Release v10 (03/09/2020)

1. Table of Contents

2. Purpose

This document provides a description of the Main Programme Data Release v10.0 dated 3rd September 2020.

Each progressive release incorporates new content, enhances existing content, and enables more effective use of the data.

This data is manifested within the Genomics England Research Environment, accessed via the Inuvika virtual desktop interface and subject to all Genomics England data protection and privacy principles.

Please see the Research Environment user guide (https://re-confluence.gel.zone/display/GERE) for detailed documentation on how to use and query the Genomics England data set (link accessible outside of the Research Environment). This page also includes instructional videos.

3. Release Overview

Data Release Version 10 provides clinical data for 89,256 participants, and 108,431 genomes from 87,383 of these participants. Of these genomes 74,233 are rare disease genomes (from 71,672 participants)[1] and 34,198 are cancer genomes (from 15,711 participants)[2].

Participants	
Rare Disease Participants	71,800
Cancer Participants	17,339
Participants Total	89,139

Genomes		
	Number of genomes	Participants
Cancer Germline	17,891	15,432
Cancer Tumour	19,333	15,593

Cancer Total	37,224	15,612
Rare Disease	74,008	71,419
Genomes Total	111,232	87,031

- The genomic data (BAMs, VCFs, and associated quality metrics) delivered to us by our sequencing provider (Illumina) are manifested in file shares. These are accessed via the user's Home directory under the subfolder '/genomes/by_date'.
- Clinical data and secondary health data ("medical history") are manifested in LabKey. Tabulated outputs from the Genomics England bioinformatics pipeline are also included in LabKey.

Approximately 10% of the genomic data are aligned against the reference genome version GRCh37 and the remaining majority (90%) against version GRCh38. The alignments were also made using different versions of Illumina's alignment pipelines V2 and V4, reflecting the versions that were applicable at the time of sequencing. The versions for each genome are identified in the Sequencing Report table. We intend to provide consistently realigned and recalled versions of all our genomes in the future.

4. Audience

The intended audience for this document is researchers that have access to the Genomics England Research Environment.

5. Identifying this data release

The clinical data, secondary data, and tabulated bioinformatic data for this data release, and the paths to the applicable genome files, are found in the following LabKey folder:

main-programme /main-programme_ v10_2020-09-03

Subsequent releases will be identified by an incremental increase in the version number and the date of data release.

Relevant genomic data produced by the Genomics England Bioinformatics pipeline (such as rare disease tiering, structural and copy-number variant reports for cancer genomes) are found in the user's Home directory, under the folder 'gel_data_resources' and then 'main_programme' (Genomics England Data).

6. Frequency of Release

The main programme data release schedule has now changed. Until V6 (Feb 2019), data releases were quarterly. As the data has increased in volume and depth, the time to process and create the data releases has extended. Since V7, there will be three data releases a year.

7. Samples Removed from this Release

In Data Release (V8), a decision was made to review certain categories of participants and their inclusion in the Genomics England's main programme data. The following scenarios were reviewed and participants discontinued from this release (v8) onwards:

- Discontinued samples* (samples which were not determined to be complete enough for continued inclusion in data releases as per the scenarios below)
    - For both Cancer and Rare Disease
        - Cases with samples that have failed QC with no replacement
        - Adults (individuals >=18 at time of release) consented as children
    - Cancer only
        - Cases for which a "sample not sent" notification has been received
    - Rare Disease only
        - Cases where the clinical data cannot be verified or resolved to a quality where it is appropriate to include them in the research environment, as determined by the Genomics England clinical team

Data held for these discontinued participants will remain in earlier Main Programme releases but will not be included in this or subsequent data releases.

In addition to the above data withdrawals, in rare occasions, we may have to completely remove the genomes of individuals across all data releases to abide by regulatory rules.

For Data Release v10, we have removed the following two platekey samples from LabKey tables:

LP3000986-DNA_B05 – This concerns a hard removal whereby genome data will be removed in its entirety, due to issues regarding third party consent. The clinical data will remain present and accessible in the system.

LP3000144-DNA_F05 – This concerns a soft removal whereby genome data will remain on the system for analysis done on previous data releases. The variant files for this sample showed truncated data, providing data only up to chromosome 9. Variant data for this sample is likely to return at a later stage in the form of Dragen realigned files. The clinical data will remain present and accessible in the system.

*Participants with discontinued samples/data will be informed directly via relevant NHS Genomic Medicine Centres.

8. Scope

8.1. In scope

Data that are in scope for this release:

- Cancer and rare disease data for the main programme participants with current consent. These data include:
    - Genomic data for participants when available
    - Whole genome sequencing (WGS) family-based quality control for rare disease, reporting sex checks and pedigree checks
    - Outputs of the Genomics England Bioinformatics Research services
        - A new aggregated Illumina gVCF for germline genomes (genomes included are from release 8). Please see the documentation here: Aggregated Variant Calls (aggV2)
        - New Principal Components for germline genomes (genomes included are from release 8)
        - New ancestry assignments for samples based on genomic data (genomes included are from release 8)
        - Genome-wide *de novo* variant dataset for 13,836 trios from 12,505 families from the rare disease programme. Please see the documentation here: The *de novo* variant research dataset for the 100,000 Genomes Project
    - Outputs of the Genomics England Bioinformatics rare diseases interpretation pipeline
        - Tiering data – rare disease
        - Exomiser results for interpreted genomes – rare disease
        - GMC outcome data ("exit questionnaire data") – rare disease - up until 16/07/2020.
    - Outputs of the Genomics England Bioinformatics cancer interpretation pipeline
        - Gold standard cancer genomes which have been through interpretation and passed quality checks
        - Tumour signature and mutational burden data
        - Annotation and tiering of small variants
            - Tiering, structural and copy number variant report
        - Cancer Principal Component Analysis (PCA). For more information on these metrics please see the following document: Cancer Analysis Technical Information Document here.
    - Primary clinical data, including formal pedigree data on rare disease participants where it is available; and
    - Secondary datasets (medical history) including:
        - Hospital Episode Statistics (HES), including HES Accident and Emergency, HES Admitted Patient Care, and HES Outpatient Care.
        - Diagnostic Imaging Dataset (DID).
        - Patient Reported Outcome Measures (PROMs).
        - Mental Health Minimum Dataset (MHMDS).
        - Mental Health Learning Disabilities Dataset (MHLDDS).
        - Office for National Statistics - Death details data (ONS).
        - Systemic Anti-Cancer Therapy Dataset (SACT).
        - Systemic Anti-Cancer Therapy Dataset - UNCURATED (SACT_UNCURATED).
        - National Radiotherapy Dataset (RTDS).
        - Cancer Registration (AV) tables.
        - Cancer waiting times (CWT).
        - Lung Cancer Data Audit (LUCADA).
        - National Cancer Registration and Analysis Service Diagnostic Imaging Dataset (NCRAS_DID).
    - Sample datasets describing:
        - Handling and quality control of DNA samples at the Genomic Medicine Centres, the biorepository and the sequencer.
        - Omics samples stored at the biorepository.
    - Orthogonal standard-of-care test data collected from GMCs for a subset of cancer patients

8.2. Out of scope

Additional time is required to update the applications/tools that are available in the RE to the current data release. Refer to the link below for the data release version used in the RE products and services.

Application Data Versions

Data out of scope for this release:

- Clinical and genomic data for participants that have withdrawn from the 100,000 Genomes Project or were otherwise ineligible (n=8351).
- Participant data from the pilot phases of the project (i.e. not main programme, n=527).

8.3. Quality Notes

- BAM and VCF genomic data files are as they have been delivered to us by our sequencing provider (Illumina). These have all passed an initial QC check based on sequencing quality and coverage. They have, however, not all undergone our full in-house quality checks and they are therefore subject to potential discrepancies or inaccuracies. Such checks include, but are not limited to, discrepancies in genetic versus reported sex and in family relationships.

        - As participants undergo the in-house checks and pass through the Genomics England interpretation pipeline, any inaccuracies we identify will be rectified in subsequent releases.
        - Any samples that have been affected prior to this release (e.g. sample swaps or samples that have been retracted as part of the in-house QC process) are listed in Section 10 below.
        - Researchers are encouraged to work on the subset of samples that have already passed our internal QC checks; these can be found below for rare disease and cancer genomes, respectively.
    - For Rare Disease genomes, it should be noted that all tiered genomes have passed through Genomics England in-house QCs and that all tiered genomes come from the pool of genomes that have had family checks applied to them, as a first step towards Genomics England tiering. For rare disease interpretation including tiering, variants are called using the Platypus variant caller. Please see the Rare Disease Results Guide here for more information: 10. Further reading and documentation.
        - Different QC filtering has been applied to the Illumina VCF files and the Platypus VCFs that are used for tiering. There may therefore, be tiered variants that have been filtered out of the Illumina VCF files, and, conversely, variants present in the Illumina VCF file that have been filtered out of the platypus VCFs.
        - Some rare disease families lack a proband due to the availability of data at the time of release. The missing data will be made complete in a future release if available.
        - Human Phenotype Ontology (HPO) terms may be missing or incomplete for some participants. They will be updated in future releases in available.
        - Pedigree data are only available for a subset of rare disease participants. This will be updated in future releases if available. Each participant's relationship to their family's proband is available for such cases; this can be used to determine family relationships instead of formal pedigree data.
        - WGS family selection quality checks are provided for rare disease genomes on GRCh38, reporting abnormalities of sex chromosomes and reported vs genetic sex summary checks (computed from family relatedness, Mendelian inconsistencies, and sex chromosome checks). Full details on why a family has failed a reported vs genetic sex check can be requested via the Service Desk.
    - For Cancer genomes, it should be noted that all 'gold standard genomes' that have been through Genomics England interpretation and passed quality checks are found in the cancer quick view table cancer_analysis. **We strongly recommend using the data from this table for *all* cancer analyses.**
    - Clinical data and secondary data have been provided as submitted and have undergone limited validation.
    - **sact_uncurated** is the table with the raw feed from PHE_NCRAS which feeds into their curation processproducing the **sact** table (both under PHE/NCRAS section), which remains the gold standard. A major point to raise is that this SACT curation does not provide tumour IDs, thus users must match this dataset to other NCRAS registries by adjusting for date. For this first release we focused on standardising date fields. A lot of familiar data fields remain in their raw non-standardised form (sex, treatmentintent, clinicaltrialindicator). Pending feedback, these fields can be normalised in subsequent releases.

8.4. Conditions of Use

- **Participants identified as TracerX in the field normalised_consent_form in the participant table in LabKey must not be used by commercial organisations.** Commercial organisations do not have access to the genomic data of TracerX participants.
- Participants with a participant ID that commences with 125 or 226 were recruited through the Scottish Genomes Partnership Research Programme. These are under the governance of a separate but linked consent and protocol to the 100,000 genomes project. Only the removal of summary level statistics is permitted. **Airlock approval will not be granted for the removal of record level data associated with these participants.**

9. Data Release Description

The Genomics England data are organised into data views (displayed within LabKey as tables) categorised into Quick View, Common, Bioinformatics, Rare Disease and Cancer. The Data Dictionary that describes the table structure and provides data definitions for this release can be found here.

9.1. Quick View

Data views that bring together data from several LabKey tables for convenient access:

Name of Table / Data View	Description
rare_di	Data for all rare disease participants including: sex, ethnicity, disease recruited for and relationship to proband; latest genome build, QC status of latest genome, path to latest genomes and whether tiering data are available; as well as family selection quality checks for rare disease genomes on GRCh38, reporting abnormalities of the sex chromosomes, family relatedness, Mendelian inconsistencies and reported vs genetic sex summary checks. Please note that only sex checks are unpacked into individual data fields; a final status is shown in the "genetic vs reported results" column.

rare_disease_analysis	
cancer_analysis	Data for all cancer participants whose genomes have been through Genomics England bioinformatics interpretation and passed quality checks, including: sex, ethnicity, disease recruited for and diagnosis; tumour ID, build of latest genome, QC status of latest genome and path to latest genomes; as well file paths to the genomes. This table includes information derived from laboratory_sample and cancer_participant_tumour. Some key data included in the table are elucidated below: *Global Tumour Mutation Burden* This is the number of somatic non-synonymous small variants per megabase of coding sequences (32.61 Mb). This metric was calculated using somatic_small_variants_annotation_vcf as input (see below for description) and all non-PASS variants were removed from the calculation. *Tumour purity* This is the tumour purity (cancer cell fraction) as calculated by Ccube (https://rdrr.io/github/keyuan/ccube/) *Mutational Signatures* The table includes the relative proportions of the different mutational signatures demonstrated by the tumour. Analysis of large sequencing datasets (10,952 exomes and 1,048 whole-genomes from 40 distinct tumour types) has allowed patterns of relative contextual frequencies of different SNVs to be grouped into specific mutational signatures. Using mathematical methods (decomposition by non-negative least squares) the contribution of each of these signatures to the overall mutation burden observed in a tumour can be derived. Further details of the 30 different mutational signatures used for this analysis, their prevalence in different tumour types and proposed aetiology can be found at the Sanger Institute Website: http://cancer.sanger.ac.uk/census. *Cancer PCA QC Statistics* The cancer analysis pipeline employs a sequencing quality control check which selects several important statistics associated with the sequencing returned by the sequencing provider, and uses them to check whether or not the sample in question is an outlier with respect to previous samples that have been run through the pipeline. It is, in effect, a safety net that can spot issues that have occurred at the tissue collection stage (i.e. at the GMC (Genomic Medicine Centre)) or at the library preparation step (i.e. at the sequencing provider), both of which may impact upon the final genomic analysis returned to the clinician. *Somatic small variants annotation vcf filepaths* The somatic_small_variants_annotation_vcf column contains file paths pointing to VCFs containing Genomics England flags for potential false positive variants as well as additional annotations (see VCF header for details). Swift and PolyPhen scores as well as new PONnoise50SNV flag were added. The flags used for annotation are: i. CommonGermlineVariant: variants with a population germline allele frequency above 1% in a Genomics England dataset ii. CommonGnomADVariant: variants with a population germline allele frequency above 1% in gnomAD dataset iii. RecurrentSomaticVariant: recurrent somatic variants with frequency above 5% in a Genomics England dataset iv. SimpleRepeat: variants overlapping simple repeats as defined by Tandem Repeats Finder v. BCNoiseIndel: small indels in regions with high levels of sequencing noise where at least 10% of the basecalls in a window extending 50 bases to either side of the indel's call have been filtered out by Strelka due to the poor quality vi. PONnoise50SNV: SNVs resulting from systematic mapping and calling artefacts The following methodology was used for the PONnoise50SNV flag: the ratio of tumour allele depths at each somatic SNV site was tested to see if it is significantly different to the ratio of allele depths at this site in a panel of normals (PoN) using Fisher's exact test. The PoN was composed of a cohort of 7000 non-tumour genomes from the Genomics England dataset, and at each genomic site only individuals not carrying the relevant alternate allele were included in the count of allele depths. The mpileup function in bcftools v1.9 was used to count allele depths in the PoN, and to replicate Strelka filters duplicate reads were removed and quality thresholds set at mapping quality >= 5 and base quality >= 5. All somatic SNVs with a Fisher's exact test phred score < 50 were filtered, this threshold minimised the loss of true positive variants while still gaining significant

improvement in specificity of SNV calling as calculated from a TRACERx truth set. A presentation entitled *PONnoise50SNV: SNVs resulting from systematic mapping and calling artefacts*, which further outlines the methodology, can be found in the *Publications and other useful links* table located on this page.

Alignment BAM files generated by Isaac Genome Alignment Software

A paper written by GeCIP members discussing the issue of **reference bias** in the computation of variant allele frequencies (VAFs) by the Illumina Isaac pipeline (caused by preferential soft clipping of reads supporting alternate alleles) can be located here: https://www.biorxiv.org/content/10.1101/836171v1

9.2. Common

Data views that are common to both the rare disease and the cancer domains. This data pertains to sample handling, genome sequencing, and participant data.

Data Relating to Participants:

Name of Table / Data View	Description
participant	Data on each individual participant in the 100,000 Genomes Project, e.g. personal information (such as relatives or self-reported ethnicity); points of contact with the Project (e.g. handling Genomic Medicine Centre or Trust); and a record of the status of their clinical review.
death_details	Data on participant deaths submitted by GMCs, likely less complete than the data collected by ONS and NHSD.

Data Relating to Samples:

Name of Table / Data View	Description
clinic_sample	Data describing the taking and handling of participant samples at the Genomic Medicine Centres, i.e. in the clinic, as well as the type of samples obtained. Because of the complexities of handling and managing tumour tissues samples in a clinical setting, there are many fields that are cancer-specific.
clinic_sample_quality_check_result	Data describing the quality control of obtaining and handling participant samples at the Genomic Medicine Centres, i.e. in the clinic.
laboratory_sample	Data describing the handling of samples at the biorepository and in preparation for sequencing, as well as the type of sample.
plated_sample	Data describing the handling and QC of samples at Illumina (the sequencing provider).
laboratory_sample_omics_availability	Availability of samples collected from participants in the 100,000 Genomes Project for the purpose of omics research. Data includes: Participant ID, Sample Type (e.g. Serum, RNA Blood), the number of aliquots of that sample type for that participant, and the availability status - whether the sample has already been used for a research project. Research proposals for the use of these samples can be submitted, via the GeCIP team, to the Scientific Advisory Committee and Access Review Committee.
lrs_laboratory_sample	Data describing the characteristics and processing methods (DNA to library preparation) of samples from participants in the 100,000 Genomes Project for which long-reads sequencing has been carried out.

9.3. Bioinformatics

Contains tables with data that are related to the genomic data and the outputs from the Genomics England interpretation pipeline data for participants from both cancer and rare disease programmes. These tables do not directly include primary and secondary sources of clinical data.

Name of	Description

Table/DataView	
sequencing_report	For each participant in the 100,000 Genomes Project, this table contains data describing the sequencing of their genome(s) and associated output, as well as the sample type that the sequence is from.
genome_file_paths_and_types	Data that specifies the genomic files and their folder locations for a given participant. Please be aware that the same genome can be released with multiple versions of mapping/variant calling pipeline. Since the Main Programme Data Release Version 10, we have added file paths to genomes that have been realigned with the Dragen pipeline. Please see the change summary below on how to select for these.
aggregate_gvcf_sample_stats	This table accompanies the aggregated Illumina gVCFs (/gel_data_resources/main_programme/aggregation/aggregate_gVCF_strelka/aggV2). Individual sample QC data was retrieved from Genomics England OpenCGA database. Most sequencing metrics are BAM file statistics provided from Illumina or Genomics England WGS data processing pipeline. The table contains principal components, a set of unrelated individuals and probabilities of ancestry membership, and more (These are crude categories to represent broad groups of ancestries. Please do not over-interpret these). Please also refer to the documentation listed here: Aggregated Variant Calls (aggV2) *This table has been significantly changed for Main Programme Data Release Version 10. Please see the change summary below.*
tiered_data	For each participant of the 100,000 Genomes Project who has been through the Genomics England interpretation pipeline, this table contains data describing the variants that are identified as plausibly pathogenic for a participant's phenotype. The tiering process is based on a number of features such as their segregation in the family, frequency in control populations, effect on protein coding, and mode of inheritance. and whether they are in a gene in the virtual gene panel(s) applied to the family. The applied panels can be found in the respective table 'panels_applied'.
tier	This table contains the frequencies of each tiered variant for every Project participant for whom we provide tiered variants.

ed_variants_frequency	
panels_applied	For each participant of the 100,000 Genomes Project, this table contains the name and version of the panel(s) that was applied to his or her genome.
exomiser	This table contains the full results from the Exomiser rare disease SNV and Indel Prioritisation Process. All rare disease cases are now run through the Exomiser automated variant prioritisation framework developed by members of the Monarch initiative: principally Dr. Damian Smedley's team at Queen Mary University London and Professor Peter Robinson's team at Jackson Laboratory, USA, with previous contributions from staff at Charité – Universitätsmedizin, Berlin and the Sanger Institute. Given a multi-sample VCF file, family pedigree and proband phenotypes encoded by Human Phenotype Ontology(HPO) terms, Exomiser annotates the consequence of variants (based on Ensembl transcripts) and then filters and prioritises them for how likely they are to be causative of the proband's disease based on: 1) the predicted pathogenicity and allele frequency of the variant in reference databases 2) how closely the patient's phenotypes match the known phenotypes of diseases and model organisms associated with the gene. Please see 1) Publication: https://www.nature.com/articles/nprot.2015.124 2) Website: https://github.com/exomiser/Exomiser
gmc_exit_questionnaire	Data reporting back from the Genomic Medicine Centres, for variants reported to them by Genomics England, to what extent a family's presenting case can be explained by the combined variants reported to them (including any segregation testing performed); confidence in the identification and pathogenicity of each variant; and the clinical validity of each variant or variant pair in general and clinical utility in a specific case (only the most recent update will be shown and only one questionnaire per report).
domain_assignment	For each participant in the 100,000 Genomes Project, this table contains: data describing the disease type to which they were recruited; the gene panel(s) applied to their genome(s); the GeCIP domain to which their genome(s) have been assigned for the purposes of administering the GeCIP publication moratorium; whether this participant is still under moratorium as of the date of release, and the end date of the GeCIP moratorium associated with their genome(s).
cancer_staging_	This table combines staging information from our primary clinical data (cancer_participant_tumour) and secondary clinical data from PHE/NCRAS (sact and av_tumour) to give a stage for each sample we have sequenced and fully interpreted on our database (cancer_analysis). The staging information may be in form of TNM combined, each component or other standards such as AJCC, or Dukes', for example. The genomic data is matched to the clinical data using a disease type (genomic data) and ICD code (clinical data) correspondence dictionary created and validated internally. Also, the clinical stage information must not be further away than one year from the date the sample has been collected. Note that, the column names have been preserved as found in the original datasets they were extracted from, except for tumour_pseudo_id found both in sact and av_tumour, where a prefix with the dataset names was added to. Also, for each staging dataset used, when more than one entry for the same patient was available the closest one to the clinical data collection has been kept. Further information on the staging table and it's generation process can be found in the document: Staging data (Cancer)

consolidated	
denovo_cohort_information	Table with cohort information for all participants included in the *de novo* variant dataset. Attributes within this table include: participant ID, sex, affection status, family ID, pedigree ID, and the path to each family's multi-sample VCF with flagged DNVs. See *De novo* variant research dataset for more information.
denovo_flagged_variants	Table of all *base_filter* pass variants for all trios within the DNV dataset. This table includes all flags from the DNV annotation pipeline for each variant. See *De novo* variant research dataset for more information.
lrs_sequencing_data	This table includes data describing long-read sequencing of a subset of 100,000 Genomes Project participants and associated output, including paths to raw and BAM files.

9.4. Rare Diseases

Rare Disease data are presented at the level of Rare Disease families (families of probands), Rare Disease pedigrees, and participants. Participants are individuals who have consented to be part of the project with the expectation that a sample of their DNA will be obtained and their genome sequenced. Pedigree members are extended members of the proband's family, this includes participants as well a small amounts of deidentified data recorded to allow a full picture of the proband's extended family. This additional information is extracted from the proband's medical record.

All Rare Disease table names are prefixed with "rare_diseases_".

Data at the Level of Rare Disease Families:

Name of Table / Data View	**Description**

rare_diseases_family	Data describing the families of rare disease probands participating in the 100,000 Genomes Project. It includes the family group type, the status of the family's pre-interpretation clinical review and the settings that were chosen for the interpretation pipeline at the clinical review.
rare_diseases_pedigree	Data describing the Rare Disease participants, linking pedigrees to probands and their family members.
rare_diseases_pedigree_member	Data describing the Rare Disease pedigree members, similar to the data about each individual participant in the participant table (common data view, see section 8.2). It may also include additional data, such as the age of onset of predominant clinical features; data on links to other family members; as well as data collected only for Phenotypes.

Data at the Level of Rare Disease Participants.

The data presented in these tables provides information on disease progression and pertinent medical history:

Name of Table / Data View	**Description**
rare_diseases_participant_disease	Data describing the rare disease participants' disease type/subtype assigned to them upon enrolment, and the date of diagnosis.
rare_diseases_participant_phenotype	Data describing the Rare Disease participants' phenotypes. For each Rare Disease participant in the 100,000 Genomes Project, there are data about whether a phenotypic abnormality as defined by an HPO term is present and what the HPO term is, as well as the age of onset, the severity of manifestation, the spatial pattern in the body and whether it is progressive or not. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_gen_measurement	For Rare Disease participants in the 100,000 Genomes Project, this table contains general measurements relevant to the disease, alongside the date that the measurements were taken on. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_early_childhood_observation	For Rare Disease participants in the 100,000 Genomes Project, this table contains measurements and milestones provided by the GMCs, related to childhood development. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_imaging	For Rare Disease participants in the 100,000 Genomes Project, this table contains various data and measurements from past scans, alongside the date of the scans. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_invest_genetic	For a proportion of Rare Disease participants in the 100,000 Genomes Project, this table contains information on any genetic tests carried out. Data characterising the genetic investigation is recorded alongside records of the sample tissue source and the type of testing laboratory. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_invest_genetic_test_result	For a proportion of Rare Disease participants in the 100,000 Genomes Project, this table contains the results of any genetic tests carried out. Following on from the rare_diseases_invest_genetic table, a summary of the results is presented and contextualised by testing method and scope. Please note that these data are only available for a subset of the rare disease participants.
rare_diseases_invest_blood_laborat	For a proportion of Rare Disease participants in the 100,000 Genomes Project, this table contains the results of any blood tests carried out. Over 400 blood values are recorded alongside type and technique of testing and the status of the participating patient in the care pathway. Please note that these data are only available for a subset of the rare disease participants.

ory_ test_re port	

9.5. Cancer

Cancer data are presented for either the patient level cancer diagnosis or “disease type” or the tumour specific sample details of participants in the Cancer arm of the 100,000 Genomes Project.

Data Relating to Cancer Participants:

Name of Table / Data View	Description
cancer_participant_disease	For each cancer participant in the 100,000 Genomes Project, this table includes data about their cancer disease type and subtype.
cancer_participant_tumour	For each cancer participant’s tumour in the 100,000 Genomes Project, this table contains data that characterises the tumour, e.g. staging and grading; morphology and location; recurrence at time of enrolment; and the basis of diagnosis.
cancer_participant_tumour_metastatic_site	For each cancer participant in the 100,000 Genomes Project, this table contains the site of their metastatic disease in the body (if applicable) at diagnosis.
cancer_care_plan	For a proportion of cancer participants in the 100,000 Genomes Project, this table contains information from their NHS cancer care plan on their treatment and care intent, in particular outcomes of MDT meetings and coded connected data (e.g. diagnoses from scans).
cancer_surgery	For a proportion of cancer participants in the 100,000 Genomes Project, this table contains details of what surgical procedures were had, as well as the specific location of the intervention.
cancer_risk_factor_general	For a proportion of cancer participants in the 100,000 Genomes Project, this table contains data on general cancer risk factors, namely smoking status, height, weight and alcohol consumption. This table was compiled with input from GeCIP members.
cancer_risk_factor_cancer_specific	For a proportion of cancer participants in the 100,000 Genomes Project, this table contains data on specific risk factors related to particular cancer types. This table was compiled with input from GeCIP members.
cancer_invest_imaging	For a proportion of cancer participants in the 100,000 Genomes Project, this table contains: coded data on imaging investigations characterising the scan, its modality, anatomical site and outcome; as well as the outcome of the imaging report in free text form.

Data derived from or relating to tumour samples:

Name of Table / Data View	Description
cancer_invest_sample_pathology	For a subset of cancer participants in the 100,000 Genomes Project, this table contains full pathology reports and other related data on and from their tumour samples around diagnosis and characterisation of the cancer. Please note that much of this information is also found in the clinic_sample and cancer_participant_tumour tables.
cancer_specific_pathology	For a subset of tumours from cancer participants in the 100,000 Genomes Project, this table contains pathology data specific to that participant’s cancer type. This may provide additional data to the cancer_invest_sample_pathology and cancer_participant_tumour tables.
cancer_systemic_anti_cancer_therapy	For a subset of tumours from cancer participants in the 100,000 Genomes Project, this table contains details the regimen and intent of the patients’ chemotherapy.
cancer_invest_circulating_tumour_marker	For a subset of tumours from cancer participants in the 100,000 Genomes Project, this table contains biomarker measurements specific to particular cancer types.

9.6. Secondary Data

Secondary data tables are the corpus of curated data we receive from national data warehouses for all eligible participants not belonging in a data restricting cohort and not registered in Northern Ireland, Wales or Scotland. They are mostly longitudinal in nature and agnostic to the recruited disease. Data at the point of release captures all activity contained in the period covered within each of the datasets up to the latest quarter published by NHSD and end of calendar year for PHE/NCRAS.

9.6.1.1. NHSD

- HES: Hospital Episode Statistics containing details of all commissioned activity during admissions, outpatient appointments and A&E attendances.
- DID: Metadata (demographics, modalities, ordering entity and dates) on diagnostic imaging tests collated from local radiology information systems.
- PROMS: Patient Reported Outcome Measures report health gain in patients undergoing major surgical operations based on responses to questionnaire pre and post procedure.
- MHMDS: Data on patients receiving care in NHS specialist mental health services. Reporting care period for this dataset is up to March '14. Will be replaced in the future with MHSDS.
- MHLDDS: Data on patients receiving care in NHS specialist mental health services. Reporting care period for this dataset us from March '14 to Dec '15. Will be replaced in the future with MHSDS.
- ONS/CEN: Office of National Statistics registry data for cancer registrations and deaths inside and outside hospitals. Issue of death certificates and cancer network registrations are a requirement for an entry to these manifests.

Table Name	Description
hes_apc	Historic records of admissions into secondary care of GeL main programme participants.
hes_cc	Historic records of admissions into critical care of GeL main programme participants.
hes_op	Historic records of outpatient attendances of GeL main programme participants.
hes_ae	Historic records of A&E attendances of GeL main programme participants.
did	Historic diagnostic Imaging records of GeL main program participants.
did_bridge	Linking file of participants to DID submissions.
proms	Questionnaire responses pre and post four operations: hip replacement, knee replacement, varicose vein and groin hernia surgery.
mhmd_v4_record	Historic records of MH related admissions of GeL main programme participants. One record per spell per patient in a provider.
mhmd_v4_event	Historic records of MH related admissions of GeL main programme participants. Episode and event tables link to the records table via spell_id.
mhmd_v4_episode	Historic records of MH related admissions of GeL main programme participants. Episode and event tables link to the records table via spell_id.
mhldds_record	Historic records of MH related admissions of GeL main programme participants. One record per spell per patient in a provider.
mhldds_event	Historic records of MH related admissions of GeL main programme participants. Episode and event table link to the records table via mhm_mhmds_spell_id.
mhldds_episode	Historic records of MH related admissions of GeL main programme participants. Episode and event tables link to the records table via mhm_mhmds_spell_id.
mh_bridge	Linking file of participants to MHMD records and the three interlinking tables (spells).
cen	Cohort Event Notification for GeL main programme participants. Captured events are death and cancer registrations. Death events are associated with date and references to the death register district and number are included. Cancer events are associated with date of cancer registration, reference number and basic cancer type characteristics - site, morphology and behaviour.
ons	Office of National Statistics - death registration and cause of death reports for the GeL main programme participants. This table has been truncated to contain date of death and cause of death details only.

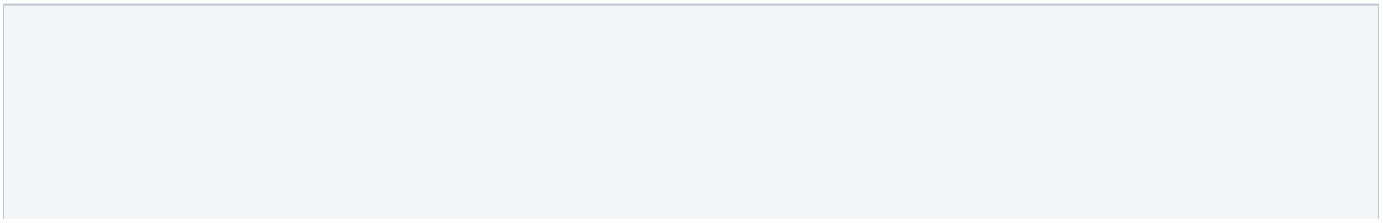
PHE/NCRAS

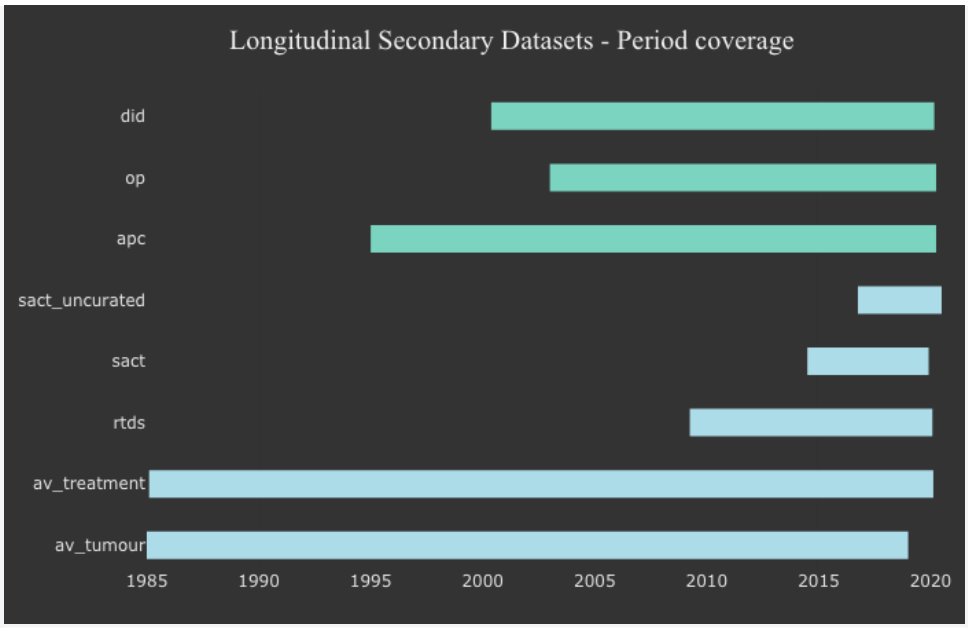
Available for patients diagnosed with Cancer (ICD10 C00-97, D00-48) from 1 January 1995 - 31 December 2017

This dataset brings together data from more than 500 local and regional datasets to build a picture of an individual's treatment from diagnosis. **Please note that pseudo_tumour_ids in AV tables and in SACT are assigned to participants by NCRAS and do not link to the tumour_ids assigned by GeL for sequencing and clinical data. Whilst (particularly in the case of single tumour) this may refer to the same cancer, caution should be applied prior to any analysis.**

Table Name	Description
av_patient	Patient information - demographics and death details.
av_tumour	Tumour catalogue and characterisation for all patients with registerable tumour. Table's <pseudo_tumour_id> is used to link treatment tables also available in NCRAS. One row per tumour (av* table specific pseudo_tumour_id), per participant at the point of registration of that cancer /tumour with NCRAS.
av_treatment	Tumour linked catalogue of treatments and sites that provided them for all patients with registerable tumour.
av_imd	The Income Deprivation Domain (IMD table) measures the proportion of the population experiencing deprivation relating to low income. The definition of low income used includes both those people that are out-of-work and those that are in work but who have low earnings.
av_rtd	Routes to Diagnosis: cancer registration data are combined with Administrative Hospital Episode Statistics data, Cancer Waiting Times data and data from the cancer screening programmes. Using these datasets cancers registered in England which were diagnosed in 2006 to 2016 are categorised into one of eight Routes to Diagnosis. The methodology is described in detail in the British Journal of Cancer article 'Routes to Diagnosis for cancer - Determining the patient journey using multiple routine datasets'.
cwt	The National Cancer Waiting Times Monitoring Data Set supports the continued management and monitoring of waiting times
sact	Systemic Anti-Cancer Therapy (chemotherapy detail) data for cancer participants from PHE covering regimens between 03/2015 and 12 /2017. One row per chemotherapy cycle, per tumour (SACT-specific pseudo_tumour_id), per participant.
rtds	The Radiotherapy Data Set (RTDS) standard (SCCI0111) is an existing standard that has required all NHS Acute Trust providers of radiotherapy services in England to collect and submit standardised data monthly against a nationally defined data set since 2009. The purpose of the standard is to collect consistent and comparable data across all NHS Acute Trust providers of radiotherapy services in England in order to provide intelligence for service planning, commissioning, clinical practice and research and the operational provision of radiotherapy services across England. Data is available from 01/04/2009. The data is linked at a patient level and can be linked to the latest available av_patient table.
ncras_did	The Diagnostic Imaging Dataset (DID) is a central collection of detailed information about diagnostic imaging tests carried out on NHS patients, extracted from local radiology information systems and submitted monthly. The DID captures information about referral source, details of the test (type of test and body site), demographic information such as GP registered practice, patient postcode, ethnicity, gender and date of birth, plus data items about different events (date of imaging request, date of imaging, date of reporting, which allows calculation of time intervals. Data is available for patients diagnosed between 1 January 2013 and 31 December 2015.
lucada_2013	The National Lung Cancer Audit (LUCADA) looks at the care delivered during referral, diagnosis, treatment and outcomes for people diagnosed with lung cancer and mesothelioma. The data items in the LUCADA dataset have been compiled to meet the requirements of audit, and are not to be confused with the data items identified as Lung Cancer in the National Cancer dataset. The audit focuses on measuring the care given to lung cancer patients from diagnosis to the primary treatment package, assessing against standards and bringing about necessary improvements. The project supports the Calman Hine recommendations, the National Cancer Plan and other national guidance (e.g. NICE guidance) as it emerges.
lucada_2014	As above. Different schema to lucada_2013.
sact_uncurated	This table extracts chemotherapy (SACT) information for cancer participants in the 100,000 genomes project from unlinked and unprocessed PHE/NCRAS chemotherapy data from 2008 until June 2020. Please refer to background and use caveats in the quality notes section of this release note.

Activity Period Coverage for the longitudinal secondary data tables





Source	Dataset	Start	End
NCRAS	av_tumour	1985-01-01	2018-12-31
NCRAS	av_treatment	1985-02-08	2020-02-14
NCRAS	rtds	2009-04-01	2020-01-30
NCRAS	sact	2014-07-01	2019-11-30
NCRAS	sact_uncurated	2016-10-02	2020-06-29
NHSD	apc	1995-01-01	2020-03-31
NHSD	op	2003-01-01	2020-03-31
NHSD	did	2000-05-19	2020-02-29
NHSD	ons	1995-09-14	2020-06-01

9.7. Genomics England Data Resources

Genomics England Data Resources are available in the following locations:

From the Inuvika Desktop:

~/gel_data_resources/

From the High Performace Compute (HPC) cluster:

/gel_data_resources/

The data resources available here are:

Tiering data for rare disease: Tiering data are available for rare disease participants who have been through the Genomics England interpretation platform. These data provide information on the pathogenicity of variants that have been identified in the proband's genome. Tiering data for rare disease probands can also be found in the designated LabKey table outlined above.

GMC exit questionnaires for rare disease: Outcomes questionnaire for interpreted genomes generated by Genomics England and Clinical Interpretation Providers.

Interpretation request data for rare disease: The following information can be found within the interpretation request JSON file: Family Pedigree and Other Family History, Analysis Panels & versions, Specific Disorder, Tiered Variants and Tiering version, HPO terms, Workspace (NHS GMC or LDP site code), Gene Panel Coverage, Disease Penetrance, Variant Classification.

Tiering, structural, and copy-number variant reports for Cancer: Annotated in JSON format. The file paths are available in the Quick View titled cancer_analysis.

Aggregated gVCF dataset (aggV2):

This is a set of multi-sample VCF files containing germline genomic data from 78,195 participants – termed the "aggV2" – from Main Programme Data Release v10. This is an increase of genomic data of ~20,000 participant compared to our original aggregated data set ("aggV1"). The file contains germline samples from both the rare disease and the cancer programs including only genomes aligned to the Homo Sapiens NCBI GRCh38 assembly with decoys. All included samples have passed a set of basic QC metrics:

- Sample Contamination (freemix) < 0.03
- Ratio of SNV Het-to-Hom calls < 3
- Total Number of SNVs Between 3.2M-4.7M
- Array Concordance > 90%
- Median Fragment Size > 250bp
- Excess of Chimeric Reads < 5%
- Percentage of Mapper Reads > 60%
- Percentage of AT Dropout < 10%

These QC metrics are provided in the LabKey table aggregate_gvcf_sample_stats. See also here.

The aggregated dataset is split into 1,371 genomic regions or 'chunks' by physical position, to process the aggregation in parallel and to ensure that the resulting output files are not too large. No variant (= site) QC filters were applied in the dataset, but the VCF filter was set to PASS for variants which passed the following parameters:

- Missingness (fully missing genotypes with DP=0) 5%
- Coverage (Median Depth) 10X
- GQ (Median GQ) 15
- ABratio (Percentage of het calls not showing significant allele imbalance for reads supporting the ref and alt alleles) 25%
- completeGTRatio (Percentage of complete sites (sites with no missing data)) 50%
- phwe_eur (p-value for deviations from HWE in unrelated samples of inferred European ancestry) 1e-5

We recommend only using variants that have PASS in the filter column in your analyses which will have passed all the parameters above. If a site does not pass the parameters above, the failing criteria/criterion will be listed in the FILTER field in place of a 'PASS' flag. See also here.

In addition to the genotypes we provide pairwise kinship and relatedness information (PLINK2 implementation of the KING-Robust algorithm), Principal Components (of which the first 20 can be found in the aggregate_gvcf_sample_stats LabKey table), and predicted ancestry probabilities for all samples.

All data can be found at:

/gel_data_resources/main_programme/aggregation/aggregate_gVCF_strelka/aggV2/

Detailed documentation can be found at:

https://re-confluence.gel.zone/display/GERE/aggV2+Details

For help with querying this data, we provide examples at:

https://re-confluence.gel.zone/display/GERE/aggV2+Code+Book

Our previous aggregated data set ("aggV1") containing germline genomic data from 59,464 participants can still be found at /gel_data_resources /main_programme/aggregated_illumina_gvcf/GRCH38/20190228/. However, we strongly recommend using the "aggV2" moving forward for all new analyses.

9.8. Cohort Metadata

Within the data release, there is genomic data and clinical data for participants that are part of non-NHS research cohorts that have been sequenced by Illumina and analysed via the Genomics England pipeline.

These research cohorts can be distinguished via their clinic ID as each has been given their own unique code. If any genomic or clinical data from the research cohorts is used in your analysis and subsequent publication, reference to the cohort organisation will need to be made.

Non-NH	Clinic ID	Rare Dis	Description	Constraints	Requirements of Use	Opportunities for further research

Cohort Name		ease/Cancer				
BreastCancerNow	BCN	Cancer	The Breast Cancer Now Tissue Bank (BCNTB) is a multi-centre tissue bank established to fill the gap in the Triple Negative breast cancer (TNBC) research community. It systematically collects high quality tissues and data under an established ethical framework. Full clinico-pathological and follow-up data is due to be made available with ongoing longitudinal data collection. This cohort is curated group of 110 treatment naïve TNBC patients. Additional tissue for many is available through the BCNTB for further matched 'omic analysis.	Consistent with Genomics England acceptable uses	Any publication referencing the Sequence Data generated, needs to ensure reference is made to the contribution of the Provider to the generation of the Sequence Data	Potential to remove identifiers for the purpose of requesting access to Breast Cancer Now biobank samples.
CLL	CLL	Cancer	The original Chronic lymphocytic leukaemia (CLL) Genomics England Pilot aimed to develop the protocols and analytical methods required to perform whole genome sequencing (WGS) at scale for patients with CLL recruited into national clinical trials as a prelude to the Genomics England main programme. This cohort is a small subset of the pilot to allow for the provision of validation data.	Consistent with Genomics England acceptable uses	Any publication referencing the Sequence Data generated, needs to ensure reference is made to the contribution of the Provider to the generation of the Sequence Data	
UKALL2003trial	ALL	Cancer	The aim of this project is to explore the genomic landscape of patients with acute lymphoblastic leukaemia at initial presentation in order identify mutations that could explain their poor response and potentially be future biomarkers. The objective was to perform whole genome sequencing and targeted screening for mismatch repair deficiency on a large well annotated cohort of patients with ALL treated on the UKALL2003 trial. This will generate, for the first time, a comprehensive genomic landscape of chemo-resistant acute lymphoblastic leukaemia.	Consistent with Genomics England acceptable uses	Any publication referencing the Sequence Data generated, needs to ensure reference is made to the contribution of the Provider to the generation of the Sequence Data	
NIHRBioresource	NB3	Rare Disease	The NIHR BioResource is comprised of volunteers from around the country who have given their consent to taking of a biological sample, and they are willing to be approached to participate in research studies and trials on the basis of their genotype, and or phenotype. This cohort consists of rare disease participants who consented to WGS as part of the 100,000 Genomes Project.	Anyone who wishes to be granted permission to contact any of the NIHR BioResource participants should follow the process of applying to the NIHR BioResource. The steps to be made can be found on the NIHR BioResource website at: https://bioresource.nihr.ac.uk/about-us/about-the-bioresource/	Any publication referencing the Sequence Data generated, needs to ensure reference is made to the contribution of the Provider to the generation of the Sequence Data	

10. Contact and Support

For all queries relating to this data release please contact the Genomics England Service Desk portal: Service Desk (accessible from outside the Research Environment). The Service Desk is supported by dedicated Genomics England staff for all relevant questions.

11. Change Summary

The change summary below summarises the changes in this release:

Data Release	Description
main_program	• Two new tables, lrs_laboratory_sample and lrs_sequencing_data, have been added to the Common and Bioinformatics table, respectively. These tables accompany the release of **long-read whole genome sequencing** data for a subset of 47 participants in the 100,000 Genomes Project. File paths to raw and BAM files are provided. Further details of the sequencing protocol and bioinformatics pipeline are here. • Data for orthogonal standard-of-care tests which were collected from GMCs for a subset of cancer patients. First ~2000 cancer genomes re-processed through Pipeline 2.0. That includes Dragen v3.2.22 for alignment and germline variant calling + Strelka 2.9.9 for somatic small variants + Canvas 1.39 for somatic CNV + Manta 1.5 for somatic SVs. Please be aware that false positives have not been filtered from Strelka calls in this release. These realigned files can be found in the genome_file_paths_and_types and sequencing_report tables in LabKey. A new variable in the delivery_version column called Dragen_Pipeline2.0 will provide users the ability to easily subset their data to realigned genomes only. The delivery_version column in genome_file_paths_and_types is new, and directly corresponds to the one found in sequencing_report.

me_v10_2020-09-03	• The **aggregate_gvcf_sample_stats** table has been refreshed for the aggV2 dataset - which can be found here: */gel_data_resources /main_programme/aggregation/aggregate_gVCF_strelka/aggV2*. There are now changes to the table which reflect the changes in sample QC from aggV1 to aggV2. Please see the Data Dictionary for full descriptions of all columns. Added Columns: karyotype, illumina_ploidy, sample_source, sample_preparation_method, sample_library_type, samtools_insert_size_standard_deviation, samtools_insert_size_average, samtools_error_rate, samtools_average_quality, samtools_raw_total_sequences, samtools_reads_mapped, samtools_reads_mapped_and_paired, samtools_reads_properly_paired, samtools_reads_unmapped, samtools_reads_duplicated, samtools_pairs_on_different_chromosomes, illumina_mean_coverage, illumina_autosome_mean_coverage, illumina_coverage_at_15x, illumina_percent_aligned_reads, illumina_percent_read_pairs_aligned_to_different_chromosomes, illumina_fragment_length_median, illumina_array_concordance, illumina_snvs_all, illumina_snvs, illumina_indels_all, illumina_deletions_all, illumina_insertions_all, illumina_snv_het_hom_ratio, illumina_snv_ts_tv_ratio, illumina_indel_het_hom_ratio, illumina_deletion_het_hom_ratio, illumina_insertion_het_hom_ratio, illumina_percent_gc_dropout, illumina_percent_at_dropout Removed Columns: paternal_platekey, maternal_platekey, samtools_reads_mapped_percent, samtools_pairs_on_different_chromosomes_percent, gc_drop, at_drop, coverage_localrmsd, coverage_med, coverage_avg, coverage_pct75, coverage_pct25, coverage_sdcoverage_gte15x, illmn_snv_ts_tv_ratio, illmn_autosome_mean_coverage, illmn_percent_aligned_reads, illmn_het_hom_ratio_del, illmn_het_hom_ratio_indel, illmn_het_hom_ratio_snv, illmn_het_hom_ratio_ins, illmn_snvs_all, illmn_indels_all, illmn_insertions_all, illmn_deletions_all . • **sact_uncurated** table is the raw feed from PHE_NCRAS which feeds into their curation process producing the **sact** table (both under PHE /NCRAS section). This table extracts chemotherapy (SACT) information for cancer participants in the 100,000 genomes project from unlinked and unprocessed PHE/NCRAS chemotherapy data from 2008 until June 2020. This is a first trial attempt by a small group within Genomics England to curate chemotherapy data. Whilst we do not possess the extensive experience and resource of Public Health England, we are providing a nearly live dataset. As such, it is likely to contain some errors, however it contains clinical therapy data that is not yet available in the curated NCRAS registries, such as SNOMED CT diagnosis codes alongside ICD10. The gold standard remains the NCRAS curated SACT table. However, for this dataset to improve and move forward, **Genomics England are keen for user feedback and for users to highlight areas for improvement.** Users will note subtle differences to the structure of the table compared to the curated SACT table and thus an additional data dictionary has been provided. A major point to raise is that this SACT curation does not provide tumour IDs, thus users must match this dataset to other NCRAS registries by adjusting for date. Genomics England hopes to continue developing this uncurated live dataset with user feedback and look forward to hearing your thoughts.

main_programme_v9_2020-04-02	• Two new columns, normalised_hpo_id and normalised_hpo_term, have been added to the rare_diseases_participant_phenotype table. These columns provide a standardised description, and HPO ID (where the ID provided by the GMCs is an alternate ID in the ontology) for each row of data. The source data was downloaded from https://hpo.jax.org/app/download/ontology in December 2019.
	• A new table, laboratory_sample_omics_availability, has been added to the Common tables. This provides a view of the samples collected from 100,000 Genomes Project participants for the purpose of omics research. Proposals for the use of these samples can be submitted to the Scientific Advisory Committee and Access Review Committee, via the GeCIP team.
	• *De novo* variant dataset:
	  • Documentation:
	  • The *de novo* variant research dataset for the 100,000 Genomes Project
	  • *denovo_cohort_information*: LabKey Table with cohort information for all participants included in the *de novo* variant dataset. Attributes within this table include: participant ID, sex, affection status, family ID, pedigree ID, and the path to each family's multi-sample VCF with flagged DNVs.
	  • *denovo_flagged_variants*: LabKey Table of all base_filter pass variants for all trios within the DNV dataset. This table includes all flags from the DNV annotation pipeline for each variant.
	  • *annotated_multi-sample_VCFs*: All multi-sample VCFs per family with DNVs flagged within the FILTER field. These VCFs are functionally annotated with VEP and accessible within the filesystem. File paths per participant are included in the denovo_cohort_information LabKey table. The data can be found in directory: /gel_data_resources/main_programme/denovo_variant_dataset
	• Mental Health and Learning Disabilities Dataset has been added to the secondary datasets extending the coverage period of activity related to mental health to 30/11/2015 and expanding the scope (from September 2014) to include people in contact with learning disability services for the first time. The tables are of the same format as the previously available MHMDS dataset.
	  • *mhldds_event*
	  • *mhldds_episode*
	  • *mhldds_record*

main_programme_v	• The `tiering_data` table has been updated to reflect an updated model for the Genomics England Tiering algorithm for rare disease (now on model version 6). Now, all variants include genomic annotation. Further changes are as such:
	  • `db_snp_id` column has been removed as this is no longer included in the raw data from the Clinical Interpretation Pipeline
	  • The allele frequency columns have been removed from the `tiering_data` table and are now all included in the `tiered_variants_frequency` table
	  • The `event_justification` column has been renamed to `segregation_pattern`
	• The `phenotype` variable in the `tiering_data` table has now been normalised so that all disease names match the official terms. It is therefore equivalent to the variable `normalised_specific_disease` rather than `specific_disease` in the table `rare_diseases_participant_disease`.
	• The `panel_identifier` column has been added to the `panels_applied` table. This is a unique hash of the panel name and the panel version. The Data Dictionary has been updated to reflect this change.
	• The `lab_sample_id` column has been added to the `genome_file_paths_and_types` table to make it easier to identify which genome deliveries are associated with a particular laboratory sample. The Data Dictionary has been updated to reflect this change.
	• The gmc_exit_questionnaire has had the column `gene_name` added which is the name of the gene where the variant resides post annotation by Ensembl VEP v98. All genes are included (semi-colon delimited). The Data Dictionary has been updated to reflect this change.

8_2019-11-28	• The gmc_exit_questionnaire has had the column `phenotypes_explained` removed. This is because of an ongoing issue at the GMC level whereby incorrect HPO terms were being entered in the Reporting Outcomes Questionnaire. Specifically, all negative HPO terms in "explainsPhenotype" checkbox were potentially being selected and included in the final report, which renders the utility of this attribute meaningless in the exit questionnaire. We recommend to use the `rare_disease_participant_phenotype` table to identify the HPO terms for the participant and link it back to the gmc_exit_questionnaire table. This is a temporary and partial solution to the issue whilst we try and fix it for the next release. We felt it better to remove potentially misleading information than to preserve it. The Data Dictionary has been updated to reflect this change.
	• The columns: dbsnpid, genomicfeature_hgnc, genomicfeature_ensemblid, and consequencetype have been removed from the `tiered_variants_frequency` table. The data still remain in the `tiering_data` table. The Data Dictionary has been updated to reflect this change.
	• laboratory_sample_id added to plated_sample table;
	• rare_diseases_participant_disease.normalised_age_of_onset created by changing values of rare_diseases_participant_disease. age_of_onset 1 or >150 to null.
	• cancer_staging_consolidated table that consolidates all the staging data in one place and aim to link more than only participant IDs, but also at the sample/tumour level.
	• In the `domain_assignment` table, the names of six GeCIP domains have been changed to the official domain names and to match those on the Genomics England website:
	  • `Inherited cancer` is now `Inherited cancer predisposition`
	  • `Immunology` is now `Immune disorders`
	  • `Haematology` is now `Non-malignant haematological and haemostasis disorders`
	  • `Response to sepsis` is now `Paediatric sepsis`
	  • `Childhood cancers` is now `Childhood solid cancers`
	  • `Head and neck` is now `Head and neck cancer`

main_programme_v7_2019-07-25	• 196 platekeys have now been remapped to different participant IDs following the in-house QC checks. **These mappings have been rectified for Version 7** and the following tables have been corrected (*sequencing_report, genome_file_types_and_paths, rare_disease_analysis, aggregate_gvcf_sample_stats*). No other tables were affected. • The affected platekeys – participant ID mappings are provided in the research environment under the folder: /gel_data_resources /main_programme/sample_remappings in the file: **corrected_sample_remapping.tsv**. Researchers working with earlier data releases should amend accordingly. • In addition, the following four platekey IDs were blacklisted following in house QC checks and have been removed from release 7: LP3001094-DNA_E08, LP3001053-DNA_C03, LP3001268-DNA_F06, LP3001327-DNA_G09. Researchers using earlier releases should remove these from their analyses. • The aggregate_gVCF _sample_stats table now includes the first 10 Principal components; a set of unrelated individuals and predicted probabilities of ancestry membership • Exomiser data now included for all interpreted cases in the LabKey table: 'exomiser'. • The panels_applied table now contains the columns: *interpretation_cohort_id*, *interpretation_request_id*, *sample_id*, and *phenotype*. See the data dictionary for the definitions of these fields. • The tiering_data table now contains the columns: *interpretation_cohort_id* and *interpretation_request_id*. See the data dictionary for the definitions of these fields. • The *sex_karyotype_pass* column has been removed from the rare_disease_analysis table as this is made redundant by the *reported_karyotypic_sex* and *inferred_sex_karyotype* columns. The *platekey* column has been renamed to *plate_key*. • The rare_disease analysis table now only includes the *latest* genome delivery per participant per genome build. This ensures that deprecated genomes are not used in analysis. • The rare_disease_analysis table now only reports the WGS *genetic_vs_reported* results for GRCh38 genomes as GRCh37 genomes were not subject to this test. • The gmc_exit_questionnaire table now contains the columns: *interpretation_cohort_id* and *interpretation_request_id*. See the data dictionary for the definitions of these fields. The *variant_details* column has been separated into four fields: *chromosome*, *position*, *reference*, *alternate*. • In the *delivery_version* column of the sequencing_table, unknown delivery versions have been recorded with the "unknown" flag. • rare_diseases_invest_genetic.sample_source_id removed from the dataset as it contains data of little use, some of which contains clinician contact details • A spelling error in one of the enumerations for rare_diseases_participant_disease.normalised_specific_disease corrected - 'Anophthalmia or microphthamia' corrected to 'Anophthalmia or microphthalmia' • The cancer_analysis table now contains the following 4 new columns: 1. *interpretation_request_id*: interpretation request and version of analysis that was released to the Interpretation Portal and returned to the Genomic Medicine Centre; 2. *tumour_purity*: tumour purity (cancer cell fraction) calculated by Ccube (https://rdrr.io/github/keyuan/ccube/); 3. *analysis_csv_filepath*: contains path to a machine-readable csv file with a summary of germline and somatic small variants that are presented in the results of Whole Genome Analysis. See Technical Information document for details of this analysis; 4. *analysis_html_filepath*: contains path to HTML file with results of Whole Genome Analysis. It includes annotation and prioritisation of somatic small variants and structural variants/copy number variants, COSMIC signatures, tumour mutation burden, tiered germline variants for cancer susceptibility genes. For FFPE samples, only analysis of small variants is included. See Technical Information document for the details of this analysis. • In the cancer_analysis table the *somatic_coding_variants_per_mb* is calculated as total number of small somatic non-synonymous coding variants per Mb of coding sequence (32.61 Mb). This metric was re-calculated using somatic_small_variants_annotation_vcf as input and all non-PASS variants were removed from the calculation; • In the cancer_analysis table, signature_1 to signature_30: COSMIC signatures (v2) were re-calculated using somatic_small_variants_annotation_vcf as input. Only signatures with contribution above 5% are shown • In the cancer_analysis table, the somatic_small_variants_annotation_vcf file has been updated: this VCF file contains Genomics England flags for potential false positive variants as well as additional annotations (see VCF header for details). Swift and PolyPhen scores as well as new PONnoise50SNV flag were added. See following description of all current flags: i. Variants with a population germline allele frequency above 1% in a Genomics England dataset (CommonGermlineVariant), ii. Variants with a population germline allele frequency above 1% in gnomAD dataset (CommonGnomADVariant), iii. Recurrent somatic variants with frequency above 5% in a Genomics England dataset (RecurrentSomaticVariant), iv. Variants overlapping simple repeats as defined by Tandem Repeats Finder (SimpleRepeat), v. Small indels in regions with high levels of sequencing noise where at least 10% of the basecalls in a window extending 50 bases to either side of the indel's call have been filtered out by Strelka due to the poor quality (BCNoiseIndel), vi. SNVs resulting from systematic mapping and calling artefacts. The following methodology was used: the ratio of tumour allele depths at each somatic SNV site was tested to see if it is significantly different to the ratio of allele depths at this site in a panel of normals (PoN) using Fisher's exact test. The PoN was composed of a cohort of 7000 non-tumour genomes from the Genomics England dataset, and at each genomic site only individuals not carrying the relevant alternate allele were included in the count of allele depths. The mpileup function in bcftools v1.9 was used to count allele depths in the PoN, and to replicate Strelka filters duplicate reads were removed and quality thresholds set at mapping quality >= 5 and base quality >= 5. All somatic SNVs with a Fisher's

	exact test phred score < 50 were filtered, this threshold minimised the loss of true positive variants while still gaining significant improvement in specificity of SNV calling as calculated from a TRACERx truth set (PONnoise50SNV) • In the cancer_analysis table, the somatic_small_variants_annotation_json column has been removed, as the somatic_small_variants_annotation_vcf file should contain the equivalent information

main_programme_v6_2019-02-28	• · Date fields have been added to the following, tables:
	  • cancer_surgery
	  • rare_diseases_invest_blood_laboratory_test_report
	  • rare_diseases_invest_genetic
	  • cancer_participant_tumour
	  • cancer_risk_factor_general
	  • cancer_invest_imaging
	  • rare_diseases_participant_phenotype
	• In rare_diseases_pedigree, pedigree_family_id was renamed rare_diseases_family_id, and in rare_diseases_pedigree_member both member_participant_id and member_participant_sk were renamed participant_id and participant_sk accordingly
	• In participant table, duplicated_participant_id was added to highlight instances where a single person has been recruited under multiple participant_ids
	• A new table, death_details, was added. It contains death data received from GMCs only
	• In the participant table both mother_affected and father_affected have been changed to Yes/No/Unknown values
	• A new table, plated_sample, has been created to accommodate plated sample-level data from the laboratory sample table, specifically:
	  • platekey
	  • well_id
	  • plate_id
	  • biorepository_dispatch_datetime
	  • illumina_qc_datetime
	  • dna_amount (renamed illumine_dna_amount)
	  • illumina_delta_cq
	  • illumina_qc_status
	  • illumina_sample_concentration
	  • illumina_sequence_gender
	  • matched_dna_germline_laboratory_sample_sk (which is now accommodated in matched_sample_type and matched_sample_ids)
	• Column mydob has been removed from apc, op, ae tables
	• Column cdsuniqueid has been removed from ae table
	• SACT table with 38 fields covering details of chemotherapy regimens recorded by PHE for cancer patients has been added.
	• The sequencing_report table now contains the column
	  • lab_sample_id
	• The sequencing_report table has the following columns removed
	  • No
	  • BAM date
	  • BAM size
	  • Status

main-programme_v5.1_2018-11-20	• cancer_analysis – 8 new columns • hes_ae – 55 new columns, 2 columns removed: lsoa01, oacode6 • hes_apc - 64 new columns, 1 column removed: oacode6 • hes_op - 52 new columns, 2 columns removed: lsoa01, pctorig02
main-prog	• This release provides clinical data for 85,070 participants, and 71,860 genomes from 62,487 of these participants. Of these genomes, 54,456 are rare disease genomes (from 54,138 participants) and 17,404 are cancer genomes (from 8,349 participants) • 15,545 families with Tier 1, 2 and 3 variants from the interpretation pipeline; 2,470 families with GMC exit questionnaires • The LabKey table domain_assignment has been updated to include Moratorium end dates for genomes associated with participants in this table • File paths to tiering and structural variants from cancer genomes added to cancer quick view

ramme_v5_2018-10-31	• New clinical LabKey tables with information on progression and medical history: cancer_surgery; cancer_risk_factor_cancer_specific; cancer_specific_pathology; cancer_systemic_anti_cancer_therapy; cancer_care_plan; cancer_invest_circulating_tumour_marker; as well as rare_diseases_imaging; rare_diseases_gen_measurement and rare_diseases_early_childhood_observation.
	• A new table tiered_variants_frequency was added between Main Programme Data Release V4 and this one (V5.1)
	• Multiple data fields were added, removed and renamed in cancer_invest_sample_pathology:
	  • The following were added: tumour_id; sample_pathology_id; topography_icd_code; topography_snomed_ct_code; topography_snomed_rt_code; topography_snomed; topography_snomed_version; sample_receipt_date; sample_taken_date; vascular_or_lymphatic_invasion_cancer; event_date
	  • The following were removed: topography_id; sample_details_id; vascular_or_lymphatic_invasion_cancer_id
	  • The following were renamed: preoperative_therapy_id renamed to preoperative_therapy; vascular_or_lymphatic_invasion_cancer_id renamed to vascular_or_lymphatic_invasion_cancer
	• cancer_invest_imaging now includes free imaging report texts (report_text) and multiple other data fields were added to this table: cancer_invest_imaging; tumour_id; imaging_modality; cns_imaging_radiological_number_of_lesions; cns_imaging_radiological_lesion_size; cns_imaging_radiological_lesion_location; cns_imaging_radiological_largest_lesion_features; cns_imaging_principal_diagnostic_imaging_type; breast_imaging_mammogram_result
	• All new genomic data added in the current data release (since July 2018) are aligned against the reference genome version GRCh38, using alignment pipelines V4
	• The following normalised diseases were renamed to match the official terms: *Cytopaenia and pancytopaenia* was renamed *Cytopenia and pancytopenia*; *Early onset dementia (encompassing fronto-temporal dementia and prion disease)* was shortened to *Early onset dementia*
	• The rare_disease_analysis quick view table now provides WGS family selection quality checks for rare disease families with genomes on build GRCh38, reporting abnormalities of the sex chromosomes, family relatedness and Mendelian inconsistencies, as well as reported vs genetic sex summary status (this contains an overall status – only sex checks are unpacked into individual data fields)
	• New outputs from the Genomics England Bioinformatics pipeline: The cancer_analysis quick view table now contains gold standard cancer genomes that have been through Genomics England Bioinformatics interpretation and passed quality checks

main-programme_v4_2018-07-31	• This release provides clinical data for 71,331 participants, and 55,681 genomes from 49,303 of these participants. Of these genomes, 43,997 are rare disease genomes (from 43,570 participants) and 11,684 are cancer genomes (from 5,715 participants). • New LabKey tables: panels_applied, rare_diseases_invest_genetic, rare_diseases_invest_genetic_test_result, rare_diseases_invest_blood_laboratory_test_report, panels_applied, cancer_invest_sample_pathology, cancer_invest_imaging, cancer_risk_factor_general, cancer_PCA_QC_stats, tumour_MB_signatures • LabKey tables removed: family_members • “Relationship to proband” field moved from family_members to rare_disease_analysis • Multiple data fields from cancer_participant_tumour and laboratory_sample added to cancer_analysis • “Disease” field changed to “disease or panel” in domain_assignment; an “origin” field has been added to domain_assignment to indicate whether the GeCIP domain applied to each participant is based on the disease they were recruited for or the panel applied to their genome • “Panel name” and “panel version” fields moved from tiering to panels applied
main-programme_v3_2018-04-30	• The dataset now includes 44,067 genomes. • Clinical data are also provided for participants with *and* without a sequenced genome, for a total of 61,554 • New LabKey tables are: family_members, genome_file_paths_and_types, rare_disease_analysis, tiering_data. • LabKey tables removed: rare_diseases_pedigree_member_disease, rare_diseases_pedigree_member_hpo_term. • Changes to LabKey tables including the new fields in the clinic_sample_level data and participant_level_data tables. • A new field genome_build was added to the sequencing_report table. This specifies 37 when the Delivery Version is V2 or before, and 38 when it is V4. • Removal of some ID fields where a human readable description of the value is available. • A new column named normalised_consent_form has been created in the participant table, assigning the free text values in consent_form to sensible categories • Pedigree diagnosis and phenotype data were removed from the research dataset
mai	• The dataset includes 31,384 genomes – an increase of 11,519 genomes from the first release.

n-programme_v2_2018-01-30	• Clinical data are also provided for participants with *and* without a sequenced genome, for a total of 53,190 participants. • A far broader set of clinical data are provided for participants, comprising 16 tables in LabKey. • In addition to Hospital Episode Statistics (HES), the secondary datasets Diagnostic Imaging Dataset (DID), Patient Reported Outcome Measures (PROMs) and Mental Health Services Data Set (MHSDS) are included in the release. • There have been significant changes to the data structure of the LabKey tables. Refer to the Data Dictionary that accompanies this release for further details.
main-programme_v1_2017-10-11	• This data release represents the baseline for subsequent releases.

[1] Some Rare Disease participants have multiple genomes, aligned to both GRCh37 and GRCh38. This excludes 86 TracerX genomes from 99 participants (refer to 6.4 for further information).

[2] Genomes which are yet to be classified as being rare disease or cancer are assigned an ‘unknown’ delivery type; therefore, the total cancer genomes + total rare disease genomes do not completely add up to the total genome count due to these ‘unknown’ delivery types. These genomes will be assigned to the rare disease or cancer programme at a later date.

Main Programme Release Note v10 and Data Dictionary Files

Data Release No...ogramme v10.pdf

Data Dictionary...gramme v10.xlsx