

Where Do Biomarkers Fit When Trying to Relate Health to Function?

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Outline

- Health and Function Conceptualized
- Models of Disablement and the WHO-ICF Framework
- Putting Biomarkers into Perspective: Tools for Measuring Health and Function?
- TBI Biomarkers: an ICF Mapping Exemplar
- Envisioning a Future Path: Biomarkers Mainstreamed in Assessing Health and Function
- Resources for Building Biomarkers as Functional Assessment Tools

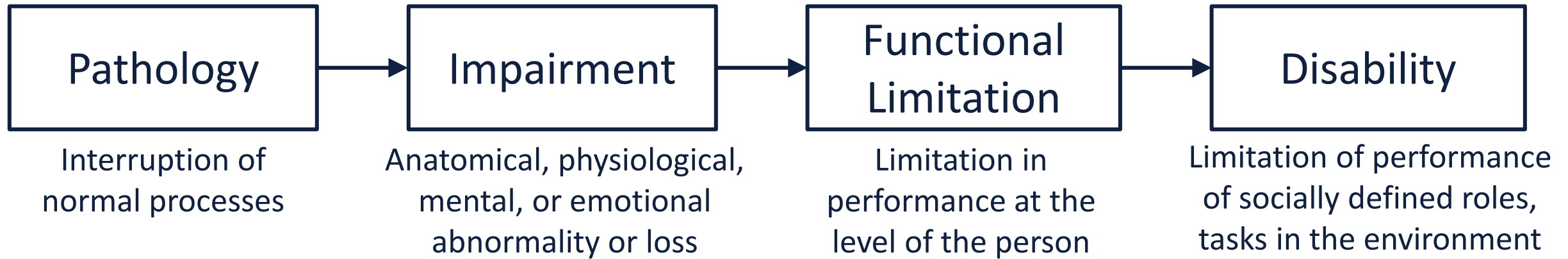
Health & Function: Core Conceptualization

- Health Defined (Sartorius: PMC2080455)
 - absence of any disease or impairment:
 - most relevant to the medical model and based on state of the science, signs, and symptoms
 - a state that allows individuals **to adequately cope** with all demands of life
 - Assumptions about health are based on level of function
 - a state of balance, or equilibrium, between individuals and their social & physical environment
 - health reflects an internal equilibrium get the most from life despite disease.
 - Incorporates values of individuals, cultures, and communities

Health and Function Interrelated Concepts:
Relevance to Disablement

Nagi's Disablement Model has its origins in the early 1960s.

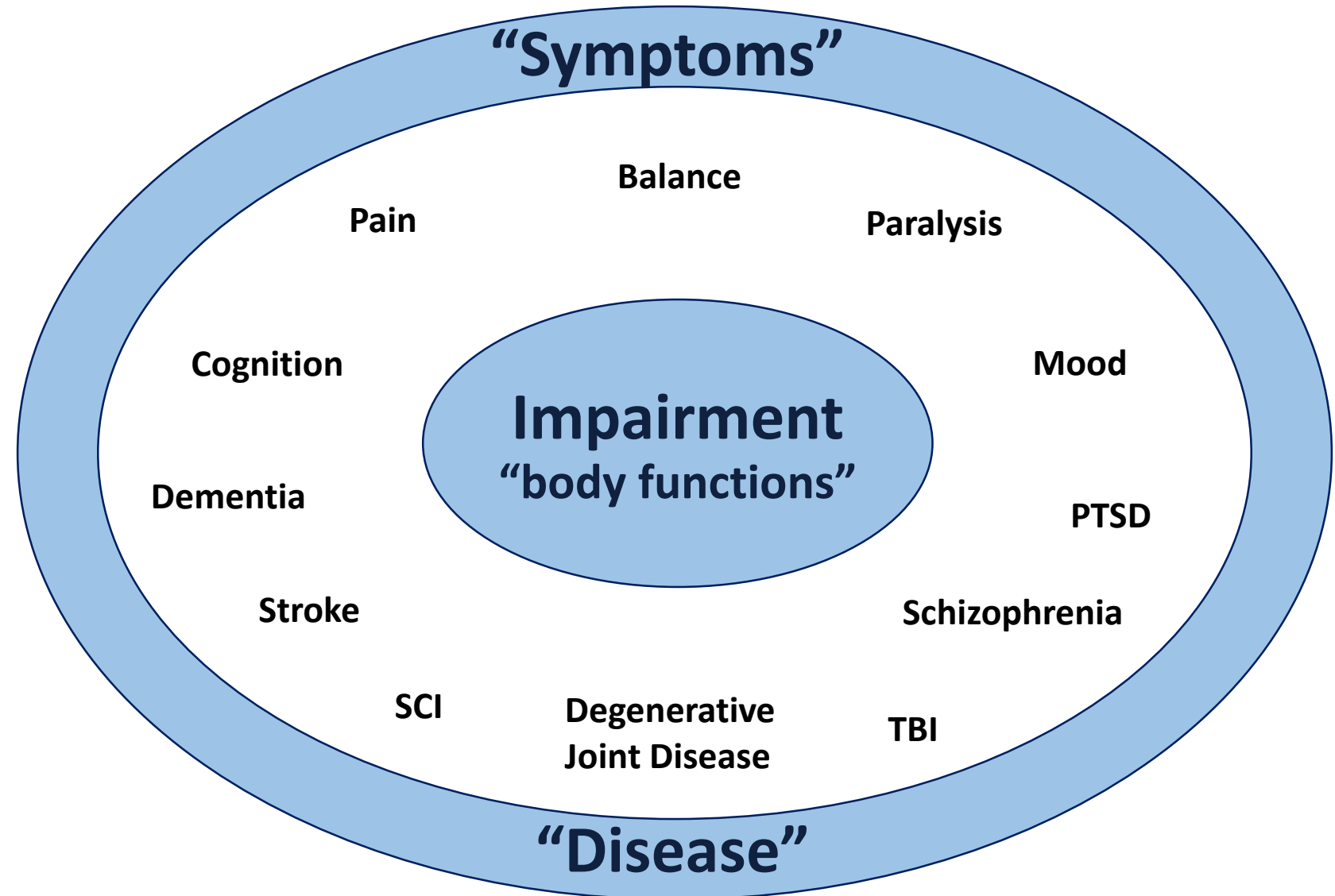
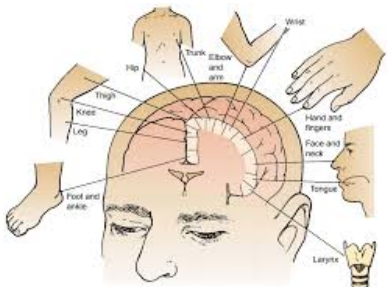
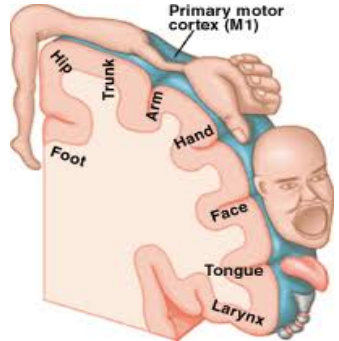
Disablement Model Viewpoint of Health and Function



In this model, participation & life satisfaction are distal outcomes of health, but can uniquely inform evidence based practice effects on health & function

How does impairment/functional limitations/disability map on to WHO-ICF Definitions?

Impairment: problems with body functions and structures that are associated with health conditions

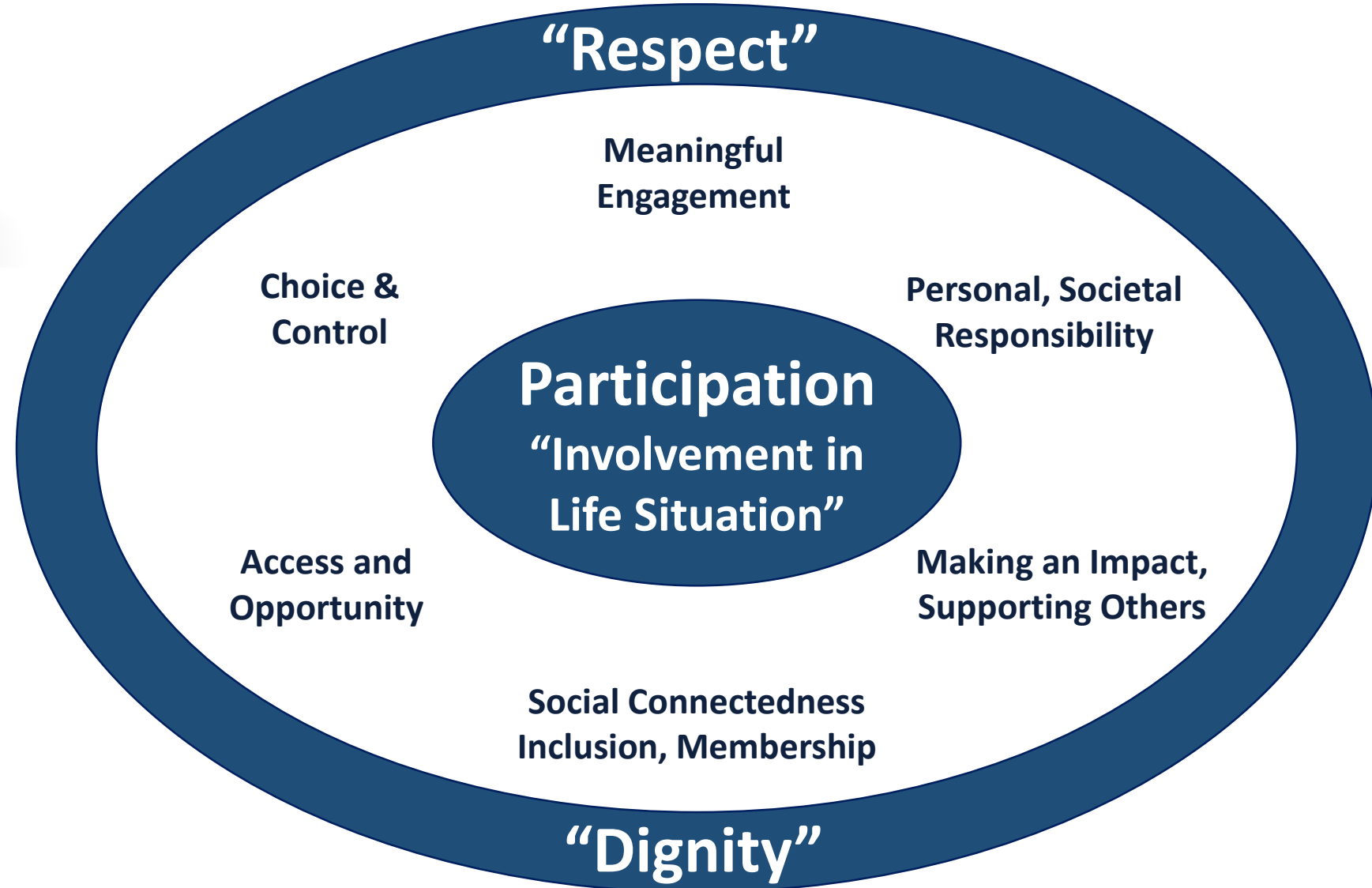


Activities: things individuals do to be independent members of the community

Activities of Daily Living



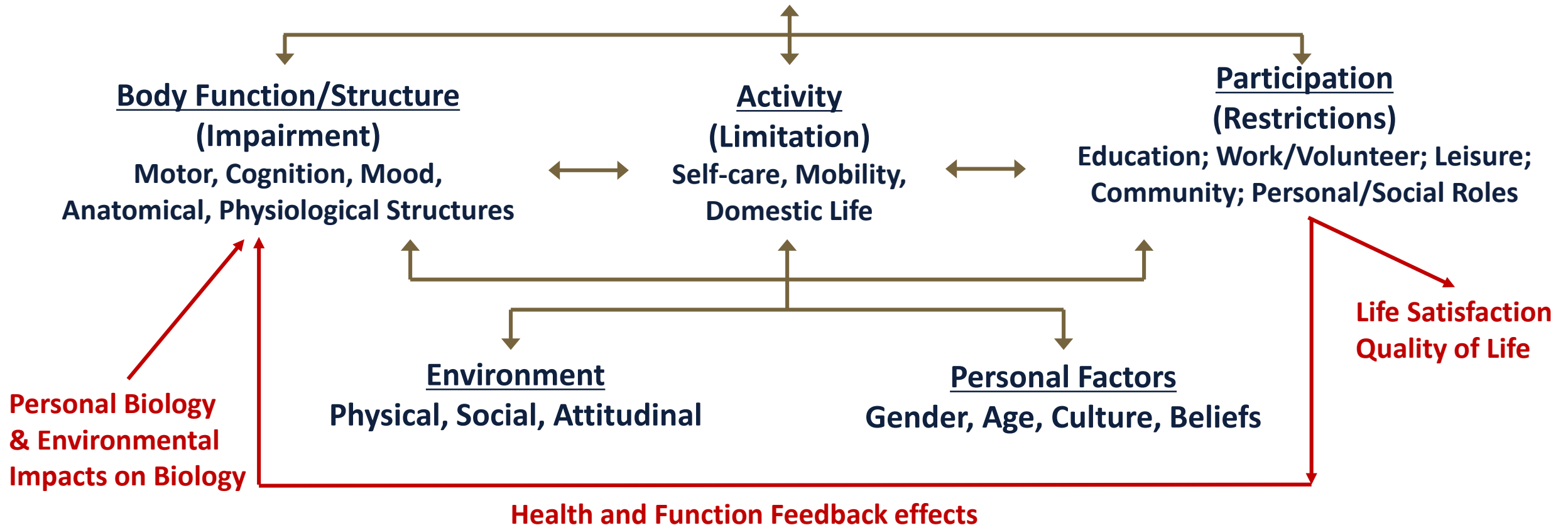
Participation: is distinguished from activity through intent and impact.



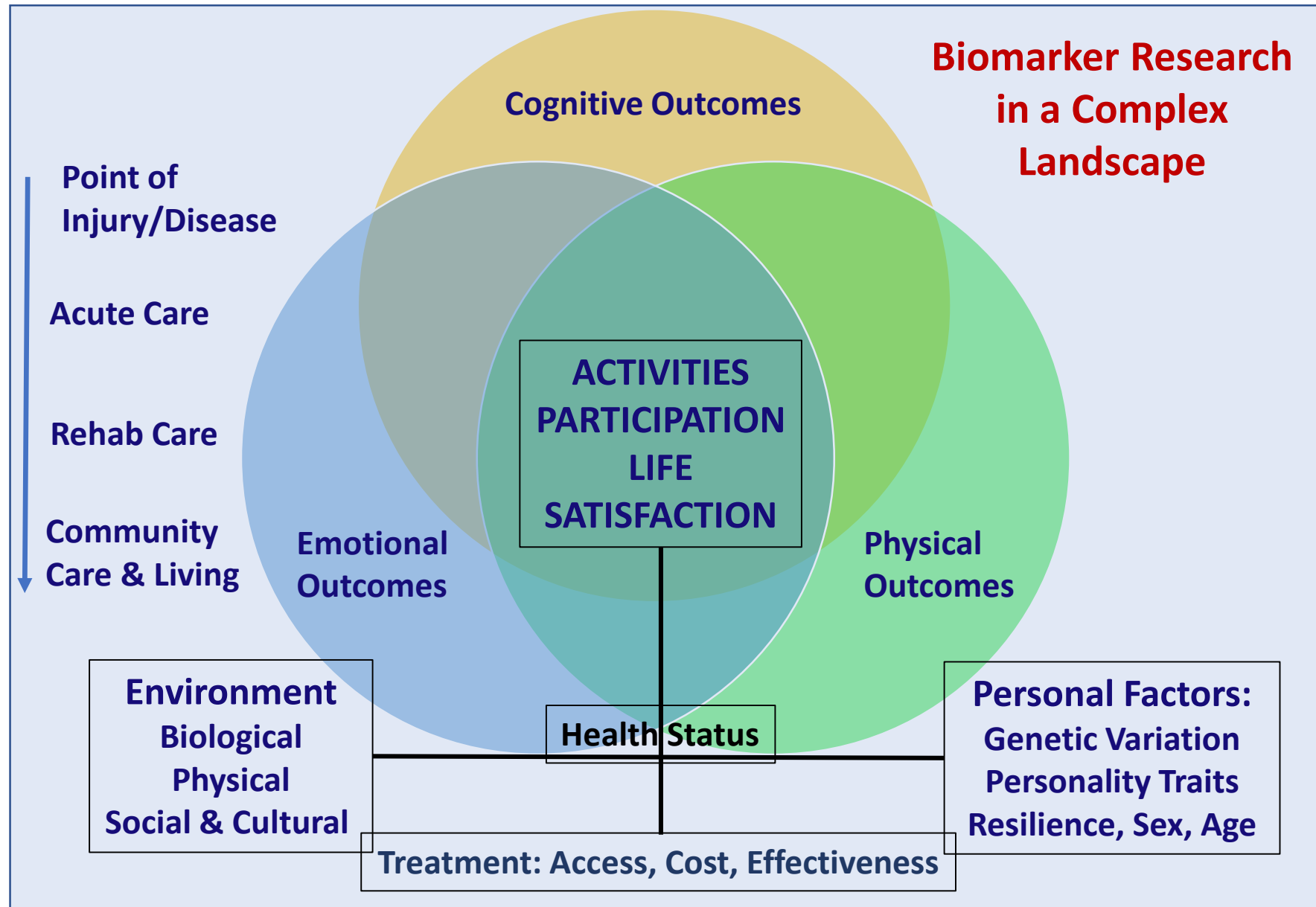
Hammel et al., What does participation mean?
Disabil Rehabil 2008
Stakeholder Interviews

(WHO, 2001) World Health Organization's International Classification of Function (ICF) Framework

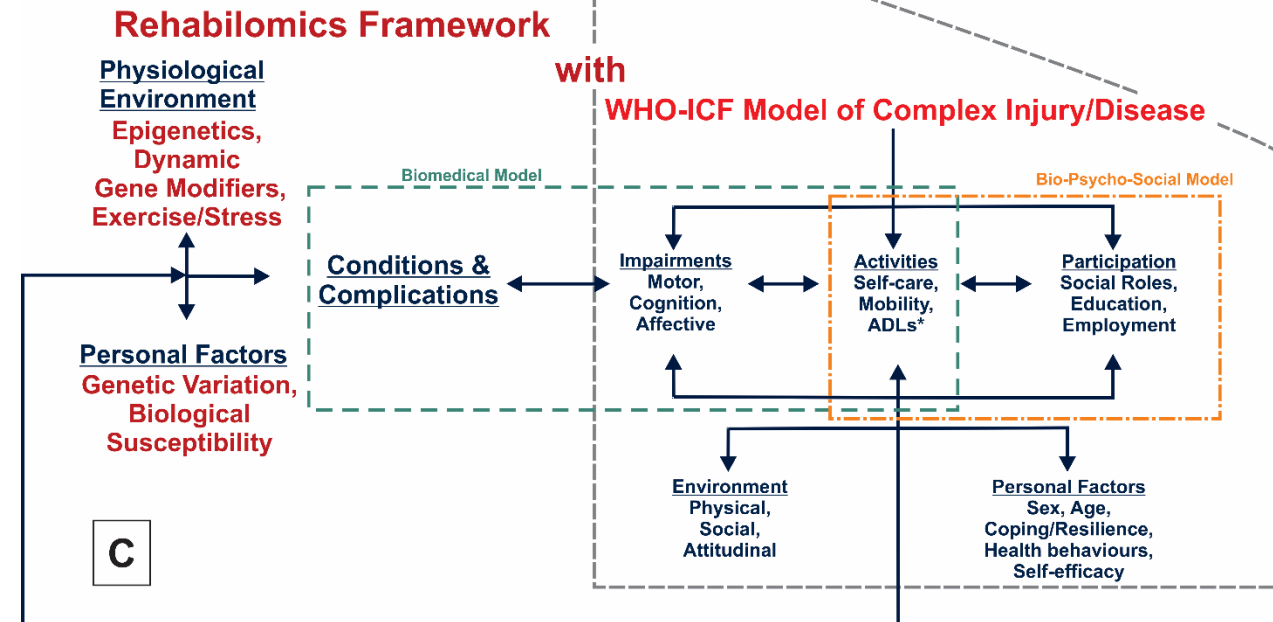
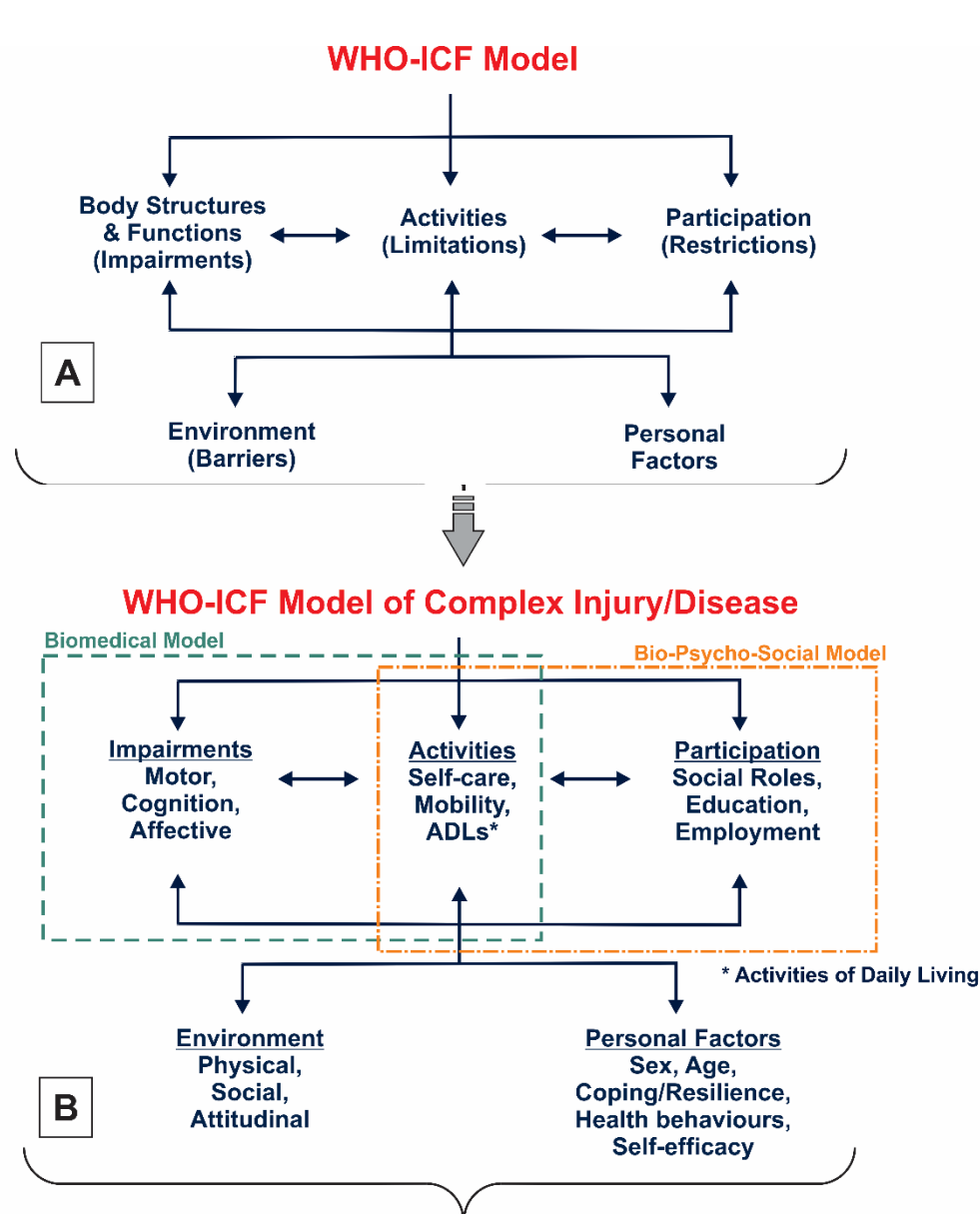
Health & Function (Disease, Disorder, Condition)



Biomarkers: An Instrument in the Tool Box to Capture Health & Function?



(WHO, 2001) World Health Organization's International Classification of Function (ICF) Framework



- Builds off of Disablement Models of Health & Function
- Allows for needs assessment across functional domains of impairment, activity, participation
- Rehabilitation and outcome evaluation
- Understanding disease beyond the medical model
- Matching interventions to specific health conditions while assessing impact on function.
- Application to precision rehabilitation approaches “Rehabilomics”

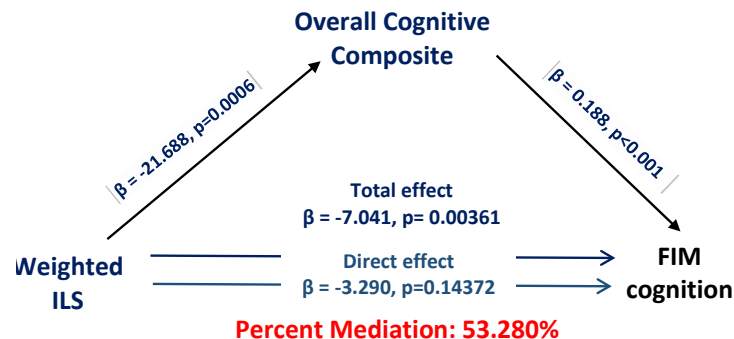
Assessing Relationships between Inflammation & Cognition

- **Cognitive impairment post-TBI** is a central component to survivor outcomes such as the ability to return to work, live independently, and participate in leisure activities.
- Used **weighted inflammatory load score**, as measure of inflammatory burden on cognition.
- Overall cognitive composite scores were created from neuropsychological test measures representing verbal fluency, memory, attention/ processing speed, and executive function

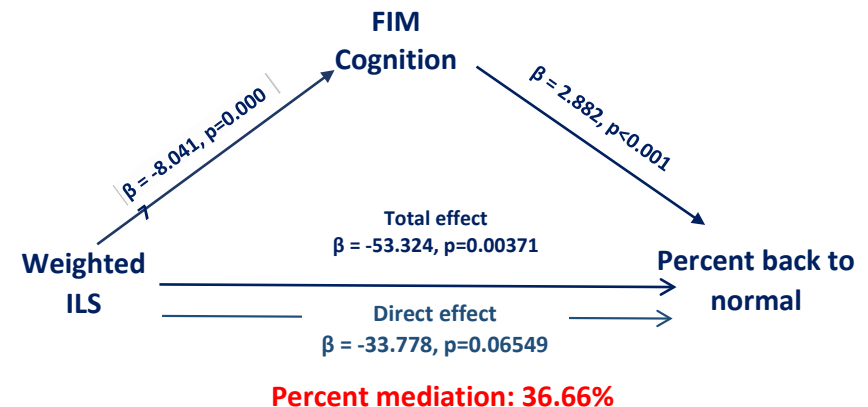
Covariate Adjusted Linear Regression – wILS vs. 12 M Overall Composite (n=112)

Variable	β	p-value	Adjusted R ²
Age	-0.02463	0.5711	0.2048 for base model 0.2803 adding ILS =0.0755 difference 36.87% improvement
Gender	-2.92971	0.1095	
Years Education	1.16724	0.0021	
Best in 24 GCS	0.91576	0.0002	
Overall Weighted ILS	-21.57313	0.0005	

Mediation Model at 12 months

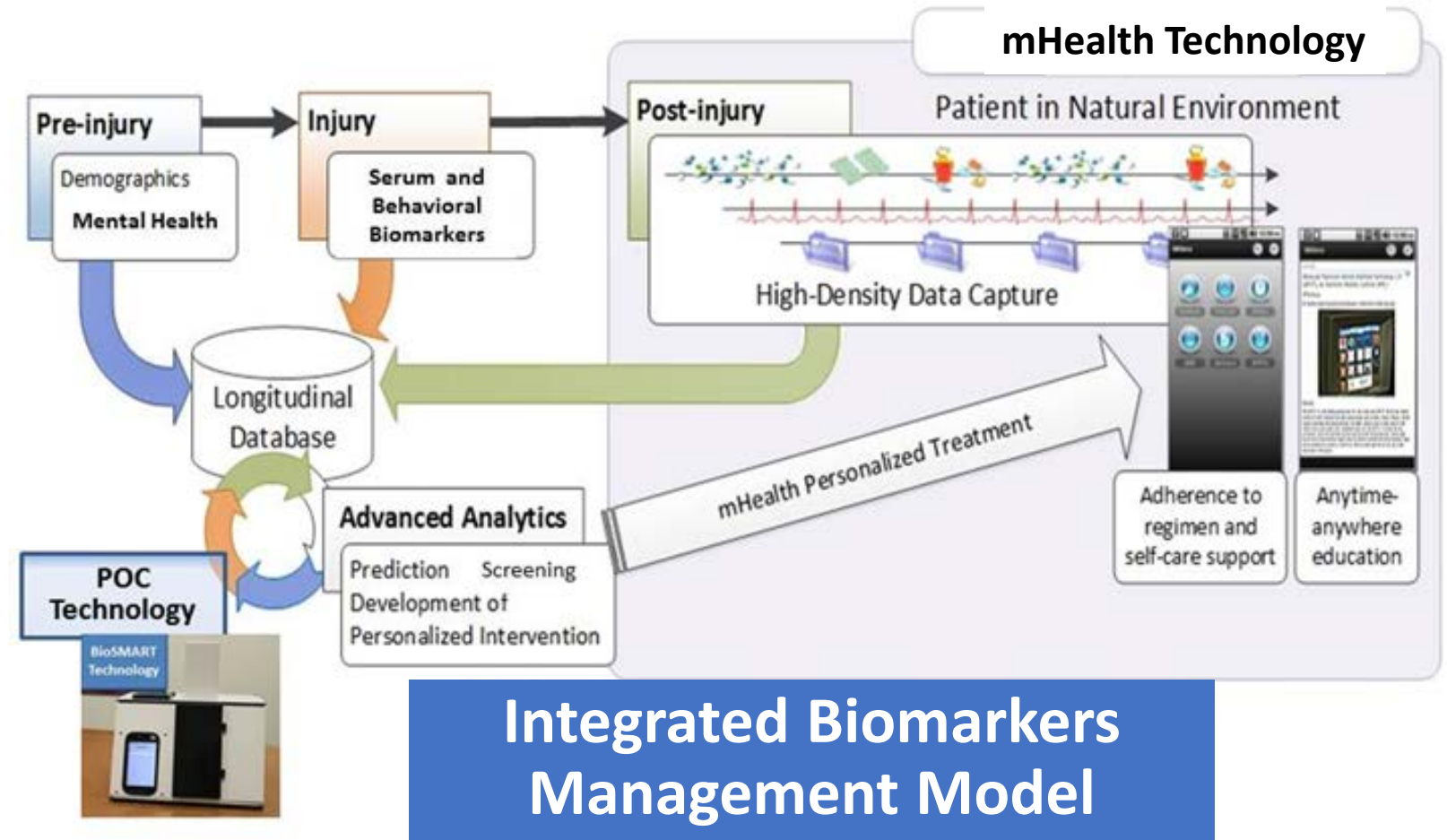


Mediation Model for 12 Months



Biomarkers: A long-term Vision for Health & Function Monitoring & Management

What are some current resources and research programs that can get us closer to the goal of using biomarker to capture function?



Overall, our long-term vision is for an integrated Point of Care Biomarker and telehealth model of chronic, community-based care for individuals provides biomarker based Personal Biology readouts reflecting health and function for populations with chronic injury or disease.

2015



The NEW ENGLAND JOURNAL *of* MEDICINE

A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

“Tonight, I am launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes----and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”

---- President Barack Obama, State of the Union Address, January 20, 2015

Precision medicine: is an emerging approach for disease prevention and treatment that takes into account people’s individual variations in genes, environment, and lifestyle

- **Near Term Focus: Cancer**
 - Already advanced in use of biomarkers and genomics
- **Long Term Focus: Health and Disease**
 - **How does disability and function fits within the PMI?**
 - **How can biomarkers research be prioritized to address functional assessment?**



Biomarkers as Functional Assessment Tools?

PMI Goals: Improve & Personalize the ways we anticipate, prevent, diagnose & treat health conditions

- Genomic Heterogeneity; Personal Biology
 - Better understanding of Disease Mechanism
- Medical and Bioinformatics
 - Molecular, cellular, clinical, behavioral, and environmental
- Adaptive Clinical Trials; Stratified Clinical Trials.
 - The right drug at the right dose to the right patient.

(2016) NIH awards \$55 million to build million-person “All Of Us” study

- NCMRR: Incorporating Principles of Health/Function with PMI enrollment & research
- Opportunities for large scale studies addressing biomarkers as functional assessment tools across spectrum.
 - Engagement with Disability Researchers and Consumers on Barriers to Participation
 - Engagement with disability advocates and populations to drive the research focus.



Biomarkers as Functional Assessment Tools?



- Million Veteran Program:
 - to learn how genes, lifestyle, and military exposures affect health and illness.
- Since launching in 2011,
 - over 825,000 Veteran partners have joined this program on genetics and health.
 - VA-DOE Big Data Science Initiative.
 - Mega-biobank for precision medicine

Ongoing Research Programs

- Predicting Breast Cancer Risk
- Genetics & Heart Disease
- Opioid Sensitivity
- Post-traumatic Stress Disorder
- Genetic Locations Linked to Smoking & Addiction.
- Cholesterol Genetics and New Treatments
- Opportunities for Consumer Engagement defining and assessing the genomics of function?

Thank-you



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