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OPEN TrialChain: Privacy-Preserving Blockchain Design for Diabetes Clinical Trials Using Open Algorithms

Kim, A. Milan C. Alsalamah, S. and Pentland, A.

Agenda

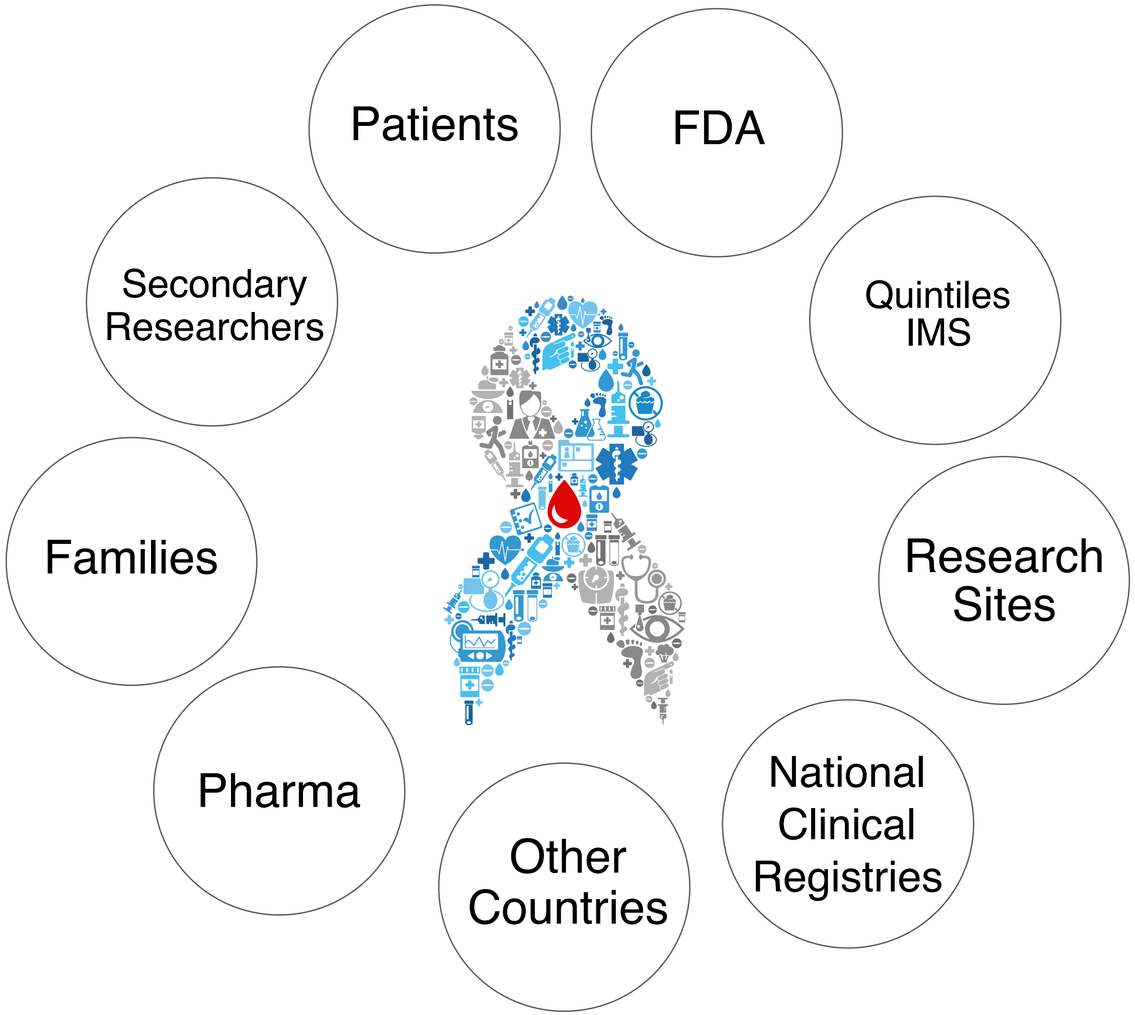
- Clinical Trials
- Clinical Trial Problems
- Type II Diabetes Case Study
- OPEN TrialChain Model
- Adopting OPEN TrialChain
- Challenges

Clinical Trials

Introduction

- Governments and pharmaceutical companies (Pharma) **spend** $100-800 **millions on clinical trials** for each drug candidate, and yet up to 25-50% go **unpublished**.
- Section 801 of the Food and Drug Administration Amendments Act (**FDAAA**) of 2007 requires the **submission** of "**basic results**" for certain clinical trials,
    - The **ambiguity** of “basic results” leads to rather **scant result submissions**.
- It is in the **best interest** of **pharmaceutical** companies to **report** as little as possible
    - Gain a **competitive advantage** over other pharmaceutical companies developing drugs in the same space
    - Maintain **patient privacy**.

Clinical Trials- Ecosystem



Clinical Trials- Ecosystem

- **FDA: Approve all clinical trials (but don't always enforce publication of trials)**
- **Quintiles IMS:** third-party that plans the logistics of clinical trials, and are often the data owners
- **Research Sites:** physical clinics that report patient metrics
- **Other Countries**: if clinical trials are done internationally (to cut cost), countries may intervene in the exportation of the data by order of the General Data Protection Regulation (GDPR)
- **Pharmaceutical companies**: develop the drugs that are being tested. Their IP is on the line and has to be protected
- **Patients**: In the case of GDPR, they have to have revoke access
- **Secondary Researchers**: In order to learn and make retrospective studies on drug development
- **Families**: In the case of pediatric trials, families may be consulted for consent

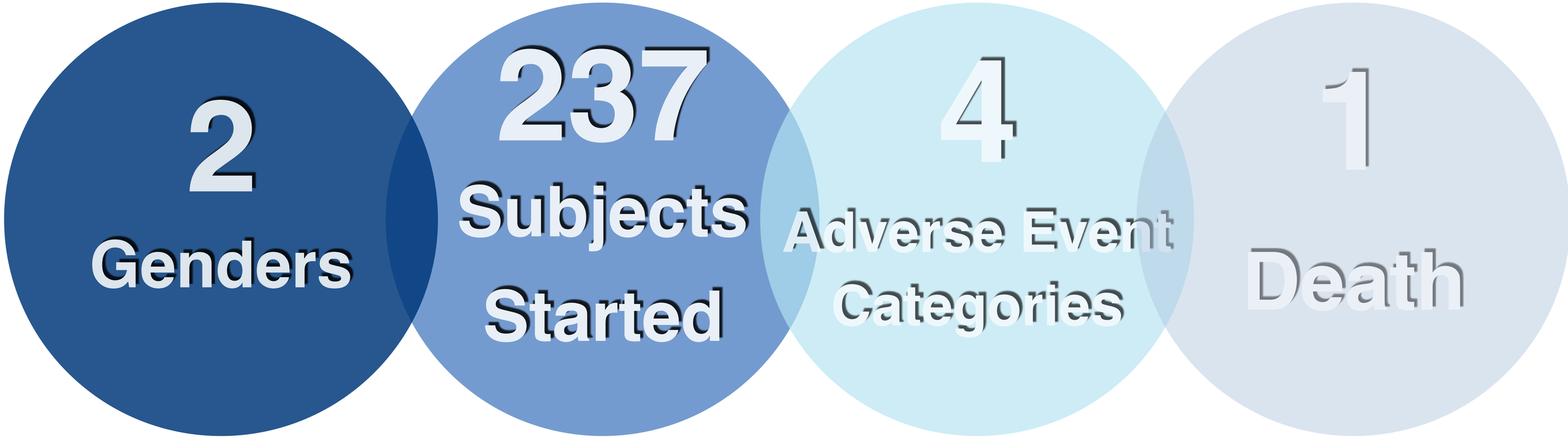
Clinical Trial Problems

Clinical Trial Problems

1. Pharmaceutical companies are **discouraged from publishing** their trial results as they do not want to lose ownership over it.
2. Even when they do publish, **reported results** are **very limited** for competitive advantage.
3. **Underrepresented groups** have **no significance** in the **results** of trials.
4. **Results** are **not illustrated** in a **meaningful** way because they could be cross-referenced and track it back to the subject under study resulting in **privacy invasion.**

Case Study: Type II Diabetes in Adults

Type II Diabetes Clinical Trials- Dataset in Adults



Diabetes Type II Clinical Trials- Dataset in Adults

	Metformin XR	Canagliflozin 100 Milligram (mg)	Canagliflozin 300 mg	Canagliflozin 100 mg + Metformin XR	Canagliflozin 300 mg + Metformin XR
Started	237	237	238	237	237
Adverse Event	4	3	7	4	8
Death	1	0	0	0	0

OPEN TrialChain Model

OPEN TrialChain Model

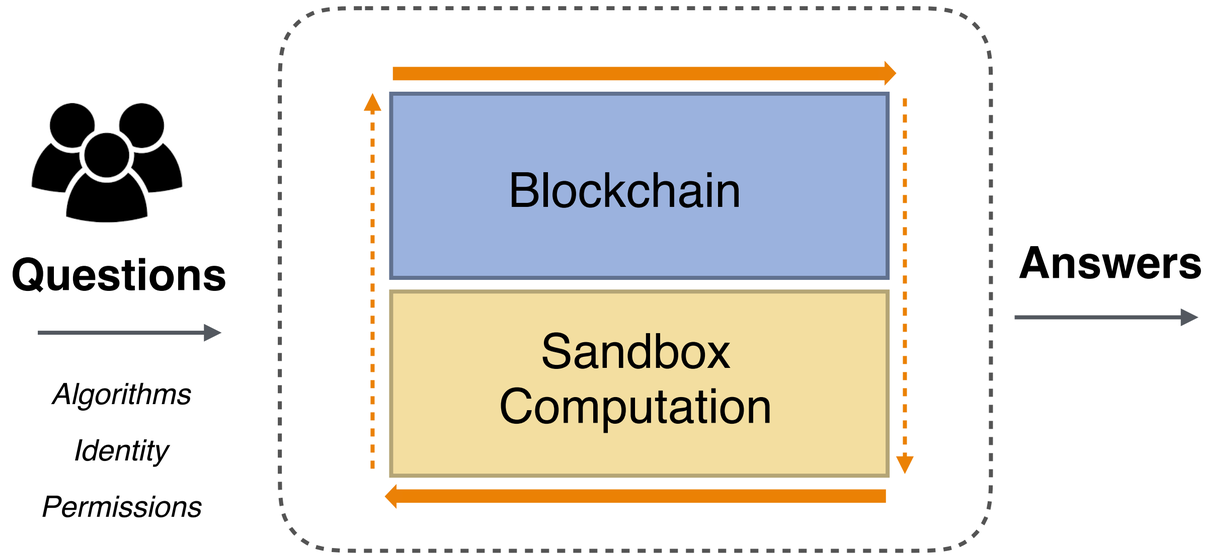
- **What is it?**
  - It is a **Blockchain-based** data sharing **infrastructure** that uses open algorithms between stakeholders of the federation in the clinical trials ecosystem.
- **Benefits**
  - OPEN TrialChain balances between the **sharing** of clinical **data** and the need for subject's **privacy protection.**
- **How?**
  - By allowing queries on decentralized raw datasets from which returns aggregated safe answers that are blinded (i.e. anonymized).

OPEN TrialChain- Components

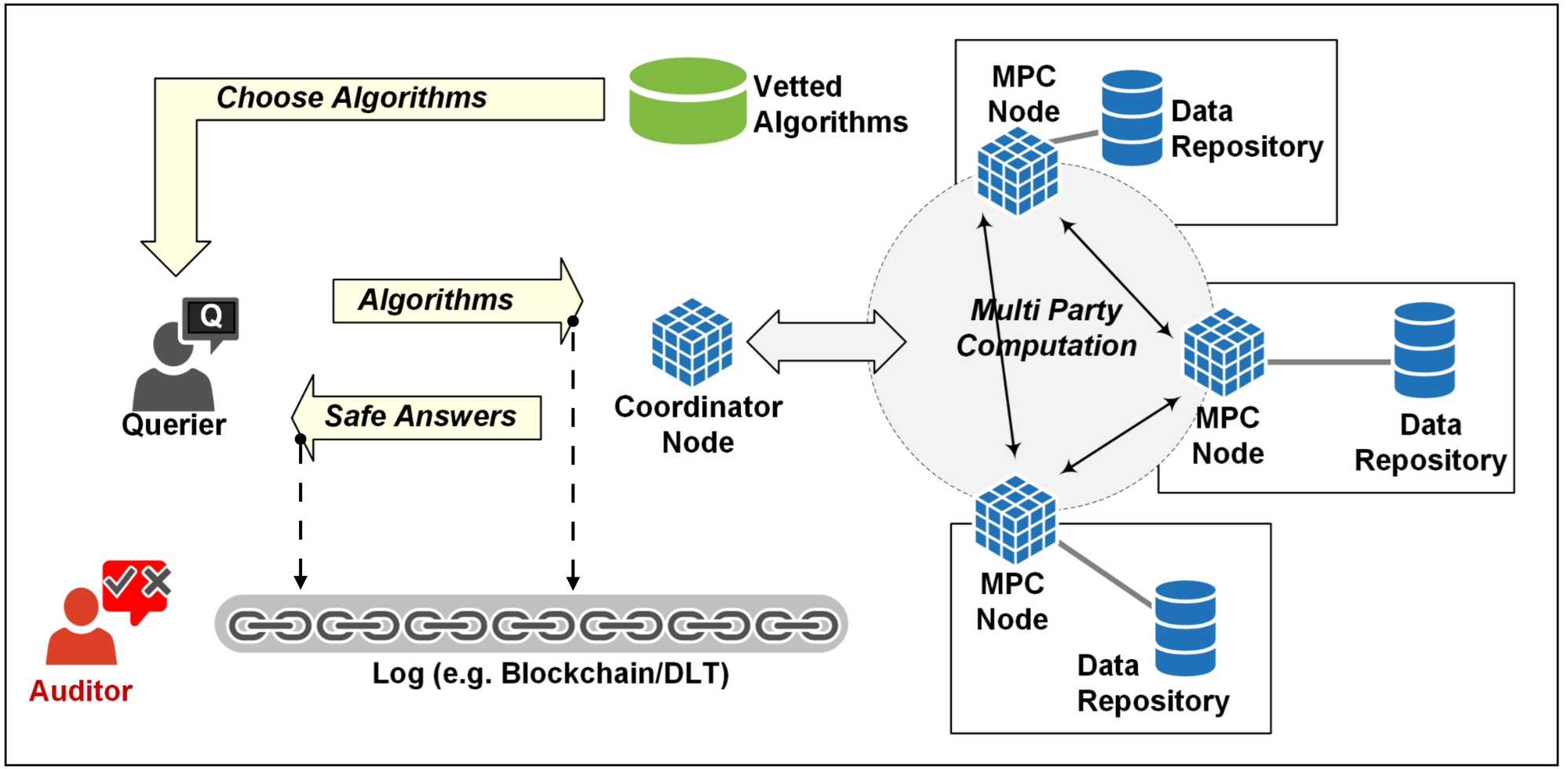
1. ***Data Providers***
   - Users owning clinical trial datasets owners who monitors other's queries over their data.
2. ***Vetted algorithms***
   - Allow users to query for specific demographics across multiple clinical trials without compromising individuals' data.
3. ***Queries Blockchain***
   - A tamper-proof, time-stamped ledger for audits and monitoring purposes.
   - FDA could use for study auditing.
   - Stakeholders use it to allow well-informed decision making processes.

OPEN TrialChain- Key Principles

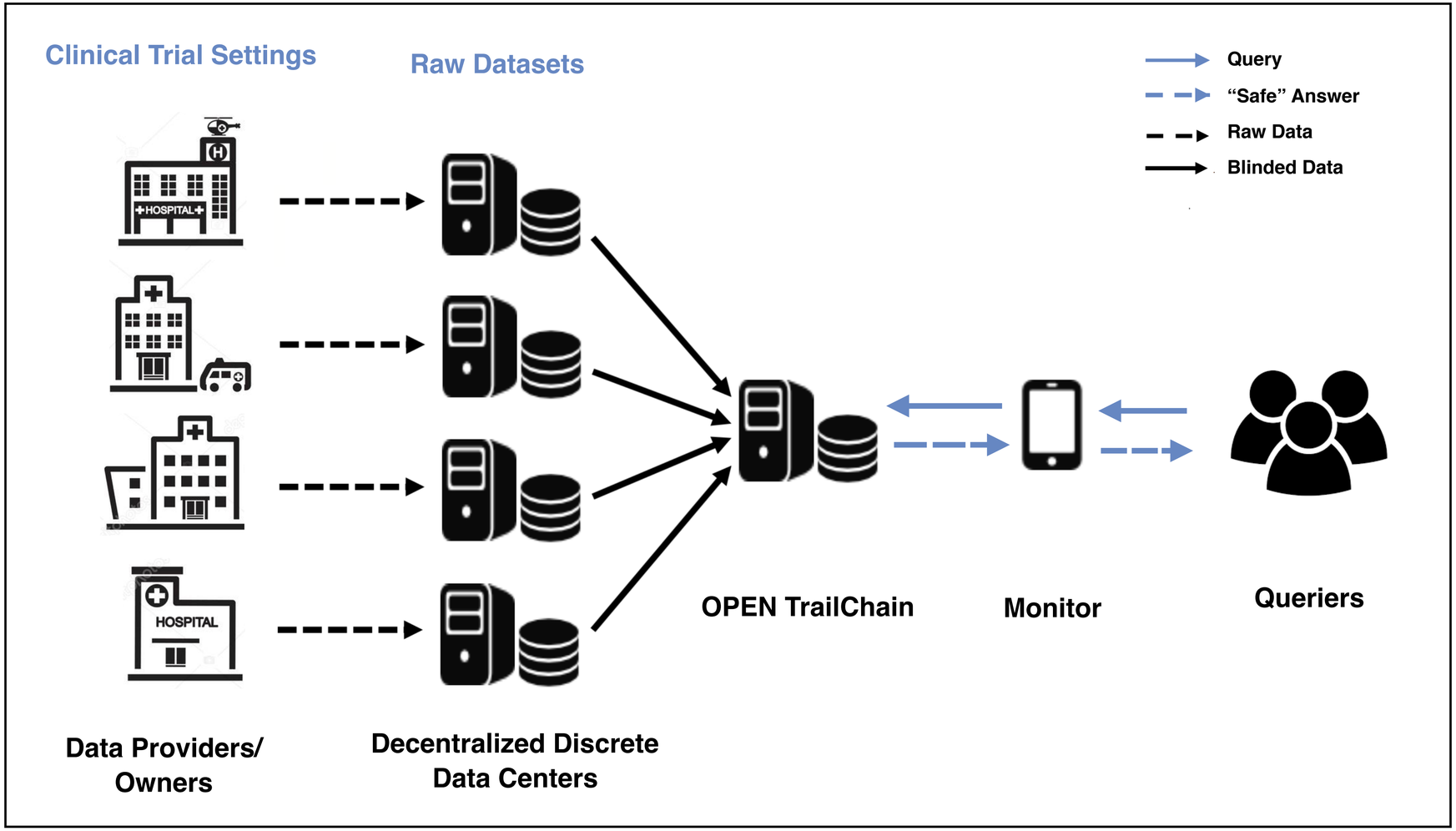
1. Keeps **data encrypted at all times**
2. Allows only **vetted algorithms**
3. Moves the **algorithm to the data**, (not vice versa)
4. Aggregates blinded data from **distributed repositories** in a decentralized infrastructure
5. Returns "**safe answers**"



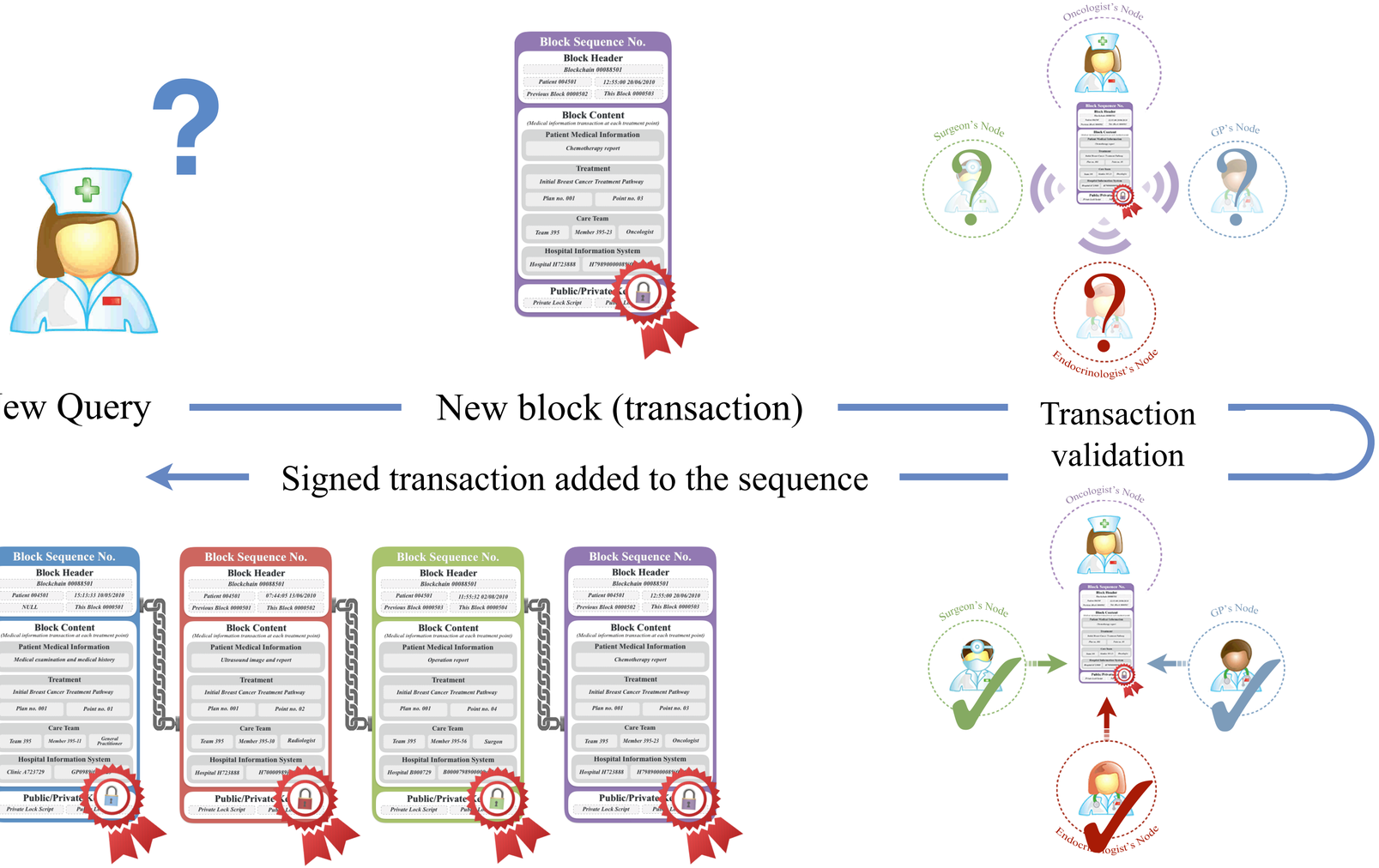
OPEN TrialChain- Model Architecture



OPEN TrialChain- Data Flow



OPEN TrialChain- Blockchain For Clinical Trials



Adopting OPEN TrialChain Model

OPEN TrialChain- Potential Users

- ***Doctors -*** *query for information relevant to their patients*
- ***FDA -*** *audit the blockchain and usage of information*
- ***Secondary Researchers -*** *conduct primary retroactive research for other potential drug developments*
- ***Pharmaceutical Companies -*** *monitor the blockchain for usage of their data in user queries*

OPEN TrialChain- In Type II Diabetes in Practice

- ***User (Doctor)***

  - *A doctor who has a **diabetic patient who is an African American female***

  - *Although there have been many diabetes trials with immediate-release Metformin, each **trial doesn't have a very significant cohort of African American women**.*

  - *Therefore, the **granularity** of the studies' results is very **coarse** in order to **protect the privacy of these few patients**.*

OPEN TrialChain- In Type II Diabetes in Practice

- ***Question / Algorithm***
  - *What are the **adverse events** for diabetic **African American females** taking **Metformin**?*

- ***Unsafe Answer***

  Detailed answers about a subject from one clinical trial that would compromise the subject's health data.

- ***Safe Answer*** *(without OPEN TrialChain)*

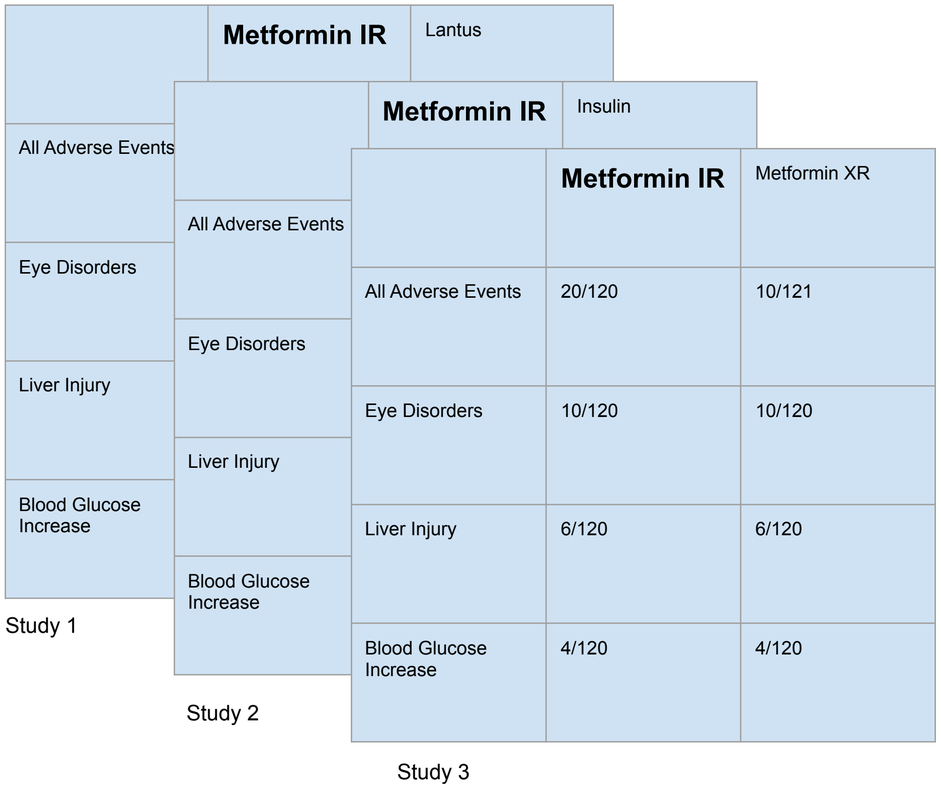
  Vague answers in disjoint tables *that protect the few African American females in a single study.*

OPEN TrialChain- In Type II Diabetes in Practice

- ***Question / Algorithm***
  - *What are the **adverse events** for diabetic **African American females** taking **Metformin**?*

- ***Safe Answer (with OPEN TrialChain)***
  - ***a safe answer would provide a blinded summary statistics** (histogram or scattered plot) that illustrates the adverse events for this particular demographic.*

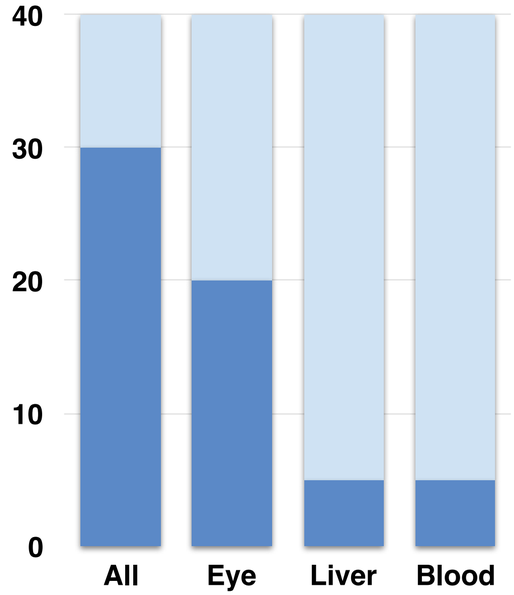
OPEN TrialChain- Aggregated Safe Answer Example



Uninformative safe answer

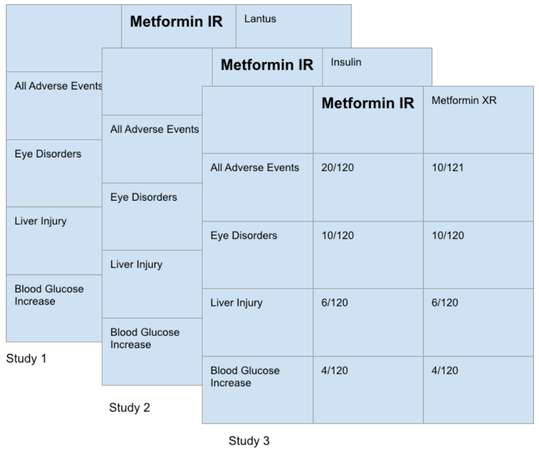
What are the adverse events for diabetic African American females taking Metformin?

	Metformin IR
All Adverse Events	30/40
Eye Disorders	20/40
Liver Injury	5/40
Blood Glucose Increase	5/40

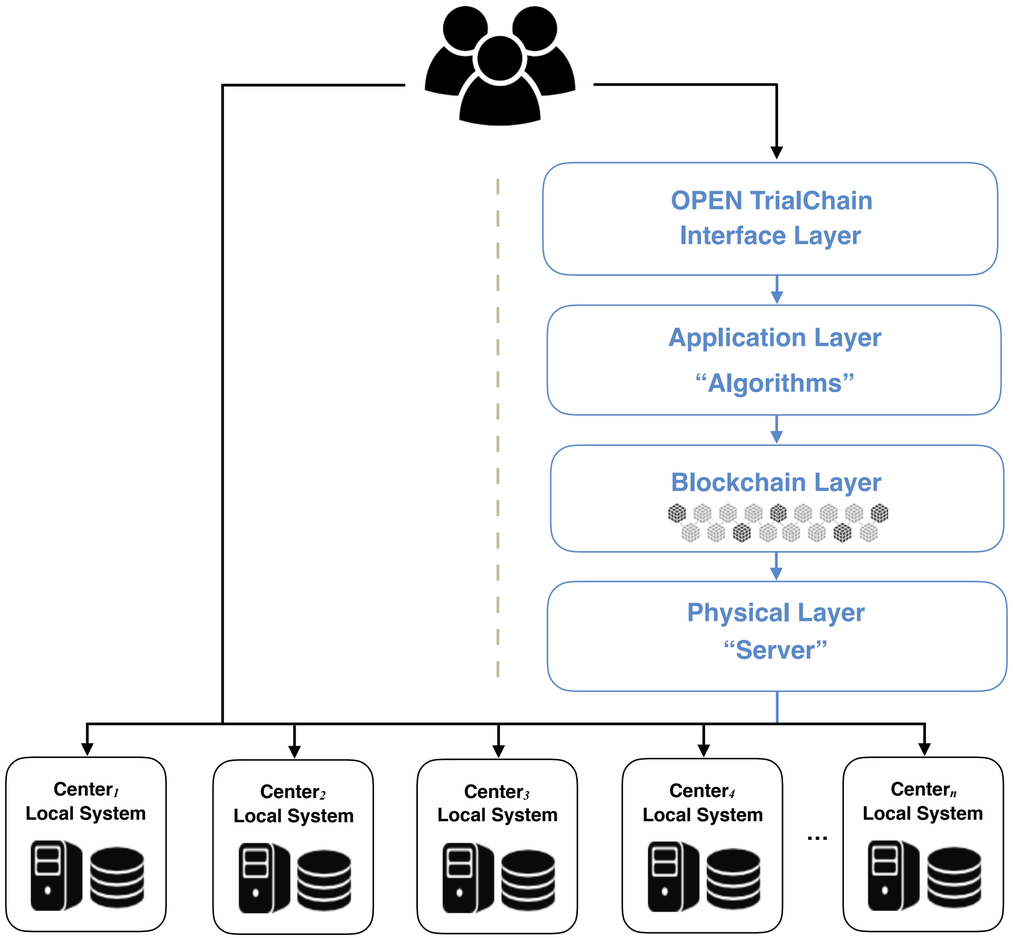


Informative safe answer with OPEN TrialChain

OPEN TrialChain- Aggregated vs. Blinded Results



Aggregated Less Informative Disjoint Table Results



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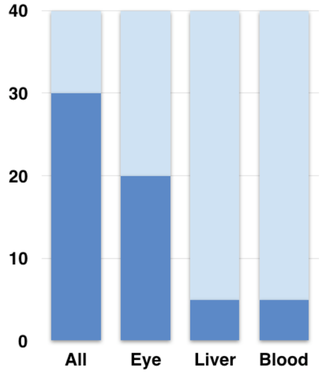

Aggregated Informative Blinded Visual Results

Addressing Clinical Trial Problems

Addressing the Problems

1. Encourages **reporting trial results** with higher fidelity **audited by the blockchain**
2. Incentives **more detailed results** in exchange for their peers' detailed results.
3. Report **safe answers** in summary statistics about the salient information (ex. effects of Metformin) without linking “unflattering” results to individual studies.
4. Returns **meaningful visualizations** that can help understand complex results and derive insights by comparing the models/diagrams.

Impact and Challenges

Impact on Ecosystem

- Eventually, OPEN TrialChain is expected to **optimize the clinical trial** ecosystem by
  - **improving patient safety,**
  - **saving lives,**
  - **cutting drug development costs,**
  - **encouraging transparent results,**
  - **preserving patients privacy, and**
  - **maintaining pharmaceuticals integrity**.

Adoption Challenges

- Early adopters would be hesitant to provide details of their data. Even if trial details would only be disclosed in safe answers, it still **dulls a company's competitive edge**.
- **Setting up OPEN TrialChain servers** for each dataset would be work that pharmaceutical companies may not be willing to invest in.
- At this time, OPEN TrialChain is **not GDPR compliant** and does not give individual subjects the ability to revoke access to their data.

Thank you