PGS Catalog access with quincunx

Introduction

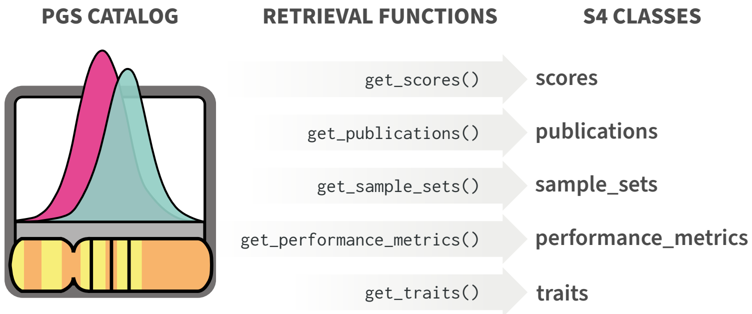
The **PGS Catalog** is a service provided by the EMBL-EBI and University of Cambridge that offers a manually curated and freely available database of published polygenic scores (PGS): `https://www.pgscatalog.org/`.

The PGS Catalog data provided by the **REST API** is organised around five core entities:

- PGS **Polygenic Scores**
- PGP **PGS Publications**
- PSS **PGS Sample Sets**
- PPM **PGS Performance Metrics**
- EFO **EFO traits**

Get PGS Catalog Entities

quincunx facilitates the access to the Catalog via the REST API, allowing you to programmatically retrieve data directly into R. Each of the five entities is mapped to an S4 object of a class of the same name.



PGS CATALOG	RETRIEVAL FUNCTIONS	S4 CLASSES
	`get_scores()`	scores
	`get_publications()`	publications
	`get_sample_sets()`	sample_sets
	`get_performance_metrics()`	performance_metrics
	`get_traits()`	traits

Query criteria for retrieval functions, e.g., PGS can be queried by either `pgs_id`, `efo_id` or `pubmed_id`. These correspond to the criteria exposed by the PGS Catalog REST API: `https://www.pgscatalog.org/rest/`.

Search by	Example	PGS	PGP	PSS	PPM	EFO
pgs_id	"PGS000001"	🟩	🟧	🟦	🟥	
pgp_id	"PGP000001"		🟧			
pss_id	"PSS000001"			🟦		
ppm_id	"PPM000001"				🟥	
efo_id	"EFO_0000249"	🟩				🟨
pubmed_id	"25855707"	🟩	🟧			
author	"Mavaddat"		🟧			
trait_term	"Alzheimer"					🟨

PGS Catalog Entities in R

PGS Catalog entities are represented as S4 classes in R. Each class represents a relational database of tidy data tables. All objects start with a table with the same name as the class. Combination of variables indicated in bold renders each row unique in each table.

S4 class scores

`scores`
- **pgs_id**
- pgs_name
- scoring_file
- matches_publication
- reported_trait
- trait_additional_description
- pgs_method_name
- pgs_method_params
- n_variants
- n_variants_interactions
- assembly
- license
- beta_unit

`publications`
- **pgs_id**
- **pgp_id**
- pubmed_id
- publication_date
- publication
- title
- author_fullname
- doi

`samples`
- **pgs_id**
- **sample_id**
- stage
- sample_size
- sample_cases
- sample_controls
- sample_percent_male
- phenotype_description
- ancestry_category
- ancestry
- country
- ancestry_additional_description
- study_id
- pubmed_id
- cohorts_additional_description

`traits`
- **pgs_id**
- **efo_id**
- trait
- description
- url

`demographics`
- **pgs_id**
- **sample_id**
- **variable**
- estimate_type
- estimate
- unit
- variability_type
- variability
- interval_type
- interval_lower
- interval_upper

`cohorts`
- **pgs_id**
- **sample_id**
- **cohort_symbol**
- cohort_name

S4 class publications

`publications`
- **pgp_id**
- pubmed_id
- publication_date
- publication
- title
- author_fullname
- doi
- authors

`pgs_ids`
- **pgp_id**
- **pgs_id**
- stage

S4 class traits

`traits`
- **efo_id**
- **parent_efo_id**
- is_child
- trait
- description
- url

`pgs_ids`
- **efo_id**
- **parent_efo_id**
- is_child
- pgs_id

`child_pgs_ids`
- **efo_id**
- **parent_efo_id**
- is_child
- child_pgs_id

3x `trait_{categories, synonyms, mapped_terms}`
- **efo_id**
- **parent_efo_id**
- is_child
- trait_{category, synonyms, mapped_terms}

S4 class sample_sets

`sample_sets`
- **pss_id**
- pgs_name
- scoring_file
- matches_publication
- reported_trait
- trait_additional_description
- pgs_method_name
- pgs_method_params
- n_variants
- n_variants_interactions
- assembly
- license
- beta_unit

`cohorts`
- **pss_id**
- **sample_id**
- **cohort_symbol**
- cohort_name

`samples`
- **pss_id**
- **sample_id**
- stage
- sample_size
- sample_cases
- sample_controls
- sample_percent_male
- phenotype_description
- ancestry_category
- ancestry
- country
- ancestry_additional_description
- study_id
- pubmed_id
- cohorts_additional_description

`demographics`
- **pss_id**
- **sample_id**
- **variable**
- estimate_type
- estimate
- unit
- variability_type
- variability
- interval_type
- interval_lower
- interval_upper

S4 class performance_metrics

`performance_metrics`
- **ppm_id**
- pgs_id
- reported_trait
- covariates
- comments

`publications`
- **ppm_id**
- **pgp_id**
- pubmed_id
- publication_date
- publication
- title
- author_fullname
- doi

`sample_sets`
- **ppm_id**
- **pss_id**

`samples`
- **ppm_id**
- **pss_id**
- **sample_id**
- stage
- sample_size
- sample_cases
- sample_controls
- sample_percent_male
- phenotype_description
- ancestry_category
- ancestry
- country
- ancestry_additional_description
- study_id
- pubmed_id
- cohorts_additional_description

`demographics`
- **ppm_id**
- **pss_id**
- **sample_id**
- **variable**
- estimate_type
- estimate
- unit
- variability_type
- variability
- interval_type
- interval_lower
- interval_upper

`cohorts`
- **ppm_id**
- **pss_id**
- **sample_id**
- **cohort_symbol**
- cohort_name

3x `pgs_{effect_sizes,classification_metrics,other_metrics}`
- **ppm_id**
- **{effect_size_id, classification_metrics_id, other_metrics_id}**
- estimate_type_long
- estimate_type
- estimate
- unit
- variability_type
- variability
- interval_type
- interval_lower
- interval_upper

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Other S4 Entities

Besides the five PGS Catalog entities, there are three other objects that can be retrieved from the REST API: `trait_categories`, `cohorts` and `releases`.

S4 class trait_categories

`trait_categories`
- **trait_category**

`trait`
- **trait_category**
- **efo_id**
- trait
- description
- url

S4 class cohorts

`cohorts`
- **cohort_symbol**
- cohort_name

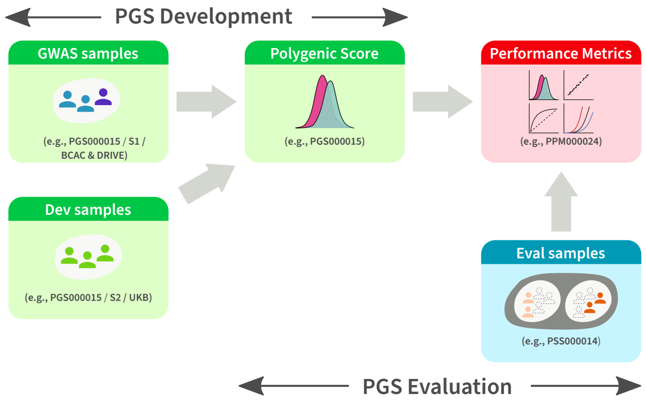
`pgs_ids`
- **cohort_symbol**
- **pgs_id**
- stage

S4 class releases

`releases`
- **date**
- n_pgs
- n_ppm
- n_pgp
- notes

3x `{pgs_ids, ppm_ids,pgp_ids}`
- **date**
- **{pgs_id, ppm_id, pgp_id}**

PGS Construction Process



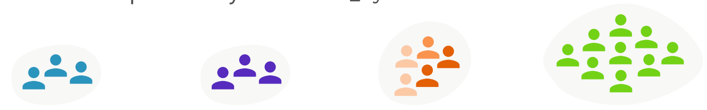
Samples and Polygenic Scores (PGS) are annotated according to their utilisation context in the PGS construction process, i.e. the `stage` variable in quincunx:

- Source of Variant Associations (GWAS): `stage="gwas"`
- Score Development/Training: `stage="dev"`
- Development: `stage="gwas/dev"` (`"gwas"` and `"dev"`)
- PGS Evaluation: `stage="eval"`

Cohorts, Samples and Sample Sets

Cohorts

A cohort is a group of individuals with a shared characteristic. Cohorts are identified in quincunx by the `cohort_symbol` variable.



(e.g., PROMIS / N=30,000) (e.g., LOLIPOP / N=30,000) (e.g., MHI / N=30,000) (e.g., UKB / N=500,000)

Samples

A sample is a group of participants associated with none, one or more catalogued cohorts. The selection from a cohort can be either a subset or its totality. Samples are not identified in PGS Catalog with a global unique identifier, but quincunx assigns a surrogate identifier (`sample_id`) to allow relations between tables.

Possible compositions of samples:

Admixture of cohorts. (e.g., PGS000011 / S2 / PROMIS & LOLIPOP / N=8,653)

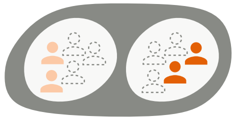
A cohort subset. (e.g., PSS000020 / S1 / MHI / N=862)

Another but disjoint subset. (e.g., PSS000020 / S2 / MHI / N=2,333)

Not associated with any cohort.

Sample Sets

A sample set is a group of samples **used in a polygenic score evaluation**. Each sample set is identified in the PGS Catalog by a unique sample set identifier (PSS ID).



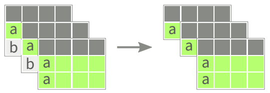
A sample set of two samples.
(e.g., PSS000020: S1 and S2)

Manipulate Cases of S4 Entities

Get a **scores** object **s** consisting of two polygenic scores (PGS):

```
s <- get_scores(pgs_id = c('a', 'b'))
```

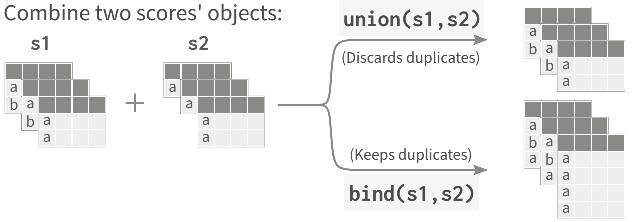
Subset object **s** by either identifier or position using `` `[` ``:



```
s['a'] # Subset by identifier
```

```
s[1] # Subset by position
```

Combine two scores' objects:



`union(s1,s2)`
(Discards duplicates)

(Keeps duplicates)
`bind(s1,s2)`

Polygenic scoring file

PGS scoring files are provided by the PGS Catalog to allow computation of polygenic scores by users. These files are hosted at the PGS Catalog FTP server: http://ftp.ebi.ac.uk/pub/databases/spot/pgs/scores/. They are labelled by their respective PGS Score ID (e.g. `PGS000001.txt.gz`). For more details please visit: https://maialab.org/quincunx/articles/pgs-scoring-file.html.

File Format

Each scoring file contains variant identification, effect alleles and respective score weights. The file is formatted as a gzipped tab-delimited text file, with a header containing brief metada about the score. You can read PGS scoring files into R with `read_scoring_file()`.

`PGS000117.txt.gz`

```
### PGS CATALOG SCORING FILE - see www.pgscatalog.org/downloads/#dl_ftp for…
## POLYGENIC SCORE (PGS) INFORMATION
# PGS ID = PGS000117
# Reported Trait = Cardiovascular Disease
# Original Genome Build = GRCh37
# Number of Variants = 267863
## SOURCE INFORMATION
# PGP ID = PGP000054
# Citation = Elliott J et al. JAMA (2020). doi:10.1001/jama.2019.22241
rsID       chr_name chr_position effect_allele reference_allele effect_weight
rs11240779 1        808631       A             G                0.00077622
rs1921     1        949608       A             G                -0.00583829
rs2710890  1        958905       G             A                -0.00182583
rs4970349  1        967658       T             C                -0.001855691
…
```

Columns

The following table lists all possible columns in a PGS scoring file. A few columns are required (R), and most are optional (O); either the `rsID` alone or the combination of `chr_name` and `chr_position` are required, with the other being optional.

Column (Requirement)	Description	Example
rsID (R/O)	dbSNP Accession ID	"rs554219"
chr_name (R/O)	Chromosome name	"11"
chr_position (R/O)	Chromosome position	69516874
effect_allele (R)	Effect allele	"G"
reference_allele (O)	Reference allele	"C"
effect_weight (R)	Variant weight	0.117
locus_name (O)	Locus name	"CCND1"
weight_type (O)	Type of weight	"log(OR)", "beta_cox"
allelefrequency_effect (O)	Effect allele frequency	0.410
is_interaction (O)	Variant interaction?	TRUE or FALSE
is_recessive (O)	Recessive inheritance model?	TRUE or FALSE
is_haplotype (O)	Is effect allele a haplotype?	TRUE or FALSE
is_diplotype (O)	Is effect allele a diplotype?	TRUE or FALSE
imputation_method (O)	Imputation method	TODO
variant_description (O)	Variant description	TODO
inclusion_criteria (O)	Score inclusion criteria	TODO
OR (O)	Odds Ratio	1.12
HR (O)	Hazard Ratio	1.08

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