U.S. Department of Health & Human Services • National Institutes of Health

National Center for Complementary and Integrative Health

New Strategies and Methodologies for Whole Person Research

Emrin Horgusluoglu, Ph.D.
Division of Extramural Research, NCCIH, NIH

Thursday, April 11, 2024

Speakers

- **Speakers**
  - Dr. Helene M. Langevin, Director, *NCCIH*
  - Dr. Patricia M. Herman, *RAND Corporation*
  - Dr. Jeffery A. Dusek, *University of California, Irvine*
  - Dr. Aaron Y. Lee, *University of Washington*

- **Moderator**
  - Dr. Emrin Horgusluoglu; Program Director, *NCCIH*

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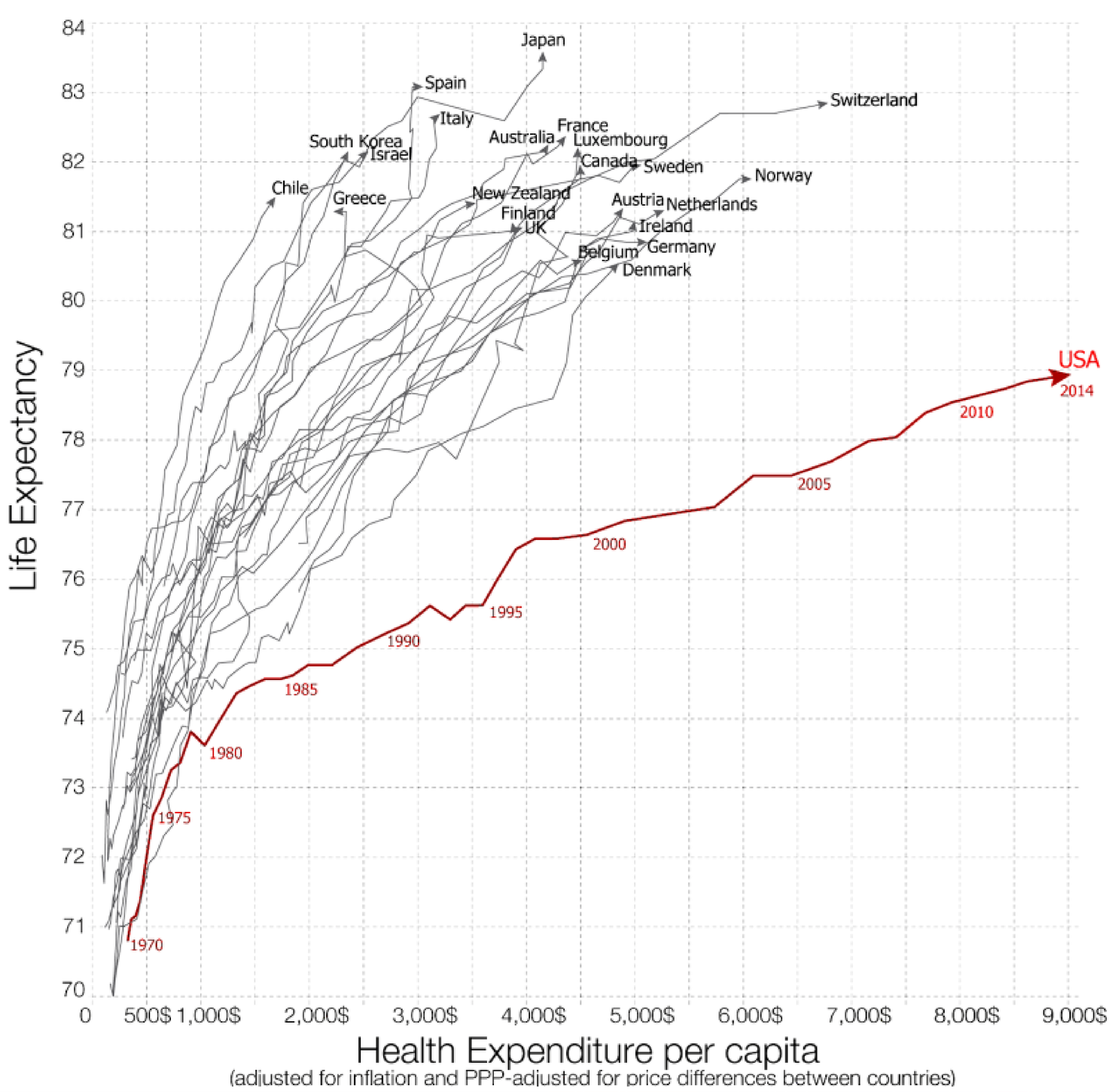
New Strategies and Methodologies for Whole Person Research

Helene M. Langevin, M.D.
Director, The National Center for Complementary and Integrative Health (NCCIH)

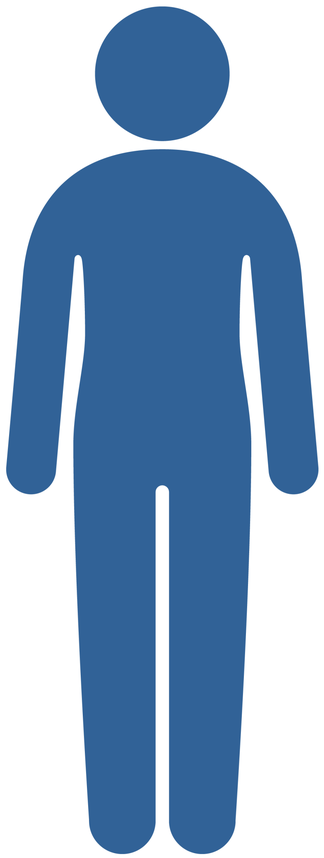
The Problem

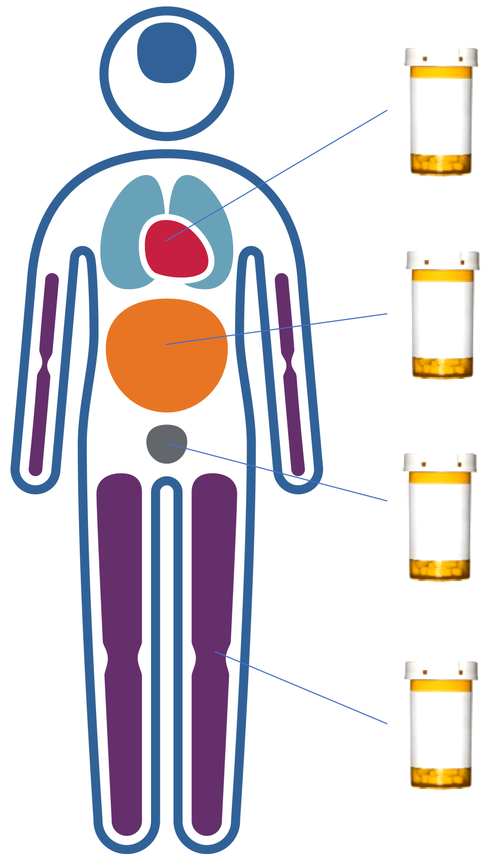


https://ourworldindata.org/financing-healthcare/

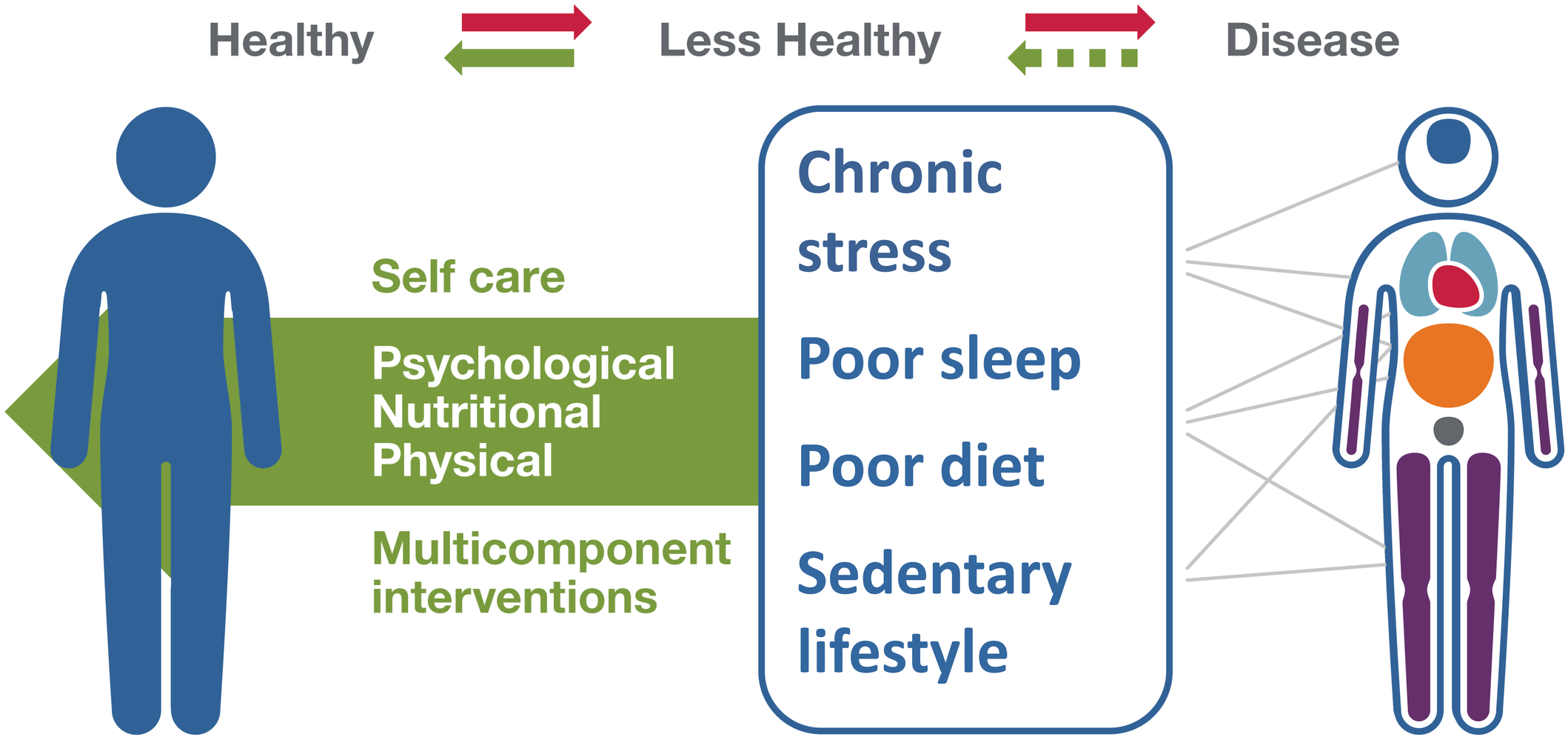
The Health Continuum

Healthy ⇄ Less Healthy ⇄ Disease



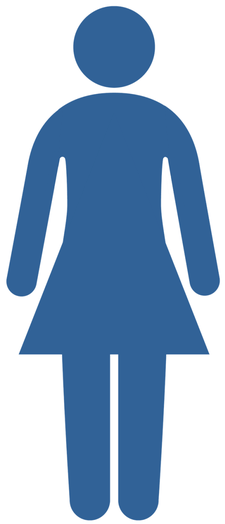


Where we need to go

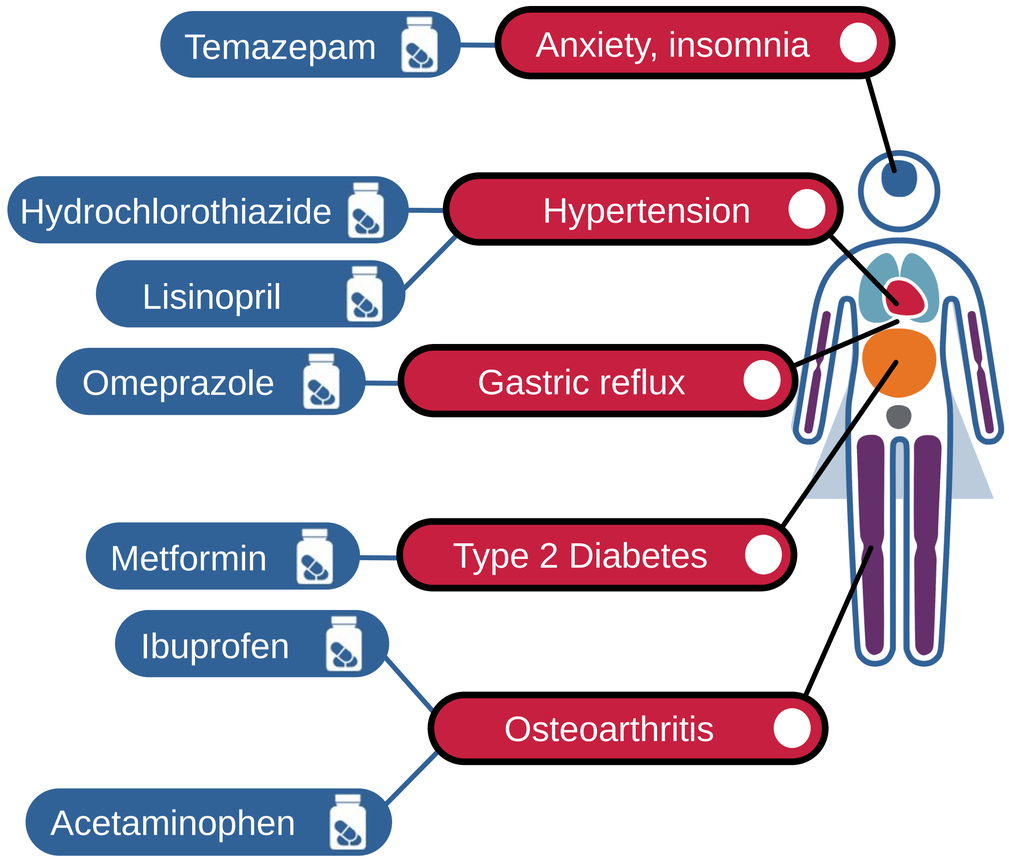


AN EXAMPLE:

Mrs. M. at age 40



Mrs. M. at age 40



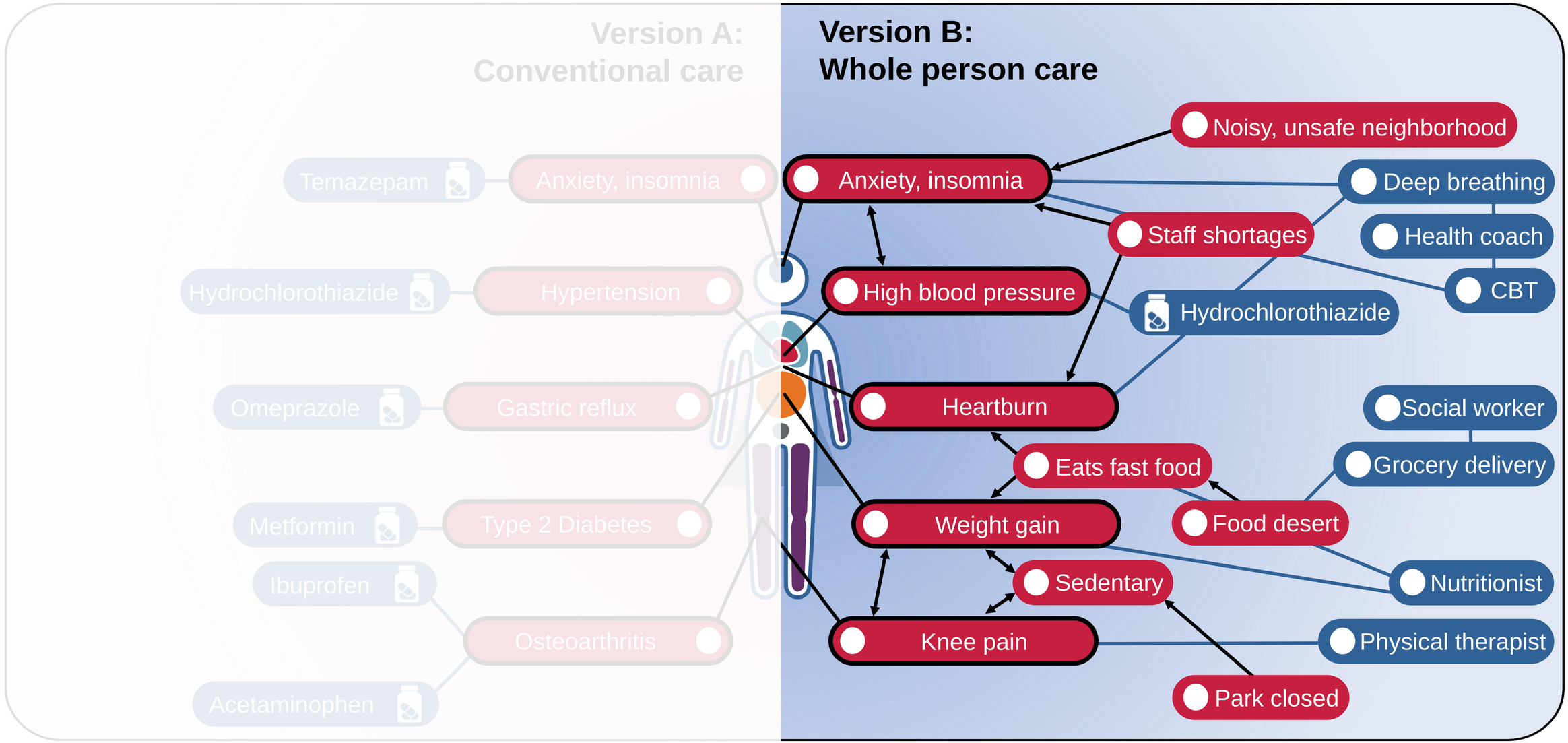
Mrs. M. at age 80

Version A: Conventional care

- Daytime somnolence
- Unsteady gait, falls
- Temazepam
- Anxiety, insomnia
- Cardiac arrhythmia
- Trazodone
- Hydrochlorothiazide
- Hypertension
- Lisinopril
- Omeprazole
- Gastric reflux
- Cognitive decline
- Nursing home
- Metformin
- Type 2 Diabetes
- Erosive gastritis
- Ibuprofen
- Oxycodone
- Osteoarthritis
- Acetaminophen

Version B: Whole person care

Mrs. M. at age 45



Mrs. M. at age 80

Version A: Conventional care

Daytime somnolence

Unsteady gait, falls

Temazepam

Anxiety, insomnia

Cardiac arrhythmia

Trazodone

Hydrochlorothiazide

Hypertension

Lisinopril

Omeprazole

Gastric reflux

Cognitive decline

Nursing home

Metformin

Type 2 Diabetes

Erosive gastritis

Ibuprofen

Oxycodone

Osteoarthritis

Acetaminophen

Version B: Whole person care

Healthy sleep

Deep breathing

BP controlled

Hydrochlorothiazide

Heartburn managed

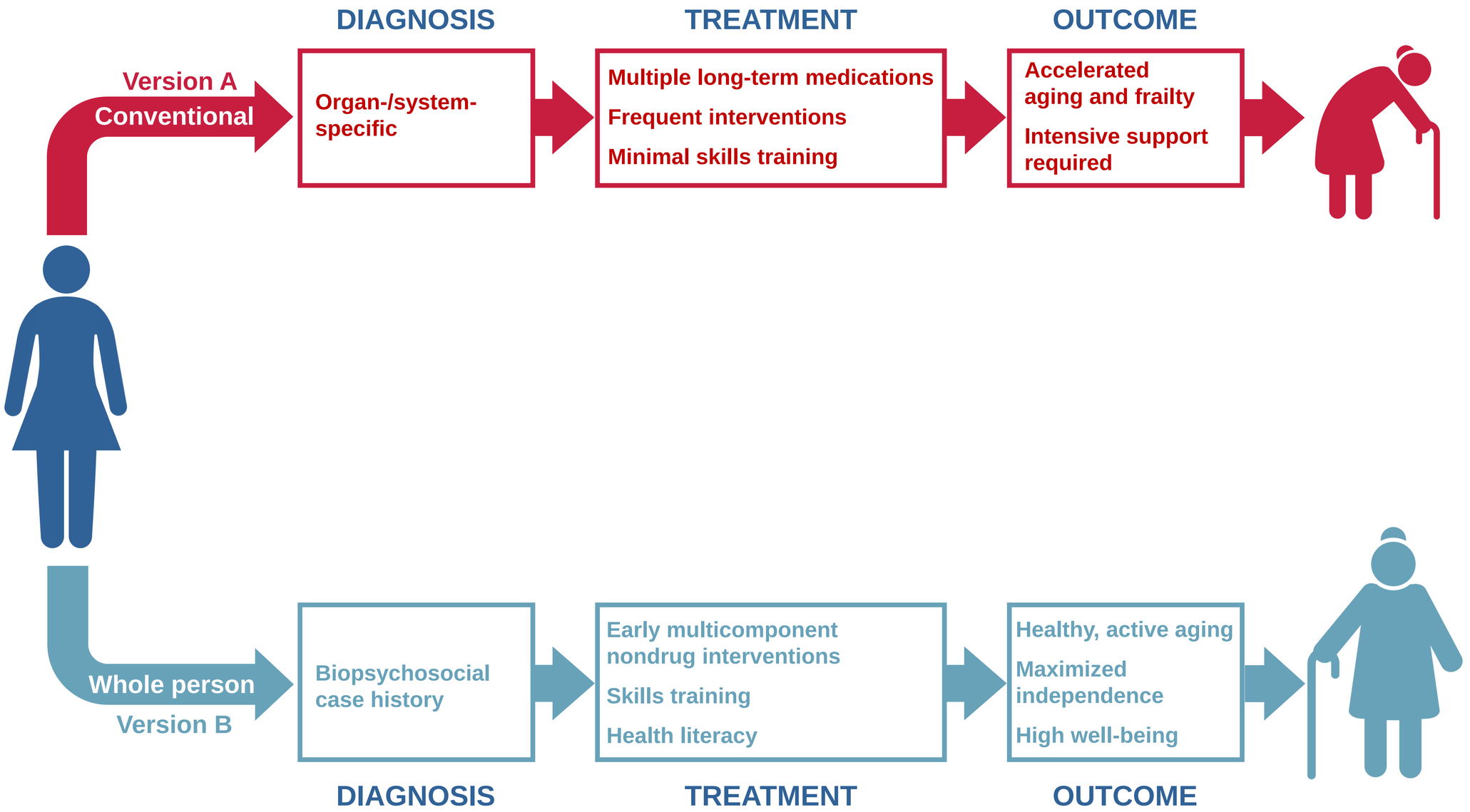
Healthy diet

Grocery delivery

Healthy weight

Regular exercise

Knee pain managed


DIAGNOSIS
TREATMENT
OUTCOME
Version A
Conventional
Organ-/system-specific
Multiple long-term medications
Frequent interventions
Minimal skills training
Accelerated aging and frailty
Intensive support required
Whole person
Version B
Biopsychosocial case history
Early multicomponent nondrug interventions
Skills training
Health literacy
Healthy, active aging
Maximized independence
High well-being
DIAGNOSIS
TREATMENT
OUTCOME

The Economics of Whole Person Health

A Hypothetical Case Study

RAND
Research Across Complementary and Integrative Health Institutions (REACH) Center

Patricia M. Herman, ND, PhD
Senior Behavioral Scientist, Codirector RAND REACH Center

Overview

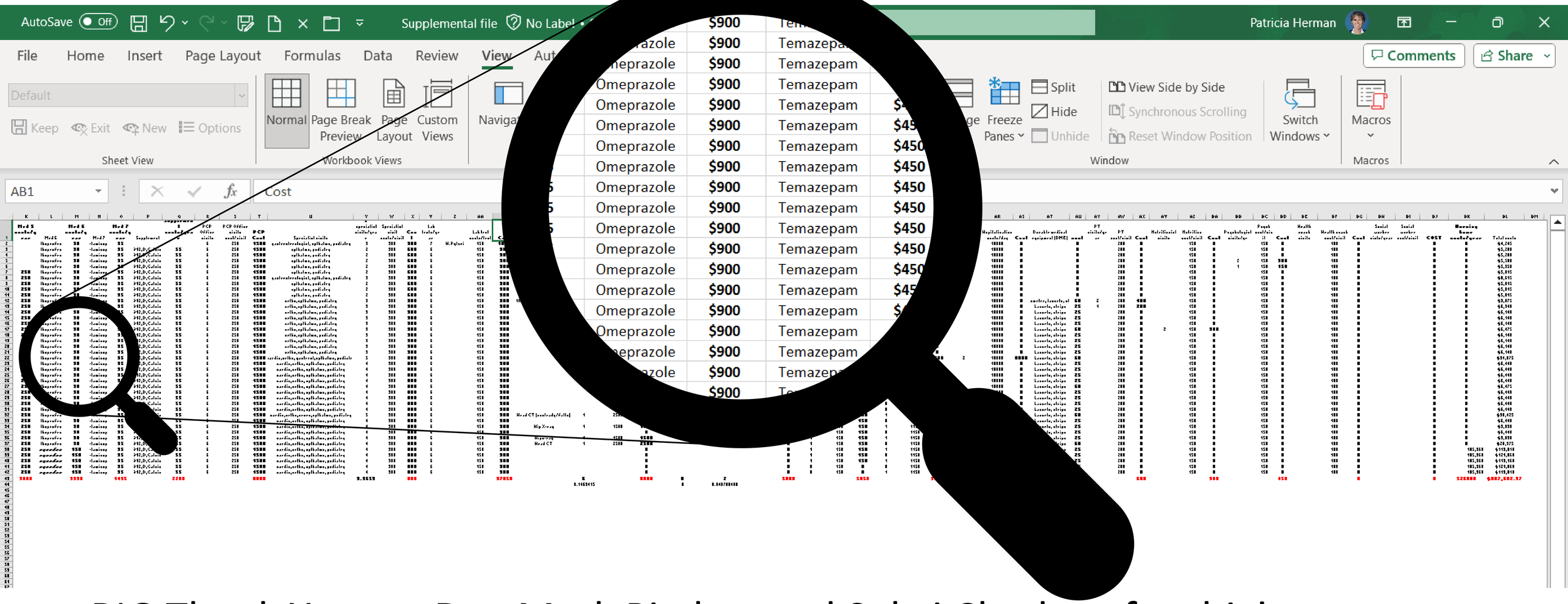
- Methods
- Detailed assumptions regarding treatments and cost
- How these assumptions play out over the years
- Estimated total healthcare costs under each scenario
- Summary

Methods

- You just heard Mrs. M's clinical case scenarios under each approach
- A PCP with experience in both laid out typical unit costs and detailed healthcare utilization for each approach
- Healthcare utilization for conventional care was vetted against data from the 2020 Medical Expenditures Panel Survey (MEPS)
- Unit costs (prices) were also vetted against MEPS and Medicare pricing
- Annual nursing home costs come from an actual cost survey of n=2438 residents of a county in Minnesota*
- All costs are presented in 2023 USD
- Future costs discounted back to Mrs. M's 40th birthday (her decision point) using a 3% discount rate

*Long KH, et al. Medical and nursing home costs. *Alzheimer's & Dementia.* 2022;18(3):393-407.

Detailed Assumptions on Healthcare Utilization by Year



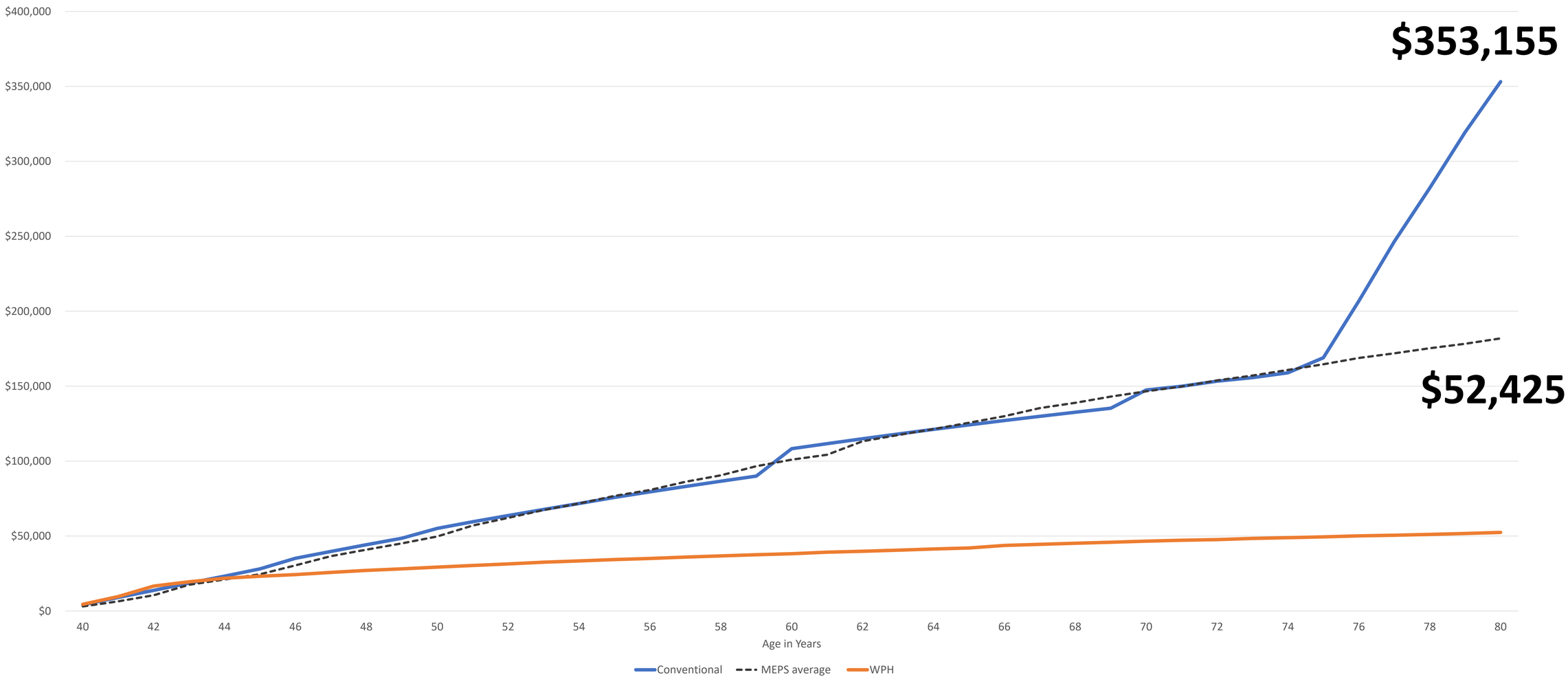
BIG Thank Yous to Drs. Mark Pitcher and Sekai Chedeya for this!

Healthcare Utilization and Costs Across Years

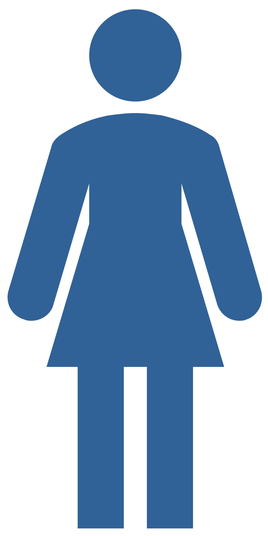
		Cumulative healthcare costs	No. of medi-cations	PCP Office visits	Specialist visits	Labs and Imaging	Urgent care & ED visits	Hospital days	Other visits*
Age 40	Conventional care	$4,121	3	6	3	7	1	0	0
	WPH care	$4,762	1	3	0	1	1	0	26
	MEPS check	$3,046							
Age 45	Conventional care	$28,153	7	6	2	6	1	0	0
	WPH care	$23,524	1	1	0	1	0	0	5
	MEPS check	$24,491							
…									
Age 80	Conventional care	$353,155	7	6	4	6	0	1	0
	WPH care	$52,425	1	2	0	2	1	0	4
	MEPS check	$181,892	← Note conventional care costs = $186,670 without skilled nursing costs.						
Healthcare utilization totals across years									
	Conventional care		275	246	138	256	47	8	8
	WPH care		41	56	1	73	18	0	199

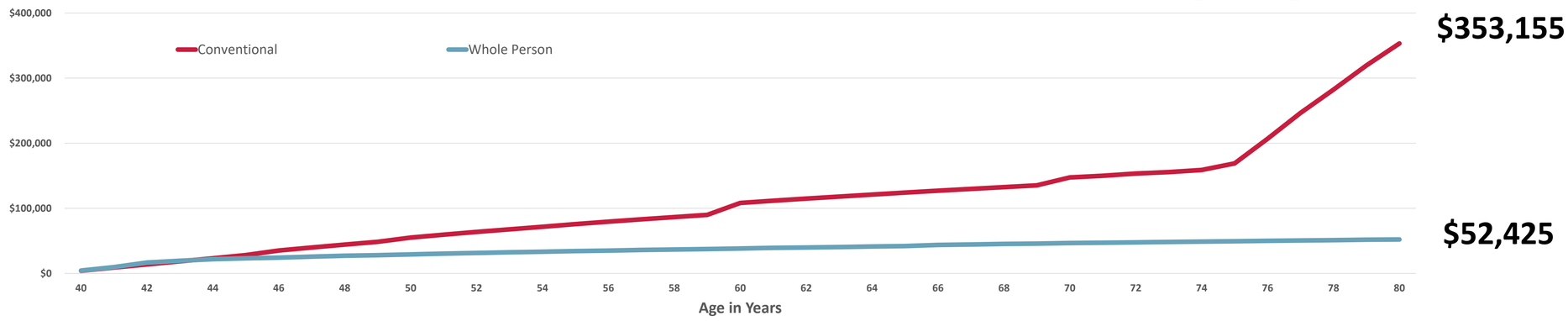
*Other visits include visits to a physical therapist, nutritionist, psychologist, health coach, and social worker.

Discounted Cumulative Total Health Care Costs for Mrs. M Starting at Age 40



	DIAGNOSIS	TREATMENT	OUTCOME
Version A	Organ-/system-specific	Multiple long-term medications Frequent interventions Minimal skills training	Accelerated aging and frailty Polypharmacy Intensive support required





Version B	Biopsychosocial case history	Early multimodal non-drug interventions Skills training Health literacy	Healthy, active aging Maximized independence High well-being

Summary

- Early investments in patient support and skill building can generate substantial benefits in terms of improved health and quality of life and reduced healthcare costs

- This case study illustrates the major challenge for implementing a whole person approach to care: the long time frame required to see cost benefits

Effectiveness of Complementary and Integrative Health Interventions

Jeffery A Dusek, PhD

Director of Outcomes Research, Susan Samueli Integrative Health Institute, University of California, Irvine

Co-Chair, BraveNet Practice Based Research Network Executive Committee

UCI Susan Samueli Integrative Health Institute

BraveNet

Objectives

1. Rationale for outcomes research in complementary and integrative health clinical settings

2. Describe BraveNet's Practice Based Research Network (PRBN)

3. Review primary findings from BraveNet's 17 site practice-based research registry study called PRIMIER

4. Recommendations for future CIH effectiveness research

BraveNet

Objective 1: Rationale for Outcomes Research

- RCTs assess the efficacy of specific interventions for specific patient populations in “controlled settings”
- But do not accurately inform the real-world practice of CIH because of the controlled nature of the RCT paradigm
- Outcomes research evaluates the effectiveness of treatments in the real-world of clinical practice.

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Objective 2: What is the BraveNet PBRN?

Mission

To conduct and disseminate high quality practice-based research that evaluates the effectiveness, safety, cost and impact on patient experience of integrative medicine approaches.

BraveNet

BraveNet Focus

- 24 site **Practice Based Research Network**
- Focus on patient reported outcomes in real world integrative health settings
- Multi-site collaboration for
  - Observational ambulatory CIH care
  - Randomized controlled trials

BraveNet Members

(circa 2024)

Seattle, WA
Osher Center for Integrative Medicine, University of Washington

Salt Lake City, UT
Osher Center for Integrative Medicine, University of Utah

San Francisco, CA
Osher Center for Integrative Medicine, University of California-San Francisco

Irvine, CA Susan Samueli Integrative Health Institute, University of California, Irvine

San Diego, CA Scripps Center for Integrative Medicine

San Diego, CA
Centers for Integrative Medicine, University of California- San Diego

Albuquerque, NM Center for Life and Integrative Medicine, University of New Mexico

Bloomington, IN
University of Indiana

Milwaukee WI, Chicago IL
Aurora Advocate Research Institute

Chicago, IL
Osher Center for Integrative Medicine, Northwestern University

Cincinnati, OH
Alliance Integrative Medicine

Columbus, OH
Center for Integrative Health and Wellness, Ohio State University

Cleveland, OH
Connor Whole Health

Nashville, TN Osher Center for Integrative Medicine, Vanderbilt University

New York, NY
Department of Family Medicine, Mount Sinai

Worcester MA U of Massachusetts Chan Medical School

Boston, MA Boston Medical Center

Philadelphia, PA Jefferson Myrna Brind Center of Integrative Medicine

Philadelphia, PA Integrative Health Program, Children's Hospital of Philadelphia

Pittsburgh, PA Center for Integrative Medicine, University of Pittsburgh Medical Center

Washington, DC
Integrative Medicine George Washington University

Durham, NC
Duke Integrative Medicine, Duke University

Calgary, Alberta ACTION Centre, University of Calgary

Sydney, Australia NICM Health Research Institute, West Sydney University

BraveNet

Objective 3: Patients Receiving Integrative Medicine Effectiveness Registry (PRIMIER) Overview

Design: **Prospective, non-randomized, observational study** conducted at 17 BraveNet clinical sites (2013)

Data Collection: *Patient Reported* data and Demographics: Primarily **REDCap,** paper forms, electronic assessment center; *Health Service Utilization*: Electronic Health Records

Primary Outcome: Health related quality of life

Patient-reported outcome measures collected at 5 time points: **index, 2, 4, 6, 12 months**.

- **PROMIS-29** (physical function, anxiety, depression, sleep disturbance, fatigue, pain interference, social roles)
- **Perceived Stress Scale-4** (PSS4)
- **Patient Activation Measure** (PAM)

Secondary Outcome: Integrative Health service utilization (from electronic health records): **ICD diagnostic codes, CPT codes, Clinician type, Visit date**

Inclusion/Exclusion criteria: 18^{+} years, seen by a provider in CIH clinics, consented to study

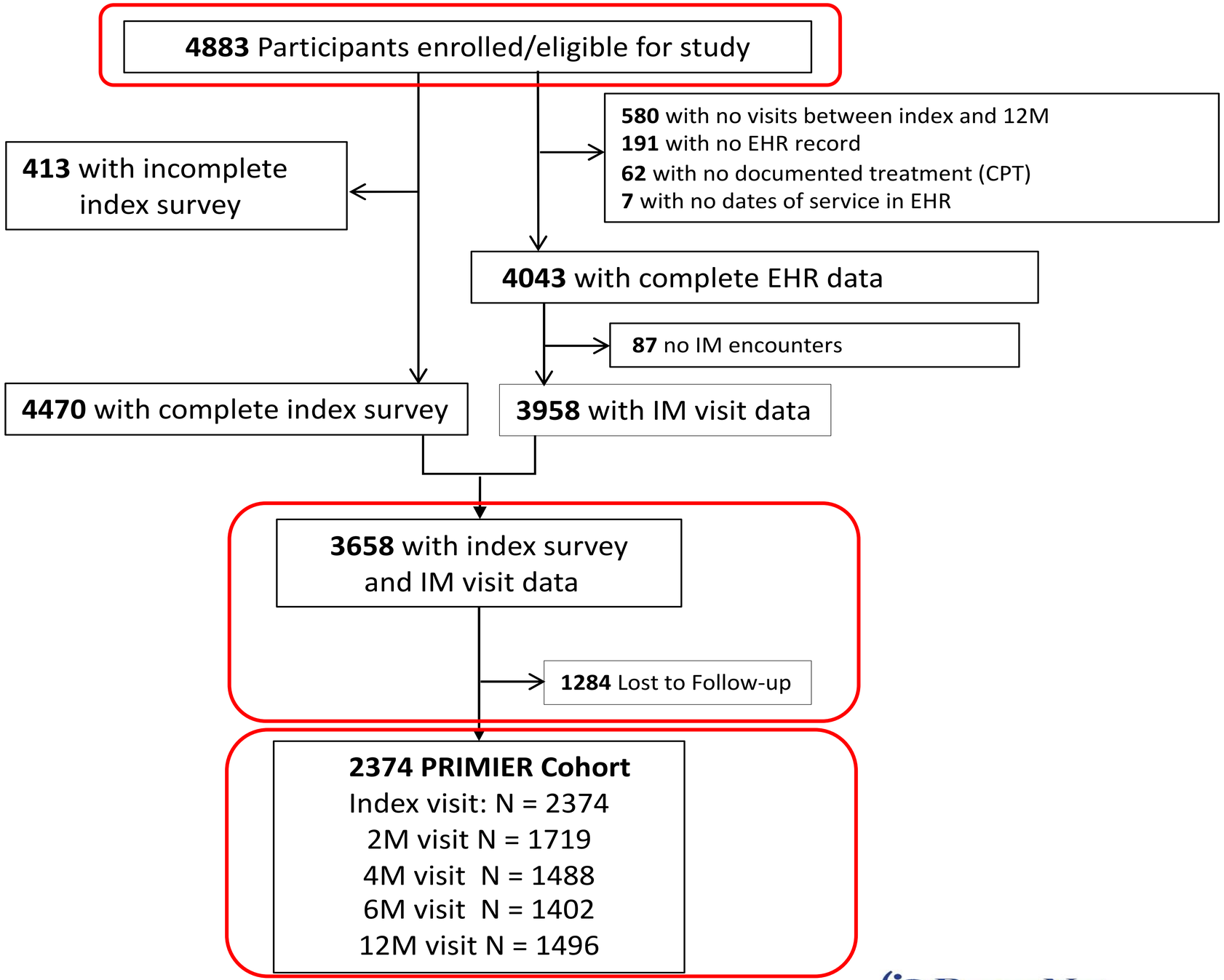
Recruitment: Fliers, QR Code in clinic, email blast to clinic patients, **Integration into clinical care**

Participant Flow

Demographics:
Participants were **white** (88.4%), **female** (79.7%), **college-educated** or beyond (78.5%) with a **mean age of 51.4 years** (SD 14.5)

T scores of 55 on Anxiety, Fatigue, Pain Interference

PSS 5.5 and **PAM** 67



Clinical Trials.gov (NCT01754038).

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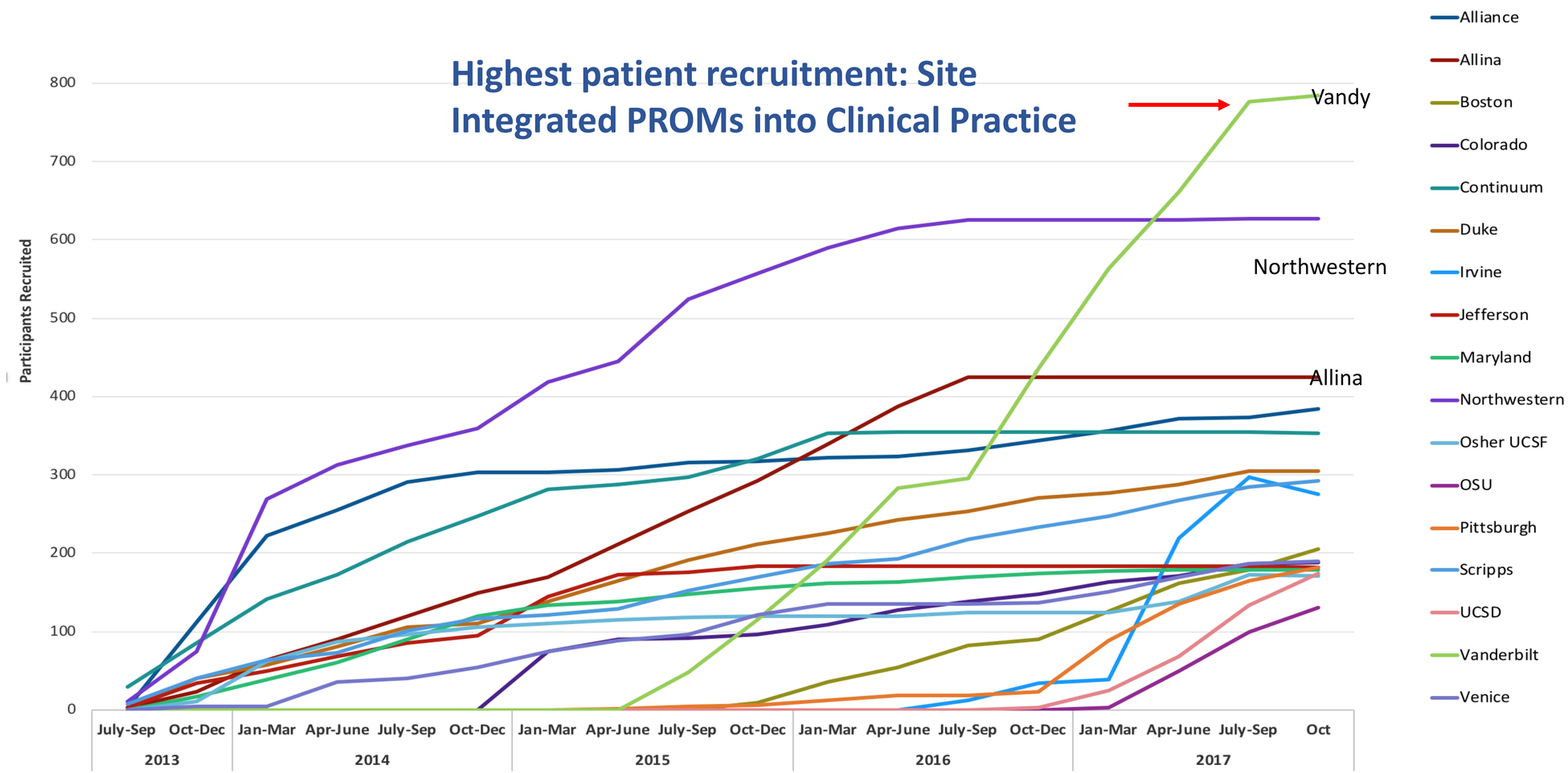
Final PRIMIER Participants Recruited by Site



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Cohort Self-Reported Symptoms at Index: Top 10

Condition*	%
Chronic Pain	**18.9%**
Acute Pain	**9.3%**
Wellness Visit	**9.2%**
Anxiety/Stress	4.9%
Cancer	4.6%
Fatigue/Chronic Fatigue	4.5%
Heart Disease	4.1%
Fibromyalgia/Myofascial Pain	3.8%
Headache/Migraine	3.1%
Inflammatory Bowel Syndrome/Irritable Bowel	2.5%

*10 patients did not complete this question on the survey at the Index visit.

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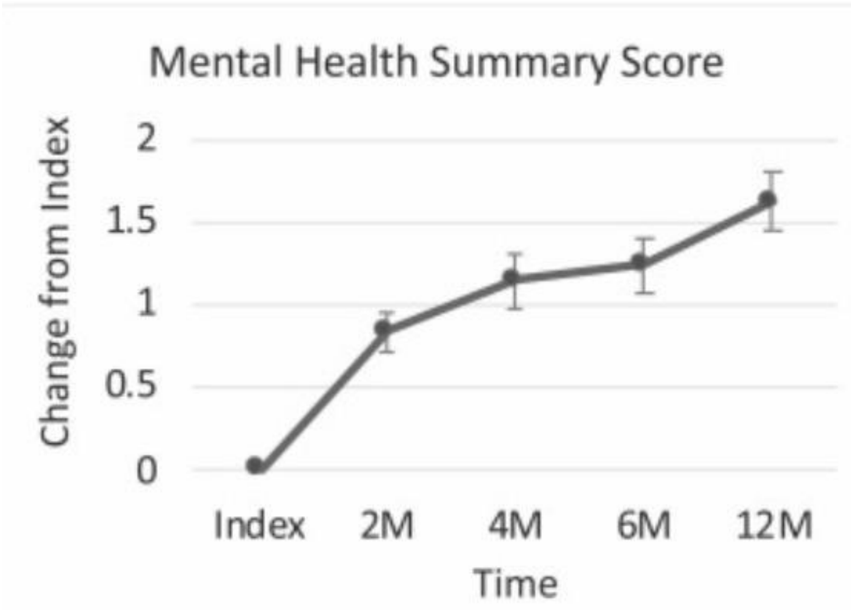
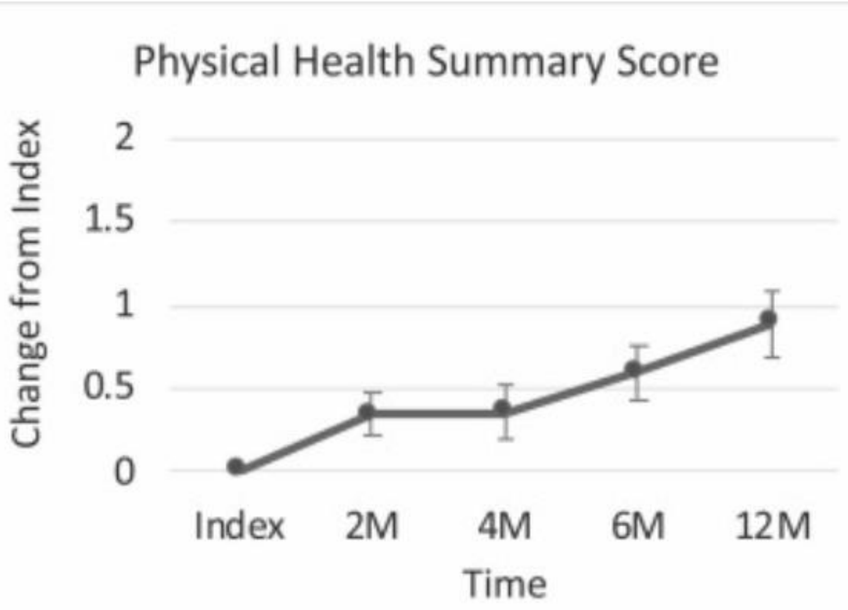
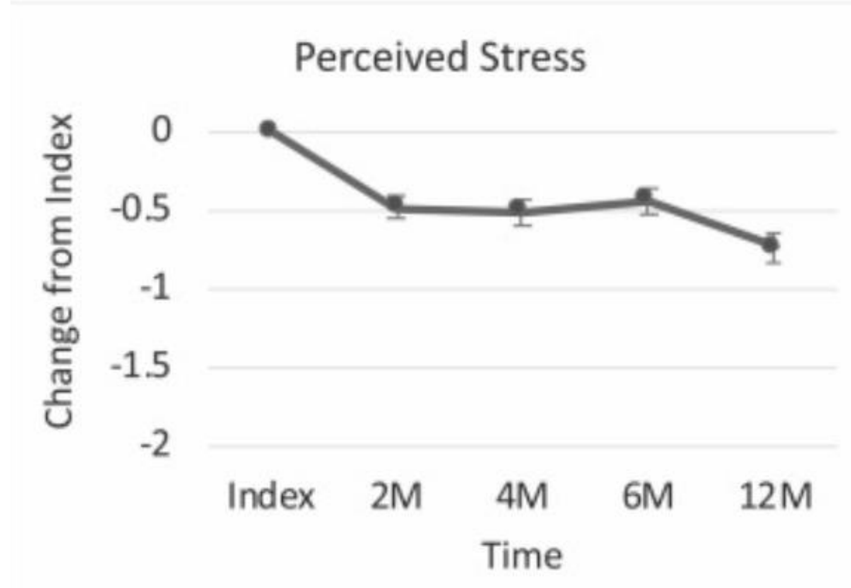
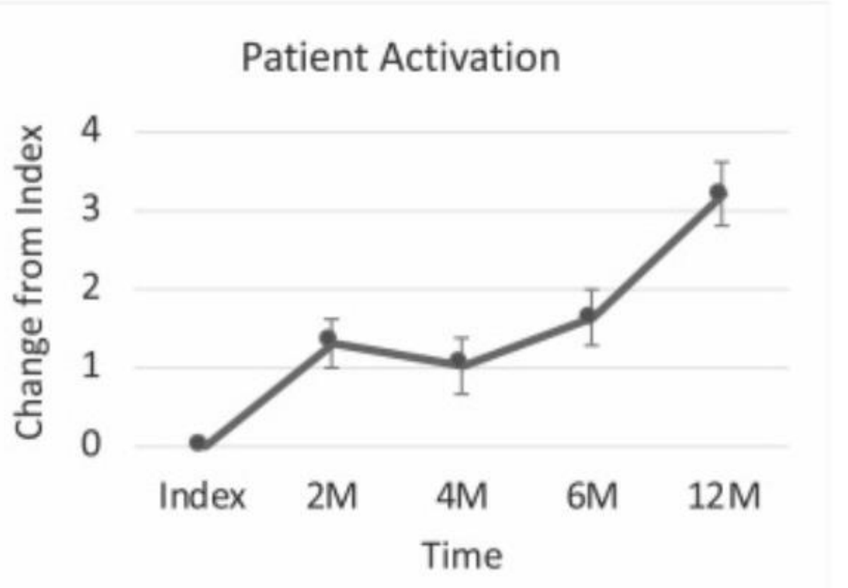
Primary Outcomes









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Adjusted Mean Changes Across PROs: Summary

Significant Improvements at 12 months ($p<0.001$)	• All PROMIS-29 subscales • PROMIS Mental Health + Physical Health Summary Scores • PROMIS Composite Score • PSS-4 • PAM
Significant improvements at all 4 time-points	• PROMIS Mental Health Summary Score • PROMIS Composite score • PSS-4

PROMIS-29: Minimal Clinically Important Difference

- **MCID** defined as **≥3 points better than index scores** at a given time point for PROMIS-29 scores

- **Mental Health Summary score**:

Timepoint	2 months	4 months	6 months	12 months
% at MCID	30.2%	34.5%	34.9%	38.5%

- **Physical Health score**:

Timepoint	2 months	4 months	6 months	12 months
% at MCID	21.8%	21.3%	24.3%	28.3%

- Common pattern of the **percentage** of responders **increasing** from 2-month to 12-month follow-up assessment

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CIH Service Utilization

IM Service	Index - 2 months	2 -4 months	4 - 6 months	6 - 12 months	Index - 12 months
Consult MD/NP	45.9%	31.2%	26.2%	38%	**67.8%**
Acupuncture	23.5%	16.6%	13.6%	17.9%	**32.9%**
Manual therapy	10.7%	8.5%	8.2%	11.3%	**19.1%**
Chiropractic	6.4%	4.9%	4.4%	6.8%	**11%**
Mind and body	6.8%	4.6%	3.4%	3.8%	**10%**
Consult coaching	5.7%	3.2%	2.9%	3.7%	**9.5%**
Energy therapy	0.8%	1%	1%	2.7%	**3.4%**
Other	0.8%	0.5%	0.4%	1.6%	**2.1%**
Any CIH	**1768 (74.5%)**	**1233 (51.9%)**	**1025 (43.2%)**	**1394 (58.7%)**	**2374 (100%)**

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Summary of Findings

- **2,374 (65%)** completed at least 1 follow-up assessment, had evaluable EHR data and >1 CIH visit through 12 months
- At index visit, **most common conditions** were **chronic pain**, **acute pain**, and **wellness**
- Significant improvements observed at 12-months on **all PROMIS-29 measures**, **PSS** and **PAM**
- At 12 months, clinically meaningful improvements found on **PROMIS-29 Mental Health** (38%) and **Physical Health** (28%) Summary scores
- **CIH service utilization** was possible (albeit painful) with EHR extracts

Limitations

- **65% retention rate**; however, within high-normal range of multisite CIH effectiveness studies

- **Limited demographic diversity** of sample
  - Though typical of those seeking CIH care, future research should strive to include more diverse samples for improved generalizability

- **No control group**

- Absence of multiple testing **adjustments**, due to exploratory nature of study

- Any patient receiving care at participating site was eligible to join PRIMIER – thus, index visit may **not** have been the **actual start** of treatment course

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Effectiveness Future Directions

- Standardize CIH documentation and data collection practices across sites using Epic EHR

  ✓PROMs: Use of Common Data Elements with customization for each clinical site's needs to **incorporate recruitment and data collection into routine clinical care**

  ✓CIH Utilization: Use of common visit types to be able to identify when CIH has occurred

- Use of Propensity Score Matching to create comparison groups

- GOAL: deliver CIH to the right patient, at the right time, at the right dose, for the most effective duration

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Complementary Therapies in Medicine 71 (2022) 102904

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Patients Receiving Integrative Medicine Effectiveness Registry (PRIMIER) of the BraveNet practice-based research network: Outcomes of the PRIMIER cohort☆

Jeffery A. Dusek [a,b,*], Qi Gao [c], Ryung S. Kim [c], Donald I. Abrams [d], Benjamin Kligler [e], Natalie L. Dyer [a], Kathryn Hansen [f], M. Diane McKee [c,g], the PRIMIER Research Group

BraveNet

Thank you

Treatment Patterns of complete cases in EMR matched (n=2374)

UCI Susan Samueli Integrative Health Institute

Boston University School of Medicine Integrative Medicine

Connor Whole Health

DukeHealth

UNM HEALTH

aim FOR WELLBEING

Scripps

AdvocateAuroraHealth Research Institute

UC San Diego CENTERS FOR INTEGRATIVE HEALTH

Children's Hospital of Philadelphia

UPMC LIFE CHANGING MEDICINE

Icahn School of Medicine at Mount Sinai

UCSF Osher Center for Integrative Health

VANDERBILT HEALTH

Northwestern Medicine Osher Center for Integrative Health

THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER

UW Medicine FAMILY MEDICINE

HEALTH UNIVERSITY OF UTAH

GW School of Medicine & Health Sciences

Marcus Institute of Integrative Health Jefferson Health

INDIANA UNIVERSITY SCHOOL OF MEDICINE

UMass Chan MEDICAL SCHOOL

NICM Health Research Institute

UNIVERSITY OF CALGARY CUMMING SCHOOL OF MEDICINE

Bridge2AI
Propelling Biomedical Research with Artificial Intelligence

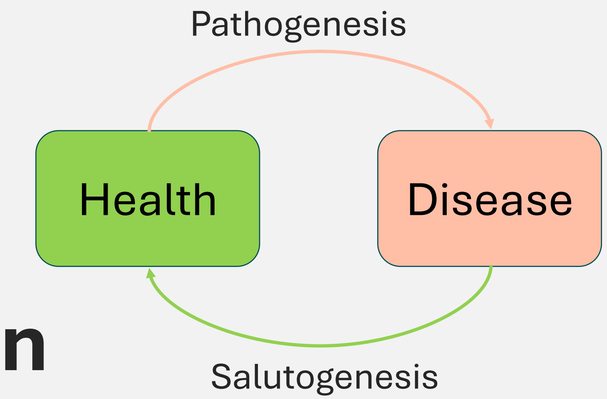
Salutogenesis Grand Challenge

AI Ready and Equitable Atlas for Diabetes Insights (AI-READI)

Aaron Y Lee, MD, MSCI

University of Washington

Introduction



The goal of the **Salutogenesis Data Generation Project** (DGP) is to create a multidimensional, ethically-sourced dataset in diverse people for studying **salutogenesis** in Type 2 Diabetes

The DGP is also referred to as the AI Ready and Equitable Atlas for Diabetes Insights (**AI-READI**) project

Data collection

Pre-visit (~1hr, at home)

Self-reporting surveys

- Initial Screening
- Demographic
- Center for Epidemiological Studies Depression Scale (CES-D) - 10
- Problem Areas In Diabetes Questionnaire (PAID-5)
- Diabetes score
- Diet
- Smoking History
- Alcohol Use, Vaping, and Marijuana Use
- General Health,
- Social Determinants of Health (SDoH)
- Visual Impairment and Eye Care Access

On-site visit (~3 to 4 hrs)

Current medical list

Driving record (accident report)

Monofilament test

Vision testing (lensometer, autorefraction, best corrected visual acuity (BCVA), letter contrast sensitivity)

Blood test (NT-proBNP, C-Peptide, Troponin-T, HgA1c, insulin, CBC, lipid panel, CRP, CMP12)

Biospecimen (blood and urine)

Urine test (albumin, creatinine)

Retinal imaging (undilated/dilated fundus photography, pupillary dilation, FLIO, OCT, OCTA)

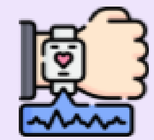
Physical Assessment (height, weight, waist and hip circumferences, blood pressure, heart rate)

ECG

MoCA

Post-visit (10 days, at home)

Continuous glucose monitoring

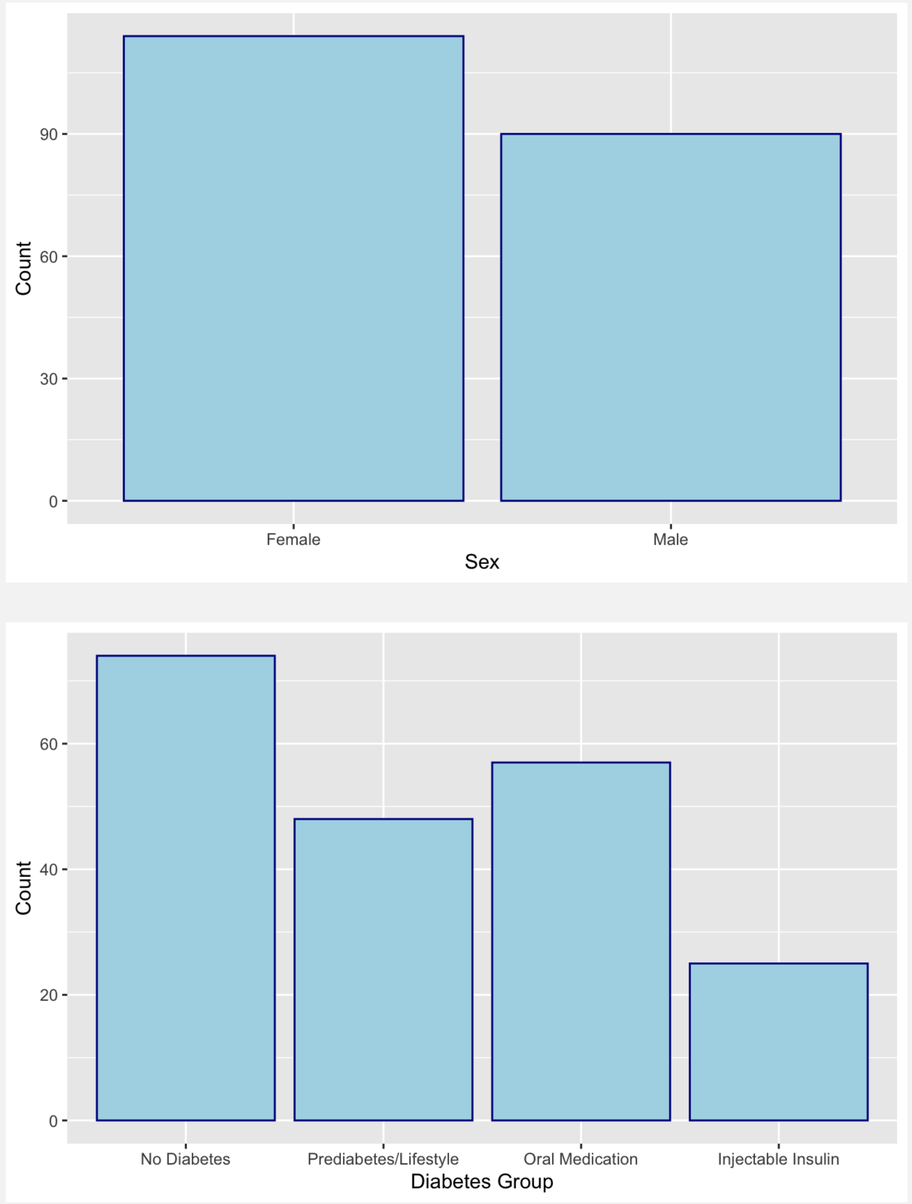


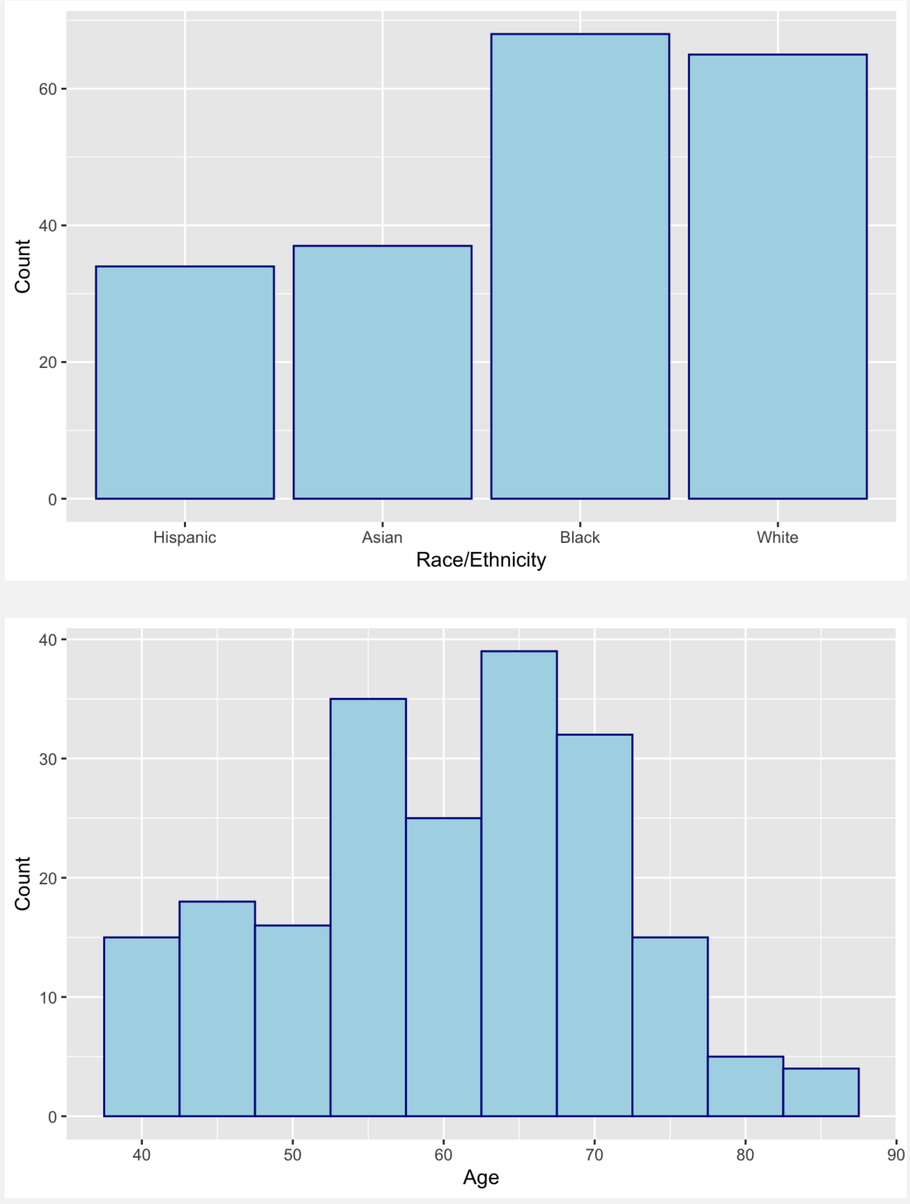
Physical Activity Monitoring (heart rate, steps, sleep phases)

Environmental sensor measurements (temperature, humidity, spectrogram, PM1.0, PM4.0, PM10.0, Nitric Oxides, volatile organic compounds)

FLIO = Fluorescence Lifetime Imaging, OCT = Optical Coherence Tomography, OCTA = Optical Coherence Tomography Angiography,
ECG = Electrocardiogram, MoCA = Montreal Cognitive Assessment, PM1.0, 4.0, and 10.0 = Particulate matter less than 1, 4, and 10 microns, respectively

Pilot participant demographics (n=204)





Preparing AI-Ready Data

OMOP

- Demographics
- Survey data
- Physical assessment data
- Medications
- Blood and urine lab values
- MOCA
- Vision testing

DICOM

- Fundus photography
- OCT
- OCTA
- FLIO

Waveform Database (WFDB)

- ECG

mHealth

- Physical activity monitor
- Continuous glucose monitor

Earth Science Data Specification

- Environmental sensor

Researchers
generating data

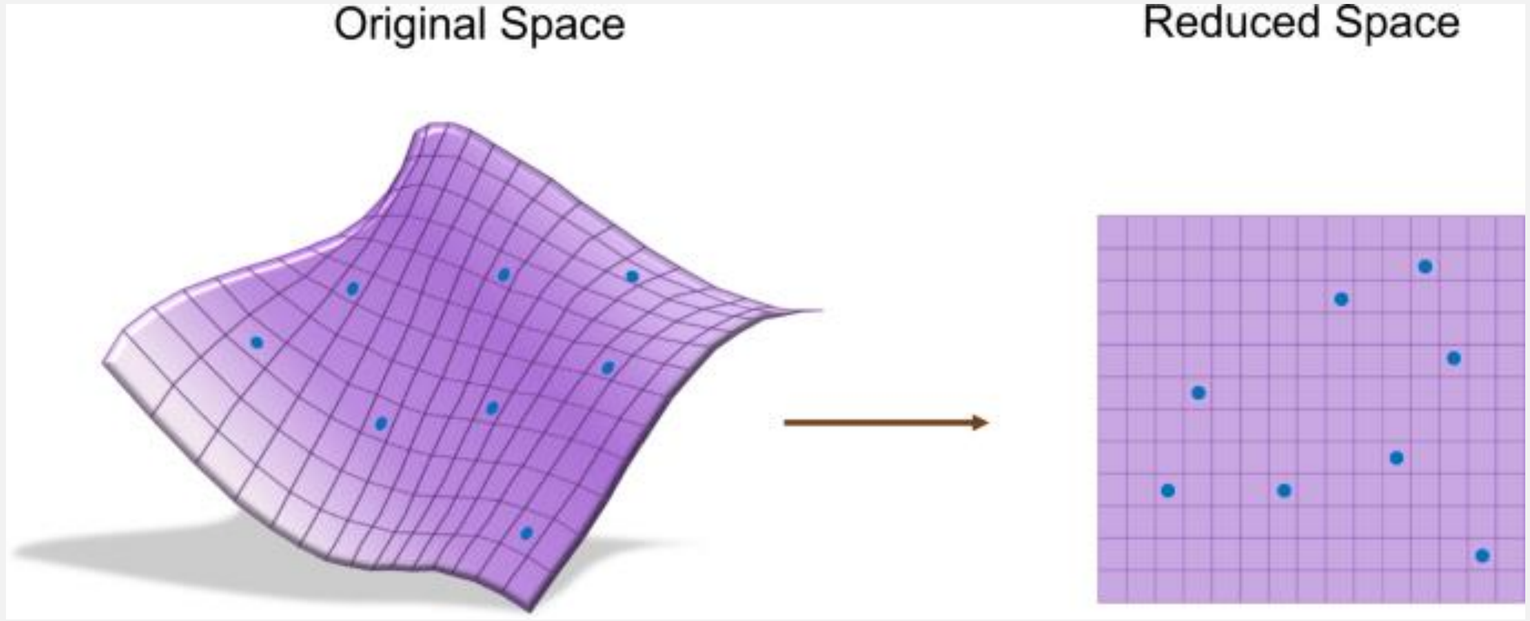
fairhub

Simplifying collection, management, and sharing of FAIR, ethical, AI-ready clinical research datasets

Researchers
reusing data

- Upload data on-the-go
- Track data collection
- Standardize data
- Generate metadata
- Share datasets

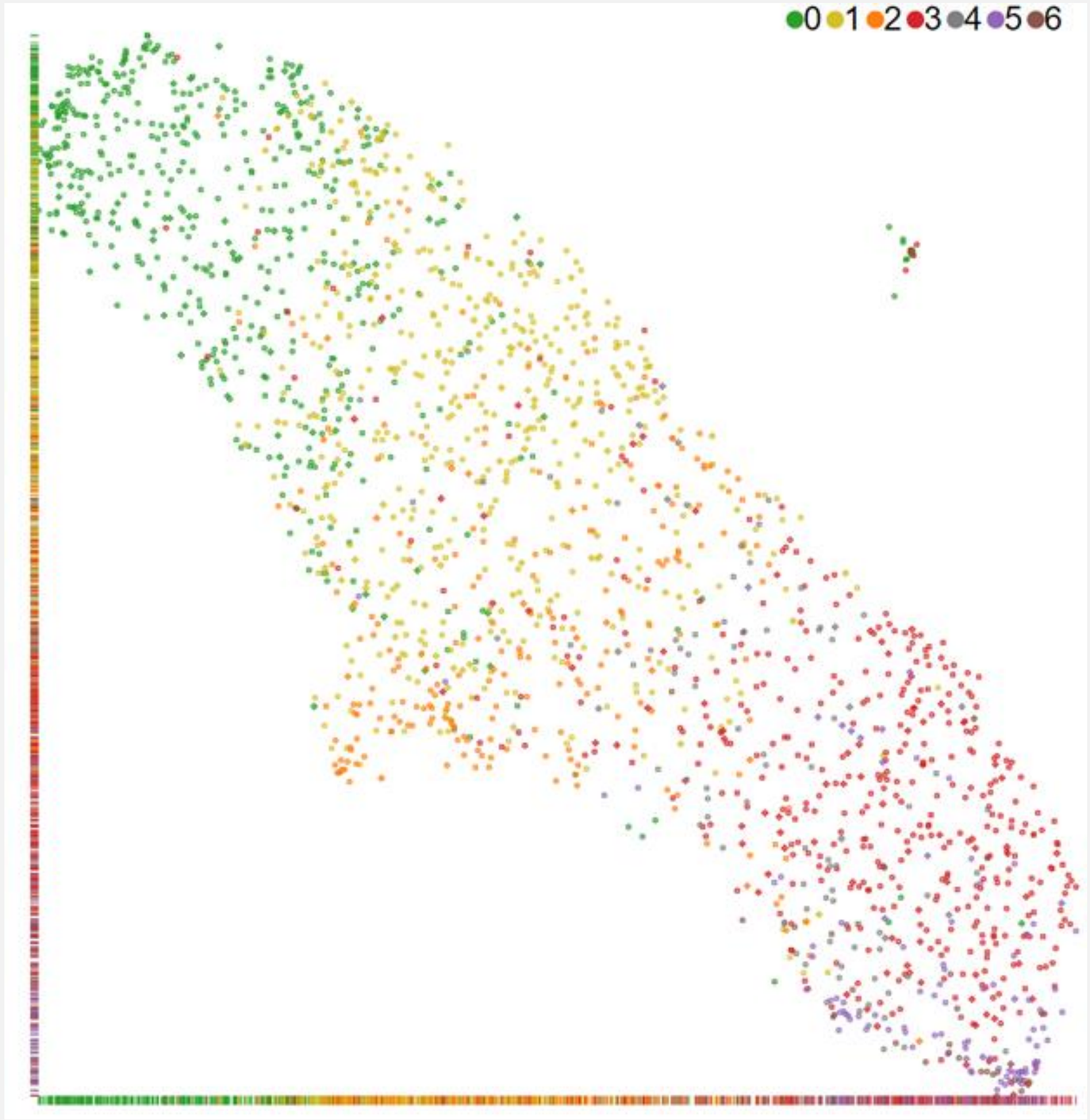
Dimension Reduction

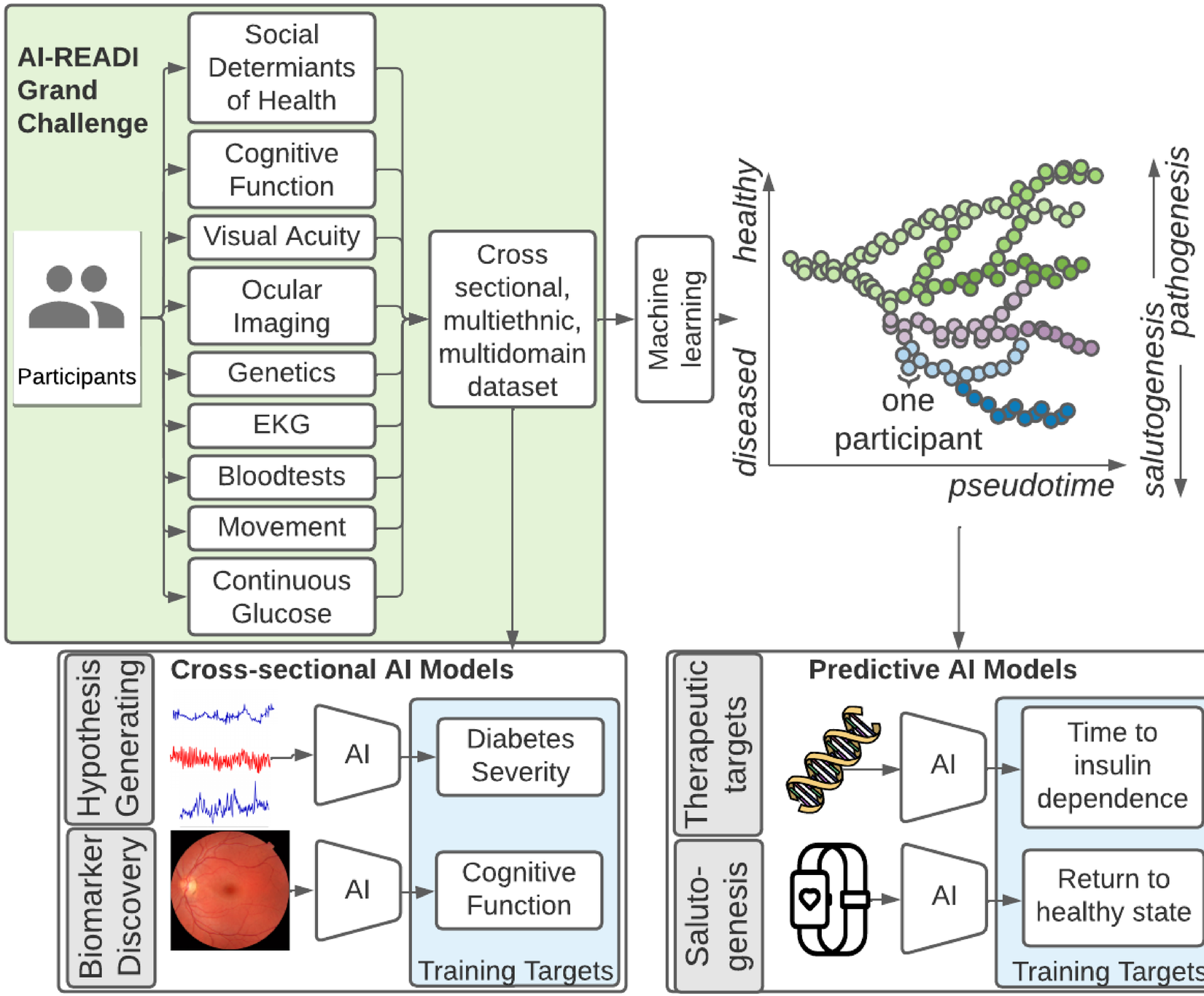


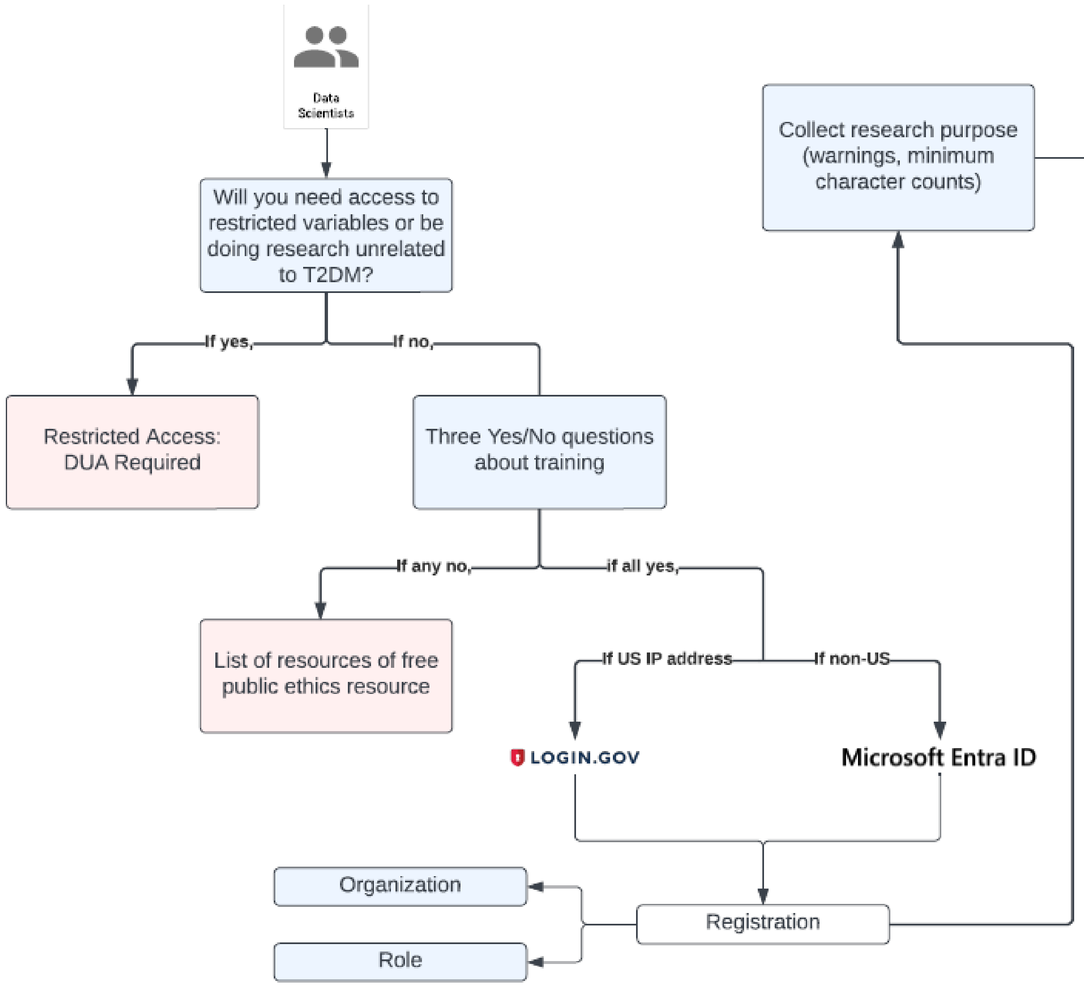
Ideally a lower dimensional latent space

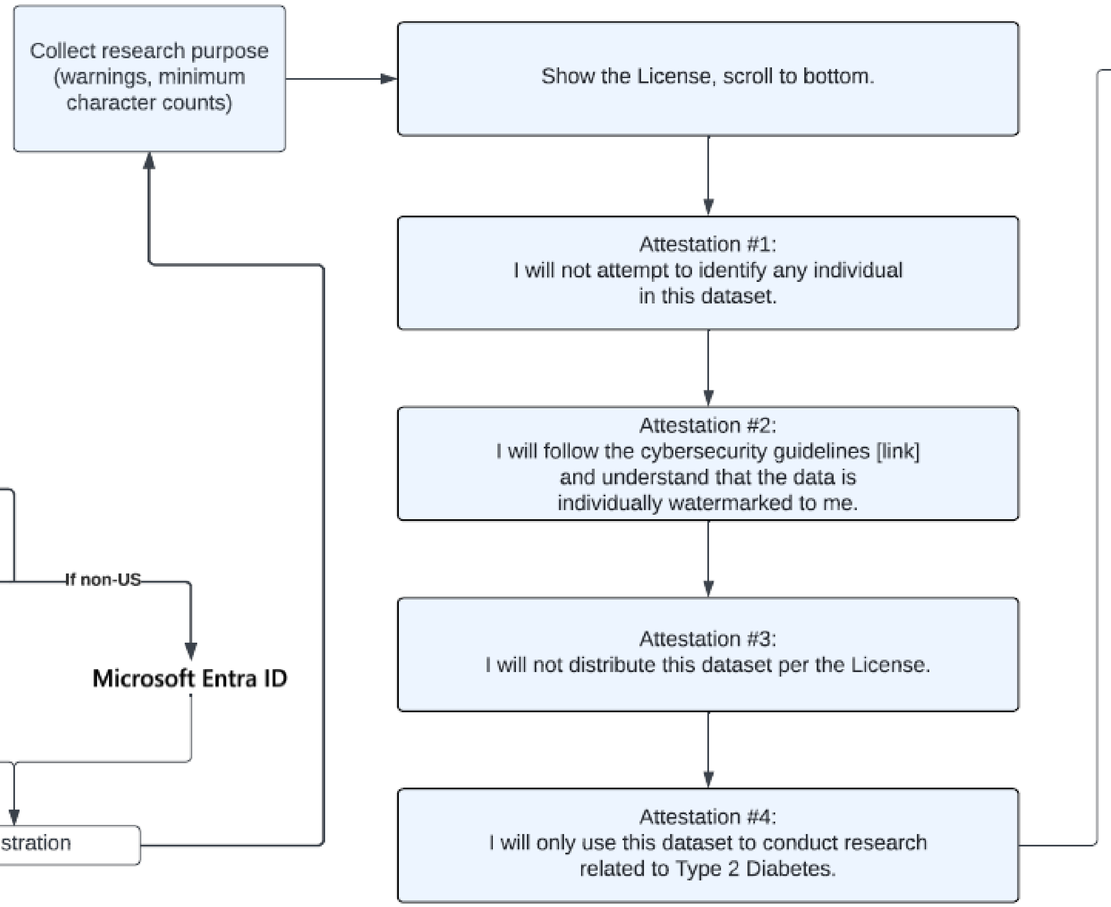
Where:

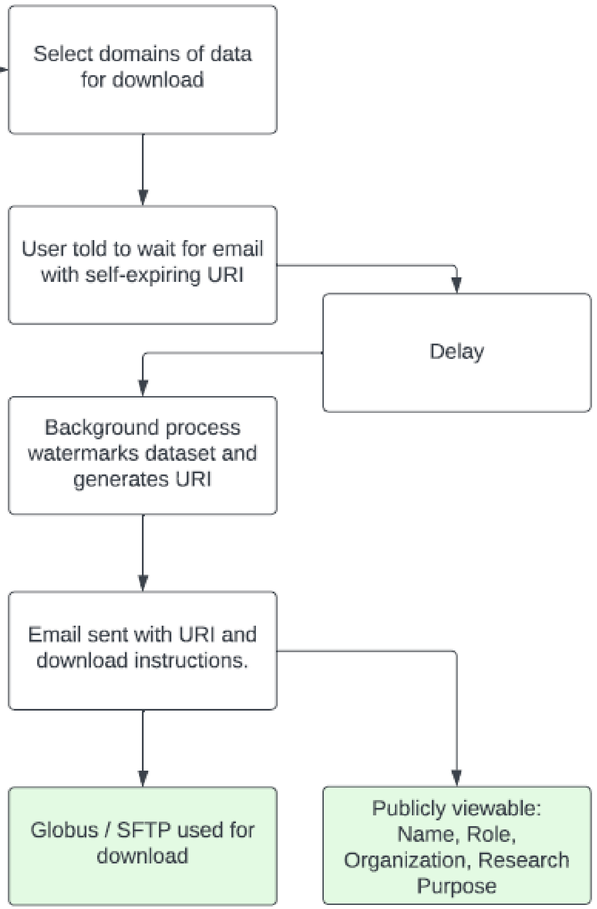
- Two points close to each other means that the input are similar
- Two points far away means that the input are very dissimilar.


0 1 2 3 4 5 6


AI-READI Grand Challenge
Participants
Social Determiants of Health
Cognitive Function
Visual Acuity
Ocular Imaging
Genetics
EKG
Bloodtests
Movement
Continuous Glucose
Cross sectional, multiethnic, multidomain dataset
Machine learning
healthy
diseased
one participant
pseudotime
salutogenesis
pathogenesis
Cross-sectional AI Models
Hypothesis Generating
Biomarker Discovery
AI
Diabetes Severity
AI
Cognitive Function
Training Targets
Predictive AI Models
Therapeutic targets
Saluto-genesis
AI
Time to insulin dependence
AI
Return to healthy state
Training Targets


Data Scientists
Will you need access to restricted variables or be doing research unrelated to T2DM?
If yes,
If no,
Restricted Access: DUA Required
Three Yes/No questions about training
If any no,
if all yes,
List of resources of free public ethics resource
If US IP address
If non-US
LOGIN.GOV
Microsoft Entra ID
Organization
Role
Registration


Collect research purpose (warnings, minimum character counts)
Show the License, scroll to bottom.
Attestation #1:
I will not attempt to identify any individual in this dataset.
Attestation #2:
I will follow the cybersecurity guidelines [link] and understand that the data is individually watermarked to me.
Attestation #3:
I will not distribute this dataset per the License.
Attestation #4:
I will only use this dataset to conduct research related to Type 2 Diabetes.


Select domains of data for download
User told to wait for email with self-expiring URI
Delay
Background process watermarks dataset and generates URI
Email sent with URI and download instructions.
Globus / SFTP used for download
Publicly viewable: Name, Role, Organization, Research Purpose

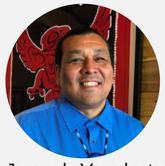
Opportunities for Engagement

Our AI-READI team is excited to be sharing the pilot dataset with you soon!

We will have several team members present at the jamboree to interact with the participants and to answer questions about the data collection protocol, the ethical considerations, the data formats and organization.

Beyond the jamboree, we will be soliciting feedback from the community.

Acknowledgement



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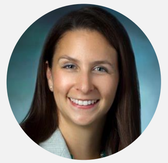

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Christopher Chute
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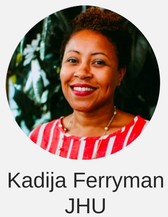

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