ODATABASE & METHODS CYBERSEMINAR SERIES

FY24 Session #12:

Centralized Interactive Phenomics Resource (CIPHER): Phenotype Library and Tool Demonstration

September 9th, 2024

Hosted by **VIReC**

Kelly Cho, PhD, MPH

Director, CIPHER & Million Veteran Program (MVP) Phenomics; Deputy Director, Cooperative Studies Program Epidemiology Center (CSPEC), Boston; Associate Professor of Medicine, Mass General Brigham, Harvard Medical School

VA Boston Healthcare System, Boston, MA

Jacqueline Honerlaw, RN, MPH

Deputy Director, CIPHER Ashley Galloway, MPH Associate Director Strategic Partnerships and Outreach, CIPHER



DATABASE & METHODS CYBERSEMINAR SERIES

Informational seminars to help VA researchers access and use VA databases.

Sessions cover...

- VA data sources & data access systems
- Application of VA data to research and quality improvement questions
- Limitations of secondary data use
- Resources to support VA data use

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First Monday of the month | 1:00pm-2:00pm ET

Date	Торіс
10/7/24	Meet VIReC: The Researcher's Guide to VA Data
11/4/24	Navigating VA Data Sources: An Overview of Commonly Used Databases

Visit the VIReC <u>Database & Methods</u> <u>Cyberseminar</u> page for more information & registration links.

Visit <u>HSR's VIReC</u> <u>Cyberseminar</u> <u>Archive</u> page to watch previous sessions. VA Health Systems Research CYBERSEMINARS

SAMPLE EMAIL

A Practical Approach to Working with VA-Purchased Community Care Data

Thursday, October 13, 2022 2:00 PM | (UTC-04:00) Eastern Time (US & Canada) | 1 hr

Please download today's slides Please click here for today's live captions

Join webinar

More ways to join:

Join from the webinar link

https://veteransaffairs.webex.com/veteransaffairs/i.php?

Where can I download a copy of the slides?

ODATABASE & METHODS CYBERSEMINAR SERIES

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Associate Director Strategic Partnerships and Outreach, CIPHER

Poll #1:

What is your primary **role** in projects using VA data?

- Investigator, PI, Co-I
- Statistician, methodologist, biostatistician
- Data manager, analyst, or programmer
- Project coordinator
- Other please describe via the chat function

Poll #2:

How many years of experience working with VA data?

- None I'm brand new to this!
- One year or less
- More than 1, less than 3 years
- At least 3, less than 7 years
- At least 7, less than 10 years
- 10 years or more





Session roadmap

Introduction to phenotyping and CIPHER program

CIPHER Online overview and live demonstration

CIPHER VA Wiki overview and live demonstration

Applications of CIPHER and future directions



Session roadmap

Introduction to phenotyping and CIPHER program

CIPHER Online overview and live demonstration

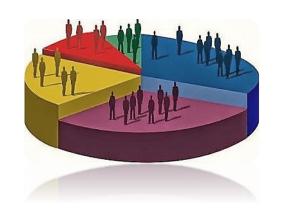
CIPHER VA Wiki overview and live demonstration

Applications of CIPHER and future directions



Poll #3:

Have you used electronic health records (EHR) data for your work?

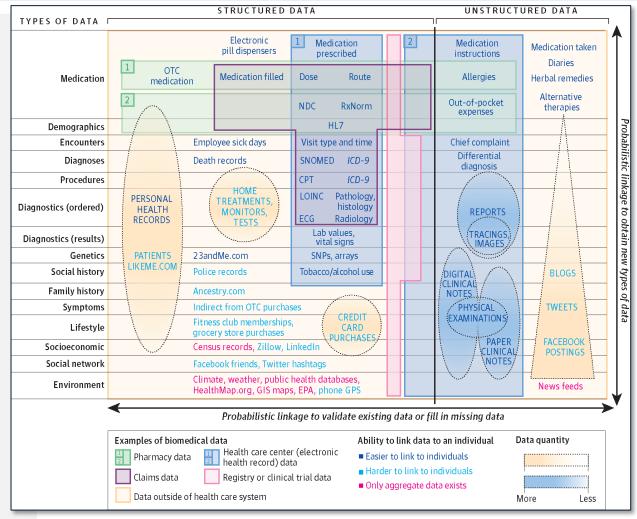


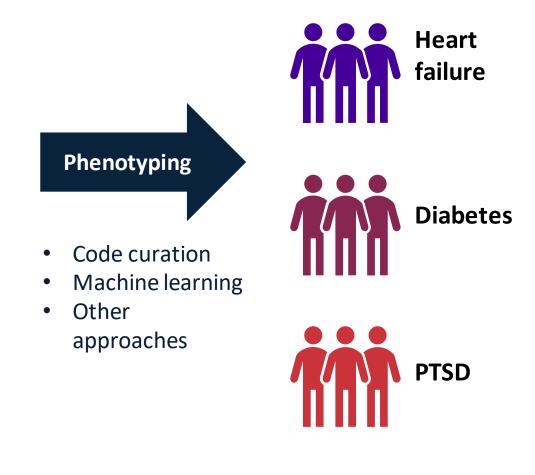
- Yes, for research
- Yes, for healthcare operations
- No, but I plan to
- No





EHRs are a rich resource for clinical research and healthcare operations





VIReC

Weber JAMA 2014

Phenotype development has its challenges



Institutional knowledge



Computing resources





System specific data variability





Centralized Interactive Phenomics Resource (CIPHER)



CIPHER Online

 A publicly accessible platform centralizing phenotype definitions and phenotyping resources

Mission: Accelerate health data innovation by providing an integrated and interactive knowledge sharing platform

CIPHER VA Wiki

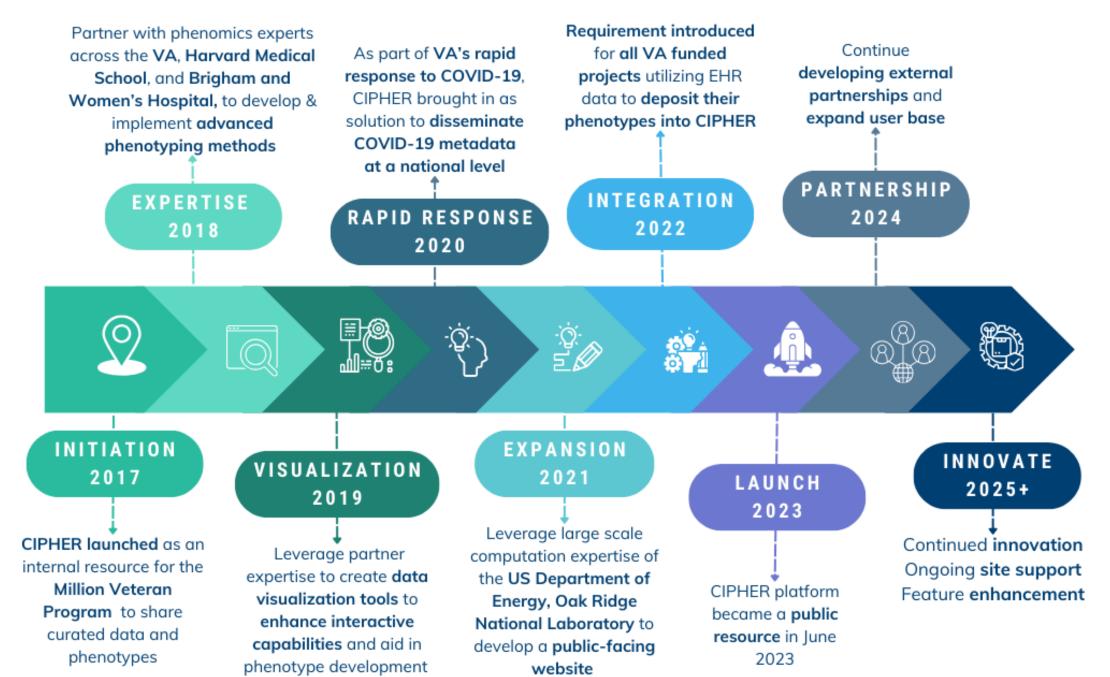
 A VA internal site with searchable data resources for the VA community

Funded by the US Department of Veterans Affairs, Office of Research and Development





CIPHER PROGRAM MILESTONES



CIPHER is integrated into the VA awards process

- VA awardees required to deposit phenotype definitions
- Successfully piloted with 12 projects and collected 46 phenotypes

URLs/hyperlinks and video clips are prohibited **except** in the *Biographical Sketch* and *Bibliography & References Cited* attachments.

CIPHER (Centralized Interactive Phenomics Resource)

Brief introduction to phenotyping and CIPHER

An electronic heath records (EHR) based phenotype is a clinical condition or characteristic derived from EHRs and linked data sources. Some examples of phenotypes include age, diabetes, asthma medications and cardiovascular disease. Phenotypes have been used in case-control studies, cohort studies, genetic research, and clinical decision support. The CIPHER (Centralized Interactive Phenomics Resource) knowledgebase aims to make EHR-based phenotyping scalable and efficient by enabling reuse and facilitating collaboration. The CIPHER platform includes electronic health record (EHR)-based phenotype definitions, algorithms, performance metrics, metadata, and data visualization tools. Additionally, users can find a number of resources for phenotype development and VA data resources.

Objective

Applicants proposing to develop new phenotype definitions as part of their VA-funded research will be required to contribute their phenotyping algorithm metadata, programming code, and validation metrics to CIPHER. Researchers are also encouraged to browse CIPHER to see if a phenotype they need is already in the library, as it currently contains thousands of phenotypes at different stages of development. You can learn more about how to contribute to CIPHER here.

Requirements

Applicants will be required to provide updates on the development of their phenotype in each Research Performance Progress Report (RPPR). Once the phenotype is finalized, it must be submitted to CIPHER, and the award number must be listed in the acknowledgement section of the phenotype page(s). Applications will also be required to include the link to their phenotype page(s) in section C. "Products of the RPPR" when it is completed or by the end of the award, whichever comes first.



CIPHER is integrated into the VA awards process

- VA awardees required to deposit phenotype definitions
- Successfully piloted with 12 projects an collected 46 phenotypes

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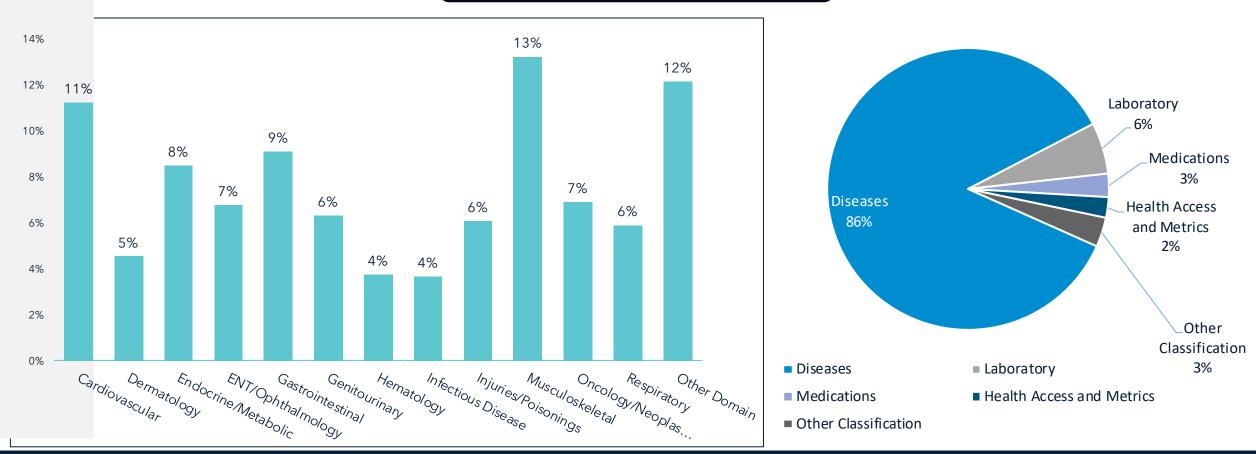
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Expanding CIPHER knowledgebase content

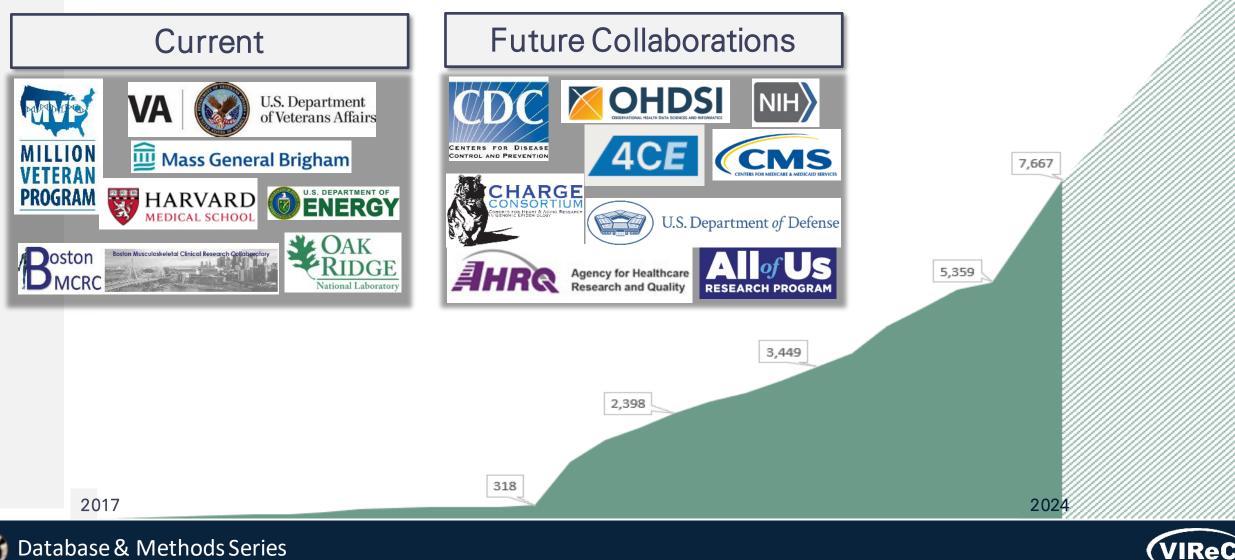
6,500+ Phenotypes





Database & Methods Series

CIPHER's userbase continues to grow





Session roadmap

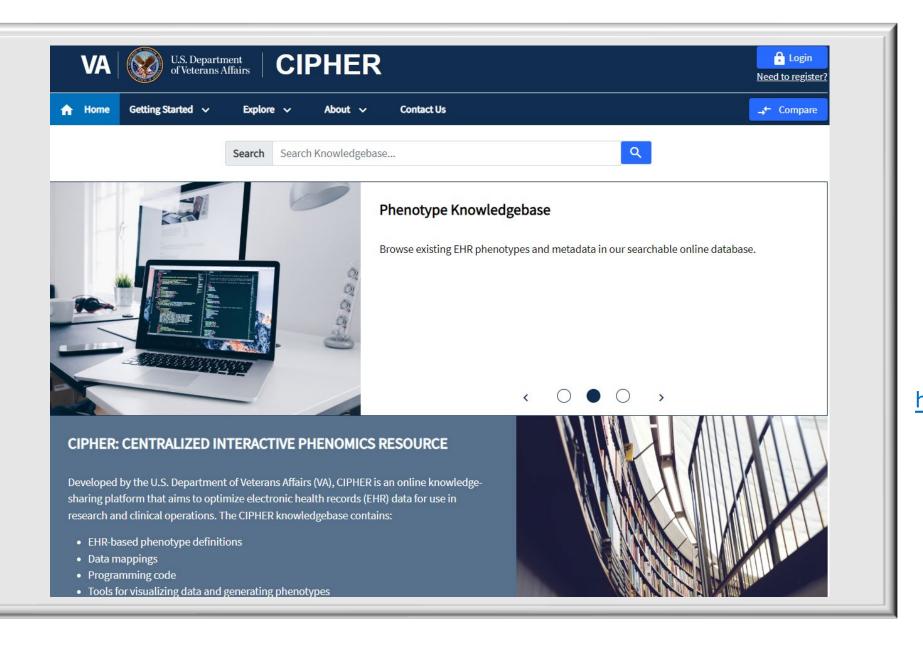
Introduction to phenotyping and CIPHER program

CIPHER Online overview and live demonstration

CIPHER VA Wiki overview and live demonstration

Applications of CIPHER and future directions





CIPHER Online

Public facing website https://phenomics.va.ornl.gov/





Searchable database of phenotype definitions

CIPHER Online (Public)

A. Phenotype knowledgebase

- B. Phenotype comparison tool
- C. Phenotype collection workflows
- D. Data visualization tools
 - Search using free text and filters
 - View phenotype version history
 - Unique URL for each phenotype
 - Metadata stored using CIPHER standard

	VA W U.S. Department of Veterans Affairs	CIPHER	Login Need to register?
A	Home Getting Started V Explor	✓ About ✓ Contact Us	→ Compare
;	Clear Filters Collapse	Knowledgebase Search	
.	Data Classification	Search dementia	٩
••	Related Disease Domain	Search results for: dementia ×	
E	Data Sources Used	Search relevance vitems per page: 10 vitems pe	> >1
÷	Algorithm components		/ /1
i:I	Role of phenotype in analysis	Dementia, All Cause (MVP Cog Working Group)	Compare
Ē	Date algorithm created	Author: MVP Cognitive Decline and Dementia During Aging Working Group, Million Veteran Program (MVP)	
		Algorithm Created: 06/01/2023	
	Author	Alzheimer's disease and related dementias among aging veterans: Examining gene-by-environn interactions with post-traumatic stress disorder and traumatic brain injury, MVP Cognitive Decli	
	MVP Cognitive Decline and Dementia During Aging Working Group (5) Million Veteran Program (MVP) (5)	Dementia During Aging Working Group, Dementia, All Cause (MVP Cog Working Group), Dement Cause (MVP Cog Working Group)_Additional Information.docx, Mark W. Logue, Richard Hauger, Merritt, and Matthew Panizzon. Phenotypes developed by the MVP Cognitive Decline and Deme During Aging Working Group, with support from VA Grants BX004192 (MWL), BX005749 (MWL), IO CX001727 (RH), and IK2 CX001952 (VM)., The Million Veteran Program (MVP) Cognitive Decline and	Victoria n tia 1
Σ	Method used	Dementia During Aging Working Croup Created a scale of nested ICD-code based dementia pher from the most restrictive (AD) to the least restrictive (all cause dementia) - see Table 1 below. Th phenotypes were developed for use in genetic studies of dementia	otypes,
F	Publication		
•	′es × ×	Alzheimer's Disease, Non-specific Dementias (MVP Cog Working Group)	Compare
		Author: MVP Cognitive Decline and Dementia During Aging Working Group, Million Veteran Program (MVP)	

https://phenomics.va.ornl.gov/web/cipher/search



CIPHER phenotype metadata standard

Phenotype Name

Phenotype Description *Phenotype purpose and aims (E.g., to maximize sensitivity)*

> Publication / Acknowledgment

Algorithm Description Logic applied to components to generate algorithm

Code Samples Programming code or code repository link

Population Population used to develop algorithm

Authors / Contacts

Data Sources Data source used to generate the phenotype

Data Classifications Disease, demographics, laboratory test, etc.

Role in Analysis Primary outcome/exposure, inclusion requirement, etc.

Related Disease Domain Cardiovascular, dermatology, genitourinary, etc.

Unique Identifier

Keywords

MeSH Terms

Methods Used Rules based, machine learning, etc.

Context of Development Research, healthcare operations, etc.

Algorithm Components Medical Vocabularies (ICD, LOINC, etc.)

Algorithm Creation Date

Lab Units / Values

Algorithm Validation / Performance Metrics Sensitivity, specificity, etc.

Attachments Tables, figures, slides, etc.

Legend

- Free Text
- Semi-controlled Authority
- Standard Vocabulary
- Empirical Value
- 🔵 Other



Honerlaw JAMIA 2023

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Comparison of phenotype metadata

CIPHER Online (Public)

A. Phenotype knowledgebase

- **B.** Phenotype comparison tool
- C. Phenotype collection workflows
- D. Data visualization tools
 - Compare metadata across up to 7 phenotypes

Compare

View List

 \checkmark

Dementia, Early Onset (TORCH)

Author: The Trajectories of Resilience, Community, and Health Lab

- K (TORCH),Identifying and Validating Complex Comorbidity Clusters in OEF-OIF Veterans, DHI 09-237
- Algorithm Created: 10/23/2019 ••••

A 😡 U.S. Departm	nent 🏫 Home Getting Started 🗸	Explore 🗸 About 🗸 Conta	act Us
henotype Com	parison		
∧ <u>Dementia, Early (</u> ✓	Dnset (TORCH)		i
Dementia (Gaziar	<u>10)</u>		ŧ
Dementia, All Cau	<u>ise (MVP Cog Working Group)</u>		Ť
ighlight - Differences -	•		
	Dementia, Early Onset (TORCH)	<u>Dementia (Gaziano)</u>	Dementia, All Cause (MVP Cog Working Group)
Method Used	Rules-Based (i.e., only structured data were used)	Rules-Based (i.e., only structured data were used)) Rules-Based (i.e., only structured data were used)
Algorithm Description	Presence of any ICD code for Alzheimer's disease (A or Frontotemporal dementia (FTD)	D) 1 inpatient or 2 outpatient ICD Codes	To quality as a case requires the presence of two or more ICD codes.

	1					
Method Used	Rules-Based (i.e., only structured data were used)	Rules-Based (i.e., only structured data were used)	Rules-Based (i.e., only structured data were used)			
Algorithm Description	Presence of any ICD code for Alzheimer's disease (AD) or Frontotemporal dementia (FTD)	1 inpatient or 2 outpatient ICD Codes	To quality as a case requires the presence of two or more ICD codes.			
ICD-9 Diagnostic Codes	4 Total	46 Total 42 Missing	27 Total 23 Missing			
	331.0, 331.1, 331.11, 331.19	046.1, 046.11, 046.19, 046.3, 290.0, 290.10, 290.11, 290.12 , 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 29 0.43, 290.8, 290.9, 291.2, 291.20, 291.21, 291.22, 291.23, 2 94.1, 294.10, 294.11, 294.8 , 331.0, 331.1, 331.11, 331.19, 331.2, 331.3, 331.4, 331.5, 331.6, 331.7, 331.81, 331.82, 33 1.83, 331.89, 331.9, 332.0, 333.0, 333.4, 797.	290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 29 0.3, 290.40, 290.41, 290.42, 290.43, 294.10, 294.11, 294.2 0, 294.21, 294.8 , 331.0, 331.1, 331.11, 331.19, 331.2, 331.5, 331.82, 332.0, 332.1, 333.4			
ICD-10 Diagnostic Codes	3 Total		20 Total 17 Missing			
	G30.9, G31.01, G31.09		A81.00, F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F 10.96, G10., G20., G30.0, G30.1, G30.8 , G30.9, G31.0, G31.01, G31.09, G31.1, G31.83, G91.2			

https://phenomics.va.ornl.gov/web/cipher/search



Standardized collection of phenotype metadata

CIPHER Online (Public)

- A. Phenotype knowledgebase
- B. Phenotype comparison tool
- C. Phenotype collection workflows
- D. Data visualization tools
 - Self-service phenotype submission & editing
 - CIPHER can assist with automated entry of large number of definitions
 - CIPHER quality review for completeness and clarity

	H
Add Algorithm Component	
2 Enter Algorithm Component Codes	
 ICD-9 Diagnostic Codes How would like to add the information? Search for a code by its name or description Perform a wildcard search by using % or * Enter codes directly. You may provide multiple codes separated by a comma. No other special characters are allowed. 	
434.% 434.0 - CEREBRAL THROMBOSIS 434.00 - CEREBRAL THROMBOSIS W/O MENTION OF CEREBRAL INFARCTION 434.01 - CEREBRAL THROMBOSIS W/ CEREBRAL INFARCTION 434.10 - CEREBRAL EMBOLISM W/O MENTION OF CEREBRAL INFARCTION 434.1 - CEREBRAL EMBOLISM 433.01 433.11 433.21 433.21	
433.81 433.91 434.01 434.11 434.9 434.91 434.0 434.1 434.9 OK Cancel	

https://phenomics.va.ornl.gov/web/cipher/contribute



Visualization tools connected to phenotype definition knowledgebase

CIPHER Online (Public)

- A. Phenotype knowledgebase
- B. Phenotype comparison tool
- C. Phenotype collection workflows

D. Data visualization tools

- Provide interactive approach to exploring metadata
- Aid in phenotype development
- Linkage to definitions in phenotype knowledgebase



KESER creates a knowledge map to allow users to visualize relatedness among diseases, treatment, procedures, and laboratory measurements.

Phecode to ICD Map assists users in developing clinically meaningful disease phenotypes by enabling the user to visualize the relationships

enabling the user to visualize the relationships between various ICD codes and Phecodes.

https://phenomics.va.ornl.gov/web/cipher/vistools



Phe:250.2

Phe:250.1
 Phe:250.11
 Phe:250.12
 Phe:250.12
 Phe:250.13
 Phe:250.41
 Phe:250.44
 Phe:250.44
 Phe:250.45
 Phe:250.55
 Phe:250.55
 Phe:250.55

Phe:250.2 Phe:250.6 Phe:250.21 Phe:250.7

Phe:250.2 Phe:250.2

ICD-9

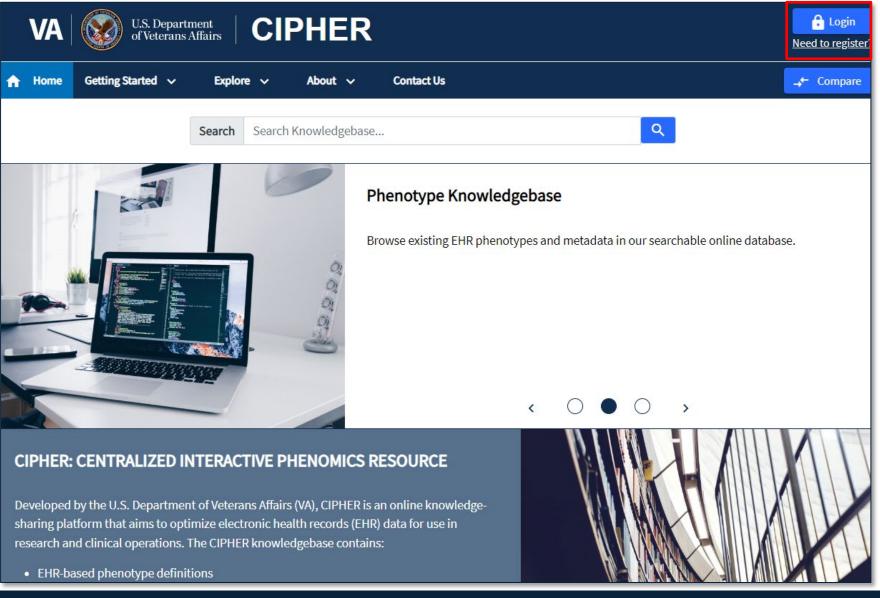
CIPHER Online Demonstration https://phenomics.va.ornl.gov/





Live Demo: CIPHER navigation

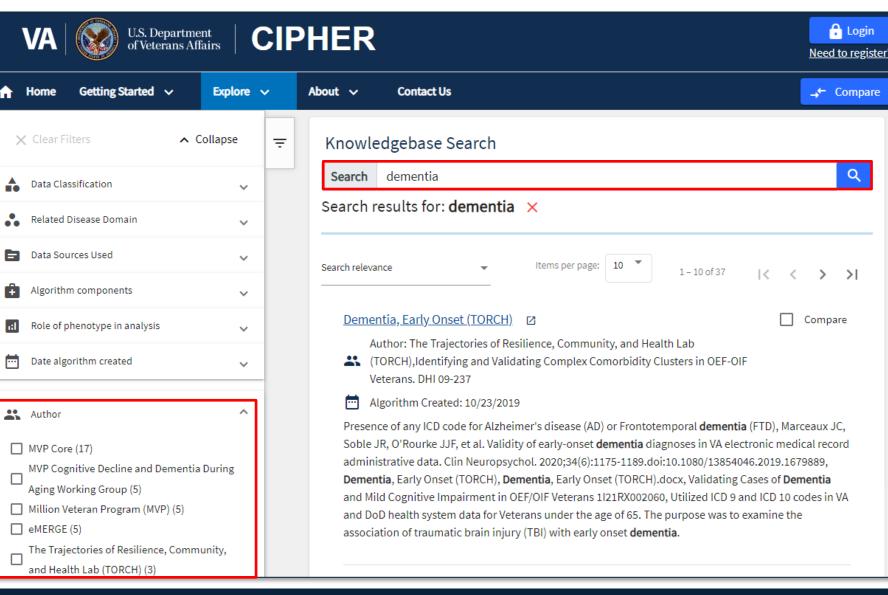
- Public facing website
- Log-in not required to browse the site





Live Demo: Phenotype knowledgebase

- Search options
 - Free text
 - Filters
- Phenotypes <u>do not</u> need to be published or validated to be accepted
- Sharing programming code is encouraged but <u>not required</u>



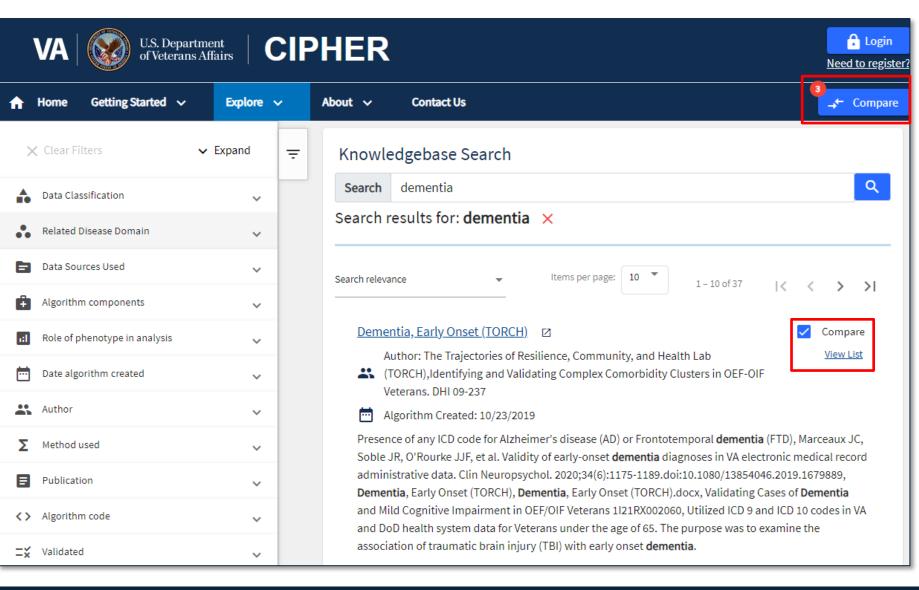




Live Demo: Phenotype comparison

- Select up to 7 phenotypes to compare metadata
- Click "view list" or "compare" to view these phenotypes side-by-side

Database & Methods Series





Live Demo: Phenotype comparison

- Use arrows to mark the "base" phenotype to use as basis for comparison (grey box)
- Highlight differences or commonalities
- May add/remove phenotypes from comparison

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		VA		U.S. Departm of Veterans A	ffairs G	IPHER						Nee	ed to register
	♠	Home	Getting	Started 🗸	Explore 🗸	About 🗸	Conta	ct Us				•	- Compare
	Back	to Knowle	<u>dgebase</u>										
	Phe	enotyp	e Com	parison									
A	$\hat{\mathbf{v}}$	<u>Dement</u>	<u>ia, Early O</u>	<u>nset (TORCH)</u>									Î
B	B Dementia, All Cause (MVP Cog Working Group). Dementias (MAP). 											Î	
С									Î				
	Highlight - Differences -							E	3		С		
				Den	nentia, Early Onset (1	<u>FORCH)</u>	Demer	ntia, All Cause	(MVP Cog Working Group)		Dementias (M/	<u>AP)</u>	
	ICD-	-9 Diagnost	ic Codes	4 Total			27 Total	23 Missing		29 Total	25 Missing		
	331.0, 331.1, 331.11, 331.19					0.3, 290.40, 2 0, 294.21, 29 , 331.0, 331.2	290.41, 290.42 9 4.8 1, 331.11, 331	.12, 290.13, 290.20, 290.21, 2 2, 290.43, 294.10, 294.11, 294 .19, 0, 332.1, 333.4	2 2, 290.20, 2 90.43, 294.	.00, 290.1, 290.10, 290 290.21, 290.3, 290.4, 2 .1, 294.10, 294.11, 294 1.00, 331.1, 331.11, 33	290.40, 290.41 4.2, 294.20, 29	, 290.42, 2 4.21	
	ICD-:	10 Diagnos		3 Total 530.9, G31.01, G3	21.00		20 Total	17 Missing	2.80, F02.81, F03.90, F03.91,	22 Total	19 Missing , F01.50, F01.51, F02,	E02 0 E02 00	E02 91 E0
				550.5, 651.01, 6.	51.03		10.96, G10.,	G20., G30.0, G		3, F03.9, F0	03.90, F03.91, G30, G3	30.0, G30.1, G3	30.8



Live Demo: Phenotype metadata

- Unique URL to enable sharing
- Programming code shared directly on CIPHER, but users may provide code repository link

VA U.S. Department of Veterans Affairs CIPHER	Login <u>Need to register?</u>
About ✓ Contact Us	→ ← Compare
Back to Knowledgebase Dementia, All Cause (MVP Cog Working Group)	Compare
Basic Information and Contact Abbreviations and Keywords Alzheimer's Disease Cognitive Decline	^
Publication ? Alzheimer's disease and related dementias among aging veterans: Examining gene-by-environment interactions with post-traumatic stress disorder and traumatic br Data Classification(s) Diseases	<u>ain injury</u>
Related Disease Mental/ Behavioral Health Neurology Author(s)	
MVP Cognitive Decline and Dementia During Aging Working Group 👫 Million Veteran Program (MVP)	

CIPHER - Dementia, All Cause (MVP Cog Working Group) (ornl.gov)



Live Demo: Phenotype metadata

- Multiple sets of validation metrics may be added to a phenotype
- For example, this phenotype has validation metrics from application at 3 health systems
 - VA Healthcare System
 - Beth Israel Deaconess
 Medical Center
 - University of Pittsburgh Medical Center

Note to Knowledgebase ong COVID-19 ■ Basic Information and Contact Abbreviations and Keywords Contact Us Contact Us Compare
ong COVID-19 Compare Basic Information and Contact
ong COVID-19 Compare Basic Information and Contact
Basic Information and Contact
Abbreviations and Keywords
COVID-19 SARS-CoV-2 PASC Post-Acute COVID-19 Syndrome Post-Acute Sequelae of SARS-CoV-2 Infection
Publication (?)
Potential pitfalls in the use of real-world data for studying long COVID
Characterization of Post-COVID-19 Definitions and Clinical Coding Practices: Longitudinal Study
Data Classification(s)
Diseases
Related Disease
Infectious Disease
Author(s)
WVP Core 4CE

CIPHER - Long COVID-19 (ornl.gov)





- Create an account to submit a phenotype through our webform
- User accounts are also needed for using Unified Medical Language System (UMLS) vocabularies
- A team can share an account to manage phenotypes together



How to Contribute

Contributing Phenotypes

We have an easy-to-use process and resources for contributing your phenotype to CIPHER.

You may start by visiting our <u>How to Use CIPHER</u> page, which gives an overview of phenotyping, how phenotypes are used, benefits of contributing your phenotype to CIPHER, and general tips for using the CIPHER website.

Next steps to contribute a phenotype:

- 1. Create a user account. Navigate to the top right-hand corner of the screen and choose to register a new account. Please enter a valid email that you have access to. You will need this to verify your account.
- Complete the Phenotype Entry Form. Open the phenotype entry form by clicking <u>Create New Phenotype</u>. You can also navigate to the form directly via the navigation bar at the top of the screen, under the Getting Started tab. You may save your work in progress and return to finish entering your phenotype at any time. To resume editing, please click on "My Phenotypes" under the "Getting Started" tab on the navigation bar.
 a. Choose the type of phenotype you would like to submit (general, lab, or medication).
 - b. Follow the instructions in the online wizard to complete the form.
- 3. Submit your phenotype. Once you have entered in all your phenotype details, you can review your entry and submit for review.
 - a. Once your phenotype is submitted it will be reviewed by the CIPHER team. If our team has any questions regarding the submission, we will reach out to the contact listed on the entry form. Once the phenotype entry is finalized by CIPHER it will be searchable within our <u>Phenotype Knowledgebase</u>.
 - b. You can check the status of your submission by navigating to "My Phenotypes" on the navigation bar under the Getting Started tab.
 - c. Should you have any questions about your submission in the meantime, please contact $\underline{\text{CIPHER}@va.gov}.$

https://phenomics.va.ornl.gov/web/cipher/contribute



Section 1: Basic Information and Contact

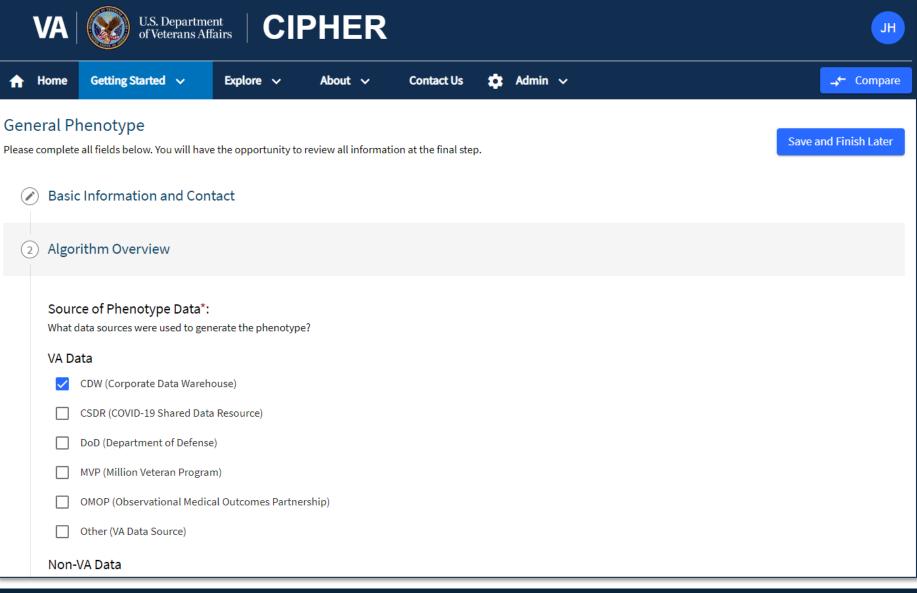
- Save and finish later
- May search against metadata already shared in the knowledgebase

	U.S. Departme of Veterans Aff	airs C	PHER					Э
↑ Home	Getting Started 🗸	Explore 🗸	About 🗸	Contact Us	*	Admin 🗸		→← Compare
General Phe Please complete al	enotype Il fields below. You will have	e the opportunity to	review all informat	tion at the final ste	ep.			Save and Finish Later
1 Basic Ir	nformation and Con	tact						
	type Name*: he name of your phenotype	2?						
	^{pe Name *} - Dementia, All Cause							
Abbrev	iations and Keyword	s*:						
	previations or keywords car		r phenotype?					
• Key	words will be used as sea	irch terms in the lib	orary.					
	the search below to sele		-					
	ne keyword is not yet store			entry with the plu	us icon.			
	remove a keyword please suggest utilizing <u>MESH</u> to							
		iniu relevant Keyw	orus.					
	Is and Abbreviations *	and Abbraviation						
# A	Search Keywords	and Abbreviations	5					



Section 2: Algorithm Overview

 May list VA and/or non-VA data sources







Section 3: Algorithm Components

- Search for code sets using standard vocabularies or enter custom fields
- Share code repository link

VA VI U.S. Department of Veterans Affairs CIPHER	HU
A Home Getting Started ✓ Explore ✓ About ✓ Contact Us Admin ✓	→ ← Compare
General Phenotype Please complete all fields below. You will have the opportunity to review all information at the final step.	Save and Finish Later
Basic Information and Contact	
Algorithm Overview	
3 Algorithm Components	
Method Used*: What logic was applied to the algorithm components to create this phenotype? (Select all that apply)	
Rules-Based (i.e., only structured data were used)	
Machine learning: Supervised	
Machine learning: Semi-Supervised	
Machine learning: Unsupervised	
Machine learning: Other machine learning approach	
Other	

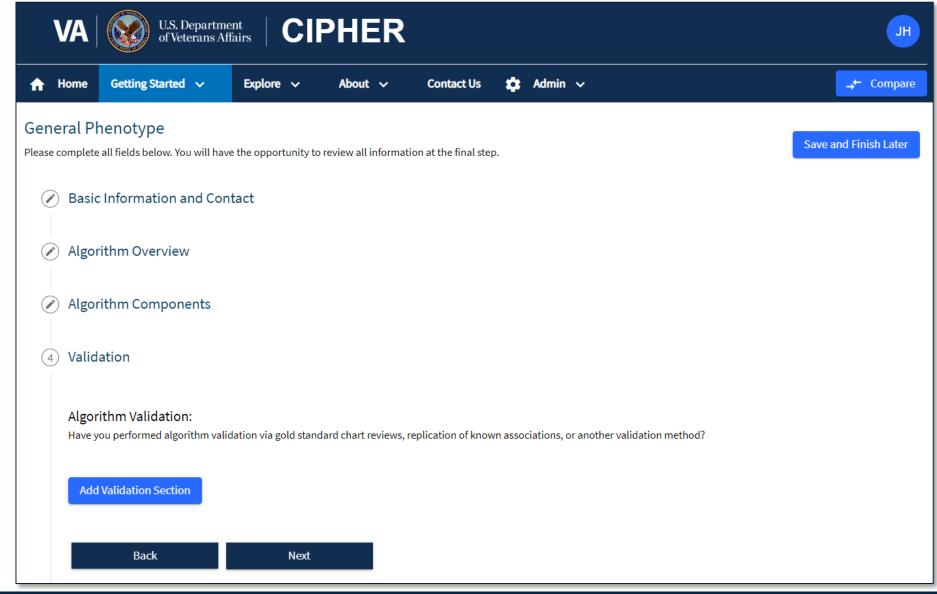


Section 4: Validation

- Add performance metrics (sensitivity, specificity)
- Store multiple validations

Section 5: Additional Information

Add attachments







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Live Demo: My phenotypes

- Store drafts here until you are ready for submission
- View phenotypes pending review by CIPHER

VA	U.S. Departme of Veterans Aff	nt airs CIP	HER								HL
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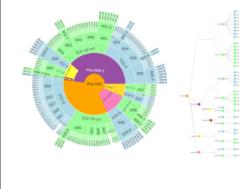
Live Demo: Visualization Tools

- Linkage from tool to phenotype definitions in CIPHER knowledgebase
- Instructional videos and use cases

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Data Visualization Tools

This page contains tools to allow users to visualize data results as well as tools to help users in developing their phenotypes. A short description is provided for each tool. Please expand the details section under each instrument to learn more about that tool and its specific utility.



Phecode to ICD map

Visualize mappings from Phecode to ICD-9 and ICD-10 codes.

Overview	Uses	Author & Citation	Video	
----------	------	-------------------	-------	--

Electronic health record (EHR)-based studies offer several advantages in research: they are cost efficient, allow for large scale longitudinal analyses, and provide the potential to analyze hundreds of human diseases, drug responses, and many observable clinical traits.

Billing codes, or International Classification of Diseases (ICD) codes, are often leveraged to define a patient's phenotype in EHR-based studies. However, these are not always organized meaningfully for the purpose of high-throughput phenotypic analyses. <u>PheCodes</u> facilitate the use of ICD codes for research by regrouping ICD-9 and ICD-10 billing codes into clinically relevant phenotypes.



Live Demo: How to cite

When reusing a phenotype:

 Cite publication, if available

Cite the unique URL



Using the CIPHER phenotype definition library

CIPHER collects phenotype metadata definitions using a standard approach developed with the VA phenomics community (JAMIA 2023).

- You can use our smart search to browse phenotype definitions and identify the most relevant definition for your use case.
- If you have feedback or questions on a phenotype definition, please email the contact listed at <u>CIPHER@va.gov</u> so that the entry can be updated with clarifications.
- If you deployed one of the phenotype definitions on your cohort and would like to share performance metrics, please email <u>CIPHER@va.gov</u> to update the phenotype page.

Guidelines for citations

Please use the following instructions for citing the use of CIPHER and any phenotypes utilized:

- Citing the CIPHER Phenotype Library
 - Please cite use of the CIPHER phenotype library by referencing the article below: Honerlaw J, Ho YL, Fontin F, Gosian J, Maripuri M, Murray M Sangar R, Galloway A, Zimolzak AJ, Whitbourne SB, Casas JP, Ramoni RB, Gagnon DR, Cai T, Liao KP, Gaziano JM, Muralidhar S, Cho K.
 Framework of the Centralized Interactive Phenomics Resource (CIPHER) standard for electronic health data-based phenomics knowledgebase. J Am Med Inform Assoc. 2023 Mar 7:ocad030. doi: 10.1093/jamia/ocad030. Epub ahead of print. PMID: 36882092.
- Citing Specific Phenotypes
 - If the phenotype has an associated publication listed on the phenotype page, please reference it.
 - If the phenotype does not include a publication, please follow the guidance in the acknowledgements section of the phenotype and/or cite the URL of the phenotype page used.

Contributing to the CIPHER phenotype library

Navigate here to contribute a phenotype to CIPHER.

Benefits of contributing your phenotype to CIPHER

- Increases the visibility of your publication, program, and/or project.
- Increases the reproducibility of your methods and the number of citations of your publications.
- Facilitates collaboration by sharing your work products, enabling collaboration requests, and opportunity to obtain feedback from the CIPHER user community.
- Provides opportunities to have your work featured in CIPHER newsletters and communications to the CIPHER user community.
- Affords you with a sharable platform to disseminate work products and supports compliance with the FAIR Data Principles.



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Learn more about CIPHER Online

Journal of the American Medical Informatics Association, 30(5), 2023, 958–964 https://doi.org/10.1093/jamia/ocad030 Advance Access Publication Date: 7 March 2023 Brief Communication

d030 2023 INFORMATICS PROPESSIONALS. LEADING THE WAY

CIPHER Metadata Standard

Brief Communication

Framework of the Centralized Interactive Phenomics Resource (CIPHER) standard for electronic health data-based phenomics knowledgebase

Jacqueline Honerlaw ⁽¹⁾, Yuk-Lam Ho¹, Francesca Fontin¹, Jeffrey Gosian¹, Monika Maripuri¹, Michael Murray¹, Rahul Sangar¹, Ashley Galloway¹, Andrew J. Zimolzak ^{2,3}, Stacey B. Whitbourne^{1,4,5}, Juan P. Casas^{1,4,5}, Rachel B. Ramoni ⁶, David R. Gagnon^{1,7}, Tianxi Cai^{1,8,9}, Katherine P. Liao^{1,4,9,10}, J. Michael Gaziano^{1,4,5}, Sumitra Muralidhar⁶, and Kelly Cho ^{1,4,5}

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Corresponding Author: Jacqueline Honerlaw, Massachusetts Veterans Epidemiology Research and Information Center

Journal of the American Medical Informatics Association, 2024, 1–9 https://doi.org/10.1093/jamia/ocae042 Research and Applications



CIPHER Design and Resources

Centralized Interactive Phenomics Resource: an integrated online phenomics knowledgebase for health data users

Jacqueline Honerlaw (1), RN, MPH^{*,1,2}, Yuk-Lam Ho, MPH^{1,2}, Francesca Fontin, MPH^{1,2}, Michael Murray, MS^{1,2}, Ashley Galloway, MPH^{1,2}, David Heise, MS³, Keith Connatser, BS³, Laura Davies, PMP³, Jeffrey Gosian, BS^{1,2}, Monika Maripuri, MBBS, MPH^{1,2}, John Russo, MS^{1,2,4}, Rahul Sangar, MPH^{1,2}, Vidisha Tanukonda, MD^{1,5}, Edward Zielinski, ALM^{1,2}, Maureen Dubreuil, MD, MSc^{2,6}, Andrew J. Zimolzak (1), MD, MMSc^{7,8}, Vidul A. Panickan, MS^{2,9}, Su-Chun Cheng, ScD^{2,9}, Stacey B. Whitbourne, PhD^{2,10,11,12}, David R. Gagnon, MD, PhD^{2,13}, Tianxi Cai, ScD^{2,9,14}, Katherine P. Liao, MD, MPH^{2,12,15,16}, Rachel B. Ramoni (1), DMD, ScD¹⁷, J. Michael Gaziano, MD, MPH^{2,10,11,12}, Sumitra Muralidhar, PhD¹⁷, Kelly Cho (2), PhD, MPH^{1,2,10,11,12}

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J. Honerlaw and Y.-L. Ho authors contributed equally.

Abstract

Honerlaw JAMIA 2023 (PMID: 36882092)

Honerlaw JAMIA 2024 (PMID: 38481028)





Session roadmap

Introduction to phenotyping and CIPHER program

CIPHER Online overview and live demonstration

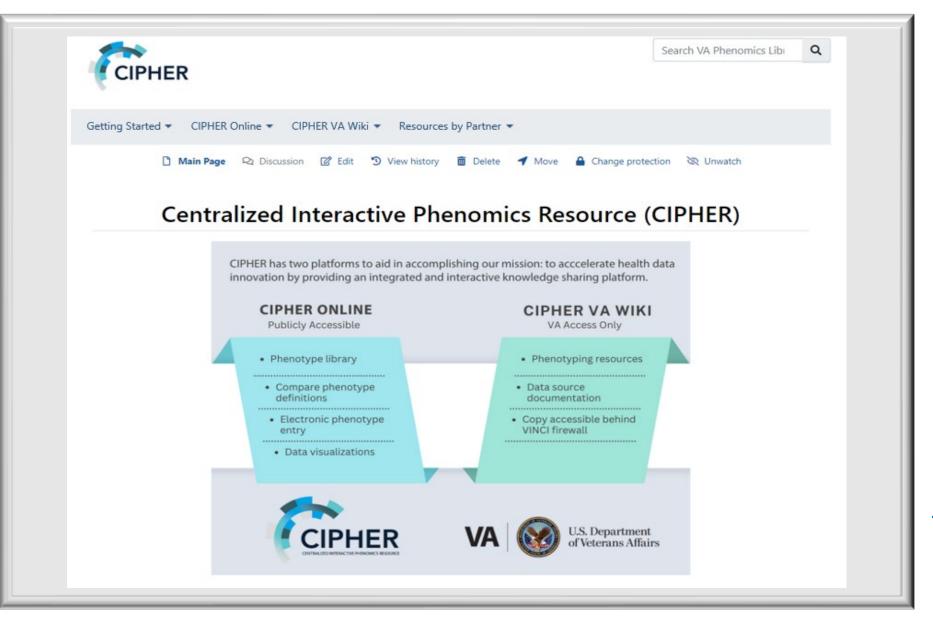
CIPHER VA Wiki overview and live demonstration

Applications of CIPHER and future directions





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CIPHER VA Wiki

VA internal website https://cipherwiki.va.gov/

VINCI workspace link https://cipher**dev**wiki.va.gov/



Resources for facilitating phenotype development

CIPHER VA Wiki (VA Internal)

A. Phenotyping resources

- B. Data source documentation
 - Phenotyping methods catalog
 - Best practices for chart review

Resource	Shared by	Description
Code QC	Boston CSP Epidemiology Center	Quality control (QC) process that the Boston CSPEC uses when reviewing code prior to manuscript submission, along with links to resources that can be utilized during QC
TRACE	Million Veteran Program (MVP) Data Core	Microsoft Access based tool developed for the purpose of chart abstraction and review.
VINCI SOPs	VINCI	Programming code developed by VINCI for pulling CDW and Cerner data

https://cipherwiki.va.gov/phenotype/index.php?title=Phenotyping_Resources

Catalogue of Phenotyping Methods

ARCH:Aggregated Narrative Codified Health

ARCH knowledge graph (KG) is a learning approach that provides a highly scalable method for effectively representing codified and narrative EHR concepts on a large scale, while recovering their network structure.

Click to Expand

Clustra:Multi-platform k-means clustering algorithm

Clustra is a package developed to use k-means clustering algorithm for analyzing longitudinal phenotypes using EHR data.

Click to Expand

(JSON)ize:Java script object notation

JSONize is a machine learning method to transform unstructured data to semi-structured documents.

Click to Expand

KOMAP:Knowledge-driven online multimodal automated phenotyping

KOMAP is a method that generates list of informative features by online narrative and codified feature search engine (ONCE), and enables the training of a multimodal phenotyping algorithm based on summary data.

Click to Expand

LATTE:Label-efficient incident phenotyping

LATTE is an algorithm developed to accurately annotate the timing of clinical events from longitudinal EHR data.

Click to Expand

Searchable data documentation

CIPHER VA Wiki (VA Internal)

A. Phenotyping resources

B. Data source documentation

Data dictionaries, trainings, tutorials, and programming code for:

- COVID-19 Shared Data Resource (CSDR)
- Million Veteran Program (MVP) Core Data
- VA Observational Medical Outcomes Partnership (OMOP)

MVP:Core Lifestyle (MVP Core Data

Contents [hide] 1 Overview

Data Dicti	onary
View Defir	nition

4 Example Query

Overview

Description: Lifestyle factors created by the MVP Data Analytics team. Reflects lifestyle factors at the tin completion.

View Name: [MVP].[CoreLifestyle_v23_1]

Contains data through: September 30, 2023

Data Dictionary

Column	Code or Value	Value Description	Definition	2.2.4 Me			
CoreLifestyleSID	MVP Core	use only		2.3.1 Vo 2.3.2 Mo			
VINCI_ID	VINCI_ID Identifier DACS team uses to assign a study mart ID in Genisis. Use this ID w VINCI for genetic analysis.						
MVPCore_id		Identifier assigned to MVP enrollees. This ID does not change over time, and can be used to unique person.					

OMOP:Observational Medical Outcomes Partnership (OMOP)

Contents [hide]							
1 VA OMOP Overview							
1.1 Rationale for a Common Data Model							
1.2 OMOP Data Model							
1.2.1 Basic OMOP Table Structure							
2 Key Resources for VA Researchers							
2.1 Available OMOP Datasets							
2.1.1 CDW OMOP							
2.1.2 Millennium OMOP							
2.1.3 DaVINCI OMOP							
2.1.4 CMS OMOP							
2.2 Getting Access to OMOP Data							
2.2.1 Preparatory to Research Access							
2.2.2 Research Access							
2.2.3 National Operation Access							
2.2.4 Medicare OMOP							
2.3 VA OMOP Release Notes							
2.3.1 Vocabulary Releases							
2.3.2 Monthly Releases							
3 OMOP Training Resources and Code Library							
be used to identify a							

https://cipherwiki.va.gov/phenotype/index.php?title=Data_Source_Documentation



Access CIPHER VA Wiki from VINCI workspace

- Copy of Wiki sent to VINCI workspace monthly
- To access:
 - Login to your Development
 Workspace or Standard
 Workspace
 - Copy/paste the following URL into the browser: <u>https://cipherdevwiki.va.gov/</u>





CIPHER VA Wiki Demonstration https://cipherwiki.va.gov/





How do CIPHER platforms differ?

	CIPHER Online	CIPHER VA Wiki	
URL	https://phenomics.va.ornl.gov/ Publicly accessible	https://cipherwiki.va.gov/ VA access only (NT account required)	
Users	<u>All</u> health data users	VA health data user community	
Scope	Public platform to develop, collect, store, and share computable phenotypes, metadata, and resources.	Platform with searchable resources for VA data users from priority initiatives; accessible on VINCI workspace.	
Content	 Phenotype knowledgebase Phenotype definition comparison Phenotype entry form Data visualization tools 	 Phenotyping resources (programming code, best practices, and methods catalog) Data source documentation (data dictionaries, trainings, and tutorials) 	
VINCI workspace	Not accessible	Copy of Wiki accessible at: https://cipher dev wiki.va.gov/	



Session roadmap

Introduction to phenotyping and CIPHER program

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Applications of CIPHER and future directions





CIPHER use case: Million Veteran Program

MVP Data Sources

Survey Data



Electronic Health Record Data



Genetic Data



Linkage to Additional Data Sources (NDI/CMS)

MVP Resources in CIPHER



.111

Phenotype algorithms

Data Visualization ToolsPhecode to ICD MapKESER Network

- PheWeb
- PheMEGA
- Metadata and results

Searchable survey data



CIPHER use case: Phenotype sharing example

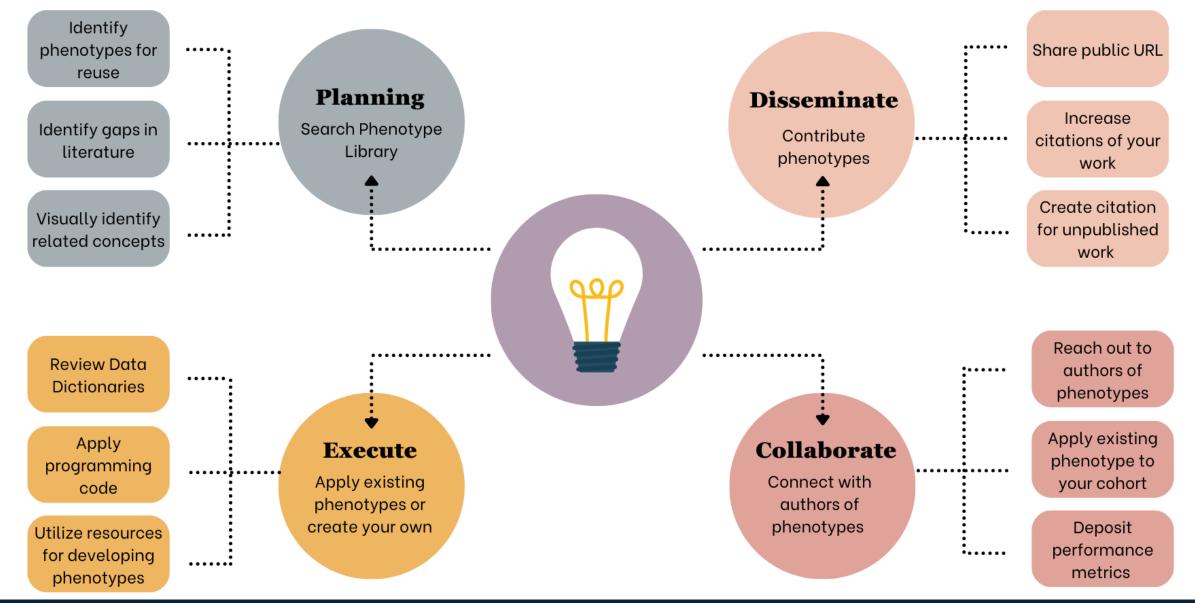
Development and validation of an electronic health record-based algorithm for identifying TBI in the VA: A VA Million Veteran Program study PMID: 39004925

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		"No TBI": Pr(having TEI)_calibrate? ~ 0.065	
semi-supervised approach (PheCAP). Nat Protoc. 2019;14 doi:10.1038/s41596-019-0227-6.	12):3426-44.	Where "main_icd" is the count of ICD for concussion as d the count of notes mentioning TBI as defined by CUI C08 notes mentioning brain concussion as defined by CUI C00 of notes mentioning Craniocerebral Trauma as defined by	76926; "C0006107" is the count of 06107, and "C0018674" is the count
View PubMed Web of Science ® Google Schola		***These details will also be shared on CIPHE community.***	R for use by the VA research
16. VA Cooperative Studies Program Epidemiology Analytics F Brain Injury (CSPEAR). 2020. https://phenomics.va.ornl.go		From the VA intranet, go to the following website to acces	ss the TBI-PheCAP phenotype:
viewer? uqid=9b5757e39c16429dee8e4a90762cfacc&name=Trau	atic_Brain_InjuryCSPE4	https://phenomics.va.ornl.gov/web/cipher/phenotype-view uqid=1c0d8fe4617041cce5ac248d5c53a6d3&name=Traur	
Google Scholar			
I7. MVP Data Core. Concussion (gwPheWAS). 2020. https://phenomics.va.ornl.gov/web/cipher/phenotype-vie/ uqid=62ecef229be54db9ae898523e163cdcb&name=Conc			Create phenotype in CIPHER
Google Scholar	or poster	Appendix 5. Guidelines for Applying the TBI-PheCAP A	-
19 MI/D Data Core Intracranial hemorrhage (inium/) (gwDheM	NEN 2020		or poster



CIPHER as part of the project lifecycle







Benefits of using CIPHER



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IReC

Poll #4:

How do you plan to use CIPHER Online? (Select all that apply)

- Browse phenotypes
- Compare phenotypes
- Submit phenotypes
- Use visualization tools
- Browse MVP gwPheWAS resources
- I do not plan to use CIPHER Online

Poll **#5**:

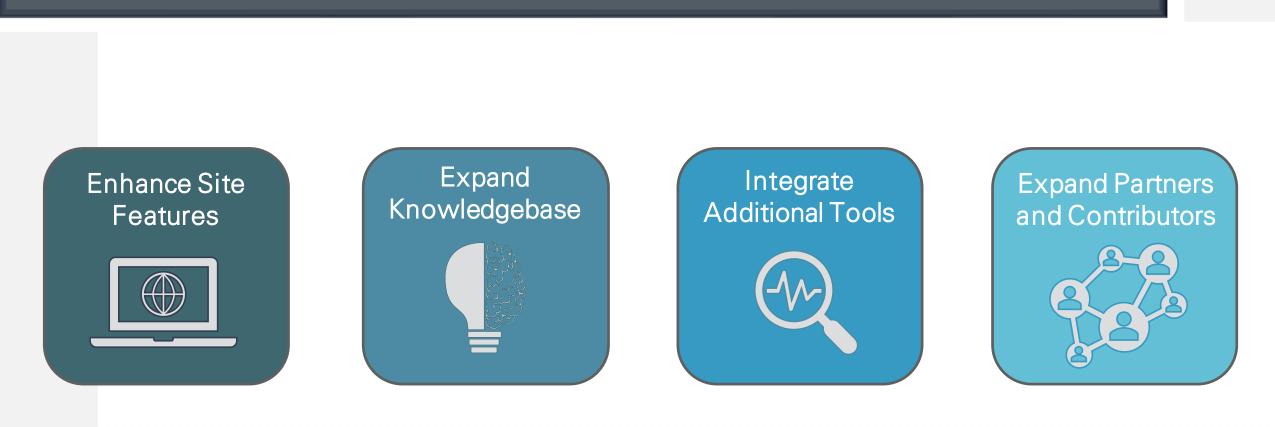
How do you plan to use CIPHER VA Wiki? (Select all that apply)

- Browse phenotyping resources
- Contribute phenotyping resources
- View OMOP, MVP, or CSDR documentation
- Access Wiki from within my VINCI workspace
- I do not plan to use CIPHER VA Wiki





Future directions





Oatabase & Methods Series

How to join the CIPHER community

- CIPHER is made possible by our collaborators.
- Here are some ways you can get involved and join the CIPHER community.



Provide Feedback Contribute your work





Highlight your work

Spread the word!



Subscribe to our newsletter



Contact Us



Acknowledgements

CIPHER Team

- Sumitra Muralidhar VACO Lead
- Kelly Cho Director
- Jackie Honerlaw Deputy Director
- Anne Ho Director for Data Operations
- Francesca Fontin Project Manager, VA Partnerships and User Experience
- Ashley Galloway Associate Director, Strategic Partnerships and Outreach
- Jeff Gosian Systems Support Librarian
- Monika Maripuri Project Manager, Clinical Phenotype Validation
- Michael Murray Lead Technical Architect
- Rahul Sangar Data Services Specialist
- Tiffany Sim Project Manager, CIPHER Online
- Joanne Sordillo SME for Environmental Exposure Data Domain
- Vidisha Tanukonda Project Manager, Clinical Adjudication
- Edward Zielinski Database Manager
- **CIPHER Online ORNL Team** David Heise, Laura Davies, Keith Connatser, Adrian Degraffenreidt
- Environment and Infrastructure Partners VINCI (Scott DuVall); MVP (Mike Gaziano); ORNL-DOE (David Heise)
- CIPHER Partners and Contributors

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Relevant Links

- <u>CIPHER VA Wiki</u> (VA Internal)
- <u>CIPHER Online</u> (Public)
- <u>CIPHER ORD Program</u> (Public)

References

- Honerlaw J, Ho YL, Fontin F, et al. Framework of the Centralized Interactive Phenomics Resource (CIPHER) standard for electronic health data-based phenomics knowledgebase. J Am Med Inform Assoc. 2023;30(5):958-964. doi:10.1093/jamia/ocad030 (<u>link</u>)
- Honerlaw J, Ho YL, Fontin F, et al. Centralized Interactive Phenomics Resource: an integrated online phenomics knowledgebase for health data users. J Am Med Inform Assoc. Published online March 13, 2024. doi:10.1093/jamia/ocae042 (<u>link</u>)

Contact Us

<u>CIPHER@va.gov</u>



Please reach out to CIPHER to schedule a demonstration, refer us to health data users who are not part of the CIPHER community, or to receive summary slides to help us spread the word at conferences or other meetings.



THANK YOU! Questions?







CONTACT INFORMATION

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O DATABASE & METHODS CYBERSEMINAR SERIES

Next session:

October 7th at 1 pm Eastern

Meet VIReC: The Researcher's Guide to VA Data



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Database & Methods BONUS SLIDES





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Resources for VA Data Users

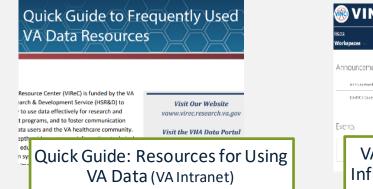
Select image to visit page







ESOURCE CENTER (VIRCC)	
VA Millennium EHR Data Documentation & Resources	
Overview	
VA Nilennium electronic health record (DIR) data documentation and renormate help new and tessaned data users with understanding the structure and contents of CDV Nilennium data and provide information or VAS transition to the Cerner Milennium electronic health neord (BHR).	Learn / VA Nill
Sign-up for VIReC product news and updates. Bmail the VIReC <u>Herobask</u> to receive notification of VIReC's new Millionnium Data products and product updates.	in childr for Da in Color
How are we doing? Take our <u>short survey</u> to shore your thoughts about the Millennium resources below. We value your feedback.	a 11 RH
Data Documentation	E Deta
Expand each type of documentation below to view these resources.	III Data













Questions about using VA Data?

HSRData Listserv

- Community knowledge sharing
- \circ ~1,800 VA data users
- Researchers, operations, data stewards, managers
- Subscribe by visiting

vaww.virec.research.va.gov/Support/HSRData-L.htm (VA Intranet)

VIReC HelpDesk

- Individualized support
- o Request Form:

varedcap.rcp.vaec.va.gov/redcap/surveys/?s=KXMEN77LXK (VA Intranet)



CIPHER Online



Find a heart failure definition to use to invite patients to a clinical trial



Learn how to query Cerner Data

CIPHER VA Wiki

- Find EHR data elements that co-occur with Type 1 Diabetes



Understand an MVP Lifestyle Survey data element

1.1	
1	

Track your own phenotype definitions and metadata



Refer to VINCI SOPs to query lab tests using best practices

