

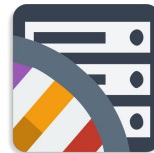
Section 4

Imputation Bot and PGS Server



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@lukfor



MICHIGAN
IMPUTATIONSERVER

Learning objectives

Participants will

1. Learn how to use Imputation bot
2. Learn how to automate job submission
3. Learn how to use the PGS Server extension

Challenges

- More and more imputation servers will be available soon
 - Additional reference panels
 - Different geographical locations
 - Example: TOPMed Imputation Server
- Challenges
 - Hard to keep track of instances, jobs and results
 - Graphical web interface not ideal for automation
 - Complex to integrate in own pipelines or scripts

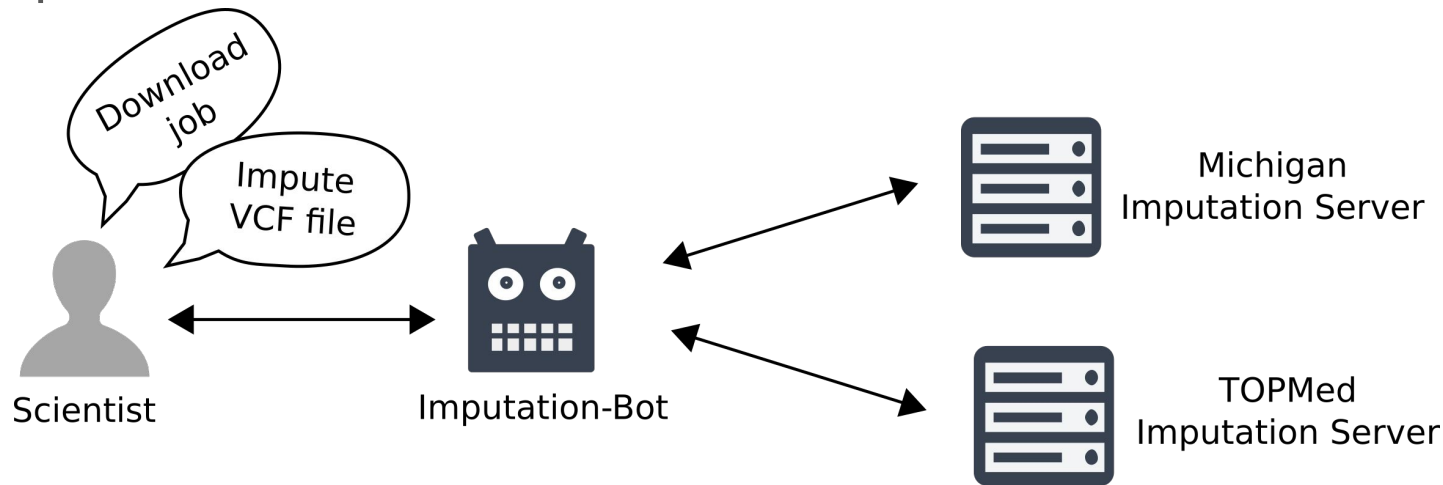


Imputation Bot

<https://github.com/lukfor/imputationbot>

Imputation Bot

- Automate remote imputation
- Submit and monitor jobs from the command line
- Different commands can easily be combined
- Improves automation

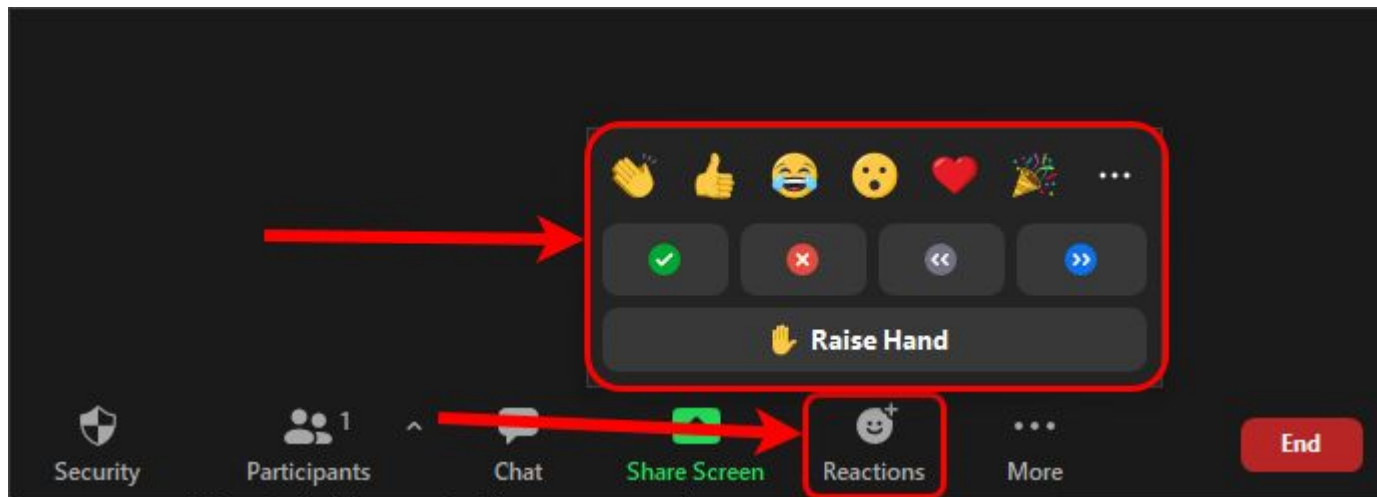


Have you used the Imputation Bot yet?

Put a "Yes" in the chat

Or

Raise your hand



1. Enable API Access

lukfor ▾

Profile

Logout



API Access

This service provides a rich RestAPI to submit, monitor and download jobs

You need a access token to use the API. [Learn more.](#)

Create API Token



API Token

Your token for this service is:

```
eyJjdHkiOiJ0ZXh0XC9wbGFpbilslmFsZyl6lkhTMjU2In0.eyJtY  
WlsjoibHVrYXMuZm9yZXJAaS1tZWQuYWMuYXQiLCJleHBp  
cmUiOiE1NzMyMjkwNTY3NTEslm5hbWUiOiJMdWthcyBGb3J  
lcilslmFwaSI6dHJ1ZSwidXNlcm5hbWUiOiJsdWtmb3lifQ.qY7i
```

OK

2. Install Imputation Bot

lukas@lukas-workstation:~/imputationbot\$

```
lukas@lukas-workstation:~/imputationbot$ curl -sL imputationbot.now.sh | bash
```

```
lukas@lukas-workstation:~/imputationbot$ curl -sL imputationbot.now.sh | bash
Installing Imputation Bot v0.8.3...
Downloading Imputation Bot from https://github.com/lukfor/imputationbot/releases
/download/v0.8.3/imputationbot-installer.sh...
  % Total    % Received % Xferd  Average Speed   Time    Time     Time  Current
                                 Dload  Upload   Total   Spent    Left   Speed
100  652    100  652    0     0   1895      0  --:--:-- --:--:-- --:--:--   1895
100 2995k    100 2995k    0     0  390k      0  0:00:07  0:00:07 --:--:--   518k
Verifying archive integrity... 100% All good.
Uncompressing Make
script=self-extrabable
scriptargs=archives makeself.sh 100%
```

Imputation Bot v0.8.3 installation completed. Have fun!

```
lukas@lukas-workstation:~/imputationbot$
```

3. Configure Imputation Bot

```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot add-instance
```



```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot add-instance
```

```
Imputation Bot 0.8.3
```

```
https://imputationserver.sph.umich.edu
```

```
(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger
```

```
Built by lukas on 2020-10-08T12:27:01Z
```

```
Imputationserver Url [https://imputationserver.sph.umich.edu]: █
```

```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot add-instance
```

```
Imputation Bot 0.8.3
```

```
https://imputationserver.sph.umich.edu
```

```
(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger
```

```
Built by lukas on 2020-10-08T12:27:01Z
```

```
Imputationserver Url [https://imputationserver.sph.umich.edu]:
```

```
API Token [None]: █
```



```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot add-instance
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Imputationserver Url [<https://imputationserver.sph.umich.edu>]:

API Token [None]: eyJjdHkiOiJ0ZXh0XC9wbGFpbIsImFsZyI6IkhTMjU2In0.eyJtYWlsIjoibHVrYXMuZm9yZXJAaS1tZWQuYWMuYXQiLCJleHBpcmUiOjE2MDQxMzkzMzAwNzYsIm5hbWUiOiJMdWthcyIsImFwaSI6dHJlZSwidXNlcm5hbWUiOiJsdWtmb3IifQ.1n0YSJr58WHXn3pi0rv8Th-FZHJVxxUb-7KVfUfadta

```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot add-instance
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

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Built by lukas on 2020-10-08T12:27:01Z

Imputationserver Url [<https://imputationserver.sph.umich.edu>]:

API Token [None]: eyJjdHkiOiJ0ZXh0XC9wbGFpbiIsImFsZyI6IkhTMjU2In0.eyJtYWlsIjoibHVrYXMuZm9yZXJAaS1tZWQuYWMuYXQiLCJleHBpcmUiOjE2MDQxMzgzMzAwNzYsIm5hbWUiOiJMdWthcyIsImFwaSI6dHJlZSwidXNlcm5hbWUiOiJsdWtmb3IifQ.1n0YSJr58WHXn3pi0rv8Th-FZHJVxxUb-7KVfUfadta

Hi Lukas

Imputation Bot is ready to submit jobs to <https://imputationserver.sph.umich.edu>
(Genotype Imputation (Minimac4)) 1.4.1)

```
lukas@lukas-workstation:~/imputationbot$
```

4. Submit a Job

```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot impute --files test-data/chr20.R50.merged.1.330k.recode.vcf.gz --refpanel 1000g-phase-3-v5 --population eur
```

```
lukas@lukas-workstation:~/imputationbot$ ./imputationbot impute --files test-data/chr20.R50.merged.1.330k.recode.vcf.gz --refpanel 1000g-phase-3-v5 --population eur
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Submitting job for 1000g-phase-3-v5 to Michigan Imputation Server...

Parameters:

refpanel: apps@1000g-phase-3-v5

files:

- test-data/chr20.R50.merged.1.330k.recode.vcf.gz

build: hg19

r2Filter: 0

phasing: eagle

population: eur

aesEncryption: no

■ Uploading files [100%]

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Submitting job for 1000g-phase-3-v5 to Michigan Imputation Server...

Parameters:

refpanel: apps@1000g-phase-3-v5

files:

- test-data/chr20.R50.merged.1.330k.recode.vcf.gz

build: hg19

r2Filter: 0

phasing: eagle

population: eur

aesEncryption: no

Uploading files [100%]

Imputation job 'job-20201008-084828-935' submitted successfully

Check the job progress on <https://imputationserver.sph.umich.edu/index.html>

#!/jobs/job-20201008-084828-935

5. Download Data

```
bash-3.2$ ./imputationbot download job-20191012-152533-884 --password mkW5oPAB-7c
```



```
bash-3.2$ ./imputationbot download job-20191012-152533-884 --password mkW5oPAB-7c
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Downloading job job-20191012-152533-884...

Downloading file job-20191012-152533-884/qcreport/qcreport.html (1/5)



```
bash-3.2$ ./imputationbot download job-20191012-152533-884 --password mkW5oPAB-7c
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Downloading job job-20191012-152533-884...

Downloading file job-20191012-152533-884/qcreport/qcreport.html (1/5)

Downloading file job-20191012-152533-884/statisticDir/snps-excluded.txt (2/5)

Downloading file job-20191012-152533-884/statisticDir/typed-only.txt (3/5)

Downloading file job-20191012-152533-884/local/chr_20.zip (4/5)

Decrypting file job-20191012-152533-884/local/chr_20.zip...



```
bash-3.2$ ./imputationbot download job-20191012-152533-884 --password mkW5oPAB-7c
```

Imputation Bot 0.8.3

<https://imputationserver.sph.umich.edu>

(c) 2019-2020 Lukas Forer, Sebastian Schoenherr and Christian Fuchsberger

Built by lukas on 2020-10-08T12:27:01Z

Downloading job job-20191012-152533-884...

Downloading file job-20191012-152533-884/qcreport/qcreport.html (1/5)

Downloading file job-20191012-152533-884/statisticDir/snps-excluded.txt (2/5)

Downloading file job-20191012-152533-884/statisticDir/typed-only.txt (3/5)

Downloading file job-20191012-152533-884/local/chr_20.zip (4/5)

Decrypting file job-20191012-152533-884/local/chr_20.zip...

Downloading file job-20191012-152533-884/logfile/chr_20.log (5/5)

All data downloaded and stored in /Users/lukas/imputationbot/job-20191012-152533-

```
bash-3.2$ █
```

Summary

- Imputation bot automates interactions with Imputation Servers
- Simplifies multi-reference and multi-study imputation
- Available: <https://github.com/lukfor/imputationbot>

More info and FAQ can be found here:
<https://imputationserver.readthedocs.io>

Extension: PGS Server

Motivation

Extend Imputation Server to simplify the application of polygenic risk scores to imputed genotypes

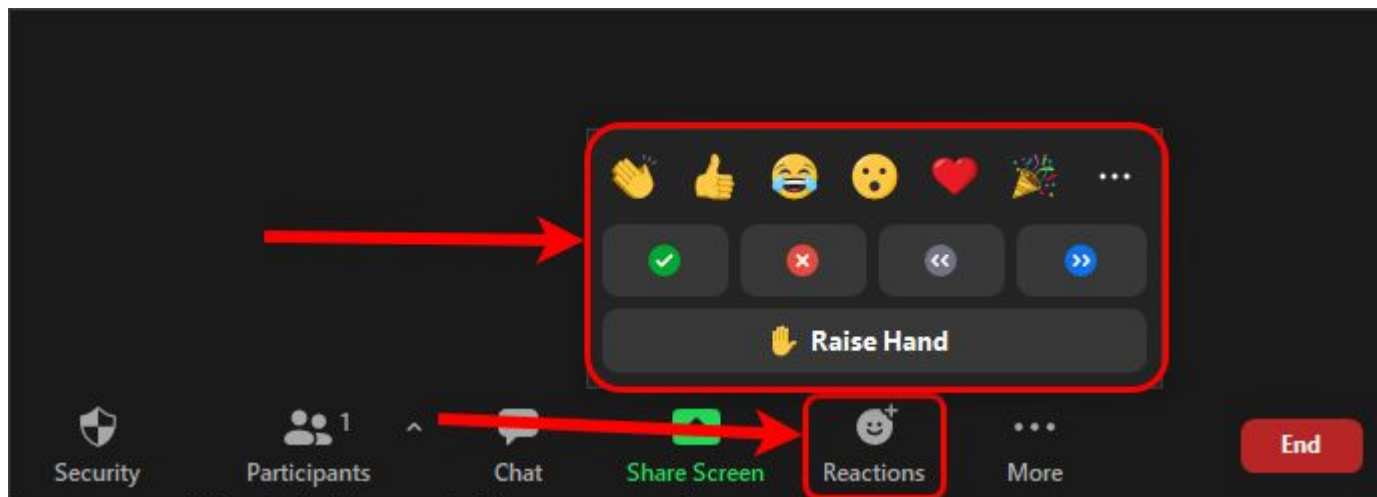
- First prototype available since April 2022
- More than 600 submitted jobs

Did you already test the PGS Server?

Put a "Yes" in the chat

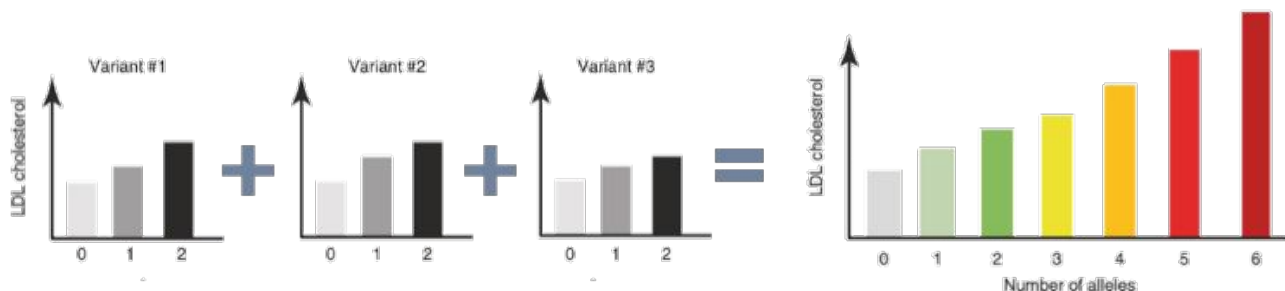
Or

Raise your hand



Polygenic Scores (PGS)

Combines the estimated effect of many genetic variants on an individual's phenotype



$$PRS_i = \sum_{j=1}^n x_{ij} \beta_j$$

counting the number of effect alleles for each individual and multiplying the count by the corresponding effect size

A higher PGS indicates a greater accumulation of risk-associated genetic variants in an individual

PGS Repositories

PGS Catalog

- The PGS Catalog is an open database of published polygenic scores (PGS)
- Each PGS in the Catalog is consistently annotated with relevant metadata
- Scores: 2,727
- <http://pgscatalog.org>

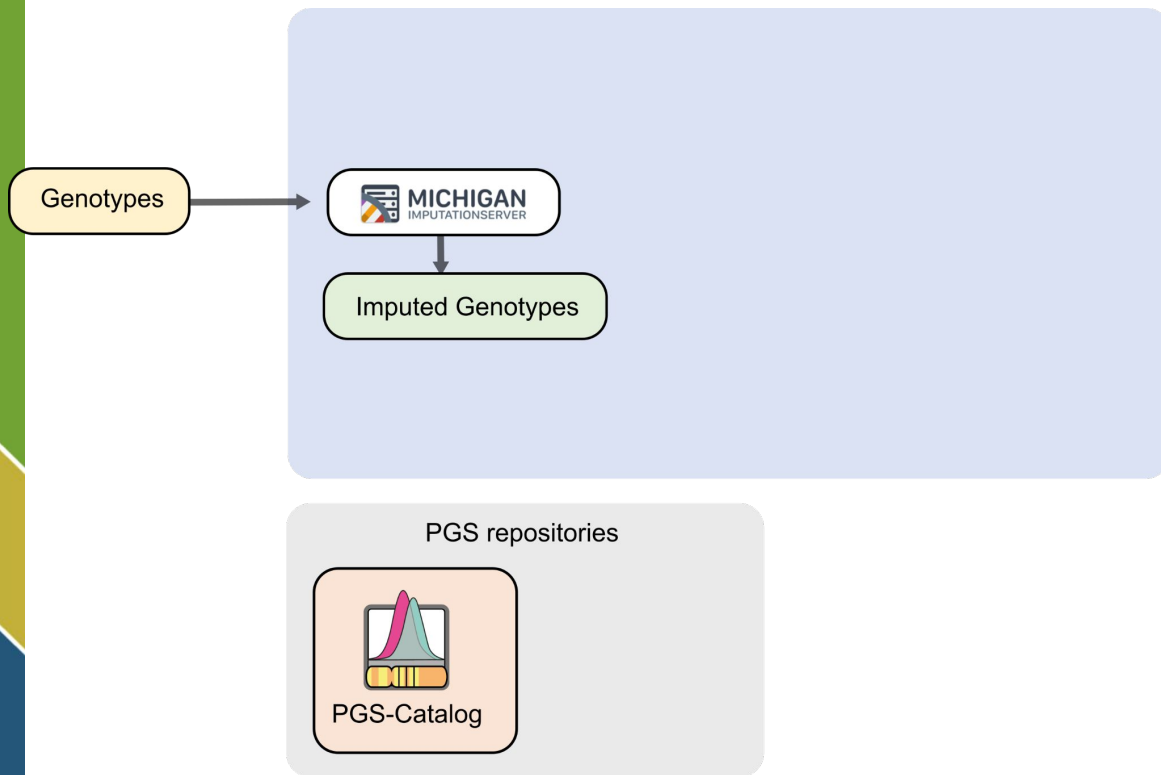
Cancer PRSWeb

- Scores: 305
- <https://prsweb.sph.umich.edu>

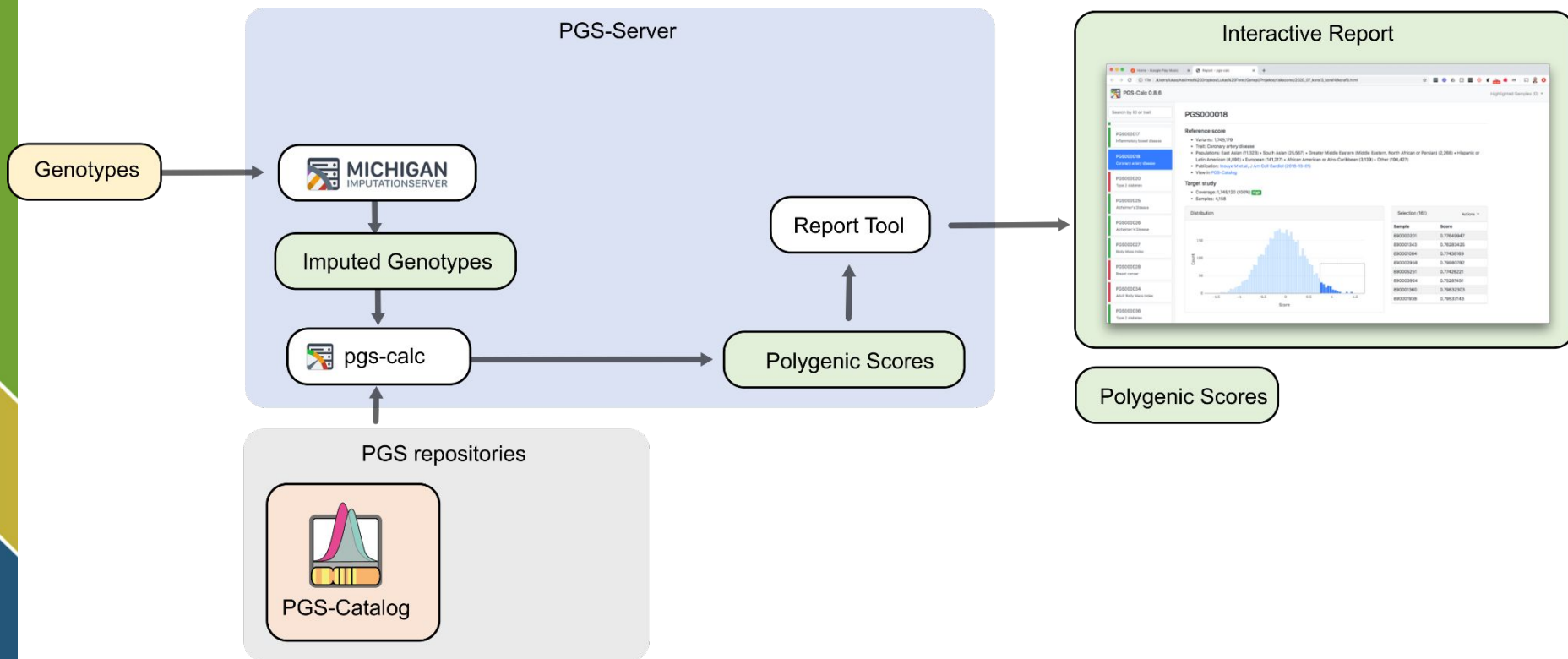
ExPRSWeb

- Scores: 514
- <https://exprsweb.sph.umich.edu>

Problem: PGS on Imputed Genotypes



PGS Server Workflow



Michigan Imputation Server

imputationserver.sph.umich.edu/index.html#!run/imputationserver%401.5.2

Michigan Imputation ServerHomeRunJobsHelpContact

lukfor

Array Build

GRCh37/hg19

Genotype Imputation (Minimac4)

Genotype Imputation and Polygenic Scores (Beta Version)

Genotype Imputation HLA (Minimac4)

Please note that the reference genome used for imputation must always match the reference genome used for the input data.

rsq Filter

off

Deprecated

Phasing

Eagle v2.4 (phasing)

Genotype Imputation (Minimac3)

Population

-- select an option --

Mode

Quality Control & Imputation

☐ AES 256 encryption

Imputation Server encrypts all zip files by default. Please note that AES encryption does not work with standard unzip programs. Use 7z instead.

☐ Generate Meta-imputation file

PGS Calculation (optional)

Please select a collection of polygenic scores to enable on the fly PGS calculation.

Scores

✓ -- select an option --

PGS Catalog v20220803 (hg19, 2620 scores)

PGS Catalog v20220803 (hg38, 2620 scores)

☐ I will not attempt to release any data from this project.

☐ I will report any inadvertent data release, security breach or other data management incident of which I become aware.

Submit Job

Search by ID or trait

PGS000017

Inflammatory bowel disease

PGS000018

Coronary artery disease

PGS000020

Type 2 diabetes

PGS000025

Alzheimer's Disease

PGS000026

Alzheimer's Disease

PGS000027

Body Mass Index

PGS000028

Breast cancer

PGS000034

Adult Body Mass Index

PGS000036

Type 2 diabetes

PGS000018

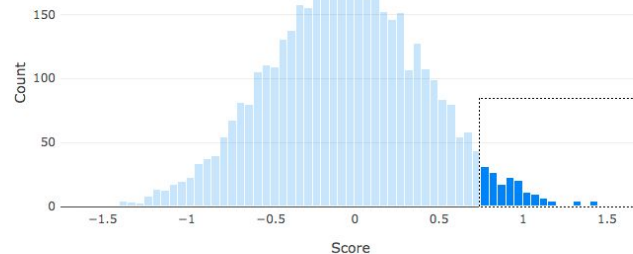
Reference score

- Variants: 1,745,179
- Trait: Coronary artery disease
- Populations: East Asian (11,323) • South Asian (25,557) • Greater Middle Eastern (Middle Eastern, North African or Persian) (2,268) • Hispanic or Latin American (4,095) • European (141,217) • African American or Afro-Caribbean (3,139) • Other (194,427)
- Publication: [Inouye M et.al, J Am Coll Cardiol \(2018-10-01\)](#)
- View in [PGS-Catalog](#)

Target study

- Coverage: 1,745,120 (100%) **high**
- Samples: 4,158

Distribution



Selection (161)

Actions ▾

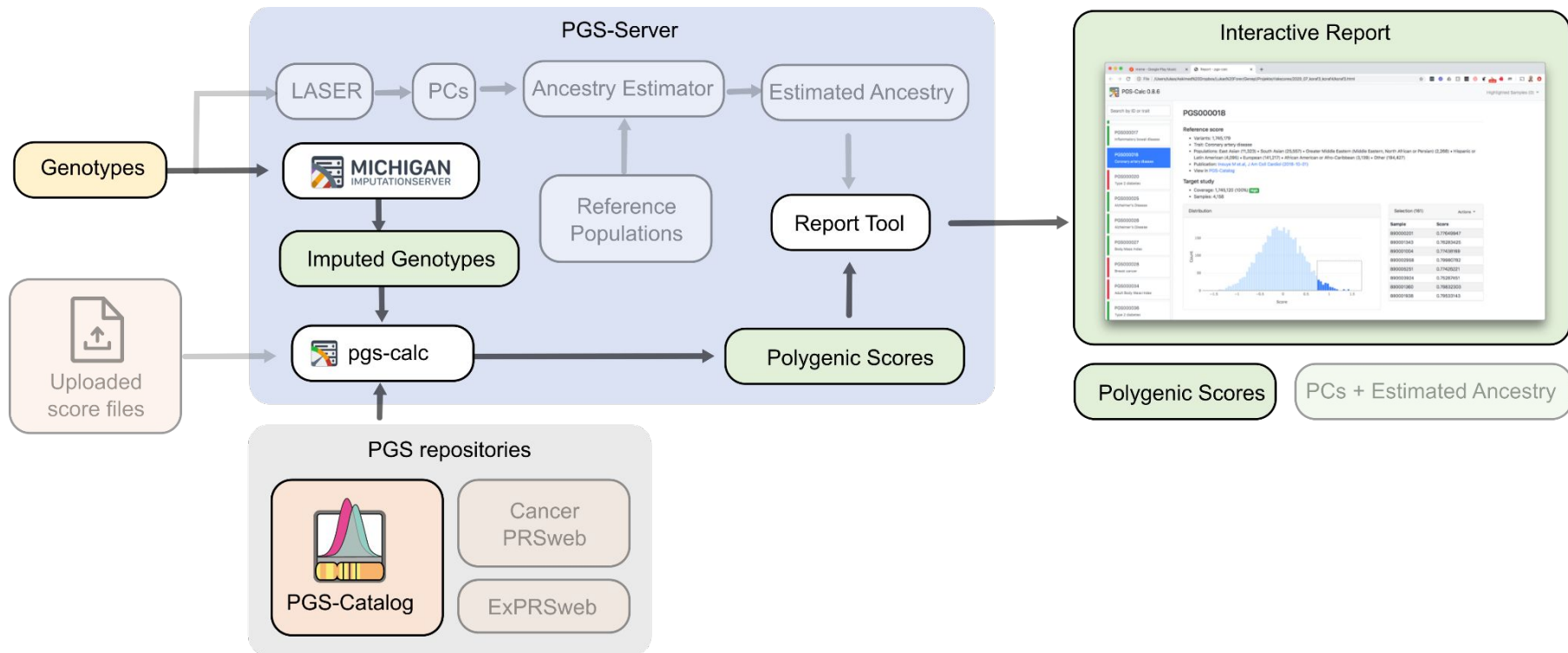
Sample	Score
890000201	0.77649947
890001343	0.76283425
890001004	0.77438169
890002958	0.79980782
890005251	0.77426221
890003924	0.75287451
890001360	0.79832303
890001938	0.79533143

PGS Server as a standalone tool

- pgs-calc is the backbone of PGS Server
- Available as a command line tool
 - No file upload required and higher flexibility
- Supports
 - Imputed genotypes from Imputation Server
 - Own score files
- Provides several filtering options (e.g. r^2 or variant list)

<https://github.com/lukfor/pgs-calc>

Work in Progress



Conclusion

- PGS became a key role in genetic research
- Has the potential to contribute to precision medicine
- Extension of Imputation Server
 - Calculates scores automatically after imputation
 - Supports PGS Catalog, CancerPRSWeb and ExPRSWeb
 - Creates interactive reports

Taking the burden out of genetic analysis