

Building a cohort based on phenotypes

Emily Perry

Research Engagement Manager

24th May 2022



Data security

- This training session will include data from the GEL Research Environment
- As part of your IG training you have agreed to not distribute these data in any way
- You are not allowed to:
 - Invite colleagues to watch this training with you
 - Take any screenshots or videos of the training
 - Share your webinar link (we will remove anyone who is here twice)
- We will record this training and distribute the censored video afterwards

Questions



Your microphones are all muted



Use the Zoom Q&A to ask questions



Upvote your favourite questions: if we are short on time we will prioritise those with the most votes.

Questions



Matthieu Vizquete-Forster
Bioinformatician -
Research Services



Christian Bouwens
Bioinformatician -
Research Services



Ronnie Rodrigues Pereira
Bioinformatician -
Research Services



Ana Lisa Taylor Tavares
Senior Clinical
Fellow in Rare
Disease Genomics
- Research
Engagement



Roel Bevers
Senior
Bioinformatician -
Research Services

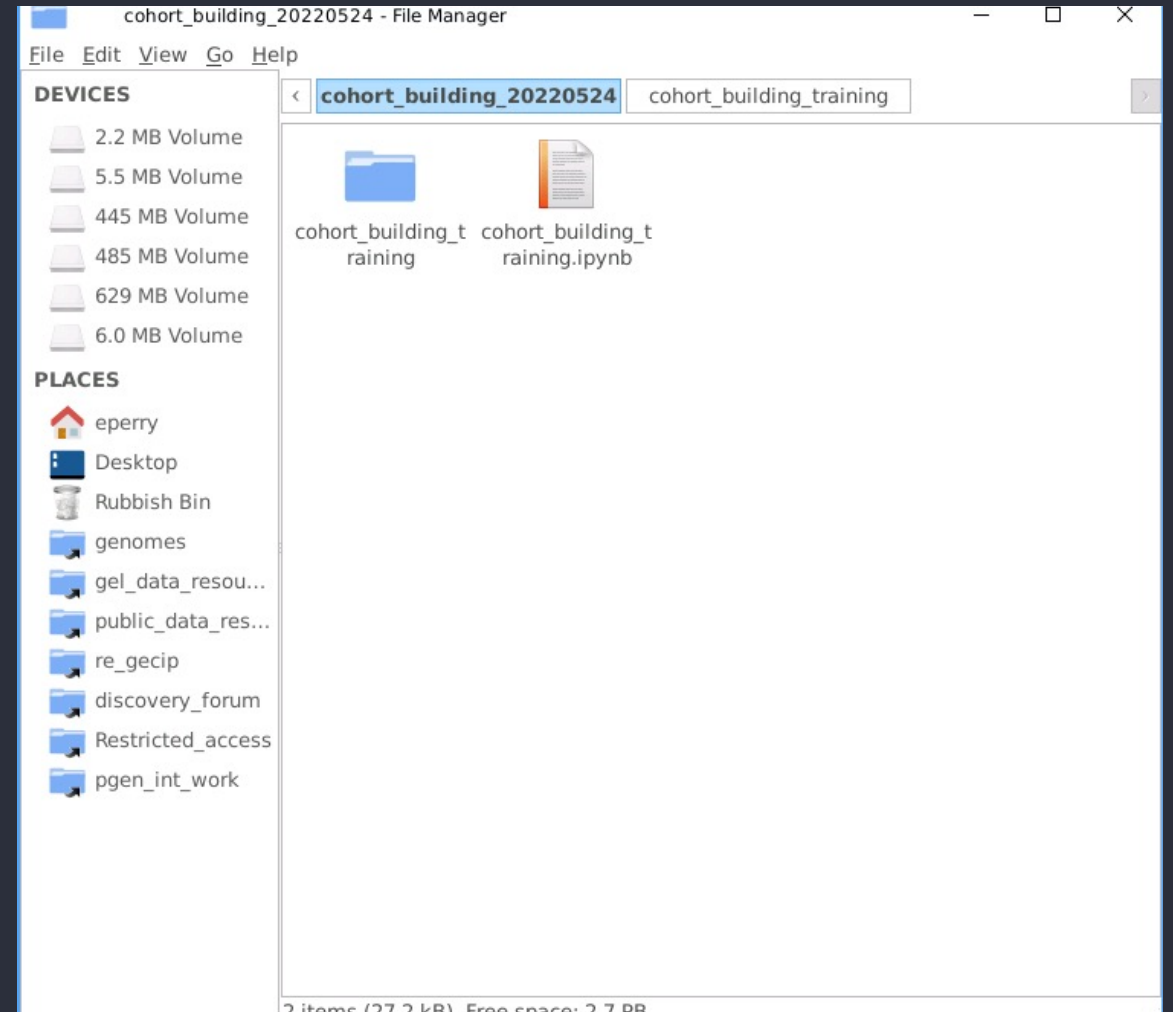
Agenda

- 1 Introduction and admin
- 2 Parameters and considerations for building a cohort
- 3 Point-and-click cohort building with Participant Explorer
- 4 Labkey tables for cohort building
- 5 Covariates in cohort building
- 6 Using the Labkey API in Python and R to build cohorts
- 7 Fetching data for downstream analysis
- 8 Getting help and questions



Materials

- Slides and video will be sent out to you after the session
- Scripts available in `/gel_data_resources/example_scripts/workshop_scripts/cohort_building_20220524`



2. Parameters and considerations for building a cohort

Phenotype data to filter by

Cancer

- Disease type
 - Recruited disease
 - Diagnosis codes in health records
- Staging
- Treatment

Rare disease

- Recruited disease
- HPO terms
- Solved? Alive?

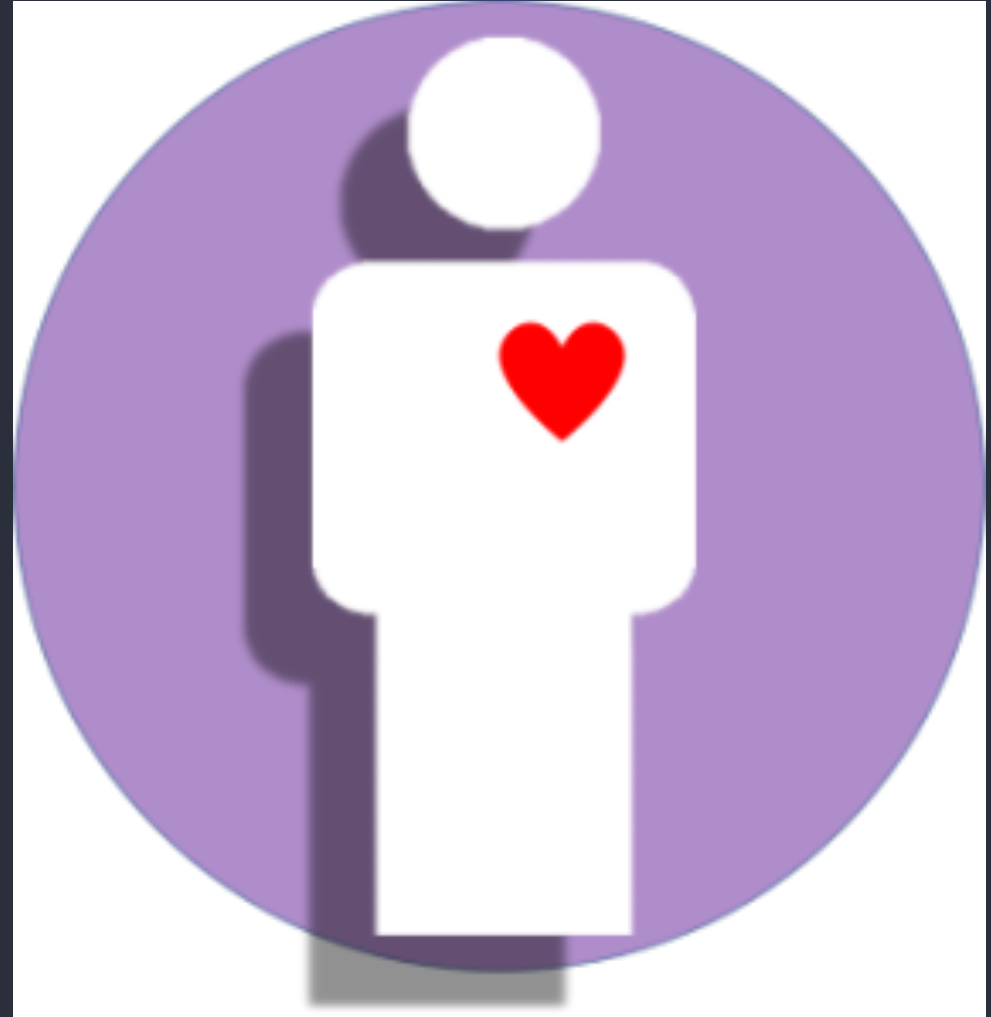
Common disease

- Rare disease relatives and cancer participants
- Diagnosis codes in health records

3. Point-and-click cohort building with Participant Explorer

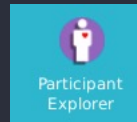
Participant Explorer

- Point-and-click tool
- Ontology-aware
- Filter by phenotypes
- Combine multiple filters



Demo: Participant Explorer





Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/smac × pcdh19_report - Jupyterl × aggregate_gvcf_sample_× rare_diseases_participan × Participant Explorer ×

← → ↻ <https://prod.terminology-service.aws.gel.ac> ☆

Genomics england Participant Explorer Search Participants Code Systems

Sign in

Username
|

Password
|

Continue

Applications Participant Explorer — ... [Terminal] 09:36

Participant Explorer — Mozilla Firefox

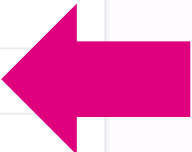
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Genomics england Participant Explorer Search Participants Code Systems

- Search by Participant ID
- Compare Multiple Participants by ID
- Search by Clinical Concept
- Search by Participant Details

Applications Participant Explorer — ... [Terminal] 09:38



Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/smac × pcdh19_report - Jupyter × aggregate_gvcf_sample × rare_diseases_participant × Participant Explorer ×

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Genomics England Participant Explorer Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any / Match None Match Any

Filter By Code Set All

Search Concepts Type at least 3 characters to search

Include descendant concepts

Search by Participant Details

Search

Applications Participant Explorer — ... [Terminal] 09:39

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/smac × pcdh19_report - Jupyter × aggregate_gvcf_sample × rare_diseases_participant × Participant Explorer ×

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Genomics England Participant Explorer Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any / Match None Match Any Filter By Clinical Conc... All

Include mapped concepts

Include descendant concepts

Search by Participant Details

Search

- All
- SNOMED CT
- Human Phenotype Ontology
- Recruited Diseases
- ICD-10
- OPCS-4
- ICD-0-3

Applications Participant Explorer — ... [Terminal] 09:40

Participant Explorer — Mozilla Firefox

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Genomics **Participant Explorer** Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any / Match None
Match Any

Filter By Clinical Conc...
All

Filter By Code Set
All

Search Concepts
colore

65 matches found for "colore" [Include all](#) < Page 1 / 7 >

Colorectal	Genomics England Cancer Type
Colorectal	OPCS Z294
Colorectal polyposis	HPO HP:0200063
Proctocolitis	SNOMED 418130002
Porter colored urine	SNOMED 720002008
Skin-colored papule	HPO HP:0025512
Coloproctostomy	SNOMED 70243005
Wears brightly colored clothes	SNOMED 225498000
Things appear vividly colored	SNOMED 247717002

Search by Participant Details

Search

Applications Participant Explorer — ... [Terminal] 09:41

Type in to search. Choose colorectal cancer.

Participant Explorer — Mozilla Firefox

Restore Session x pgen_int_work/BRS/smac x pcdh19_report - Jupyter I x aggregate_gvcf_sample_x rare_diseases_participan x Participant Explorer x +

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Genomics England Participant Explorer Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any / Match None
Match Any

Genomics England Cancer Type | Colorectal Descendant concepts included

Filter By Clinical Conc... All Filter By Code Set All Search Concepts Type at least 3 characters to search

Include mapped concepts Include descendant concepts

Search by Participant Details

Search

Applications Participant Explorer — ... [Terminal] 09:42

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

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Genomics England Participant Explorer Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any / Match None
Match Any

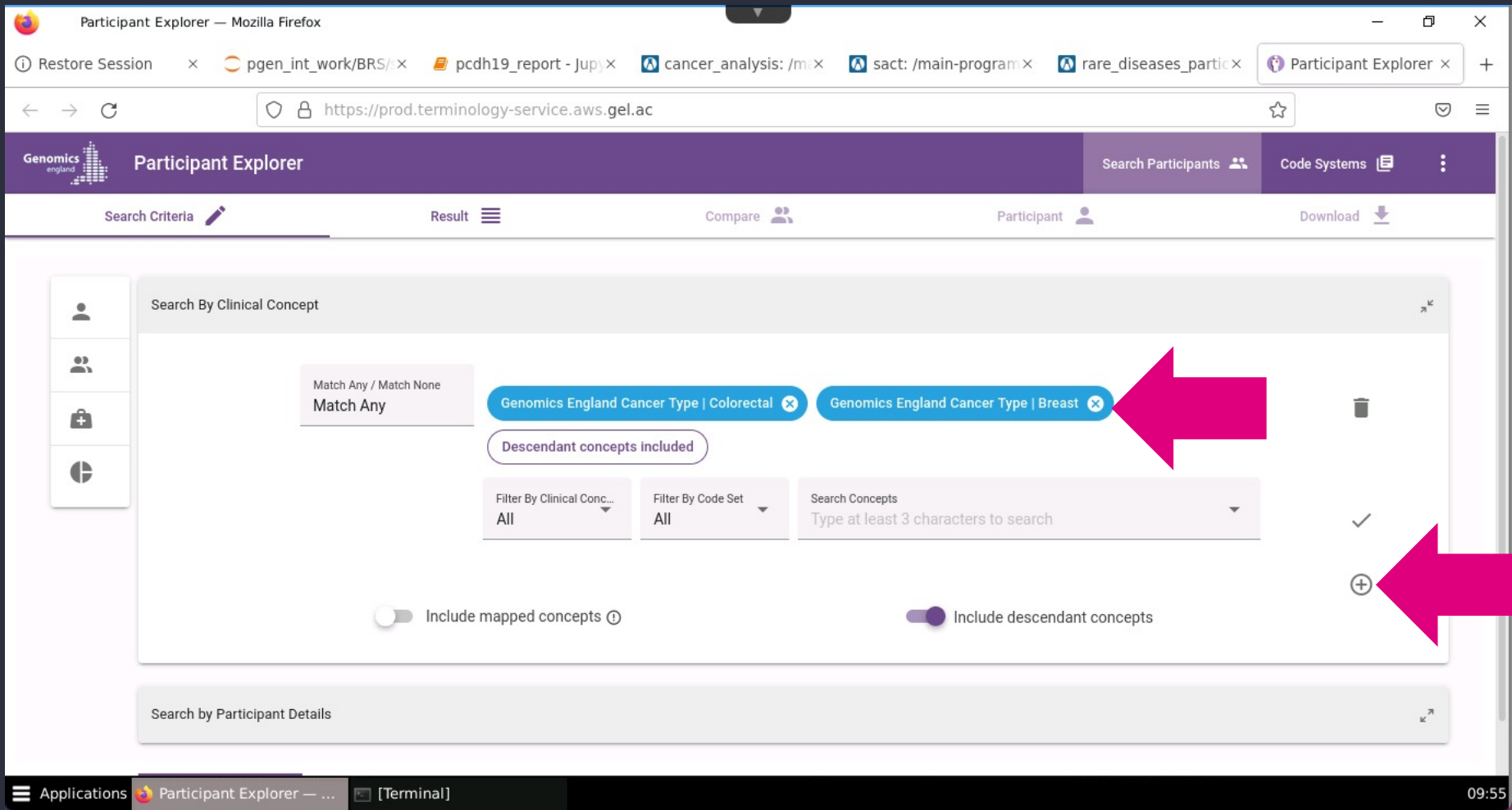
Genomics England Cancer Type | Colorectal × Genomics England Cancer Type | Breast ×

Descendant concepts included

Filter By Clinical Conc... All Filter By Code Set All Search Concepts Type at least 3 characters to search

Include mapped concepts Include descendant concepts

Search by Participant Details



Terms appear together with Match Any/None logic. For AND logic, click on +

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/:× pcdh19_report - Jup)× cancer_analysis: /m:× sact: /main-program× rare_diseases_partic× Participant Explorer × Participant Explorer

← → ↻ https://prod.terminology-service.aws.gel.ac

Genomics **Participant Explorer** Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any Genomics England Cancer Type | Colorectal Genomics England Cancer Type | Breast Descendant concepts included

And / Or And None Filter By Clinical Conc... All Filter By Code Set All Search Concepts |Type at least 3 characters to search

Include mapped concepts Include descendant concepts

Search by Participant Details

Search

Applications Participant Explorer — ... [Terminal] 09:58

Search the same but now includes and And/Or option

Participant Explorer — Mozilla Firefox

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https://prod.terminology-service.aws.gel.ac

Genomics England Participant Explorer Search Participants Code Systems

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any Genomics England Cancer Type | Colorectal Genomics England Cancer Type | Breast Descendant concepts included

And / Or And Match Any / Match None Match Any Filter By Clinical Conc... All Filter By Code Set All Search Concepts tonsille|

Include mapped concepts

Search by Participant Details

Search

28 matches found for "tonsille" Include all Page 1 / 3

Tonsillectomy	SNOMED 173422009
Dissection tonsillectomy	SNOMED 173424005
Guillotine tonsillectomy	SNOMED 173425006
Histology tonsillectomy	SNOMED 276748006
Radiofrequency tonsillectomy	SNOMED 854041000000104
Remnant tonsillectomy	SNOMED 173428008
Tonsillectomy planned	SNOMED 183979001

Applications Participant Explorer — ... [Terminal] 09:59

Participant Explorer — Mozilla Firefox

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Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any

Genomics England Cancer Type | Colorectal Genomics England Cancer Type | Breast Descendant concepts included

And / Or And Match Any / Match None Match Any

SNOMED | 173422009: Tonsillectomy Descendant concepts included

Filter By Clinical Conc... All Filter By Code Set All Search Concepts Type at least 3 characters to search

Include mapped concepts Include descendant concepts

Search by Participant Details

Search

Applications Participant Explorer — ... [Terminal] 10:00

Select Include mapped concepts

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/× pcdh19_report - Jup× cancer_analysis: /m× sact: /main-program× rare_diseases_partic× Participant Explorer ×

https://prod.terminology-service.aws.gel.ac

Search Criteria Result Compare Participant Download

Search By Clinical Concept

Match Any

Genomics England Cancer Type | Colorectal Genomics England Cancer Type | Breast Descendant concepts included

Mapped concepts found: 0

And / Or And Match Any / Match None Match Any

SNOMED | 173422009: Tonsillectomy Descendant concepts included Mapped concepts found: 9

- ↔ OPCS | F346: Excision of lingual tonsil ↔ OPCS | F342: Bilateral guillotine tonsillectomy
- ↔ OPCS | F343: Bilateral laser tonsillectomy ↔ OPCS | F344: Bilateral excision of tonsil NEC
- ↔ OPCS | F345: Excision of remnant of tonsil ↔ OPCS | F348: Other specified excision of tonsil
- ↔ OPCS | F349: Unspecified excision of tonsil ↔ OPCS | F347: Bilateral coblation tonsillectomy
- ↔ OPCS | F341: Bilateral dissection tonsillectomy

Filter By Clinical Conc... All Filter By Code Set All Search Concepts Type at least 3 characters to search

Applications Participant Explorer — ... [Terminal] 10:01

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

https://prod.terminology-service.aws.gel.ac

And / Or And Match Any / Match None Match Any

SNOMED | 173422009: Tonsillectomy Descendant concepts included Mapped concepts found: 9


- ↔ OPCS | F346: Excision of lingual tonsil ↔ OPCS | F342: Bilateral guillotine tonsillectomy
- ↔ OPCS | F343: Bilateral laser tonsillectomy ↔ OPCS | F344: Bilateral excision of tonsil NEC
- ↔ OPCS | F345: Excision of remnant of tonsil ↔ OPCS | F348: Other specified excision of tonsil
- ↔ OPCS | F349: Unspecified excision of tonsil ↔ OPCS | F347: Bilateral coblation tonsillectomy
- ↔ OPCS | F341: Bilateral dissection tonsillectomy

Filter By Clinical Conc... All Filter By Code Set All Search Concepts Type at least 3 characters to search

Include mapped concepts Include descendant concepts

Search by Participant Details

Search



Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/B × pcdh19_report - × cancer_staging_ × sact: /main-prog × rare_diseases_pr × mortality: /main- × Participant Explor ×

← → ↻ <https://prod.terminology-service.aws.gel.ac> ☆

Search by Participant Details

Programme

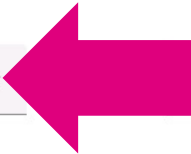
Year of Birth Range: 1900 — 2020 [Search by details help](#)

Phenotypic Sex Life Status Ethnic Category Genome Build

Rare Disease Programme specific search fields

Proband/Relative Affection Status Family Group Type Family Case Solved

Applications Participant Explorer — ... [Terminal] 11:17



Expand any of the categories and select

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/E × pcdh19_report - × cancer_staging_ × sact: /main-prog × rare_diseases_pe × mortality: /main- × Participant Explor ×

← → ↻ https://prod.terminology-service.aws.gel.ac

Search by Participant Details

Year of Birth Range

Programme

1900 2020

Search by details help

Phenotypic Sex Life Status Genome Build

Rare Disease Program

Proband/Relative Affection Status Family Case Solved

- Other Ethnic Groups: Any other ethnic group
- Other Ethnic Groups: Chinese
- White: Any other White background
- White: British
- White: Irish
- empty

Search

Applications Participant Explorer — ... [Terminal] 11:18

Select White British then search

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

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Genomics england Participant Explorer

Search Participants Code Systems

Search Criteria Result 32 Compare Participant Download

Participant ID	Compare (0 of 20 max)	Programme	Proband/Relative	Recruited Disease	Year of Birth	Phenotypic Sex	Ethnic Category	Consent Form	Life Status	Genome Build	Family
[blurred]	<input type="checkbox"/>	Cancer		Breast, Ductal		Female	White: British	Adult C1		GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Colorectal, Adenocarcinoma		Male	White: British	Adult C1		GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Colorectal, Unknown		Male	White: British	Adult C1	Deceased	GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Breast, Unknown		Female	White: British	Adult C1		GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Breast, Unknown		Female	Not Stated	Adult C1			
[blurred]	<input type="checkbox"/>	Cancer		Colorectal, Adenocarcinoma		Female	White: British	Adult C1		GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Breast, Lobular		Female	White: British	Unknown			
[blurred]	<input type="checkbox"/>	Cancer		Breast, Ductal		Female	Not Known	Adult C1		GRCh38	
[blurred]	<input type="checkbox"/>	Cancer		Colorectal, Adenocarcinoma		Male	White: British	Adult C1			
[blurred]	<input type="checkbox"/>	Cancer		Breast, Ductal		Female	Other Ethnic Groups: Any other ethnic group	Adult C1		GRCh38	

Rows per page: 10 1-10 of 32

Applications Participant Explorer — ... [Terminal] 10:03

Table of matching participants. Click on download

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

← → ↻ https://prod.terminology-service.aws.gel.ac

Genomics **Participant Explorer** Search Participants Code Systems

Search Criteria Result 32 Compare Participant Download

Available Columns

Participant +

Ethnic Category Family ID Family Group Type Consent Form

Recruited Disease +

Cancer Disease Type Cancer Disease Sub Type Rare Disease Group

Rare Disease Sub Group Specific Rare Disease

Rare Diseases Family Case Report +

Interpretation Request ID Family Case Solved Additional Comments

Condition / Observation / Procedure +

Clinical Concept Code System Code Description Source Code

Genome Sequence +

Selected Columns

Participant -

Participant ID Programme Proband/Relative Year of Birth Date of Death

Phenotypic Sex

Notes:

- The result contains unique rows only.
- The result may contain multiple rows per participant, when columns with multiple values are selected. For example, multiple values for Genome Build are rendered as separate rows.
- Rare Diseases Family Case Report, Condition/Observation/Procedure and Genome Sequence columns cannot be combined in the same result.
- When Participant ID is not selected, a column is included with the count of participants in the search result for each unique row.

Download

Applications Participant Explorer — ... [Terminal] 10:07

Select which columns you want to include in your downloaded table

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

← → ↻ <https://prod.terminology-service.aws.gel.ac> ☆

Available Columns

Participant +

Ethnic Category Family ID Family Group Type Consent Form

Recruited Disease +

Cancer Disease Type Cancer Disease Sub Type Rare Disease Group

Rare Disease Sub Group Specific Rare Disease

Rare Diseases Family Case Report +

Interpretation Request ID Family Case Solved Additional Comments

Condition / Observation / Procedure +

Clinical Concept Code System Code Description Source Code

Genome Sequence +

Genome Build Platekey Type Sample Date Delivery Date Delivery ID

Delivery Version Path

Selected Columns


Participant -

Participant ID Programme Proband/Relative Year of Birth Date of Death

Phenotypic Sex

Notes:

- The result contains unique rows only.
- The result may contain multiple rows per participant, when columns with multiple values are selected. For example, multiple values for Genome Build are rendered as separate rows.
- Rare Diseases Family Case Report, Condition/Observation/Procedure and Genome Sequence columns cannot be combined in the same result.
- When Participant ID is not selected, a column is included with the count of participants in the search result for each unique row.

Download 

Applications Participant Explorer — ... [Terminal] 10:08

If you want to access the genome files, select their location. Select download when ready

Participant Explorer — Mozilla Firefox

Restore Session × pgen_int_work/BRS/ × pcdh19_report - Jup × cancer_analysis: /m × sact: /main-program × rare_diseases_partic × Participant Explorer ×

← → ↻ <https://prod.terminology-service.aws.gel.ac> ☆

Available Columns

Participant +

Programme Proband/Relative Date of Death Ethnic Category Family ID

Family Group Type Consent Form

Recruited Disease +

Cancer Disease Sub Type Rare Disease Group Rare Disease Sub Group

Specific Rare Disease

Rare Diseases Family Case Report +

Interpretation Request ID Family Case Solved Additional Comments

Condition / Observation / Procedure +

Clinical Concept Code System Code Description Source Code

Genome Sequence +

Genome Build Platekey Type Sample Date Delivery Date Delivery ID

Delivery Version

Selected Columns

Participant -

Participant ID Year of Birth Phenotypic Sex

Recruited Disease -

Opening participant-search-result-2022-04-20T09 09 52.csv

You have chosen to open:

participant-search-result-2022-04-20T09 09 52.csv
which is: CSV document (4.3 KB)
from: blob:

What should Firefox do with this file?

Open with Gvim (default) ▾

Save File

Do this automatically for files like this from now on.

Cancel OK

Download

Applications Participant Explorer — ... [Terminal] 10:10

Participant Explorer pros/cons

- ✓ Easy to use point and click interface
- ✓ Natural language search, don't need to know the codes
- ✓ Can combine clinical concept filters with participant details such as sex, life status and ethnicity
- ✓ Many concepts that are disparate in Labkey are consolidated in PXA (eg death, diagnoses)

- ✗ Not all of the data in the LabKey tables available to be searched
- ✗ Not possible to save searches and return to them for new releases or small tweaks
- ✗ Underlying data not exposed in results, making it difficult to verify in bulk

4. Labkey tables for cohort building

Labkey

- Participant details and family relationships
- Sample details
- Genomic file locations
- Clinical data
 - Primary data: GEL
 - Secondary data: NHS, PHE and ONS
- Bioinformatics analysis results



Cancer disease

- Recruited disease
 - `cancer_analysis.disease_type`
- Diagnosis codes
 - Hospital episode statistics: `hes_###.diag##`
 - Accident and emergency: `hes_ae`
 - Admitted patient care: `hes_apc`
 - Critical care : `hes_cc`
 - Outpatient: `hes_op`

Common to use `cancer_analysis.disease_type` to find participants, then verify with diagnosis codes from secondary data

Cancer staging

- cancer_staging_consolidated
 - TNM (Tumour, Node, Metastasis)
 - AJCC (American Joint Committee on Cancer)
 - Dukes (bowel)
 - Gleason (prostate)
 - FIGO (uterine)
 - HER, ER and PR status (breast)
- cancer_participant_tumour, sact and av_tumour
 - cancer_staging_consolidated comprises data from these tables
 - cancer_staging_consolidated does not have all participants and you may find more participants that fit your criteria by expanding your search to these tables

Cancer treatment

- Systemic anti-cancer therapy: `sact`
 - `analysis_group` – all the drugs the participant was treated with
 - `drug_group` – the drug being referred to in this line of the table
 - Details of how/when the drug was administered

Rare disease phenotype

- rare_disease_analysis.normalised_specific_disease
- rare_diseases_participant_disease
 - Name and categorisation of the disease
- rare_diseases_participant_phenotype
 - HPO term and definition
 - HPO term present?
 - Onset, progression and severity

Rare disease cases

If you're looking for rare disease cases that have not been solved yet, or you want to learn more about solved cases (e.g., for eligibility to participate in a clinical trial), you can filter by:

- `gmc_exit_questionnaire.case_solved_family`
- `death_details`

Common disease

- Diagnosis codes
 - Hospital episode statistics: `hes_###.diag##`
 - Accident and emergency: `hes_ae`
 - Admitted patient care: `hes_apc`
 - Critical care : `hes_cc`
 - Outpatient: `hes_op`

5. Covariates in cohort building

Covariates to consider

- Age
- Sex
- Ethnicity
- Alive?

Age

- We don't have Age stored
 - You need to calculate it from `year_of_birth` (participant table)
 - Age will always be an approximation, since we only have year and not full date: this is particularly important for anything in small children
- What age do you want to know?
 - Age now (`current year – participant.year_of_birth`)
 - Age at sampling (`clinic_sample.clinic_sample_datetime – participant.year_of_birth`)
 - Age at diagnosis (`hes_###.###date – participant.year_of_birth`)
 - Age at death (`death_details.death_date – participant.year_of_birth`)

Sex

- participant.participant_phenotypic_sex: male/female/indeterminate
- participant.participant_karyotypic_sex: XX/XY + aneuploidies
- participant.participant_stated_gender: male/female/not stated

Ethnicity

- `participant.participant_ethnic_category`: what they have ticked on a form
- `aggregate_gvcf_sample_stats.pred_ethnicity_ancestry`: 0-1
 - Ethnicities are 1000 Genomes super-populations: African, South Asian, East Asian, European, American
 - If score ≥ 0.8 , participant is this population
 - If all scores < 0.8 , participant is admixed

Alive?

- death_details
- mortality
- cen (cohort event notification)
- av_patient
- ons (Office of National Statistics)

We can be certain that a participant is dead, but not that they are alive. They could have died since the last data freeze.

6. Using the Labkey API in Python and R to build cohorts

LabKey API

Labkey API allows you to:

- Combine data and filters from multiple tables
- Work in a variety of programming languages, but most support for Python and R
- Work both locally and on the HPC

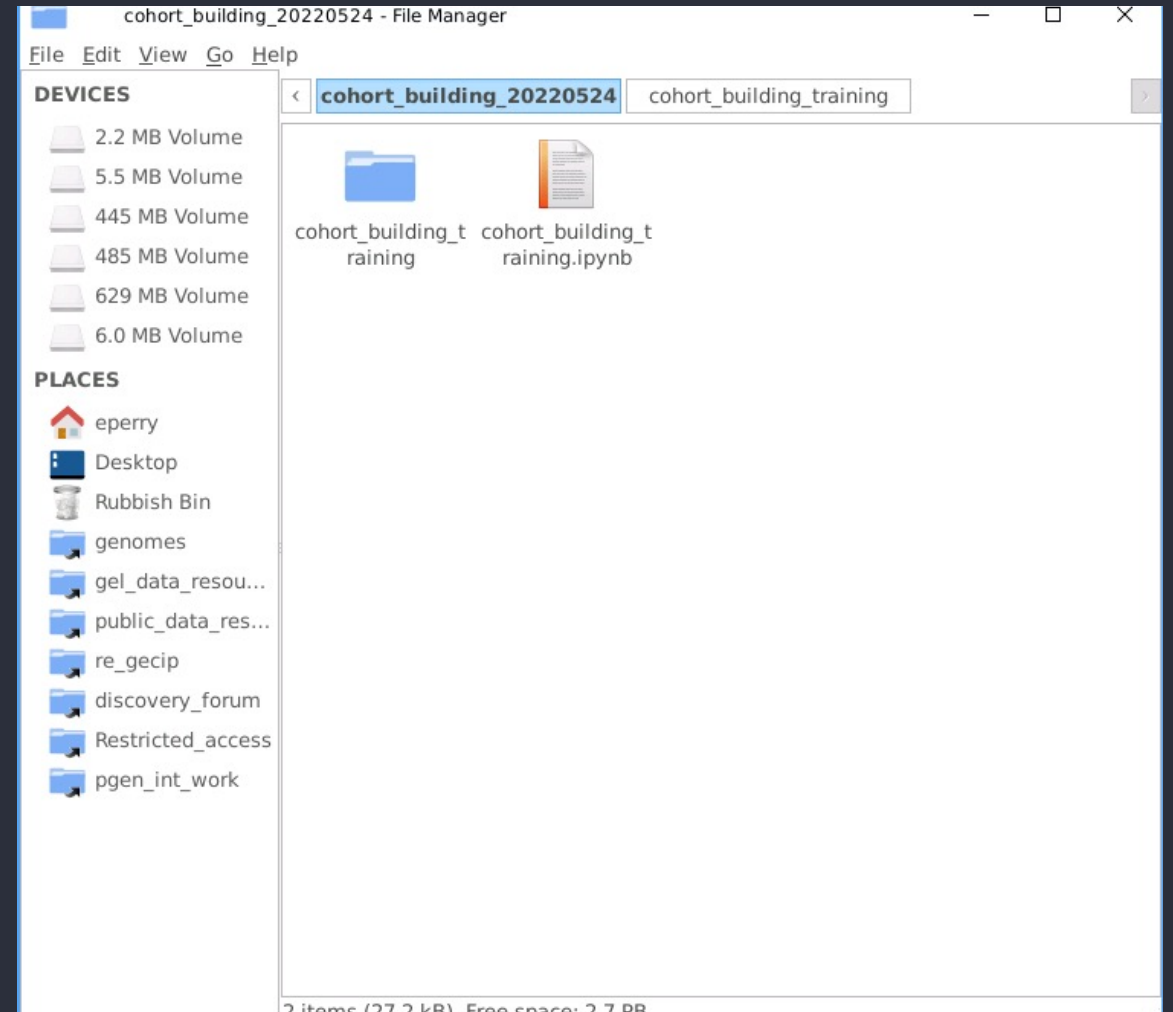


Set up .netrc

- You can access the same data via the LabKey API as you can through other means
- You will need to configure access to the LabKey API with your username and password
 - In your home directory
 - On the HPC
- You do this by editing a file called .netrc

Materials

- Slides and video will be sent out to you after the session
- Scripts available in `/gel_data_resources/example_scripts/workshop_scripts/cohort_building_20220524`



Accessing the notebooks

Python

```
module load python/3.8.1  
jupyter notebook --port  
<four digit port number>
```

Open link in browser

R

```
module load R/4.0.2  
rstudio
```

Demo: Labkey API



7. Fetching data for downstream analysis

Data to include

- genome_file_paths_and_types
 - gvcfs
 - SV/CNV files
- For filtering out data from gene-centric pipelines (Gene-Variant workflow, gene-centric SNV report)
 - participant_id
- Phenotype files (for AVT and GWAS downstream analysis):
 - Platekey
 - Phenotype: 0, 1 or score
 - Covariates: age, sex etc

8. Getting help and questions

Key takeaways

Use Participant Explorer for point-and-click

Labkey tables contain loads of data for creating cohorts

Copy-and-paste whatever code snippets you need from the notebooks!

Getting help



Check our documentation:

- <https://research-help.genomicsengland.co.uk/>
- Click on the documentation icon in the environment



Contact our Service Desk:

- ge-servicedesk@genomicsengland.co.uk

Questions



Your microphones are all muted

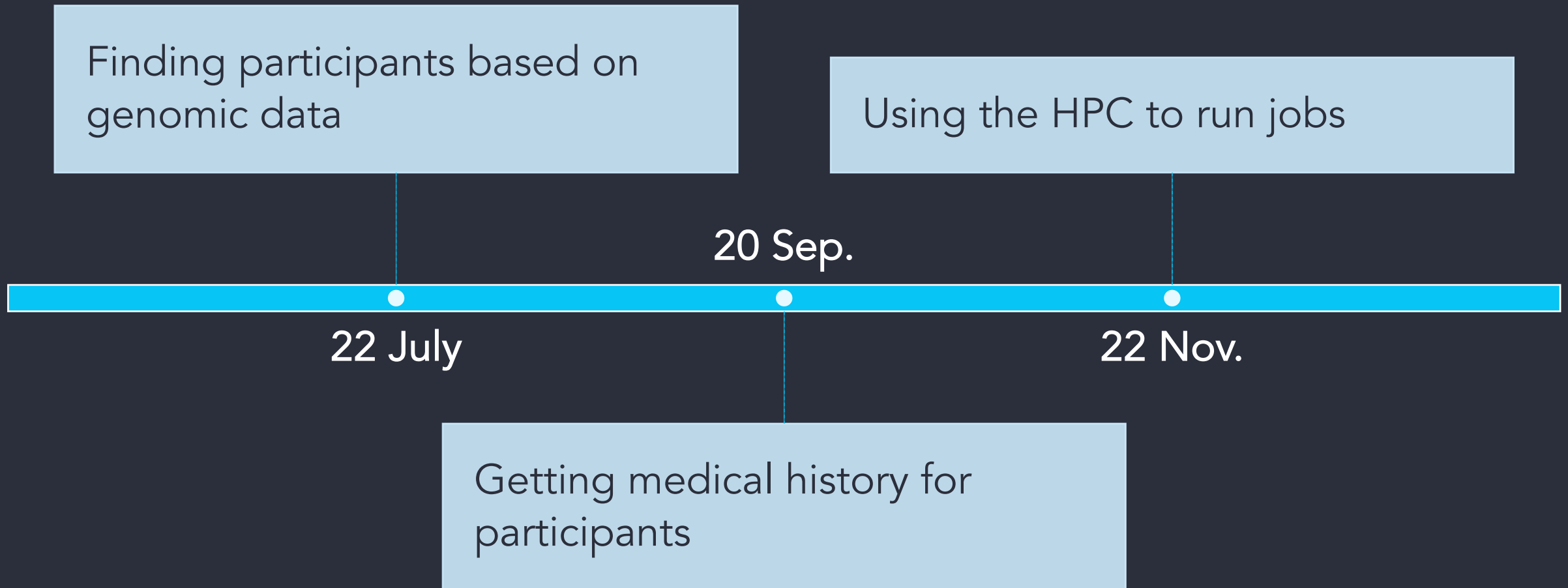


Use the Zoom Q&A to ask questions



Upvote your favourite questions: if we are short on time we will prioritise those with the most votes

Future sessions



Feedback

Thank you