PrivGenDB: Efficient and privacy-preserving query executions over encrypted SNP-Phenotype database

Sara Jafarbeiki, Amin Sakzad, Shabnam Kasra Kermanshahi, Raj Gaire, Ron Steinfeld, Shangqi Lai, Gad Abraham

Abstract—Searchable symmetric encryption (SSE) has been used to protect the confidentiality of genomic data while providing substring search and range queries on a sequence of genomic data, but it has not been studied for protecting single nucleotide polymorphism (SNP)-phenotype data. In this article, we propose a novel model, PrivGenDB, for securely storing and efficiently conducting different queries on genomic data outsourced to an honest-but-curious cloud server. To instantiate PrivGenDB, we use SSE to ensure confidentiality while conducting different types of queries on encrypted genomic data, phenotype and other information of individuals to help analysts/clinicians in their analysis/care. To the best of our knowledge, PrivGenDB construction is the first SSE-based approach ensuring the confidentiality of shared SNP-phenotype data through encryption while making the computation/query process efficient and scalable for biomedical research and care. Furthermore, it supports a variety of query types on genomic data, including count queries, Boolean queries, and \( k \)-out-of-\( k \) match queries. Finally, the PrivGenDB model handles the dataset containing both genotype and phenotype, and it also supports storing and managing other metadata like gender and ethnicity privately. Computer evaluations on a dataset with 5,000 records and 1,000 SNPs demonstrate that a count/Boolean query and a \( k \)-out-of-\( k \) match query over 40 SNPs take approximately 4.3s and 85.4s, respectively, outperforming the existing schemes.

Index Terms—Searchable symmetric encryption, genomic data privacy, secure outsourcing.

I. INTRODUCTION

Advances in genotyping technology have enabled the genotyping of large human cohorts and biobanks, (e.g., UK Biobank [1], [2], NIH All of Us [3], the Million Veteran Program [4], and others). Such large datasets are critical for advancing our understanding of human health and disease and their genetic components, for improving treatment practices, and for better delivery of healthcare. Specific examples include diagnosing a genetic predisposition to disease and precision medicine (e.g., predict the outcome of a specific drug or treatment) [5], [6]. In addition to these large projects, hospitals and research institutions often collect similar data (on a smaller scale) and store them in local databases with limited resources, while the volume of data can be very large.

Single nucleotide polymorphisms (SNPs) are the most common type of genetic variation, and many genetic analyses involve identifying associations between SNPs and traits or diseases. There are some useful queries/analyses that can help genome-based researchers with their studies, e.g., SNP-disease association study.

S. Jafarbeiki, A. Sakzad, R. Steinfeld and S. Lai are with the Faculty of Information Technology, Monash University, Melbourne, Australia. S. Jafarbeiki and R. Gaire are with CSIRO Data 61, Australia. S. Kasra Kermanshahi is with the School of Computing Technologies, RMIT University, Melbourne, Australia. G. Abraham is with the Systems Genomics Laboratory, Baker Institute, Melbourne, Australia (e-mails: sara.jafarbeiki@monash.edu; ron.steinfeld@monash.edu; shangqi.lai@monash.edu; raj.gaire@data61.csiro.au; shabnam.kasra.kermanshahi@rmit.edu.au; gad.abraham@baker.edu.au).

Examples of such queries include count queries, adding negation terms to the query predicates, and sequence similarity search. Other queries such as Boolean query and \( k \)-out-of-\( k \) match can also help clinicians in medical care.

One of the key challenges with such large datasets is managing and maintaining them securely while enabling appropriate access to authorised individuals. One solution is the use of cloud computing. However, cloud-based servers can be vulnerable to cyber breaches, and the information residing on the servers may be exploited by an adversary capable of violating security [7]–[9]. Therefore, privacy preservation remains an essential factor in the development of electronic frameworks for storing/managing genomic data [10], [11].

Balancing the privacy and security of sensitive information with the need to share and analyse information for research purposes is challenging. While analysing genomic data is valuable to researchers, the increased availability of such data has major consequences for individual privacy; notably, because the genome has some essential features, such as (i) connection with individual characteristics and certain disorders, (ii) identification capability, and (iii) disclosure of family relationships [12]. Measures need to be taken to ensure this data stays in the right hands. With more sensitive information (genomic information), the need to preserve privacy rises considerably.

Traditional ways of privacy protection for medical data, such as de-identification, are often not sufficient. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) [13] provides guidelines about how to handle sensitive information through de-identification. To maintain privacy during data processing and storage, as well as during subsequent data analysis tasks, organisations also consider government policies and regulations [14]. Nowadays, most de-identification approaches struggle to defend against re-identification attacks, and lead to utility loss [15], [16]. Therefore, cryptographic solutions are more attractive for privacy-preservation.

Several existing cryptographic solutions have been utilised in different schemes [17]–[24] for encrypting genomic data and running queries on this encrypted data. Moreover, following privacy patterns can be defined when outsourcing genomic data and conducting different queries against it: Data Privacy (DP), Query Privacy (QP), and Output Privacy (OP) [17] (see definitions in Section III-C). Table II summarises the method, cryptographic primitive, solution type, types of dataset used, supported queries, and privacy considerations taken into account by these schemes.

As illustrated in the table, previous schemes do not execute a set of valuable queries (count, Boolean for retrieving data, \( k \)-out-of-\( k \) match, negation) altogether on encrypted genomic data efficiently and they are not scalable to benefit cutting-edge biomedical applications. Moreover, they provide limited support for storing and managing dataset containing additional information (like gender and ethnicity) apart from the genomic data and phenotypes privately. Some of those solutions are only software-based ones, while others are hybrid, meaning they exploit both...
and search phases), storage size, and communication costs of our queries. We evaluate the computational costs (of the initialisation predicates (see Section II-A.2 for detailed information about these k count query, Boolean query, search and higher efficiency [26]–[31]. SSE has also been studied for preserving SNP-phenotype data privacy. One of the most significant celebrated SSE methods is Oblivious Cross Tag (OXT), studied for preserving SNP-phenotype data privacy. One of the most significant celebrated SSE methods is Oblivious Cross Tag (OXT), introduced in [34]. OXT enables searches over encrypted data in the form of Boolean queries efficiently. Our work proposes a novel model, PrivGenDB, which utilises SSE scheme motivated by OXT, to provide privacy, functionality, and scalability.

A. Our Contributions

We present a new model, which we call PrivGenDB, for providing privacy of outsourced genomic data stored on the cloud supporting data confidentiality and query privacy. Our model also provides output privacy for all the sensitive information retrieved from the server. (see Table II: Privacy). PrivGenDB is the first model that provides the privacy patterns without relying on hardware (e.g., using SGX) and is based on symmetric cryptographic primitives only. Inspired by OXT scheme of [34], we construct the first secure and efficient SSE scheme to instantiate PrivGenDB. We also prove that PrivGenDB achieves the same security guarantees as those in [34]. To facilitate such a construction, we present a novel encoding method for genomic data, and construct an inverted index based on that encoding. Hence, our model can handle datasets containing genotype and phenotype (the exact disease) and other information like gender and ethnicity (see Table II: Dataset). In terms of functionality, our PrivGenDB enables us to handle rich queries on genomic data (see Table II: Queries), such as count query, Boolean query, k-out-of-k match query and negation predicates (see Section II-A.2 for detailed information about these queries). We evaluate the computational costs (of the initialisation and search phases), storage size, and communication costs of our PrivGenDB scheme and compare these against the state-of-the-art schemes. We have conducted several experiments and the results show the effectiveness of our SSE-based PrivGenDB in comparison with previous works, which were mainly based on the Paillier Encryption algorithm. For example, for a count query on a dataset of 5,000 records and 1,000 SNPs, it takes approximately 130.8 s in [17], while PrivGenDB improves the query execution time to 1.3 s only.

II. PRELIMINARIES

A. Biology Background

This section provides background on genomic data, phenotype, and some common queries against this type of dataset.

1) Genomic data and Phenotype: The human genome consists of DNA (deoxyribonucleic acid) with two long complementary polymer chains of four units called nucleotides, A (Adenine), C (Cytosine), G (Guanine), and T (Thymine). Single nucleotide polymorphism (SNP) is a position in the genome where more than one base (A, T, C, G) is observed in a population. Most SNPs are biallelic and only two possible variants (alleles) are observed. The set of specific alleles carried by an individual is called its genotype. Together, SNPs account for a large proportion of the genetic variation underlying many human traits such as height and predisposition to disease (also called phenotype).

Table II illustrates one type of data representation in a database of SNP genotypes for a number of individuals [17], [19], together with the individuals’ phenotype.

| Record | SNP₁ | SNP₂ | SNP₃ | SNP₄ | Phenotype |
|--------|------|------|------|------|-----------|
| 1      | AG   | CC   | TT   | AG   | Cancer A  |
| 2      | AA   | CT   | AG   | ...  | Cancer B  |
| 3      | AG   | CT   | CC   | AA   | Cancer A  |
| 4      | AG   | CC   | TT   | AG   | Cancer C  |
| 5      | AA   | CC   | TT   | AG   | Cancer B  |
| 6      | AA   | CC   | TT   | GG   | Cancer A  |
| 7      | AG   | CT   | CT   | AG   | Cancer B  |

2) Queries on Genomic Data: While biobanks contain individuals’ genomic data, different types of queries need to be performed on the data to help researchers analyse and correlate diseases and genome variations such as SNPs. Here are some types of queries on genomic data:
a) Count Query: A count query determines the number of records that match the query predicates in the database and helps in computing several statistical measurements for genetic association studies. An example of a count query on the dataset represented in Table I is as follows:

```
Select count from sequences where diagnoses = Cancer B AND SNP2 = CC AND SNP4 = AG
```

The total number of SNPs specified in the query predicate is called the query size. In the above example, the query size is 2, and the answer to the mentioned query is 2 (i.e., records 2 and 5).

b) Boolean Query: A query from clinicians can be about identifying patients who have specific genotypes, so that they can contact them to provide personalised medication or inform them about their predisposition for drug allergy or vaccine. This can be done by extracting the IDs whose genotypes match the query symbols, then using those IDs to extract other information needed by the clinician. An example of a Boolean query on the dataset represented in Table I is as follows:

```
Retrieve IDs from sequences where diagnoses = Cancer B AND SNP2 = CC OR SNP4 = AG
```

The answer to the above query is a list of records’ IDs that match the predicates and is: {2,5,7}.

c) \(k'\)-out-of-\(k\) match Query: Sometimes the answer to this query can be yes/no when the query symbols are being checked for a particular record. In this case, we can check if the SNPs for a particular record has the query predicates’ characteristics or not by some threshold defined. In our scenario, presented in algorithms in Section IV the IDs related to records who have this threshold matching can also be retrieved to check their other information like diseases or medications. Examples of a threshold query on the dataset represented in Table I are as follows:

- **Does record number 7 have at least \(k'\) = 2 matches out of \(k = 3\):** ID = 7 AND SNP2 = CC AND SNP3 = CT AND SNP4 = AG. If this ID satisfies the query predicates, the answer will be the ID, which means yes. Otherwise, it will return 0, which means no. Answer: yes.
- **Retrieve IDs from sequences where at least \(k'\) = 2 matches out of \(k = 3\):** diagnoses = Cancer B AND SNP2 = CC AND SNP3 = CT AND SNP4 = AG. The answer to this query is a list of records’ IDs that match the first predicate and have at least 2 of the rest predicates. Answer: {2,5,7}.
- **Negation predicates:** In all of the above queries, negation terms can be added as predicates. For instance, select count from sequences where diagnoses = Cancer B AND SNP2 \(\neq\) CC AND SNP4 = AG. Answer: 1 (Record 7 satisfies the query predicates).

B. Cryptographic Background

This section reviews the cryptographic primitives we opted for in our proposed model.

1) Searchable Symmetric Encryption (SSE): One significant work in the area of Searchable Encryption is the scheme proposed by Cash et al. [34] called Oblivious Cross Tag (OXT), which is important due to its functionality as it supports conjunctive search and general Boolean queries. OXT provides a solution for searches over multiple keywords in the form of general Boolean queries. A special data structure called tuple-set or TSet is used for single keyword searches. An additional dataset called XSet is used for multiple keyword searches to verify if the identified documents for the first keyword also satisfy the remaining query. The OXT scheme achieves sublinear search time even though the search query is of a Boolean type and not just a single keyword. This time is proportional to the number of documents with the least common keyword stem [34]. The syntax of SSE is as follows:

```
EDBSetup(\(\lambda\), DB): Given security parameter \(\lambda\) and a database DB, this algorithm outputs the encrypted database EDB.

Search(q, EDB): Inputs the search query \(q\) and the encrypted database EDB, then outputs the search result (This protocol first uses the TokenGeneration algorithm to generate tokens and then perform the search on encrypted database).
```

We review the TSet instantiation below since we use it in our construction, and we refer the interested readers to the full paper [34] for the complete OXT syntax and more details.

TSet Instantiation. Cash et al. instantiate a TSet in [34] as a hash table with \(B\) buckets of size \(S\) each. A database \(DB = (ind_i, wi)\) is a list of (identifier, keyword) pairs. Based on the total number \(N = \sum_{w \in W} |T[w]|\) of tuples in \(T\), the setup procedure lets the parameters \(B\) and \(S\) in such a way that after storing \(N\) elements in this hash table, the likelihood of an overflow of any bucket is a sufficiently small constant; and the total size \(B.S\) of the hash table is \(O(N)\). It consists of the following algorithms:

```
TSet.Setup(T): This algorithm takes as input an array \(T\) of lists of equal-length bit strings indexed by the elements of \(W\), in which for each \(w \in W\), \(T[w]\) is a list \(t = (s_1, \ldots, s_{T[w]})\) of strings. \(T[w]\) contains one tuple per each DB document which matches \(w\), i.e., \(T[w] = [DB(w)]\). It outputs a pair \(TSet, KY\).

TSet.GetTag(KY, w): This algorithm takes \(KY\) and \(w\) as inputs and outputs stag.

TSet.Retrieve(TSet, stag): This algorithm inputs TSet, stag and returns a list of strings, \(t\) (returns the data which is associated with the given keyword).
```

2) Pseudorandom Functions (PRFs): In our framework, we use PRFs as the deterministic encryption to hide the search queries and tokens. It has also been used in the generation of TSet for confidentiality of indexes and keywords. A PRF [35] is a set of effective functions, where no efficient algorithm can differentiate between a randomly selected function from the PRF family and a random oracle (a function whose outputs are fixed completely at random), with a substantial advantage. Pseudorandom functions are essential tools in the construction of cryptographic primitives, defined as follows:

```
Let \(X\) and \(Y\) be sets, \(F: \{0, 1\}^\lambda \times X \rightarrow Y\) be a function, \(\mathsf{s} \rightarrow \mathsf{S}\) be the operation of assigning to \(s\) an element of \(S\) chosen at random, \(\mathsf{Fun}(X, Y)\) denote the set of all functions from \(X\) to \(Y\), \(\mathsf{Adv}_{PRF, \mathcal{A}}(\lambda) = \Pr[\hat{F}^{(K, \cdot)}(1^\lambda) = 1] - \Pr[\hat{F}^{(\mathcal{K} \cdot)}(1^\lambda) = 1] \leq \mathsf{negl}(\lambda)\), where the probability is over the randomness of \(A\). \(K \overset{\$}{\rightarrow} \{0, 1\}^\lambda\), and \(\mathsf{f} \overset{\$}{\rightarrow} \mathsf{Fun}(X, Y)\).

3) Bloom Filter: A Bloom filter BF [36] is a probabilistic data structure used to test the membership of an element in a set of \(N\) elements. The idea is to select \(k\) independent hash functions, \(\{H_i\}_{1 \leq i \leq k}\). The Bloom filter consists of an \(m\)-bit binary vector,
all bits set to 0. The bits at positions \( \{ H_i(n) \}_{1 \leq i \leq k} \) are modified to 1 for each element \( n \) in the set, in order to set up BF for the set. We search if \( b \) has 1’s in all positions \( \{ H_i(q) \}_{1 \leq i \leq k} \) to verify membership of \( q \) in the set and if so, we infer \( q \) is in the set with a high probability. Otherwise, \( q \) is not in the set with probability 1. There are possible false-positive matches when \( q \) is not in the set, and yet the membership test returns 1. The false-positive probability for \( q \) over a uniformly random choice of \( \{ H_i \}_{1 \leq i \leq k} \) is: \( P_e \leq (1 - e^{-k/N/m})^k \). We use the Bloom filter to keep a part of encrypted database in a small fraction of RAM on the server.

### III. System Design and Security Model

In this section, first, the used notations are given and then, a general architecture of PrivGenDB, and threat model is illustrated. Finally, privacy requirements and security definitions are discussed.

#### A. Notations

Frequently used notations in this paper are listed in Table III.

| Notation | Description |
|----------|-------------|
| ID\(_O\) | Data Owner’s unique ID |
| ID\(_D\) | Encrypted Data Owner’s ID |
| \( \Theta_s \) | The set of all SNP indexes \( s \) |
| \( G_s \) | \( \{ g \in s \mid \theta_s \in \Theta_s \} \) |
| \( C_s \) | The set of all keywords \( g \) related to phenotypes |
| \( G_D \) | \( \{ g \in \Theta_s \mid \theta_s \in \Theta_s \} \) |
| \( GDB(g) = \{ ID_O : g \in ID_O \} \) | List of all keys ID\(_O\) has, which defines the \( g \) in the database |
| \( GDB \) | Genotype-Phenotype Database |
| \( EDB \) | Encrypted Genotype-Phenotype Database |
| \( \varnothing \) | The least frequent \( g \) among predicates in the query |
| \( \{ g \} \) | Other predicates \( g \) in the query (except \( \varnothing \)) |

#### B. System Design Overview

The proposed system is composed of different entities, as shown in Fig. 1. Their functions are described as follows:

- **Data owner (O):** A data owner is a person whose data is gathered. When a data owner arrives at a medical institution like a gene trustee, as a study participant or a patient, her data is collected and recorded while her consent is given to the trustee to use her genome data for future research or treatment.
- **Data provider or Trustee (T):** A medical institution, such as gene trustees, acts as a data provider in PrivGenDB. \( T \) keeps a list of collected genome data with consent related to them. We assume that the data provider is trustworthy. The main responsibilities of this entity are: (i) encoding data and generating an inverted index, (ii) encrypting the generated inverted index, (iii) managing the cryptographic keys.

#### C. Privacy Patterns/Requirements

The following privacy patterns can be defined when outsourcing genomic data and conducting different queries against it [17]:

- **Data Privacy (DP):** the genomic data stored in the cloud server should be protected, and no information about the data should be leaked. The confidentiality of the data should be preserved, even though the cloud server is compromised.
- **Query Privacy (QP):** entities such as the cloud server, data owners, and the compromised server should not learn anything beyond what is predicted about the query, which is executed by a researcher/clinician.
- **Output Privacy (OP):** the result of the query should not be revealed to other entities except the intended recipient.
The purposes behind requiring these privacy patterns are: (i) to protect the individuals’ data from data server or any other entity trying to get their information (DP), (ii) to preserve the clinicians’ patients’ records or analysts’ research objectives from the server (QP), and (iii) to provide privacy for individuals whose records are retrieved and privacy for analystsclinicians’ objectives (OP).

For privacy leakage through output, some privacy policies through V can be considered, like defining threshold for the count query output or referring to a logbook for checking the queries already submitted to the system by a particular user not to let her conduct another particular query. These policy decisions can be made by the organisation and limit the privacy leakage, which can be gained through output results. This part is out of the scope of this research. We discuss leakages to the $U$ in Section III-D.

D. Security Definitions of Our Protocol

Here, we discuss the security definitions for our model and its leakage profile $L = \{L_D, L_U\}$.

1) Privacy against Data Server: The security definition of our protocol, $\Pi_G$, is parameterised by a leakage function $L_D$ (knowledge about the database and queries gained by the data server $D$ through interaction with a secure scheme). This shows $D$’s view in an adaptive attack (database and queries are selected by $D$) can be simulated using only the output of $L_D$. Below, we define a real experiment $\text{Real}^{\Pi_G}_A(\lambda)$ and an ideal experiment $\text{Ideal}^{\Pi_G}_A, Sim(\lambda)$ for an adversary $A$ and a simulator $Sim$, respectively:

$\text{Real}^{\Pi_G}_A(\lambda)$ chooses a DDB and a list of queries $q$. The experiment then runs $(K, \text{EGDB}) \leftarrow \text{Initialisation}(\lambda, \text{DDB})$ and gives EGDB to $A$. Then $A$ repeatedly chooses a query $q^i(\lambda)$. The experiment runs the algorithm $\text{QEncode}$ on input $q^i(\lambda)$ to get $q^i(g)$ and $\text{TokGen}$ on inputs $(q^i(g), K)$, and returns search tokens to $A$. Eventually, $A$ returns a bit that experiment uses as its output.

$\text{Ideal}^{\Pi_G}_A, Sim(\lambda)$: The game starts by setting a counter $i = 0$ and an empty list $q$. $A(1^\lambda)$ chooses a DDB and a query list $q$. The experiment runs $\text{EGDB} \leftarrow \text{Sim}(L_D(\lambda), \text{DDB})$ and gives EGDB to $A$. Then, $A$ repeatedly chooses a query $q$. To respond, the experiment records this query as $q^i$, increments $i$ and gives the output of $\text{Sim}(L_D(\lambda), q^i)$ to $A$. where $q$ consists of all previous queries as well as the latest query issued by $A$. Eventually, the experiment outputs the bit that $A$ returns.

Definition 1 (Leakage to Data Server): We define $L_D^{\Pi_G}(\lambda, \text{DDB}, q)$ of our scheme for $\text{DDB} = \{(\text{ID}_D, g)\}$, $r$ equals number of Data Owners and $q = (g_1, g_2, ..., g_r)$, where $g_1$ is the sterm and $g_x$ is the sters in the query, as a tuple $(N, s, SP, RP, IP, XP, QT, NP)$, where the first six components are exactly those appeared in the leakage function of [34] and the last two components are:

- QT (Query Threshold): is equal to $k$ which is the threshold given to $D$ in the token so that $D$ can respond to the $k'$-out-of-$k$ query.

- NP (Negation Pattern): The number of negated and non-negated predicates $g$, which are sters $g_x$ in the query, and will be sent in two different tokens $\text{gToken}_1$ and $\text{gToken}_2$ to the data server.

Remark 2: The first six leakages mentioned in $L_D^{\Pi_G}(\lambda, \text{DDB}, q)$ are derived from OXT leakage in [34]. The other ones are minor leakages related to the fact that SSE is being exploited in a different way in our protocol and our scheme supports other queries on the genomic dataset.

Definition 2 (Security): The protocol $\Pi_G$ is called $L_D$-semantically-secure against adaptive attacks if for all adversaries $\mathcal{A}$ there exists an efficient algorithm $Sim$ such that $Pr[\text{Real}^{\Pi_G}_A(\lambda) = 1] - \text{Pr}[\text{Ideal}^{\Pi_G}_A, Sim(\lambda) = 1] \leq \text{neg}(\lambda)$.

2) Data Server Content Privacy against Users: We define the leakage to the defined users in each query execution as the final output, which is vetted and is revealed to the users.

Definition 3 (Leakage to Users): For each users’ class (analystsclinicians), $L_U(\lambda, \text{DDB})$ is defined as they are allowed to conduct different queries. The leakages to the analysts and clinicians are denoted by (CN) and (CN, DOR), respectively and defined as:

- CN (Count Number): is equal to the number of data owners whose genomic/phenotypic data matches the predicates in the query.

- DOR (Data Owner Record): is the records of patients that contains some individual information of that patient when it needs to be given to the clinician for treatment purposes.

IV. PRIVGENDB: PRIVACY-PRESERVING QUERY EXECUTIONS ON GENOMIC DATA

This section provides a detailed architecture of PrivGenDB with the designed algorithms. PrivGenDB consists of four phases: $\Pi_G = (\text{PrivGenDB.Initialisation}, \text{PrivGenDB.QuerySubmission}, \text{PrivGenDB.Search}, \text{PrivGenDB.ResGeneration})$. The sequence diagram of our proposed model is depicted in Fig. 2 which summarizes the steps of our model.

![Sequence diagram of PrivGenDB](image)

PrivGenDB.Initialisation($\lambda, \text{DDB}$): This process is depicted in Algorithm 1. The Trustee $T$ runs this algorithm. Given security parameter $\lambda$ and a genotype-phenotype database DDB containing genotypes $\Theta$ for each SNP$_s$, phenotypes $\in \Theta_p$, other information $\in \Theta_D$, this algorithm outputs the encrypted database EGDB.

This algorithm uses following sub-algorithms:

- GeEncode(DDB): $T$ generates the keywords $g \in G_s$ by concatenating the index of SNP to each $\Theta_s, g = s | \theta_s$. For example, based on Table 1 there would be three defined keywords for SNP$_1$, those are: IAG, IGG, IAA. When $T$ receives the blood samples, sequences it and extracts the variations from it, creates a table like Table 1. Apart from the genotype for each SNP, $T$ collects other information of the data owner, including phenotype, gender, and ethnicity. The $T$ also creates $G_p$ for
Algorithm 1 PrivGenDB.Initialisation

PrivGenDB.Initialisation(λ, GDB)
Input : λ, GDB
Output : EGDB, K

1: G ← GeEncode(GDB)
2: INNX ← Blmv(G, GDB)
3: (EGDB, K) ← EGDB.Setup(λ, INNX, GDB)
4: T russe outsources EGDB to the D.
5: T russe sends K = (K_S, K_X, K_f, K_Z, K_P) to the Vetter.

GeEncode(GDB)
Input : GDB
Output : G
1: k ← the number of SNPs in GDB
2: for S = 1, ..., k do
3: G_s ← {} //for non-negated terms
4: for each distinct genotype θ_s in column:“SNP_s” do //for negated terms
5: generate g = s|θ_s
6: G_s ← G_s ∪ g
7: end for
8: end for
9: G ← {G_s} s∈S ∪ G_o ∪ G_s.

Blmv(G, GDB)
Input : G, GDB
Output : G

1: Initialize INNX to an empty array indexed by keywords in G
2: for each keyword g ∈ G do
3: Output (g, IDO)
4: end for
5: for each keyword g ∈ G do
6: for all IDO appended to g do
7: GDB(g) ← IDO
8: end for
9: INNX ← (g, (GDB(g)))
10: end for
11: return INNX

EGDB.Setup(λ, INNX)
Input : λ, INNX
Output : EGDB, K

1: Select key K_S for PRF F and keys K_X, K_f, K_Z for PRF F_P using security parameters λ, and G a group of prime order p and generator h.
2: Parse GDB as (IDO, g) and S_G ← {}
3: for g ∈ G do
4: Initialize inv ← {}; and let K_e ← F(K_S, g).
5: for IDO ∈ GDB(g) do
6: Set a counter c ← 1
7: Compute XIDQ ← F_P(K_f, IDO), z ← F_P(K_Z, g|c); y ← XIDQ−1, IDO P ← E(P, IDO). Do
8: Set τ g ← h F_P(XIDQ−1, IDO) and S_G ← S_G ∪ τ g
9: Append (y, IDO) to inv and c ← c + 1.
10: end for
11: INNX[g] ← inv
12: end for
13: Set (InvG, K_f) ← TSet.Setup(INNX) and let EGDB = (InvG, S_G).
14: return EGDB and K = (K_S, K_X, K_f, K_Z, K_P)

Algorithm 2 PrivGenDB.QuerySubmission

PrivGenDB.QuerySubmission(I U, q(g1, ..., g_k), K)
Input : I U, q(g1, ..., g_k), K
Output : gToK, γ

1: b ← ReqV(I U, q(g1, ..., g_k))
2: if b then
3: q(g1, ..., g_k) ← QEncode(q(g1, ..., g_k))
4: (gToK, γ) ← TokGen(q(g1, ..., g_k), K)
5: Vetter sends gToK to D.
6: end if
7: else reject the request and inform the I U

TokGen(q(g1, ..., g_k), K)
Input : q(g1, ..., g_k), K
Output : q(g1, ..., g_k), K

1: Computes τ g ← TSet.GetTag(K_f, q1).
2: V sends τ g to D.
// Based on the type of the query, V generates gToK:
  BooleanCount, k' out-of-k match Query

phenotype and G_Δ for other columns containing information, like gender and ethnicity. For example, for Table II we have: {G_s}_s∈S = {1A, 1A, 1G, 1G, 2C, 2C, 3C, 3C, 2C, 3T, 3T, 4A, 4A, 4G, 4G}, G_o = {Cancer A, Cancer B, Cancer C}.

Blmv(G, GDB): T runs this algorithm, which takes the keywords in G and the database GDB to generate an inverted index INNX. This generates the pairs of (g, IDO) for all the keywords g ∈ G = {G_s}_s∈S ∪ G_o ∪ G_Δ.

EGDB.Setup(λ, INNX, GDB): T executes this algorithm that takes the security parameter λ, generated inverted index INNX, and the database GDB as inputs and outputs the encrypted database EGDB = (InvG, S_G) along with the set of keys, K. The InvG is an array that presents equal-sized lists for each g that has been defined and created, and the S_G is a lookup table that contains elements computed from each (g, IDO) pair. For encrypting IDO, which is the ID of the data owner, a key has been generated by using a PRF function to generate a key for each keyword g and use that key for all IDO having that particular g. The EGDB is stored in the D, and the keys are sent to the V to generate tokens for the search. In this algorithm, we run TSet.Setup(INNX), which resembles TSet Setup phase of the OXT scheme [34].

PrivGenDB.QuerySubmission(I U, q(g1, ..., g_k), K): I U runs this algorithm (see Algorithm 2), which takes the query q, the key set K and user I U as inputs, and outputs the search token gToK by running below algorithms:

1: ReqV(I U, q(g1, ..., g_k)): I U authorizes the access of the I U and also checks the query legitimacy. This algorithm outputs bit b = 1 if I U is allowed to execute the submitted query q and b = 0 otherwise. PrivGenDB supports queries from researchers.
(who are interested in statistical analysis) and clinicians (who want to treat diseases of their patients or diagnose and prevent diseases by personalised medicine). Therefore, in this phase, $\mathcal{V}$ checks the accessibility of researchers and clinicians and lets them execute their related queries.

- **QE Encode** ($q_1, \ldots, g_n$): Based on the predicates in the query $q$, the $\mathcal{V}$ generates the keywords for sending to $\mathcal{D}$. The predicates related to the genotypes for SNPs will be encoded, and the new query will be generated as $q[g_1, \ldots, g_n]$. Query encoding happens similar to the Initialisation phase. As an example, let the query be: Select count from sequences where: SNP = CC and SNP = AG and diagnoses = CancerB. This is encoded to: $q_1 = 2\text{CC}$ and $q_2 = 4\text{AG}$ and $q_3 = \text{CancerB}$.

- **Tok Gen** $(q_1, \ldots, g_n, K)$: This algorithm takes the new query predicates and the key set as inputs, so it generates the token for the search, gToK. The TSet.GetTag($K_T$, $g_1$) from TSet in OXT [34] is invoked here. $\mathcal{V}$ generates tokens as follows:
  - $\tau_0$ is generated based on the least frequent term, which in our database is the phenotype as $g_1$.
  - $\gamma$ is sent to $\mathcal{D}$ to let it process the queries based on their corresponding type.
  - For count/Boolean queries, one token is generated for non-negated requested genotypes/phenotypes/other information, and one token is generated for negated terms.
  - For $k$-out-of-$k$ match query, $\mathcal{V}$ generates one token, since there are no negated terms and the process is just to check the number of matches based on some threshold ($k'$). Alongside the token and $\gamma$, $k'$ is also sent to $\mathcal{D}$.

PrivGenDB. Search(gToK, EGDB): This algorithm takes the search token gToK and the encrypted database EGDB as inputs, then outputs the search result. Based on different tokens as the input for different queries (Boolean/Count/k-out-of-k), the $\mathcal{D}$ performs different processes and outputs the result of the query. The TSet.Retrieve($\text{Inv}_{G}$, $\tau_0$) is used here, which resembles TSet in OXT scheme [34]. The whole process is described in Algorithm 3 (for Boolean/Count queries, please only follow the blue and black lines and for k-out-of-k, please read the black and red lines.)

PrivGenDB. ResGeneration($\text{RSet}$/ $\text{RSet}[g_1], T, K)$: The $\mathcal{V}$ runs this algorithm by getting the result input (based on the query and its result searched by $\mathcal{D}$) and outputs ResG which will be sent to the $\mathcal{U}$. If the output of Search algorithm is a set, the two algorithms Retrieve and OutV1 will be executed by the $\mathcal{V}$. If the output is a number, then the $\mathcal{V}$ runs the OutV2 algorithm, see Algorithm 4.

- **Retrieve** ($\text{RSet}, g_1, K$): This algorithm takes the RSet and $g_1$ as inputs and outputs the set of ID$_{\mathcal{D}}$ by decrypting all the ID$_{\mathcal{D}}$ in the RSet and puts them in a new set IDSet.

- **OutV1**($\text{IDSet}$): This algorithm takes the IDSet as the input and retrieve information based on the executed IDs, if needed. Then, the vetter puts the result in ResG and sends it to the User.

- **OutV2**($\text{RSet}, T$): This algorithm is executed when the output of the search is the number of matched records with the predicates in the query. The input of this algorithm is $\text{RSet}$ and $T$ which is the threshold for the output. So, the $\mathcal{V}$ checks the output based on the possessed threshold and put the result in ResG and sends it to the User if it satisfies the threshold.

**V. Security Analysis**

In this section, we prove the security of our protocol against honest-but-curious data server and the compromised users.

---

4Different authentication/authorization mechanisms exist that can be utilised in this model, but discussing them is out of the scope of this work.
Algorithm 3 PrivGenDB.Search

PrivGenDB.Search(gToK, EGDB)
Input: gToK, EGDB
Output: RSet
D performs the search based on input γ
1: RSet ← {} 10: j ← 0
2: inv ← TSet.Retrieve((invG, Tπ)) 11: for i = 2, . . . , n do
3: for c = 1, . . . , |inv| do 12: if gToken[c, i] ∈ SG then
4: Retrieve (ID|γ, y) from the c-th tuple in inv 13: j ← j + 1
5: if γ = 1 or 2 then 14: end if
6: if gToken1[c, i] ∈ SG for all i = 2, . . . , n in gToken1 and 15: end for
7: RSet ← RSet ∪ {ID|γ} 16: if j ≥ k′ then
8: end if 17: Res ← Res ∪ {ID|γ}
9: else 18: end if

Algorithm 4 PrivGenDB.ResGeneration

PrivGenDB.ResGeneration(RSet\{RSet\}, g1, T, K)
Input: RSet\{RSet\}, g1, T, K
Output: ResG
The V performs:
1: if the output is a set RSet then 5: IDSet ← IDSet ∪ {ID|γ}
2: IDSet ← Retrieve(RSet, g1, K) 6: end for
3: ResG ← OutV1(IDSet) 7: return IDSet
4: end if
8: OutV2(RSet, T) 9: Vetter sends ResG to the User

Retrieve(RSet, g1, K)
Input: RSet, g1, K
Output: IDSet
1: IDSet ← {} 5: IDSet ← IDSet ∪ {ID|γ}
2: Vetter sets Kc ← F(Kg, g1) 6: end for
3: for each ID|γ ∈ RSet received do 7: return IDSet
4: Compute ID|γ ← Dec(Kc, ID|γ)

\begin{align*}
\Pr\left(\text{Real}_{A} = 1\right) - \Pr\left(\text{Ideal}_{A} = 1\right) & \leq \\
\Pr\left(\text{Real}_{OXT} = 1\right) - \Pr\left(\text{Ideal}_{OXT} = 1\right) & \leq \text{negl}
\end{align*}

Therefore, since OXT is secure and its advantage is negligible, our protocol’s advantage is negligible.

VI. ANALYTICAL PERFORMANCE COMPARISON

This section presents the performance comparison of our PrivGenDB with existing related works from different perspectives. The overall comparison is presented in Table IV.

Remark 3: In terms of functionality, our model is independent of the authentication method that can be used in PrivGenDB. Therefore, to calculate the computational cost of PrivGenDB, initialisation, building the inverted index, and encrypting the database are considered. The token generation of PrivGenDB, query submission phase in our model has been considered as the search (Vetter) complexity, and the whole PrivGenDB search phase of our model has been considered as search (Data Server) complexity.

A. Initialisation Computational Cost

In the initialisation/setup phase of all the schemes in Table IV except [17], the computational cost is in the order of the number of records (r) multiplied by the number of columns in the original database, x (which is the number of SNPs + 1 for phenotype + the number of other characteristics if they support, e.g., gender, ethnicity) [18]–[21]. The tree structure proposed in [17] needs the encryption of all nodes in the setup phase. The number of nodes increases by the number of SNPs. As acknowledged by the author of [17], in our correspondence, if the number of records in the database increases, the number of nodes increases as well. We also assume that each SNP can have three possibilities of genotypes, and when the number of records increases, the possibility of having a new genotype for the SNPs increases. This assumption is completely dependent on the genotypes distribution in the dataset. The computational complexity of PrivGenDB in this phase is in the order of \(rx\). All methods in Table IV are linear in \(rx\), except [20] which does not encrypt all the data and [17] which depends on the number of nodes (increases by \(x\) and \(r\)). The proposed methods in [23], [24] have the same computation/communication complexities’ behavior as that of [17], since they proposed their scheme based on the index tree in [17], with some added functionality or improvements.

B. Search Computational Cost

The computational costs are split between the client/trusted-entity/vetter and the server during the search process. In PrivGenDB, the vetter represents the client, as it is the entity that interacts with the server to perform the search against the database. As it is obvious from the Table IV the computational cost of the search through server is in the order of the number of records in [18]–[21]. Based on the index tree proposed in [17], their scheme’s search cost depends mostly on the number of SNPs. However, increasing the number of records also increases the number of nodes in their index tree to cover all the genotype possibilities (it is discussed in part A as well). PrivGenDB’s search complexity depends on the number of IDs that match the first predicate in the
query ($\alpha$). As the phenotype was selected as the first predicate, which is the least frequent term in our database, PrivGenDB’s search complexity is sublinear to the number of records in the database. This implies that, even by increasing the number of records, if the number of matched records to the first predicate (or phenotype) does not change, the search complexity remains unchanged.

1. **Storage Size**

We now investigate the storage size of PrivGenDB and compare it to other schemes. PrivGenDB stores $\text{InvG}$ and the Bloom filter of $\mathcal{G}$ in EDBG, while [18]–[21] store the encrypted data and [17] stores the encrypted tree in the database. The size of $\text{InvG}$ equals $rx(T_D + T_F + \ell_T)$, which is the number of pairs $((y, \text{ID}_D$ in the construction)], multiplied by the size of each pair. The size of Bloom filter $m$ is approximately $1.44 - kr \times x$ to attain a negligible probability of false-positives. Other schemes’ storage size also depends on $rx$, except [17], which only supports the count query and stores the counts in the tree and depends on the number of nodes.

2. **Interaction Rounds and Bandwidth**

In PrivGenDB, the first interaction between the $\mathcal{V}$ and the $\mathcal{D}$ happens when the $\mathcal{V}$ sends the search tokens to the $\mathcal{D}$. Based on the type of the submitted query and its size, the size of the result sent to the $\mathcal{V}$ differs, which defines the next interaction. Therefore, when the $\mathcal{V}$ generates the $\tau_p$, sends it to the $\mathcal{D}$. Then, depending on the number of retrieved IDs for the $\tau_p$, the $\mathcal{V}$ generates the $G$token and sends them to $\mathcal{D}$, which checks a set membership against $\mathcal{S}_G$. Communication overhead in [17] depends on the number of nodes that need to be accessed during the search to perform the query.

### VII. EXPERIMENTAL RESULTS

This section presents the implementation results of PrivGenDB with a different number of records/SNPs/query-sizes as well as different types of queries. The source code is written in Java programming language, and our machine used to run the code is Intel(R) Core(TM) i7-8850H CPU @ 2.60GHz processors with 32 GB RAM, running Ubuntu Linux 18.04. We consider the following aspects in order to assess the efficiency of our proposed method:

- **Initialisation Time**: $T$ to perform Binv and EGDB.Setup.
- **Query Execution Time**: $\mathcal{V}$ to execute TokGen and $\mathcal{D}$ to run PrivGenDB.Search.
- **Storage Analysis**: Storage space needed to store the database.
- **Communication Overhead**: The data transferred between the $\mathcal{V}$ and the $\mathcal{D}$ to perform the query.

To improve the runtime performance of our implementation, we leverage an in-memory key-value storage Redis [37] to keep the generated $\text{InvG}$ for querying purposes. In addition, we deploy the Bloom filter from Alexandr Nikitin [38] as it is the fastest Bloom filter implementation for JVM. The false-positive rate of the bloom filter is set to $10^{-6}$, which enables our implementation to keep the $\mathcal{S}_G$ in a small fraction of RAM on the server. We used the Java Pairing-Based Cryptography Library (JPBC) [39]. We use both real-life and synthetic datasets for evaluation of PrivGenDB. The real-life data are taken from The Harvard Personal Genome Project (PGP) [40], where we took data of 58 patients with 2,000 SNPs, their phenotype, gender, and ethnicity. These patients have had different types of cancer such as breast, brain, thyroid, uterine, kidney, melanoma, colon, prostate as the phenotype, or they were Covid-19 positive/negative recently. Then, we created several synthetic datasets based on the above mentioned real dataset to evaluate PrivGenDB with a different number of records (500 – 40,000) and different number of SNPs (500 – 2,000).

#### A. Initialisation Time

Initialisation time includes the time needed for generating the inverted index and encrypting it. Genomic data encoding time is negligible. Fig. 4 illustrates the initialisation time of PrivGenDB when the number of SNPs increases or the number of records ($r$) in the dataset increases. The time consumption for the generation of inverted index and encrypting it with 5,000 records, 1,000 SNPs, different phenotypes, gender and ethnicity is around 518 seconds in PrivGenDB, while it is 47 min and 257 min in [17] and [20], respectively. Note that we encrypt all the information in our database to support different queries and this phase is needed to be performed once only.

#### B. Storage Analysis

Since PrivGenDB needs to support different queries and has the capability of retrieving the IDs, it encrypts all the related information and not just the count of different SNPs. Table IV presents the implementation results of PrivGenDB with a different number of records/SNPs/query-sizes as well as different types of queries. The source code is written in Java programming language, and our machine used to run the code is Intel(R) Core(TM) i7-8850H CPU @ 2.60GHz processors with 32 GB RAM, running Ubuntu Linux 18.04. We consider the following aspects in order to assess the efficiency of our proposed method:

- **Initialisation Time**: $T$ to perform Binv and EGDB.Setup.
- **Query Execution Time**: $\mathcal{V}$ to execute TokGen and $\mathcal{D}$ to run PrivGenDB.Search.
- **Storage Analysis**: Storage space needed to store the database.
- **Communication Overhead**: The data transferred between the $\mathcal{V}$ and the $\mathcal{D}$ to perform the query.

To improve the runtime performance of our implementation, we leverage an in-memory key-value storage Redis [37] to keep the generated $\text{InvG}$ for querying purposes. In addition, we deploy the Bloom filter from Alexandr Nikitin [38] as it is the fastest Bloom filter implementation for JVM. The false-positive rate of the bloom filter is set to $10^{-6}$, which enables our implementation to keep the $\mathcal{S}_G$ in a small fraction of RAM on the server. We used the Java Pairing-Based Cryptography Library (JPBC) [39]. We use both real-life and synthetic datasets for evaluation of PrivGenDB. The real-life data are taken from The Harvard Personal Genome Project (PGP) [40], where we took data of 58 patients with 2,000 SNPs, their phenotype, gender, and ethnicity. These patients have had different types of cancer such as breast, brain, thyroid, uterine, kidney, melanoma, colon, prostate as the phenotype, or they were Covid-19 positive/negative recently. Then, we created several synthetic datasets based on the above mentioned real dataset to evaluate PrivGenDB with a different number of records (500 – 40,000) and different number of SNPs (500 – 2,000).

### VII. EXPERIMENTAL RESULTS

This section presents the implementation results of PrivGenDB with a different number of records/SNPs/query-sizes as well as different types of queries. The source code is written in Java programming language, and our machine used to run the code is Intel(R) Core(TM) i7-8850H CPU @ 2.60GHz processors with 32 GB RAM, running Ubuntu Linux 18.04. We consider the following aspects in order to assess the efficiency of our proposed method:

- **Initialisation Time**: $T$ to perform Binv and EGDB.Setup.
- **Query Execution Time**: $\mathcal{V}$ to execute TokGen and $\mathcal{D}$ to run PrivGenDB.Search.
- **Storage Analysis**: Storage space needed to store the database.
- **Communication Overhead**: The data transferred between the $\mathcal{V}$ and the $\mathcal{D}$ to perform the query.

To improve the runtime performance of our implementation, we leverage an in-memory key-value storage Redis [37] to keep the generated $\text{InvG}$ for querying purposes. In addition, we deploy the Bloom filter from Alexandr Nikitin [38] as it is the fastest Bloom filter implementation for JVM. The false-positive rate of the bloom filter is set to $10^{-6}$, which enables our implementation to keep the $\mathcal{S}_G$ in a small fraction of RAM on the server. We used the Java Pairing-Based Cryptography Library (JPBC) [39]. We use both real-life and synthetic datasets for evaluation of PrivGenDB. The real-life data are taken from The Harvard Personal Genome Project (PGP) [40], where we took data of 58 patients with 2,000 SNPs, their phenotype, gender, and ethnicity. These patients have had different types of cancer such as breast, brain, thyroid, uterine, kidney, melanoma, colon, prostate as the phenotype, or they were Covid-19 positive/negative recently. Then, we created several synthetic datasets based on the above mentioned real dataset to evaluate PrivGenDB with a different number of records (500 – 40,000) and different number of SNPs (500 – 2,000).
lists the amount of spaces required to store the original data and encrypted data. The left column represents the number of records in the dataset ranging from 500 to 40,000. The original dataset of size 1.5MB is encrypted to 113.4MB, while it is 188MB in [17]. The expansion in the encrypted tree size of [17] is due to encrypting the data using the Paillier Encryption. It is worth mentioning the growth ratio in the storage overhead (expansion factor) of PrivGenDB is around 80, while it is 180 in [17], and it is in the order of 1024 (key bit length) in [18], [21].

C. Query Execution Time

To calculate the query execution time, we executed a number of queries with different sizes on the encrypted database. The queries we used were determined by randomly selecting 10, 20, 30, and 40 SNP sequences with other information like gender and ethnicity. PrivGenDB works with sublinear search capability, making it a proper solution for large databases. Below, we discuss our results and show our model’s scalability with respect to different characteristics of our database. Retrieve time is negligible.

1) Scalability of PrivGenDB in terms of the number of SNPs: We first experimented the effect of the number of SNPs on the query execution time. As it is obvious from Fig. 5, the time needed to perform a particular query on a dataset with 5,000 records does not change when the number of stored SNPs for each record increases.

2) Scalability of PrivGenDB in terms of the number of records: The search complexity depends on the number of matched IDs to the first predicate (α) in the query, which we selected as phenotype. Therefore, even in a large database, the search complexity is in the order of the number of returned IDs for the phenotype. Fig. 6 illustrates the time taken for a query to be performed on a database when the number of records that match the phenotype differ. This experiment shows the token generation and search time depend only on α.

To explicitly show the scalability of PrivGenDB, we explored the query execution time on datasets with 500, 1,000, and 1,500 records, while they have the same number of IDs with particular cancer or Covid19+/. Fig. 7a represents different datasets with the same number of records for some phenotypes. Fig. 7b shows that, for example, when the query’s first predicate is thyroid cancer in \( r = 1,000 \) and \( r = 1,500 \) database, the search complexity is the same since both have 250 records with this disease. Moreover, the number of records with brain cancer is 50 in all three datasets, and it is obvious from Fig. 7b that the token generation time and search time is the same in these three datasets.

3) Scalability of PrivGenDB in terms of \( k' \)-out-of-\( k \) match query for one patient: Our experiments show that the query execution time for conducting \( k' \)-out-of-\( k \) match query for a particular patient, when a clinician is interested, is mostly dependent on the time taken for the \( D \) to search for the ID in \( S_G \), which is the first predicate in this query. Token generation on \( V \) side and checking the genotypes on \( D \) side depends on the query size, but the whole process takes around 70\( \mu \)seconds (see Fig. 8).

4) Performance comparison: Table VI compares the query execution time of PrivGenDB with [17]–[20]. The times of [17]–[20] are reported directly from their original paper. The query execution time of our model depends mostly on the number of records matching the first predicate (α), which is the phenotype in our model, whereas it is linear to the number of records (\( r \)) for [18]–[20] and linear to the number of SNPs in [17]. In comparison to [17], which is the only other model that supports storing the phenotype in the database, PrivGenDB takes only 5.2 seconds to execute a query of size 50 on our 5,000 database. It is worth mentioning that it may take less time if the number of IDs that match a phenotype is less than that in the experiment. Whereas, [17] takes around 130 seconds to execute the query on the encrypted tree structure. The query execution time in [21] is in the order of the number of records stored in the data server.
Fig. 6. Query execution time on dataset with 40,000 records in total (different number of records satisfy the phenotype in the query).

Fig. 7. Query execution time on different datasets with same number of records satisfy the phenotype in the query.

Fig. 8. $k'$-out-of-$k$ match query execution time for one patient on dataset with 5,000 records and 1,000 SNPs.

D. Communication Overhead

The amount of data transferred between the $D$ and the $V$ is depicted in Fig. 9. This is the data amount to execute the query with different query sizes while $\alpha$ changes. This overhead increases if the query size ($n$) or the number of records match the phenotype ($\alpha$) increase, which defines the tokens generated by $V$ and transmitted to the $D$ for searching. Both the query execution time and communication cost generally depend on these two parameters, linearly. Query privacy is not provided in [21], and [20] does not encrypt the query. This overhead increases linearly if the number of nodes need to be accessed to perform a query increase in [17], and increases linearly by the number of records in [18], [19].

VIII. Conclusion and Future Works

In this paper, we proposed a new secure and efficient model, named PrivGenDB, for outsourcing Single Nucleotide Polymorphism (SNP)-Phenotype data to the cloud server. To the best of our knowledge, PrivGenDB is the first model that ensures the confidentiality of shared SNP-phenotype data by employing searchable symmetric encryption (SSE) and makes the computation/query process efficient. PrivGenDB constructs an inverted index using a novel encoding mechanism for genotypes, phenotypes, gender, and ethnicity; then encrypts it. By employing SSE, the vetter can generate tokens, and the data server can execute different query operations. We have compared PrivGenDB to the state-of-the-art privacy-preserving query executions on SNP-Phenotype data both analytically and numerically. Our experimental results on real and synthetic data demonstrate that the proposed model outperforms the existing schemes in terms of query execution time.

Similar to the other existing related works, PrivGenDB has some leakages that might lead to vulnerabilities to some attacks (e.g., statistical attacks). This can be avoided by countermeasures like adding noise to hide the search frequencies. We leave studying
them as a future work. Finally, PrivGenDB is flexible to support consent, which we can further take into consideration as another promising research direction.

**REFERENCES**

[1] C. Sudlow, J. Gallacher, N. AllenSudlow, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med.*, 12, e1001779, Mar. 2015.

[2] C. Bycroft, C. Freeman, D. Petkova, et al. The UK Biobank resource with deep phenotyping and genomic data. *Nature*, 2018.

[3] NIH All of Us Research Program. [https://allofus.nih.gov/](https://allofus.nih.gov/)

[4] Million Veteran Program (MVP). [https://www.mvp.va.gov/](https://www.mvp.va.gov/)

[5] PM. Visscher, NR. Wray, Q. Zhang, P. Sklar, MI. McCarthy, MA. Brown, J. Yang. 10 Years of GWAS: Discovery, Biology, Function, and Translation. *The American Journal of Human Genetics*, 101:5-22, 2017.

[6] G. Ginsburg, KA. Phillips. Precision medicine: from science to value. *Health Aff (Millwood)*, pages 694-701, 2018.

[7] Y. Al-Issa, MA. Ottom, A. Tamrawi. ehealth cloud security challenges: A survey. *Journal of healthcare engineering*, 2019.

[8] T. Ermakov, B. Fabian, R. Zanneckow. Improving individual acceptance of health clouds through confidentiality assurance. *Appl Clin Inform.*, 2016:7983-93.

[9] A.M.-H. Kuo. Opportunities and challenges of cloud computing to improve health care services. *Journal of Medical Internet Research*, 13(3):e67, Sep. 2011.

[10] Y. Erlich and A. Narayanan. Routes for breaching and protecting genetic privacy. *Nature reviews. Genetics*, 2014, 15(6): 409–21.

[11] Y. Erlich, JB. Williams, D. Glazer, et al. Redefining genomic privacy: trust and empowerment. *PLoS Biol.*, 2014; 12: e1001983.

[12] M. Naveed, E. Ayday, E.W. Clayton, J. Fellay, C.A. Gunter, J.P. Hubaux, B.A. Malin, and X. Wang. Privacy in the genomic era. *ACM Computing Surveys (CSUR)*, 48(1):1–44, 2015.

[13] Guide to hipaa privacy rule and compliance, HIPAA. [http://www.hipaa-101.com/](http://www.hipaa-101.com/)

[14] J. Andreu-Perez, C.C.Y. Poon, R.D. Merrifield, S.T.C. Wong, and G.Z. Yang. Big data for health. *IEEE Journal of Biomedical and Health Informatics*, 19(4):1193–1208, Jul. 2015.

[15] B. Berger and H. Cho. Emerging technologies towards enhancing privacy in genomic data sharing. *Genome Biology*, 20(1), Dec 2019.

[16] M. Gynbrek, A. L. McGuire, D. Golam, E. Halperin, and Y. Erlich. Identifying personal genomes by surname inference. *Science*, 339(6177):321–324, Jan. 2013.

[17] M.Z. Hasan, Md.S.R. Mahdi, Md.N. Sadat, and N. Mohammed. Secure count query on encrypted genomic data. *Journal of biomedical informatics*, 81:41–52, 2018.

[18] M. Kantarciglu, W. Jiang, Y. Liu, and B. Malin. A cryptographic approach to securely share and query genomic sequences. *IEEE Trans Inform Technol Biomed*, 12(5):606–617, Sep. 2008.

[19] M. Canim, M. Kantarciglu, and B. Malin. Secure management of biomedical data with cryptographic hardware. *IEEE Trans Inform Technol Biomed*, 16(1):166–175, Jan. 2012.

[20] R. Ghasemi, Md.M. Al Aziz, N. Mohammed, M.H. Dekordi, and X. Jiang. Private and efficient query processing on outsourced genomic databases. *IEEE journal of biomedical and health informatics*, 21(5):1466–1472, 2016.

[21] M. Nassar, Q. Malluhi, M. Atallah, and A. Shikfa. Secure aggregation queries for dna databases. *IEEE Trans. on Cloud Computing*, 2017.

[22] W. Chenghong, Y. Jiang, N. Mohammed, F. Chen, X. Jiang, Md.M. Al Aziz, Md.N. Sadat, and S. Wang. Scotch: Secure counting of encrypted genomic data using a hybrid approach. In *AMIA Annual Symposium Proceedings*, volume 2017, page 1744.

[23] L. Chen, Md M. Aziz, N. Mohammed, X. Jiang. Secure large-scale genome data storage and query. *Computer methods and programs in biomedicine, Elsevier*, Vol. 165, pages 129-137, 2018.

[24] Md.S.R. Mahdi, Md.N. Sadat, and N. Mohammed. X. Jiang. Secure Count Query on Encrypted Heterogeneous Data. 2020 Intl Conf on (DASC/Com/CBDCom/CyberSciTech), pages 548-555, 2020.

[25] R. Zhang, R. Xue, L. Liu. Searchable encryption for healthcare clouds: a survey. *IEEE Transactions on Services Computing, Vol. 11, No. 6*, pages 978-996, 2017.

[26] S. Lai, S. Patranabis, A. Sakzad, J.K. Liu, D. Mukhopadhyay, R. Steinfeld, S. F. Sun, D. Liu, C. Zuo. Result pattern hiding searchable encryption for conjunctive queries. *Proceedings of the 2018 ACM CCS*, pages 745-762, 2018.

[27] S. F. Sun, X. Yuan, J.K. Liu, R. Steinfeld, A. Sakzad, V. Vo, S. Nepal. Practical backward-secure searchable encryption from symmetric puncturable encryption. *Proceedings of the 2018 ACM CCS*, pages 763–780, 2018.

[28] S. Kasa Kermanshahi, J.K. Liu, R. Steinfeld, S. Nepal, S. Lai, R. Loh, C. Zuo. Multi-client Cloud-based Symmetric Searchable Encryption. *IEEE Trans. Dependable Secure Comput.*, 2019.

[29] S. Kasa Kermanshahi, V.F. Sun, J.K. Liu, R. Steinfeld, S. Nepal, W.F. Lau, M.H. Au. Geometric range search on encrypted data with forward/backward security. *IEEE TDSC*, 2020.

[30] Sh. Lai, X. Yuan, Sh. Sun, J.K. Liu, Y. Liu, D. Liu. GraphSE2: An Encrypted Graph Database for Privacy-Preserving Social Search. *Proceedings of the ACM Asia CCS*, 2019.

[31] Sh. Sun, R. Steinfeld, Sh. Lai, X. Yuan, A. Sakzad, J.K. Liu, S. Nepal, D. Gu. Practical Non-Interactive Searchable Encryption with and Backward Privacy. *NDSS Symposium.*, 2021.

[32] Y. Uchide, N. Kunihiro. Searchable symmetric encryption capable of searching for an arbitrary string. *Security and Communication Networks, Vol. 9, No. 12*, pages 1726-1736, 2016.

[33] W. Sun, N. Zhang, W. Lou, Y. Th. Hou. When gene meets cloud: Enabling scalable and efficient range query on encrypted genomic data. *IEEE INFOCOM*, pages 1-9, 2017.

[34] D. Cash, S. Jarecki, C. Jutla, H. Krawczyk, M-C. Roşu, and M. Steiner. Highly-scalable searchable symmetric encryption with support for Boolean queries. In *Annual cryptography conference*, pages 353–373. Springer, 2013.

[35] J. Katz, Y. Lindell. Introduction to modern cryptography book. *CRC press*, 2020.

[36] B H. Bloom. Space/time trade-offs in hash coding with allowable errors. *Communications of the ACM*, Vol. 13, pages 422-426, 1970.

[37] Redis Labs. Redis. [https://redis.io/](https://redis.io/)

[38] A. Nikitin. Bloom Filter Scala. [https://alexandrinikitin.github.io/blog/bloom-filter-for-scala/](https://alexandrinikitin.github.io/blog/bloom-filter-for-scala/)

[39] Angelo De Caro and Vincenzo Iovino. *jpbc: Java pairing based cryptography*. In *ISCC 2011*, pages 850–855. IEEE, 2011.

[40] PersonalGenomes.org. The Personal Genome Project: Harvard Medical School. [https://pgp.med.harvard.edu/data](https://pgp.med.harvard.edu/data) (accessed Dec 2020).