Bridging Open Science and Privacy Protection in research with Synthetic HIV Cohort Data

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Introduction

Hypothetically, you found a procedure X is associated with survival with a small cohort, now, you want to generalize this finding to a larger cohort.

How difficult it is to get a hand on the data?

- Application, Concept sheet, Approval waiting time...
- CITI, HIPAA training, Data center training
- Access the data only in facility or use VPN
- Rules of storing and sending the data

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Introduction

Journal or funding agency request the data you use for analysis as supplements:

What about publishing the data?

- Re-identification risk/ Privacy concern/ Patient stigmatized
- HIPAA, General Data Protection Regulation (GDPR)
- Data sharing agreement
- Loss of information when de-identifying and adding noise

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Introduction

Currently, privacy regulation is a gap for open science

How difficult it is to get a hand on the data?

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... What can we do?

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Synthetic Data

Synthetic data with Machine Learning

- **No real record/patient is in the data**, but it reflects the true data
- **Since it is not real, it provides a workaround of current regulations**

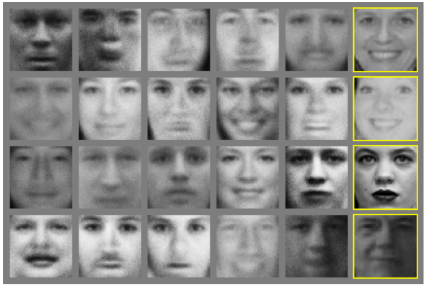

Figure 1: Goodfellow, Ian, et al. "Generative adversarial nets." Advances in neural information processing systems 27 (2014).

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Synthetic Data

Synthetic data with Machine Learning

- **No real record/patient is in the data**, but it reflects the true data
- **Since it is not real, it provides a workaround of current regulations**
- Minimum assumptions or constraints with respect to the associations between variables
- And there has been example that using both real and synthetic data together can increase accuracy
- There are already freely available synthetic databases for research i.e., The Synthetic Data Vault

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Synthetic Data

To Recap:

- No real patient information is in it
- It has most of the information in the real data

So, can we use synthetic data to bridge the gap of open science and privacy protection?

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Introduction

- Caribbean, Central and South America Network for HIV Epidemiology (CCASAnet)
- 59208 participants from Argentina, Brazil, Chile, Haiti, Honduras, Mexico, Peru
- **To develop a synthetic dataset for the CCASAnet that replicates the original dataset's structure and variable associations, facilitating its public use for**
  - Reproducible research and
  - **Hypothesis generation**

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Method

Generative Adversarial Network (GAN) Model

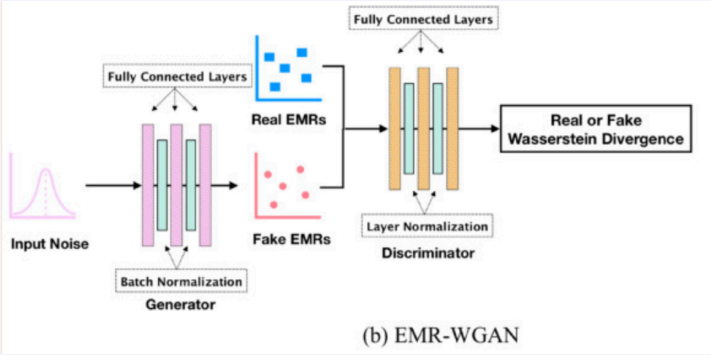

Figure 2: EMR-WGAN: Zhang, Ziqi et al. JAMIA vol. 27,1 (2020)

1. A **Generator** is trained on the real data to **generate similar records**
2. A **Discriminator** is trained to **identify fake/generated records**
3. Generator **competes** with Discriminator until Discriminator cannot identify the fake data

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Training Data

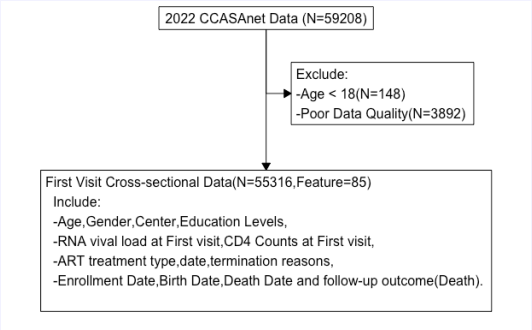

Figure 3: Training Data Set

- We use CCASAnet dataset enrolled before 2022.
- Need to transform into Machine Learning Format
- Data was split into training(80%) and testing set
- There is a detailed tutorial and code by Chao Yan available online

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Evaluation

- **Utility**: How well the synthetic data reflect the real data: We will look into data distribution and associations
- **Privacy**: How well the synthetic data protect the real data: We will use two common used metrics to evaluating risk of information leakage and re-identification
- **Real Application**: How well the synthetic data can be used in real analysis

  Mortality and loss to follow-up among HIV-infected persons on long-term antiretroviral therapy in Latin America and the Caribbean

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Result

Data Utilities

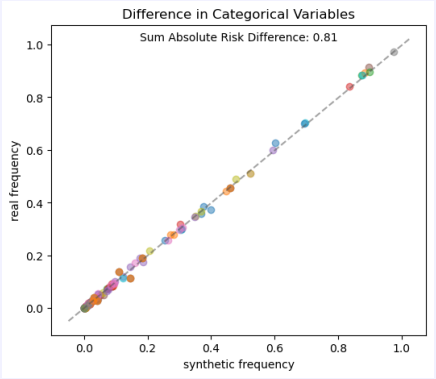

Figure 4: Absolute Difference in Prevalence of Catagorical Variables

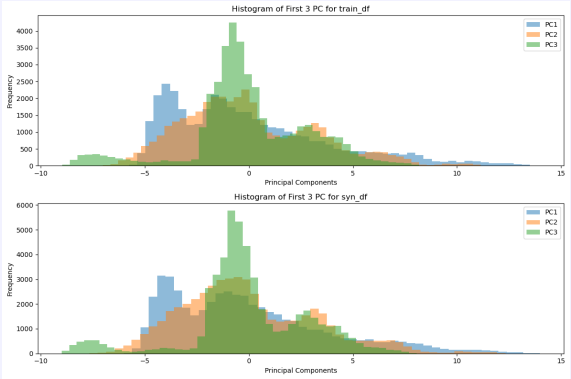

Figure 5: Principle Component

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Data Privacy

- Attribution Risk: How likely unknown attribute values of interest are predicted from a set of leaked attribute values(with a trained model from the synthetic data)
- Membership Risk: How likely a real record can be reconstructed from a leaked generative model

Table 1: Privacy Risk

	Attribution Risk	Membership Risk
Synthetic	0.32	0.37
Real	0.51	0.83

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Study Reproduciblity

Cox proportional hazards models (Time to Death) were stratified by CCASAnet site and adjust for:

sex, calendar year, age, CD4 count, clinical AIDS at ART initiation and ART regimen class

Variable	HR-Synthetic	HR-Training
Diff. in 100 CD4 Counts	0.902 (0.885-0.919)	0.856 (0.842-0.869)
Diff. in 10 Years Between Enrollment	0.793 (0.745-0.844)	0.710 (0.674-0.748)
Diff. in 10 Years of Enrollment Age	1.193 (1.155-1.232)	1.241 (1.206-1.277)
AIDS at Enrollment	1.816 (1.678-1.967)	1.783 (1.671-1.903)
Other vs NNRTI	2.336 (2.129-2.564)	1.857 (1.702-2.026)
PI vs NNRTI	1.029 (0.905-1.172)	1.070 (0.958-1.196)

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Study Reproduciblity

- We modeled the first visit data, and use patient profile to predict their survival(time-to-event), this imposes the assumption that the survival is only related the first visit.

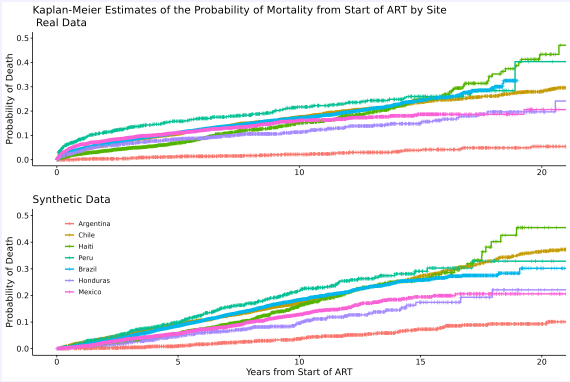

Figure 6: K-M estimate of Survival(Top: Real vs Bottom: Synthetic Data(best performance))

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Roadmap

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Adapt to longitudinal models

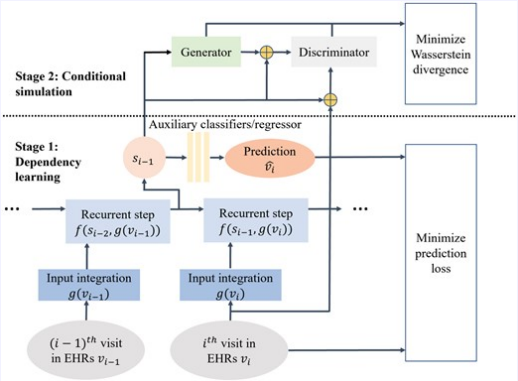

Figure 7: "SynTEG": Zhang, Ziqi, et al. JAMIA 28.3 (2021): 596-604.

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Future works

- Missingness is an attribute in EHR data, we want our synthetic data to reflect the missing pattern in the real data when published
- So far, because of the limitation of algorithm and computation time, we only used single-imputation for training
- Rare Event ($p<0.001$) cannot be properly captured by the model
- It is encouraged to check the data for abnormalities post-generation (i.e., male record with Cervical cancer)
- Further improve privacy protection
- Develop a evaluation method that shows confidence of any hypothesis generated from the synthetic data

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Summary

- We developed a version of synthetic dataset for the CCASAnet that replicates the original dataset's structure and variable associations
- It allows researchers to use the data to reproduce the study, identify problems, come up with their own hypothesis with the synthetic data and produce more results
- It shows a path forward for open science, but one must also keep in mind the quality and privacy risk of the data when published and used.

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Other Methods

We chose the GAN model because our team has experts in this field and it (SynTEG) is used as a comparison standard in most recent papers.

We want to point out that other methods are available and produce similar or better results depending on the characteristics of the data.

1. Theodorou, B., Xiao, C. & Sun, J. Synthesize high-dimensional longitudinal electronic health records via hierarchical autoregressive language model. Nat Commun 14, 5305 (2023).
2. Clinical knowledge base simulation
3. Conditional Model for research specific data

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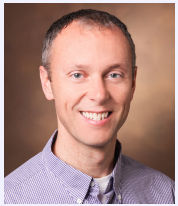
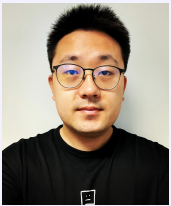
QUESTION?



Bryan E. Shepherd, PhD



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Thank you

NIH and CCASAnet fund this project <= Link to Bio to find this slides

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