait locus.

- Use already determined penetrance parameters to calculate the conditional probability that a particular individual has a heterozygous genotype given their risk factors and their families phenotypes and risk factors can include linked genetic markers.

- Conditional probability: $P(H|D) = \dfrac{L(H \cap D)}{L(D)}$

- where H is the individual's underlying genotype and D is all the other data (individual and family).

- Two copies of the pedigree in the pedigree file, one to calculate numerator and one to calculate denominator.

Today's Tutorial has two examples

- Example 1:
  - Uses one of the available generalized linear models, the Gamma distribution, with the link function = log.
  - Parameters estimated using MendelEstimatePenetrances.jl
  - The pedigree and cholesterol phenotypes: Schrott et al. (1972) Ann Int Med 76:711–720.
  - Determine the risk that a child (IV11) of a women with abnormally high cholesterol has a heterozygous genotype.

- Example 2:
  - Uses a penetrance file where values are stratified by sex and age.
  - The pedigree and penetrance are for BRCA1 and breast cancer and come from analyze.myvariant.org
  - Determine how probable a currently unaffected 38 year old woman (individual 18) has a heterozygous genotype.

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  - Type "notebook()"
  - Go to webpage and drill down to the directory with the jupyter notebooks for this tutorial
  - Click on MendelGeneticCounselingTutorial.ipynb

- If you are using Binder
  - Click on the MendelGeneticCounselingTutorial.ipynb

- **When Finished: go to File Tab and select Close and Halt**

- If extra time click on CalculatePhenotypeRisk.ipynb

Learning more about Julia and Open Mendel

On line Julia tutorials

- For Julia beginners:

https://www.youtube.com/watch?v=8h8rQyEpiZA&t=

- Links some other good online tutorials.

https://julialang.org/learning/

- statistical computing in Julia, see Prof. Hua Zhou lecture notes:

http://hua-zhou.github.io/teaching/biostatm280-2019spring/schedule.html

Open Mendel

https://github.com/OpenMendel

- Come to an Open Mendel workshop

- Wellcome course: "Genetic Analysis of Mendelian and Complex Disorders uses Open Mendel" as well as other statistical analysis programs.

GENETIC ANALYSIS OF MENDELIAN AND COMPLEX DISORDERS

15-21 July 2020
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