SQUiD: Ultra-Secure Storage and Analysis of Genetic Data for the Advancement of Precision Medicine

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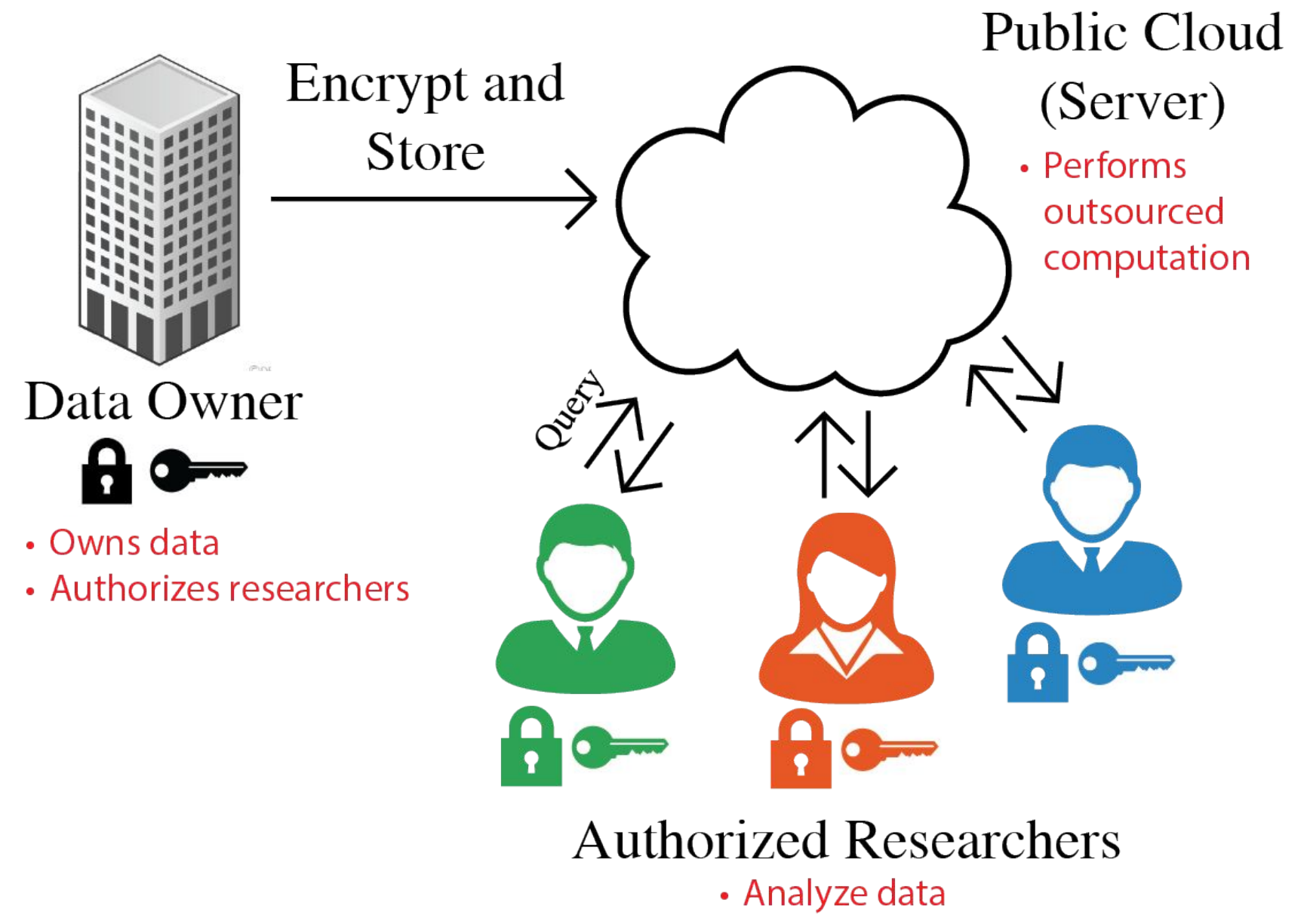
Problem Statement and Goal

- Queryable databases are needed for storing extensive, sensitive patient disease, and genetic information
- Large amount of data necessitates cloud storage, which necessitates strong security measures due to its sensitive nature

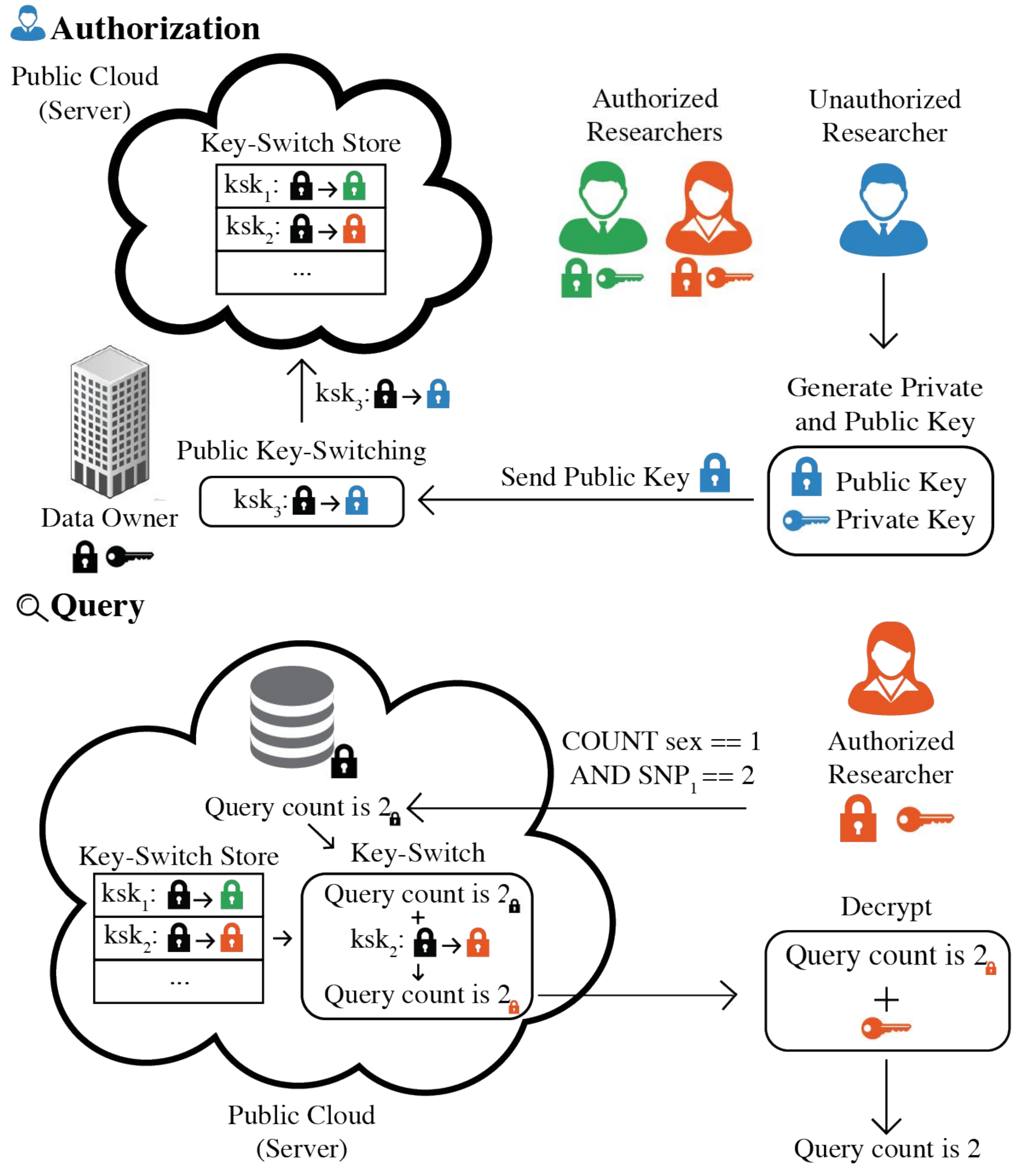
Goal: Ensure the data is secure from both cloud vulnerabilities and unauthorized users, yet accessible for authorized researchers to safely perform queries and analyses

Scenario



- **SQUiD** (**S**ecure **QU**eryable genotype-phenotype **D**atabases) is designed for a multiparty setting with a data owner, a public cloud, and multiple researchers
- SQUiD utilizes homomorphic encryption (HE) to securely compute on the data, which can be stored in the public cloud

Enabling multiparty queries with public key-switching



- We developed a new cryptographic primitive, "public key-switching", to eliminate the sharing and sending of private keys
- Each party generates their own set of keys:

  Public Key
  Private Key

- Only the public key is sent to the data owner to produce a key-switching key
- Key-switching re-encrypts a ciphertext, *ct* into a ciphertext, *ct'* such that the client can decrypt *ct'* with their private key
- Having a key-switching key inside the store, grants the researcher access to the data

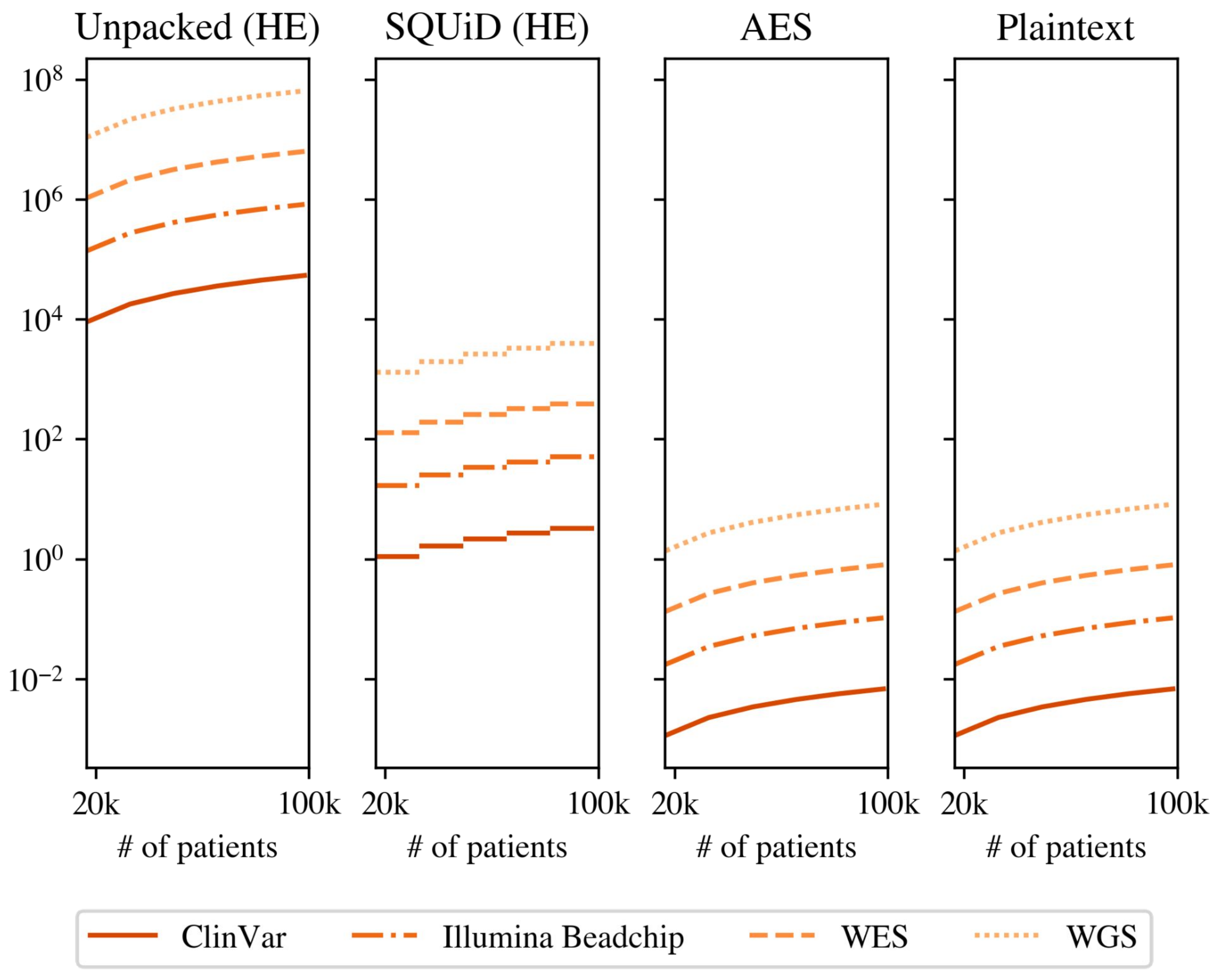
Overcoming high storage costs by utilizing vertical packing

- SQUiD vertically packs columns of genotypes and phenotypes from multiple individuals into single ciphertexts

ID	SNP$_1$	SNP$_2$	⋯	SNP$_K$	sex	smoker	disease
0	0	1	⋯	1	0	0	3
1	1	0	⋯	0	1	1	2
2	0	1	⋯	0	1	0	3
⋮	⋮	⋮		⋮	⋮	⋮	⋮
N	0	0	⋯	2	0	1	0

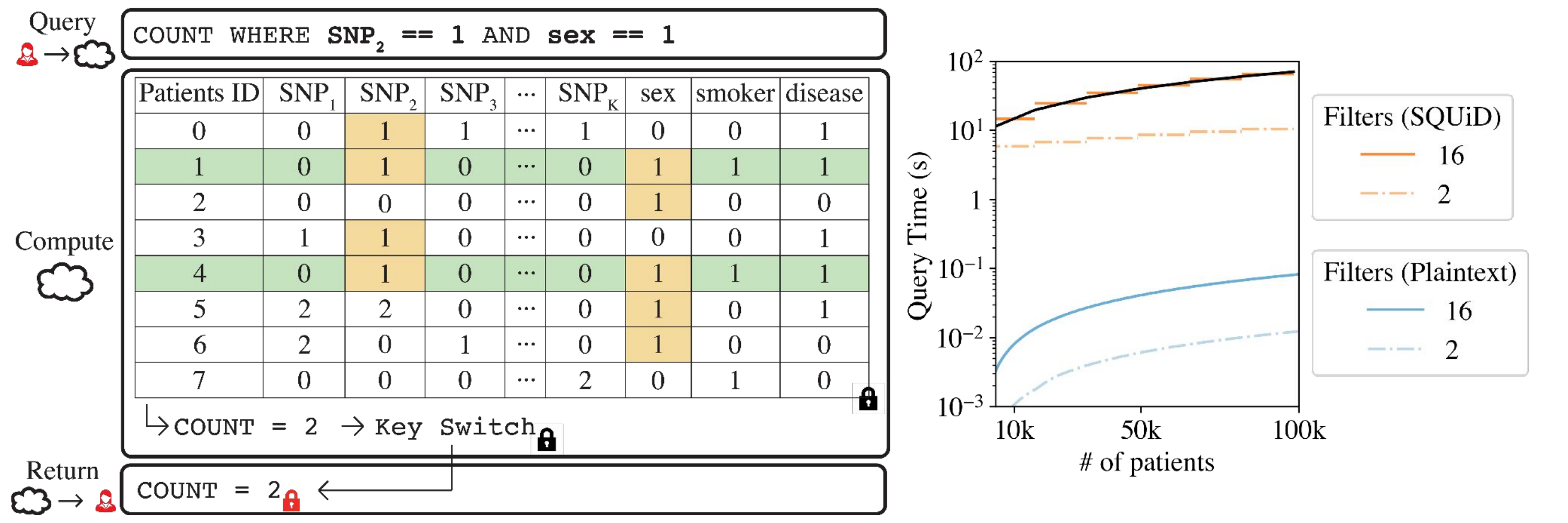
Columns are packed into single ciphertext

ID	SNP$_1$	SNP$_2$	⋯	SNP$_K$	sex	smoker	disease
0	c_0	c_1	⋯	c_{K-1}	c_K	c_{K+1}	c_{K+2}
1							
2							
⋮							
N							



Providing scalable query performance

A - Count Query



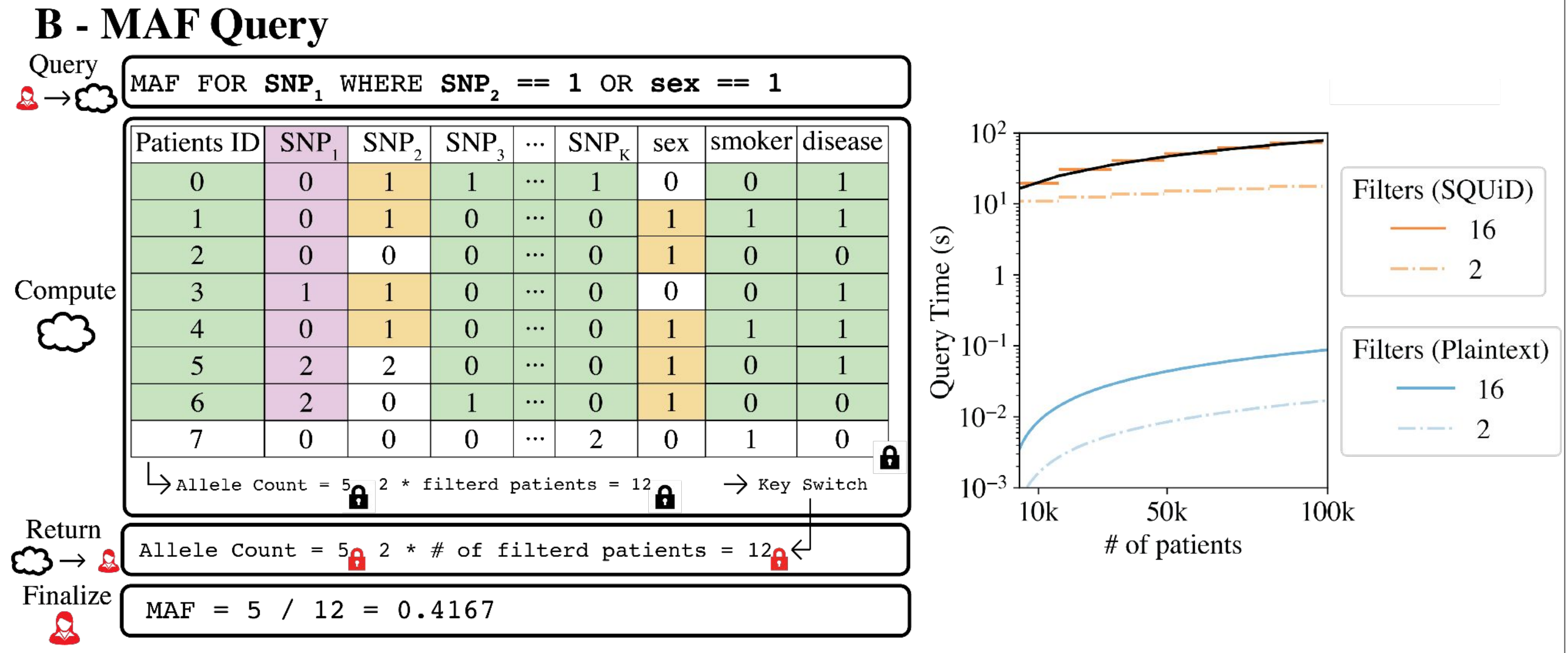
COUNT WHERE **SNP$_2$** == 1 AND **sex** == 1

Patients ID	SNP$_1$	SNP$_2$	SNP$_3$	⋯	SNP$_K$	sex	smoker	disease
0	0	1	1	⋯	1	0	0	1
1	0	1	0	⋯	0	1	1	1
2	0	0	0	⋯	0	1	0	0
3	1	1	0	⋯	0	0	0	1
4	0	1	0	⋯	0	1	1	1
5	2	2	0	⋯	0	1	0	1
6	2	0	1	⋯	0	1	0	0
7	0	0	0	⋯	2	0	1	0

↳COUNT = 2 → Key Switch

COUNT = 2 ←

B - MAF Query



MAF FOR **SNP$_1$** WHERE **SNP$_2$** == 1 OR **sex** == 1

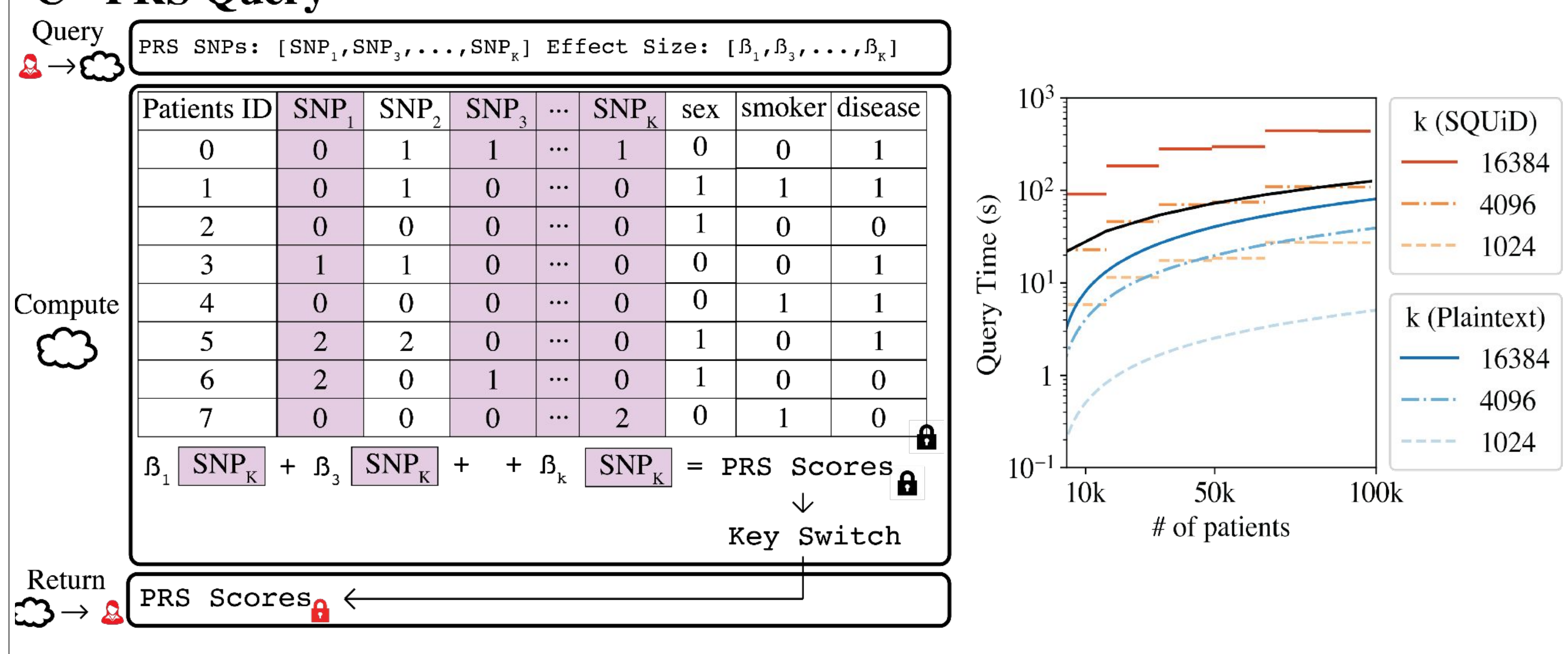
Patients ID	SNP$_1$	SNP$_2$	SNP$_3$	⋯	SNP$_K$	sex	smoker	disease
0	0	1	1	⋯	1	0	0	1
1	0	1	0	⋯	0	1	1	1
2	0	0	0	⋯	0	1	0	0
3	1	1	0	⋯	0	0	0	1
4	0	1	0	⋯	0	1	1	1
5	2	2	0	⋯	0	1	0	1
6	2	0	1	⋯	0	1	0	0
7	0	0	0	⋯	2	0	1	0

↳Allele Count = 5 2 * filterd patients = 12 → Key Switch

Allele Count = 5 2 * # of filterd patients = 12 ←

MAF = 5 / 12 = 0.4167

C - PRS Query



PRS SNPs: [SNP$_1$,SNP$_3$,...,SNP$_K$] Effect Size: [ß$_1$,ß$_3$,...,ß$_K$]

Patients ID	SNP$_1$	SNP$_2$	SNP$_3$	⋯	SNP$_K$	sex	smoker	disease
0	0	1	1	⋯	1	0	0	1
1	0	1	0	⋯	0	1	1	1
2	0	0	0	⋯	0	1	0	0
3	1	1	0	⋯	0	0	0	1
4	0	0	0	⋯	0	0	1	1
5	2	2	0	⋯	0	1	0	1
6	2	0	1	⋯	0	1	0	0
7	0	0	0	⋯	2	0	1	0

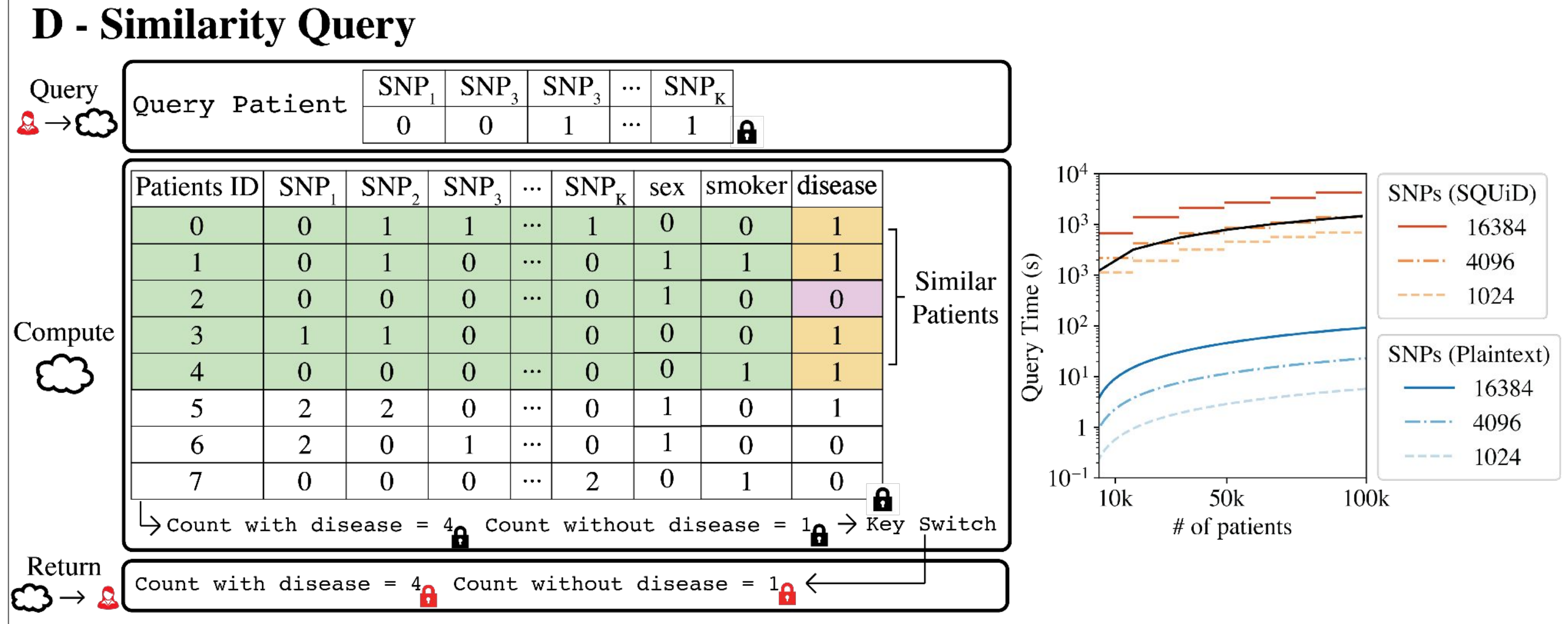
ß$_1$ SNP$_K$ + ß$_3$ SNP$_K$ + + ß$_k$ SNP$_K$ = PRS Scores

↓

Key Switch

PRS Scores ←

D - Similarity Query



Query Patient

SNP$_1$	SNP$_3$	SNP$_3$	⋯	SNP$_K$
0	0	1	⋯	1

Patients ID	SNP$_1$	SNP$_2$	SNP$_3$	⋯	SNP$_K$	sex	smoker	disease
0	0	1	1	⋯	1	0	0	1
1	0	1	0	⋯	0	1	1	1
2	0	0	0	⋯	0	1	0	0
3	1	1	0		0	0	0	1
4	0	0	0	⋯	0	0	1	1
5	2	2	0	⋯	0	1	0	1
6	2	0	1	⋯	0	1	0	0
7	0	0	0	⋯	2	0	1	0

↳Count with disease = 4 Count without disease = 1 → Key Switch

Count with disease = 4 Count without disease = 1 ←

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Github repository of SQUiD with an API for quick deployment: