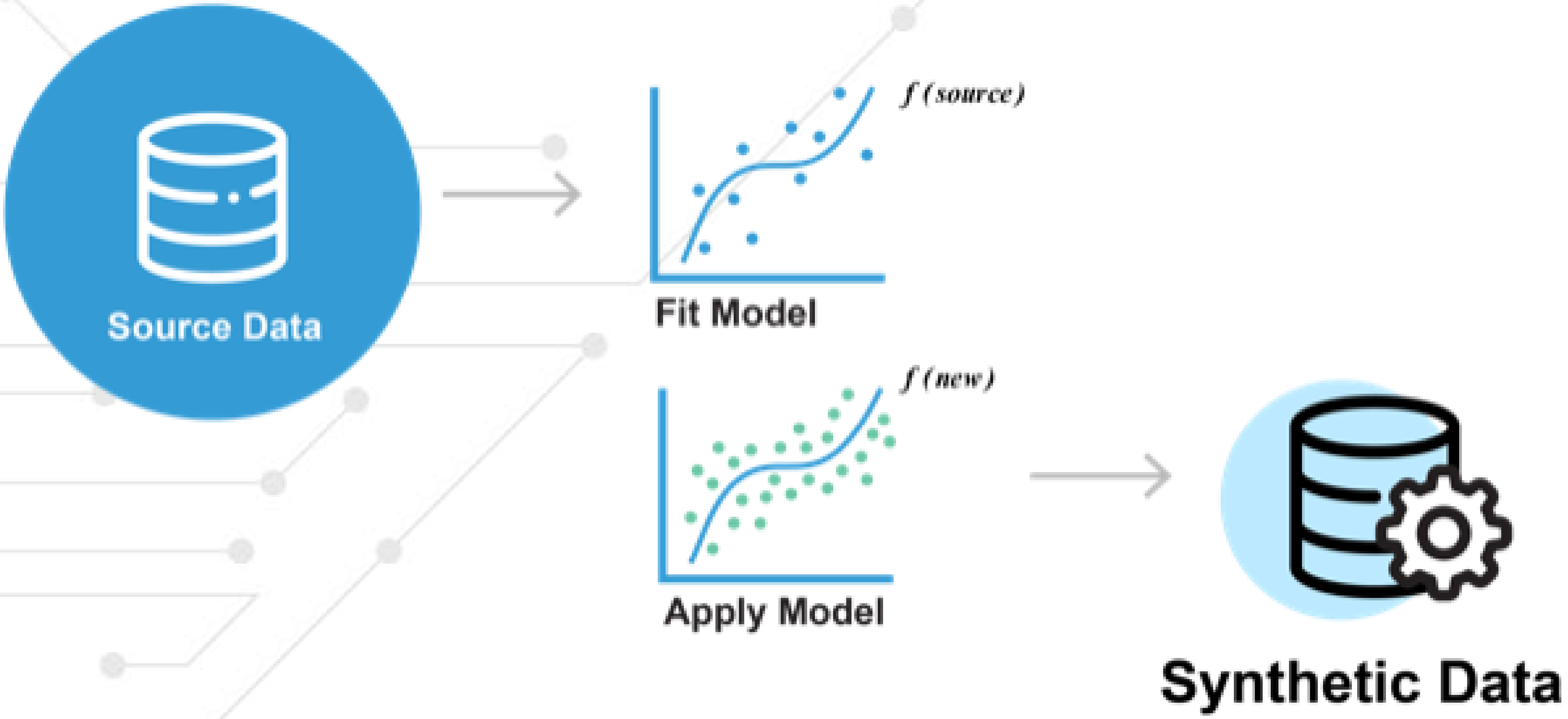
Synthetic Clinical Trial Data

Methods, Practice, and Experience

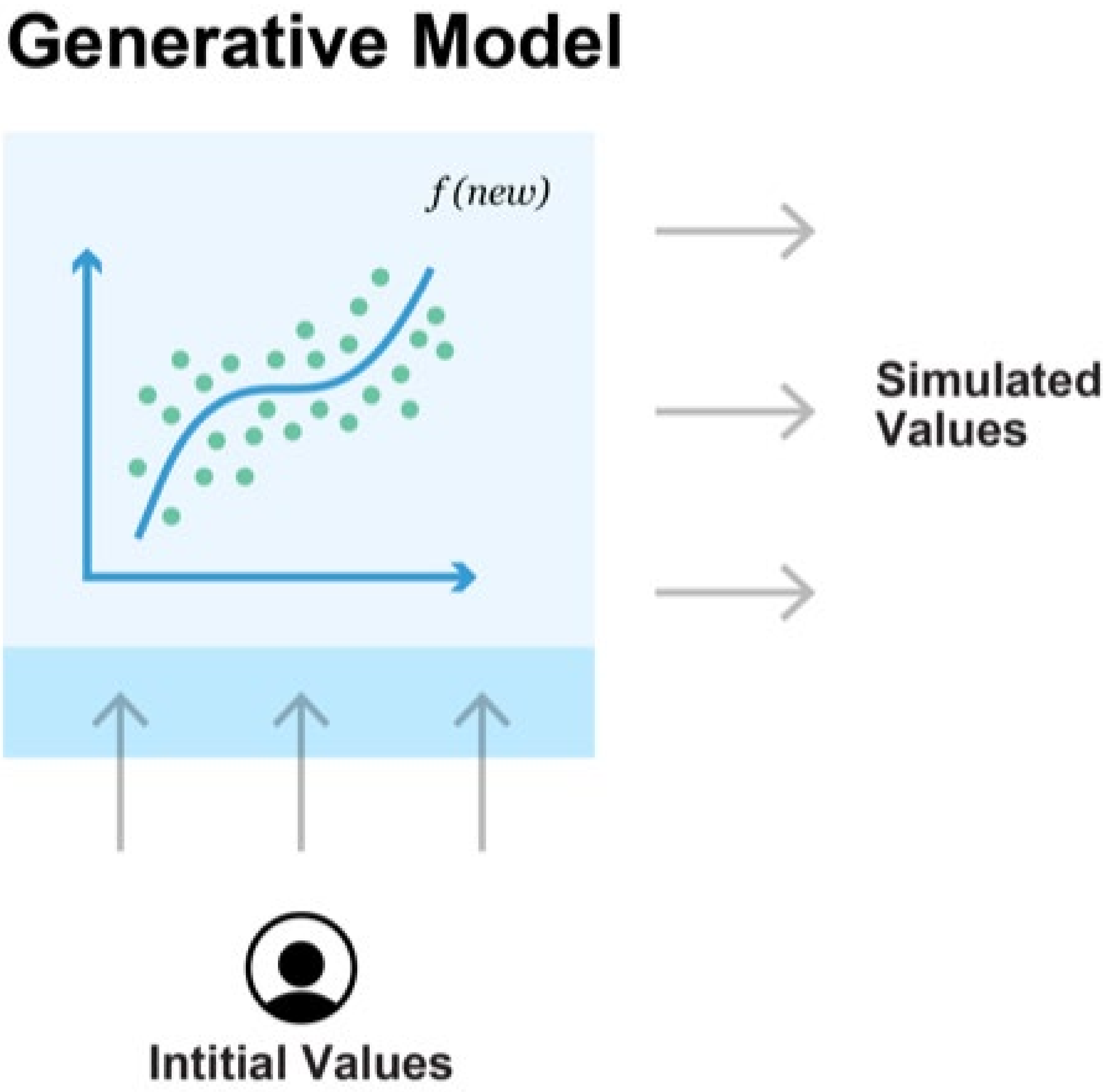
Khaled El Emam

4th June 2020

The Synthesis Process



Synthesis As Simulation

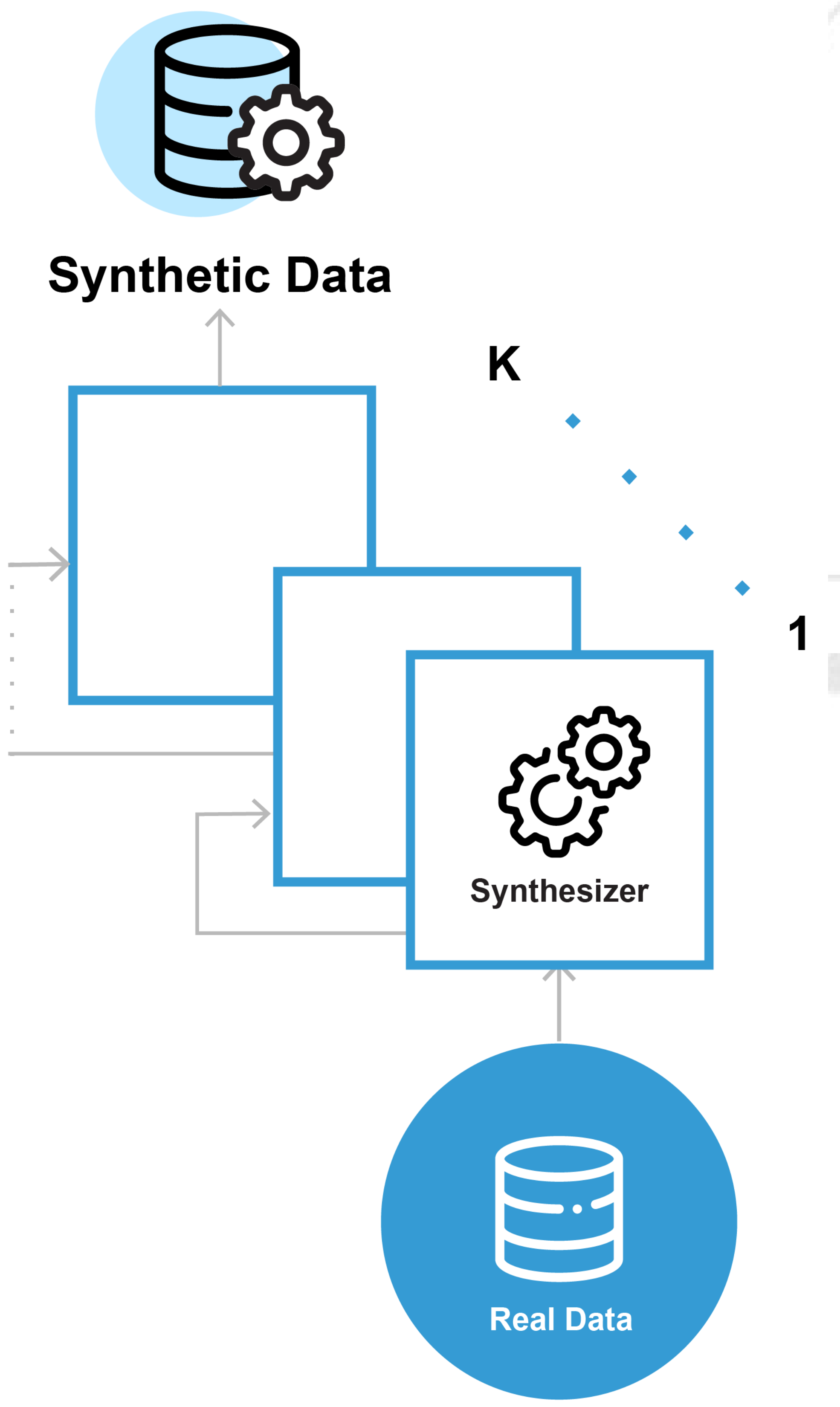


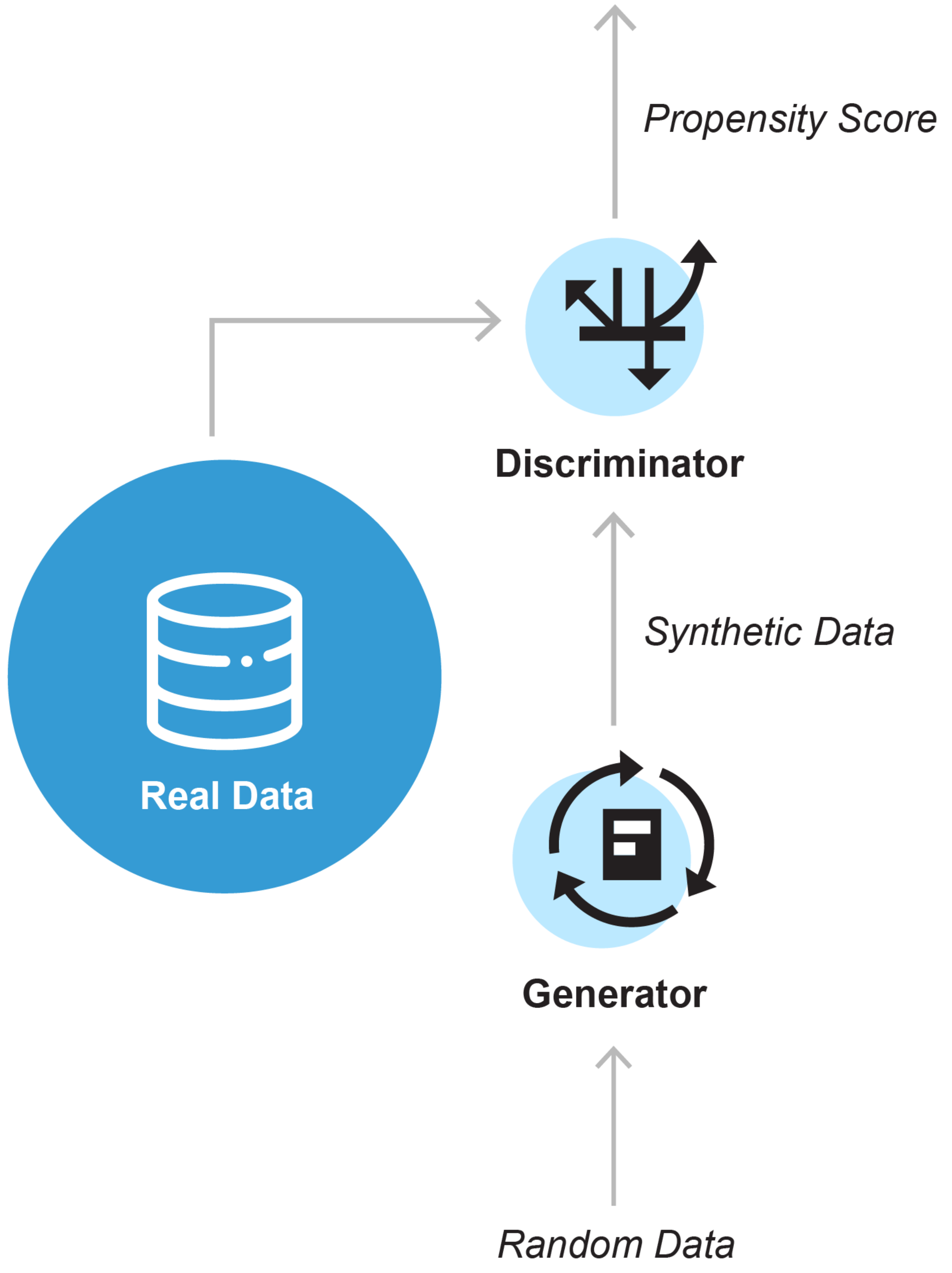
Generative Model

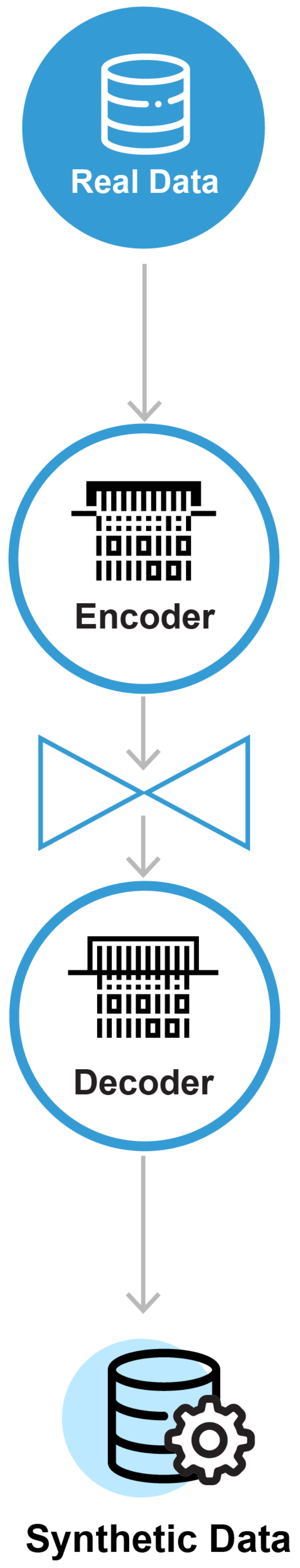
Simulated Values

Intitial Values

Synthesis Techniques







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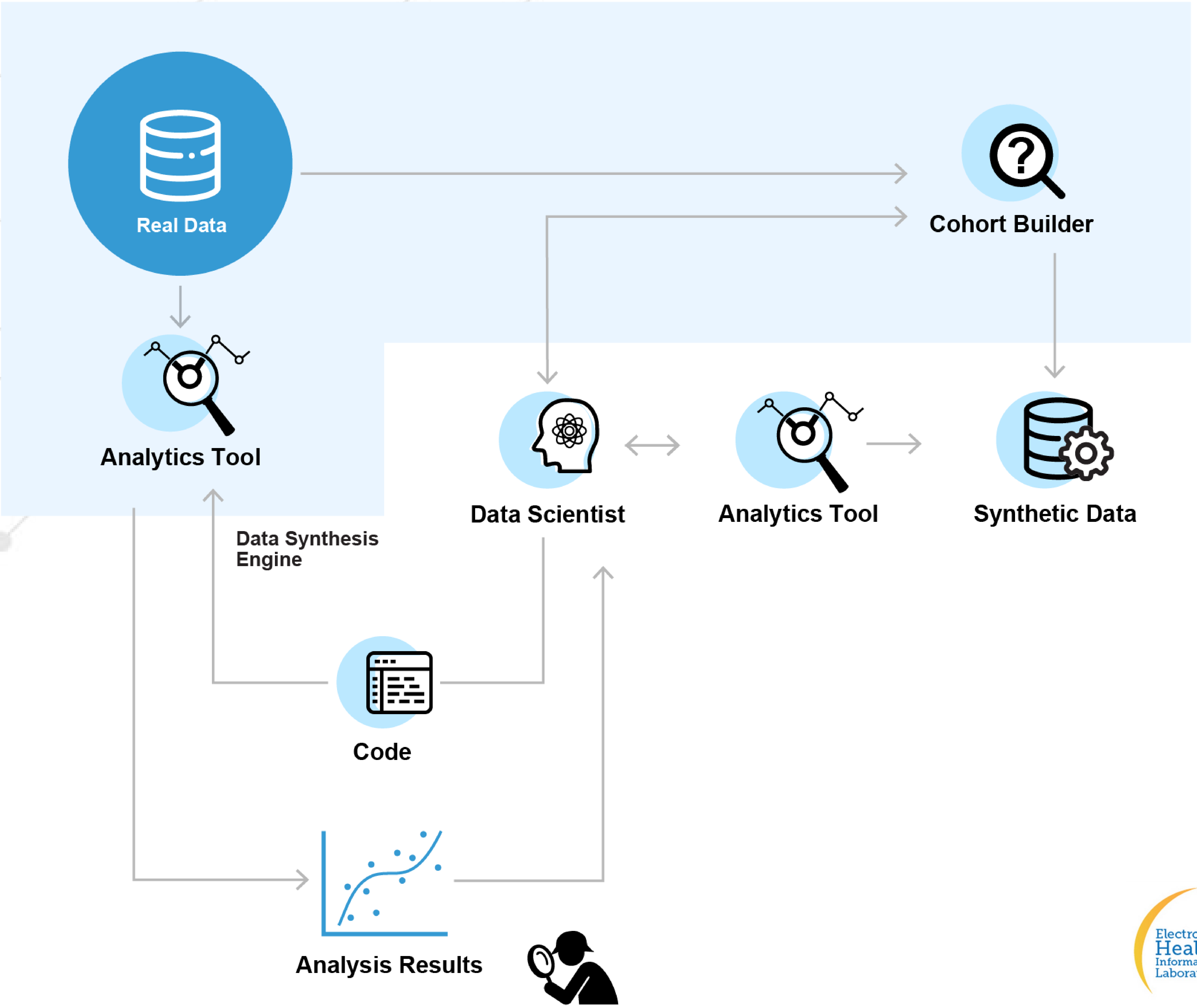
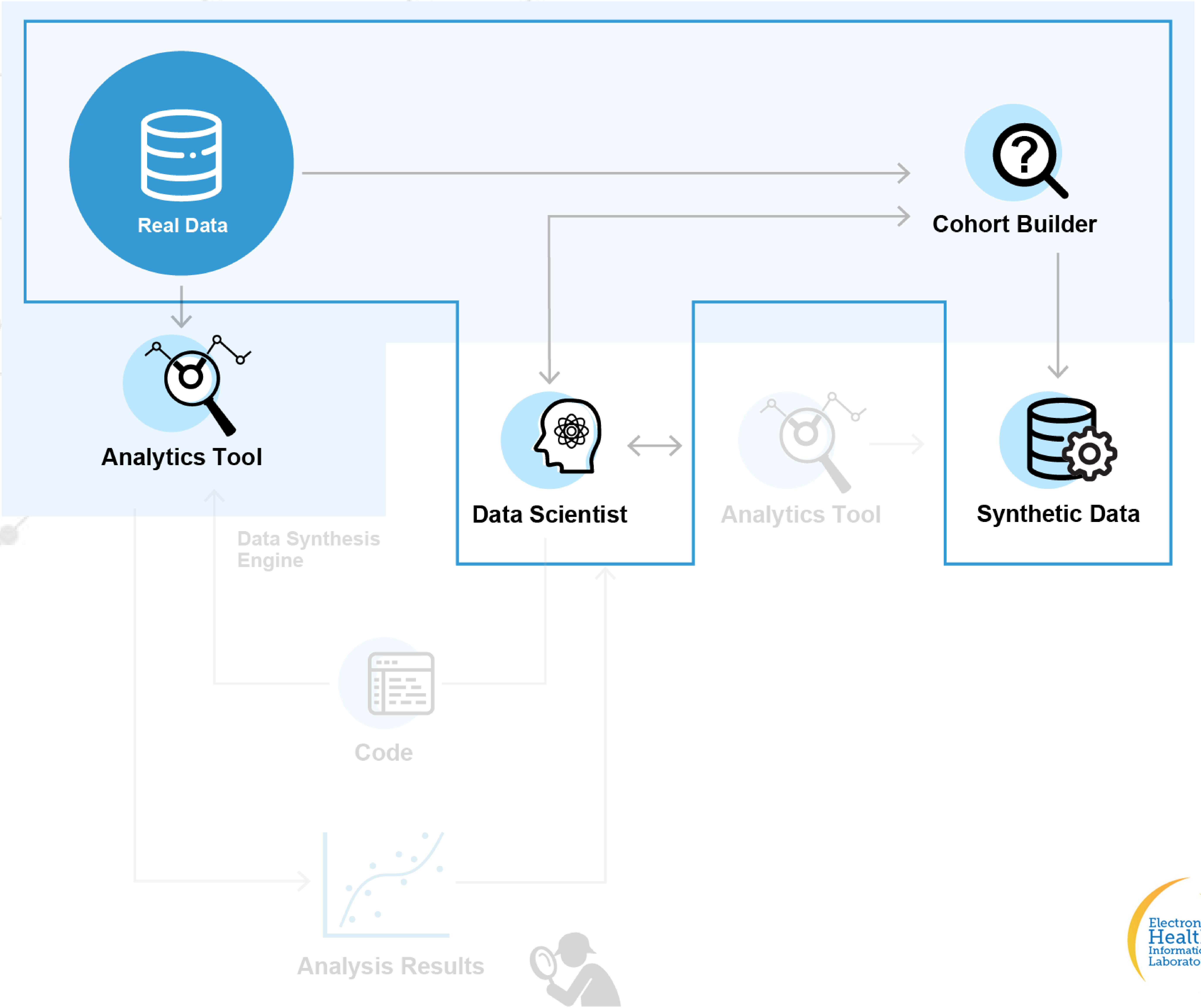
Replica Analytics

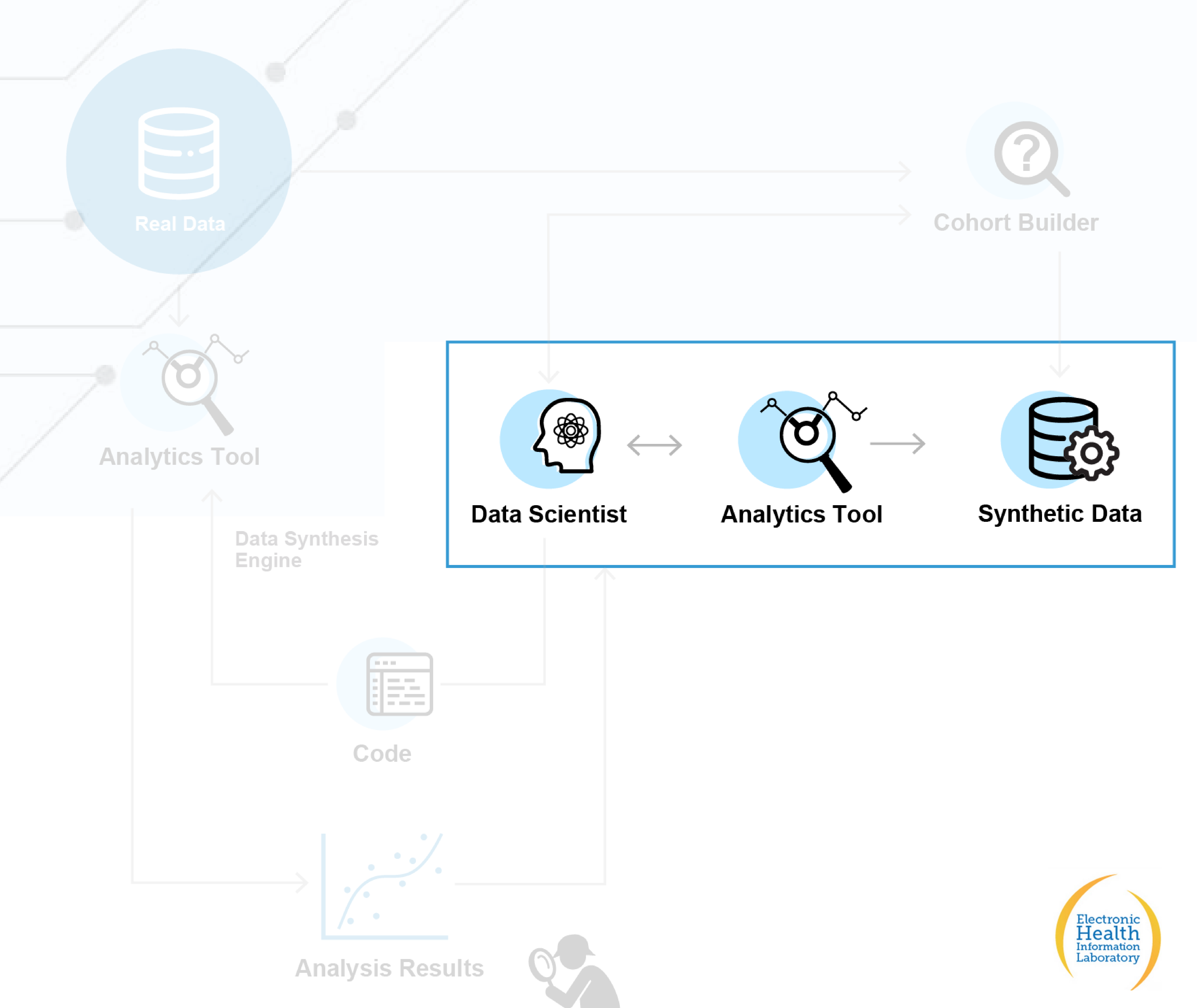
Synthesis as a Platform



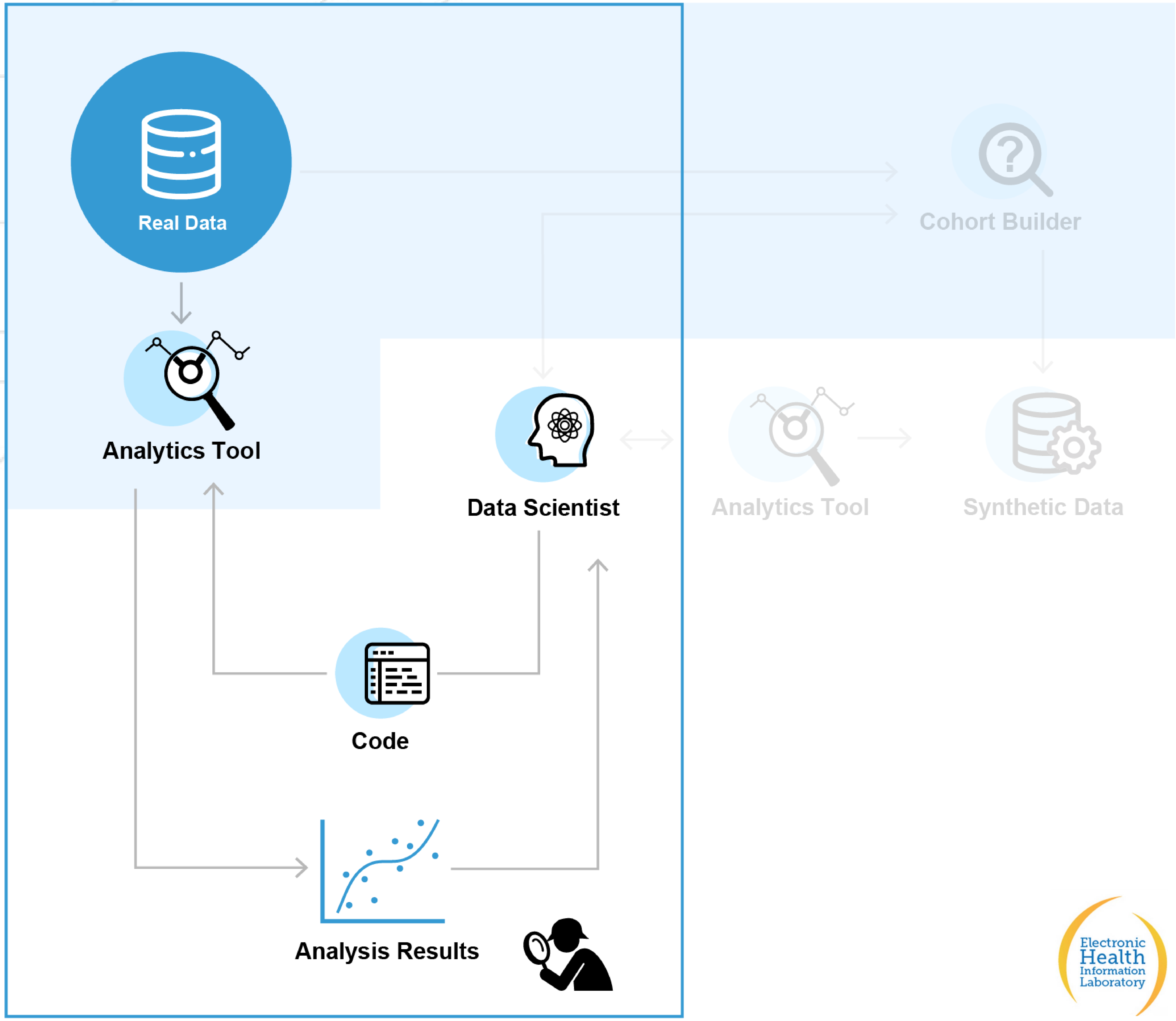
Synthetic Cohort Builder



Analysis on Synthetic Data



Validation Server



Complex Data – Clinical Trials

- Small datasets – is there enough signal to capture the patterns in the data
- Complex relational data models
- Unique patient relationships rather than tabular relationships – the RELREC problem
- Large number of heterogeneous events over an extended period of time

Replicated Analysis

- N0147 trial: Effect of cetuximab on survival among patients with resected stage III colon cancer
- Randomized trial run between 2004 and 2009
- In total, 2,686 adult patients with stage III colon cancer, with two arms:
- Control: adjuvant regimens of folinic acid, fluorouracil, and oxaliplatin / fluorouracil, leucovorin, and irinotecan
- Treatment: cetuximab + control regimens
- Replication was published in 2018 in *Surgery*

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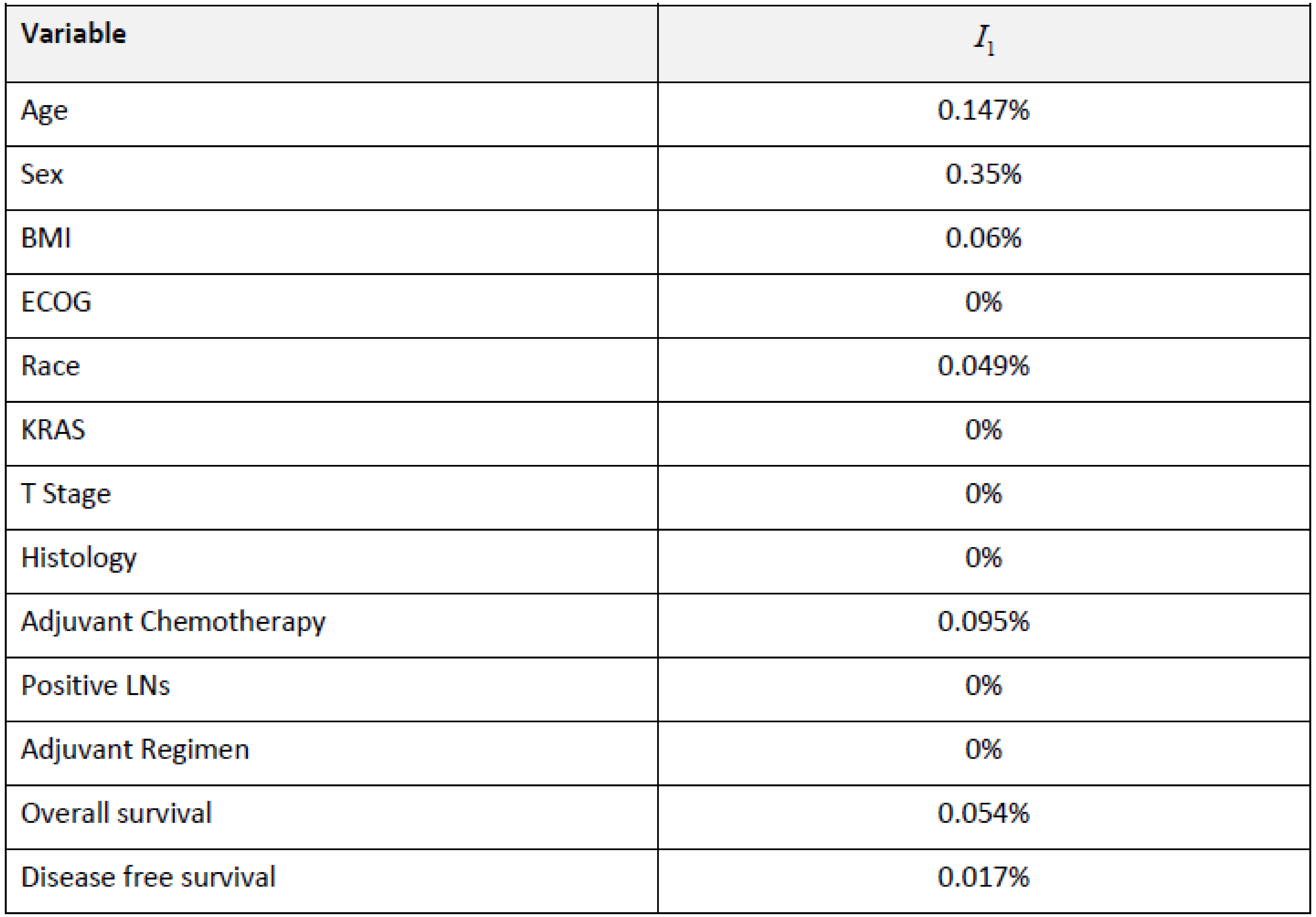
Replicated Analysis

- Only the control arm, N=1,543
- **Objective:** understand the impact of obstruction on overall survival and disease-free survival
- **Covariates:** cancer staging, lymph node involvement, histology, baseline ECOG performance status, KRAS biomarker, demographics and BMI
- **Statistics:** Descriptive statistics, bivariate relationships, cox model

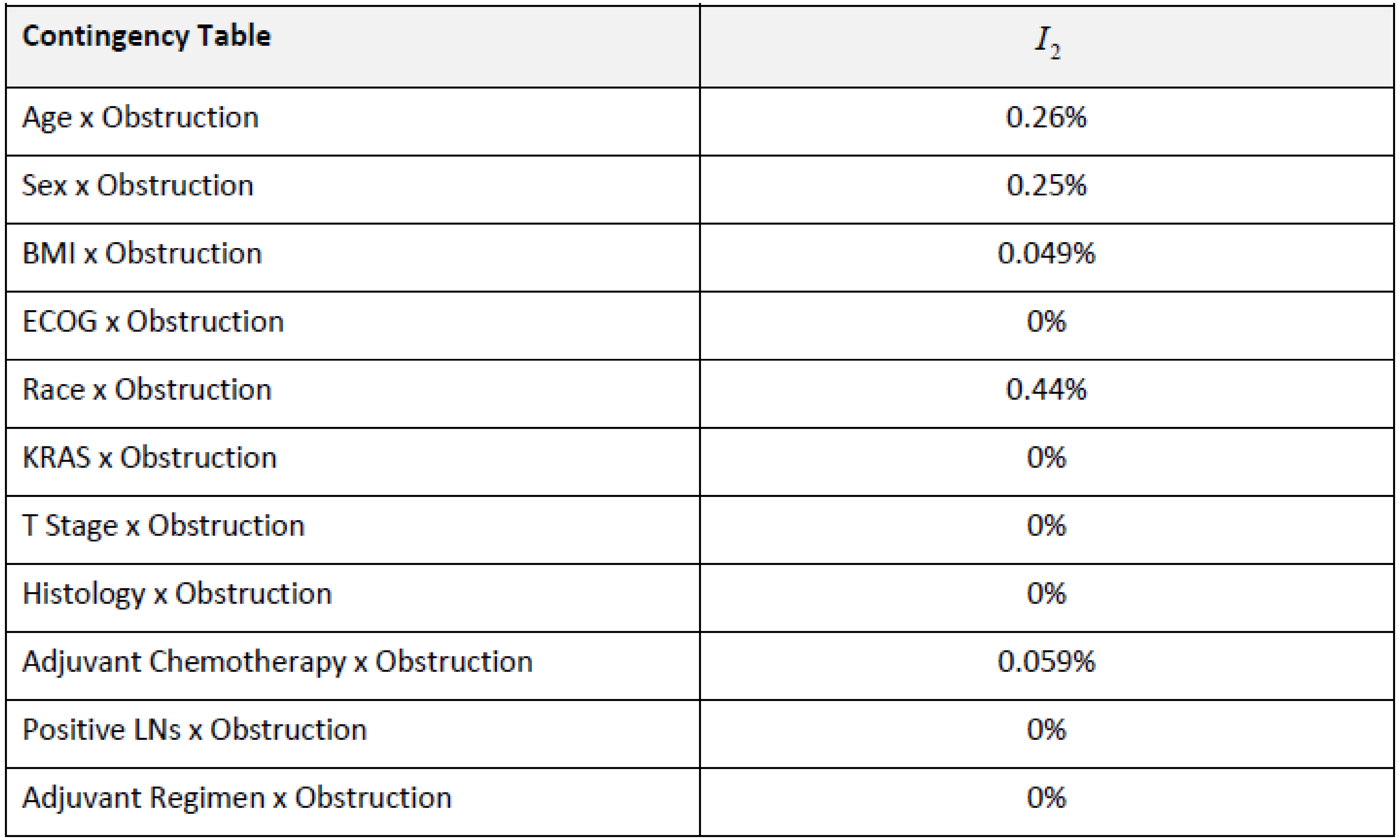
Descriptive Statistics



Variable	I_1
Age	0.147%
Sex	0.35%
BMI	0.06%
ECOG	0%
Race	0.049%
KRAS	0%
T Stage	0%
Histology	0%
Adjuvant Chemotherapy	0.095%
Positive LNs	0%
Adjuvant Regimen	0%
Overall survival	0.054%
Disease free survival	0.017%

% information loss due to using synthetic data as opposed to the real data

Bivariate Statistics



Contingency Table	I_2
Age x Obstruction	0.26%
Sex x Obstruction	0.25%
BMI x Obstruction	0.049%
ECOG x Obstruction	0%
Race x Obstruction	0.44%
KRAS x Obstruction	0%
T Stage x Obstruction	0%
Histology x Obstruction	0%
Adjuvant Chemotherapy x Obstruction	0.059%
Positive LNs x Obstruction	0%
Adjuvant Regimen x Obstruction	0%

% information loss due to using synthetic data as opposed to the real data

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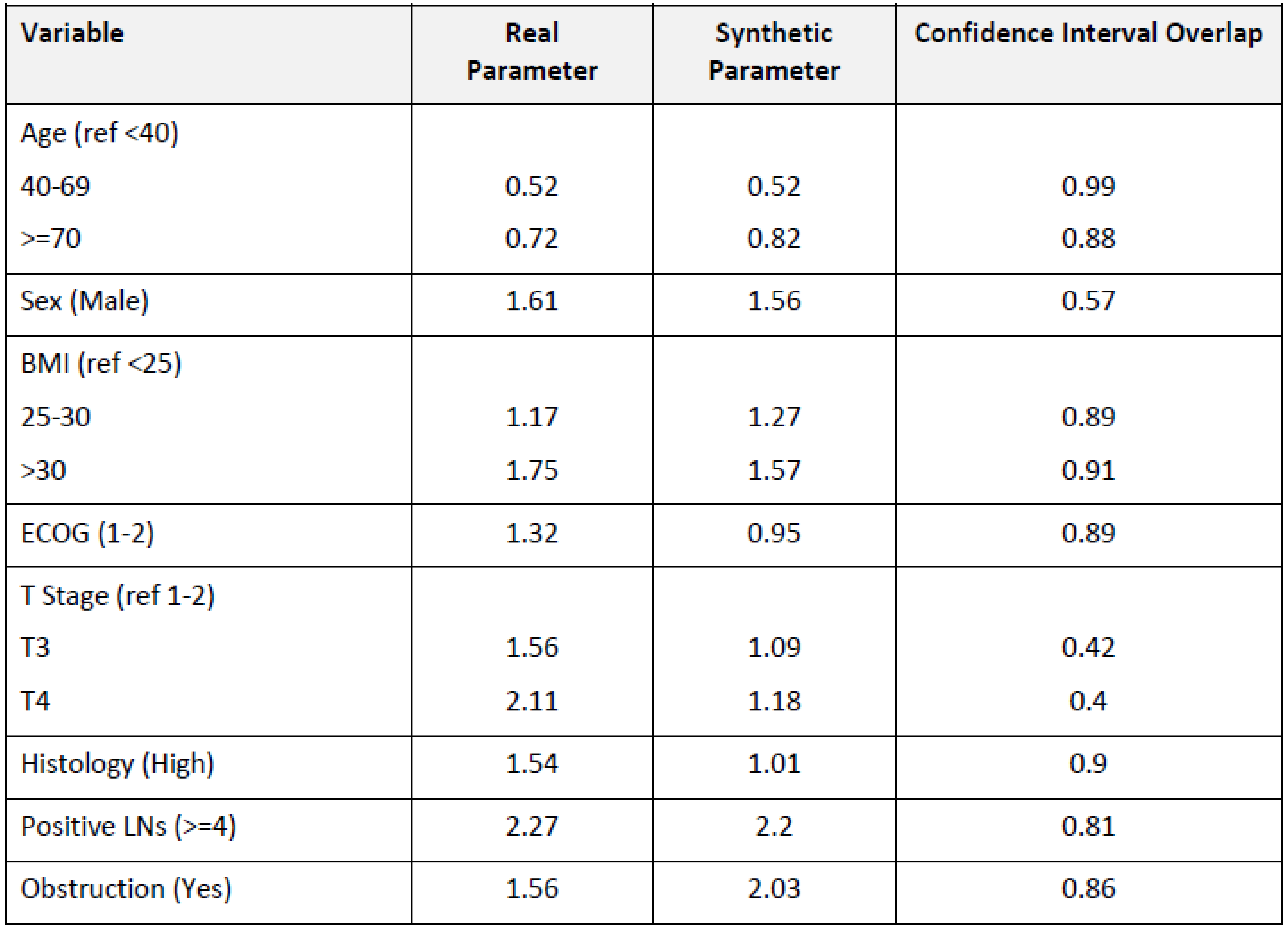
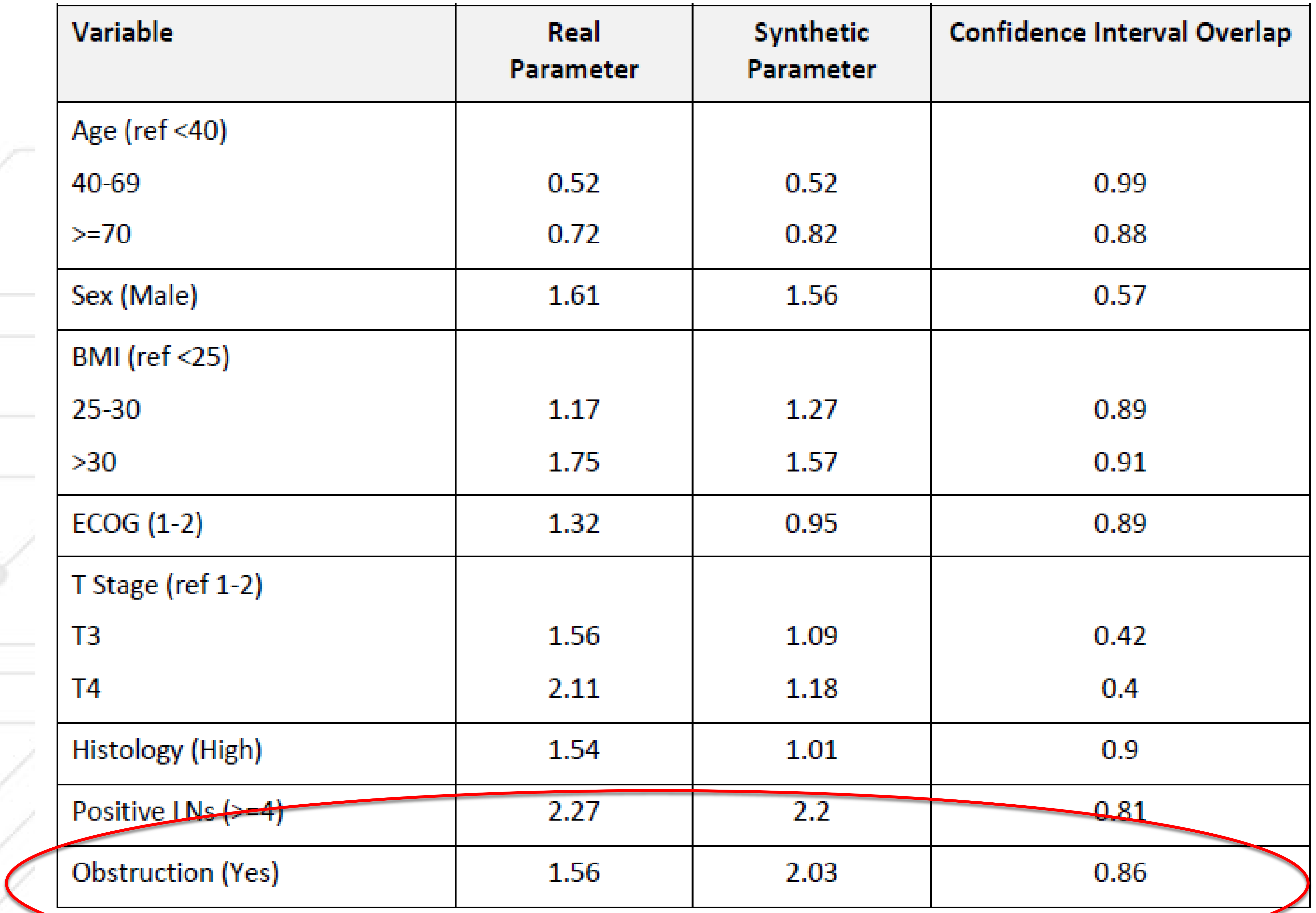
Impact of Obstruction on Overall Survival



Variable	Real Parameter	Synthetic Parameter	Confidence Interval Overlap
Age (ref <40)			
40-69	0.52	0.52	0.99
>=70	0.72	0.82	0.88
Sex (Male)	1.61	1.56	0.57
BMI (ref <25)			
25-30	1.17	1.27	0.89
>30	1.75	1.57	0.91
ECOG (1-2)	1.32	0.95	0.89
T Stage (ref 1-2)			
T3	1.56	1.09	0.42
T4	2.11	1.18	0.4
Histology (High)	1.54	1.01	0.9
Positive LNs (>=4)	2.27	2.2	0.81
Obstruction (Yes)	1.56	2.03	0.86

Proportion of confidence interval overlap

Impact of Obstruction on Overall Survival



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Conclusions

- It was possible to replicate the analysis and draw the same conclusions given the objectives of the study
- The combination of cohort builder and validation server enable reliable analytics with synthetic data, as well as faster access to data

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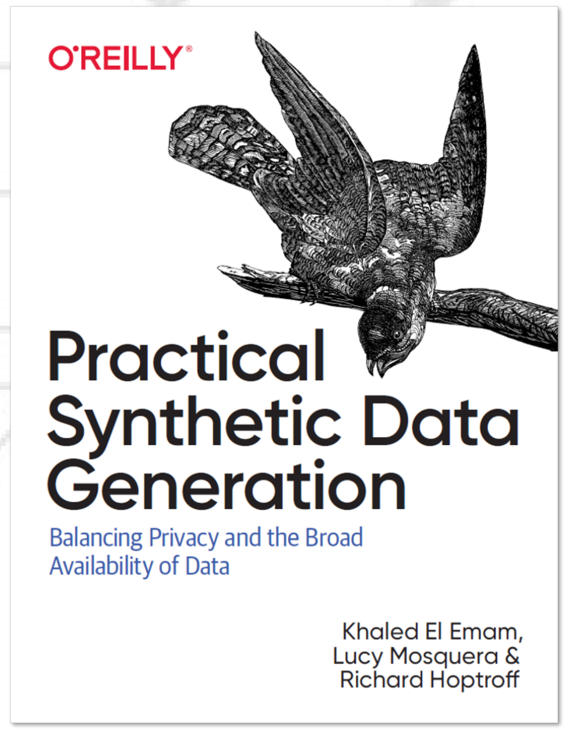
- Read our introductory report and book on the topic

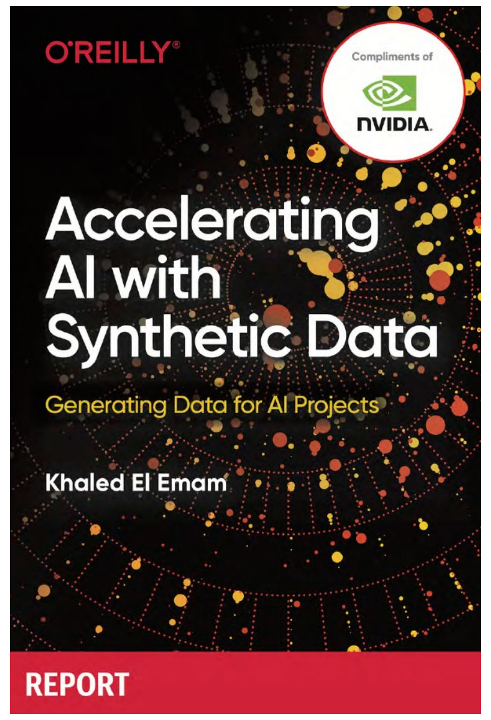


O'REILLY

Practical Synthetic Data Generation

Balancing Privacy and the Broad Availability of Data

Khaled El Emam, Lucy Mosquera & Richard Hoptroff



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Compliments of NVIDIA

Accelerating AI with Synthetic Data

Generating Data for AI Projects

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REPORT

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