PHEBR-summary

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PHEBR

Population Health Equity Bioinformatics Resource

The Population Health Equity Bioinformatics Resource (PHEBR) is a key tool for developing understanding of neurophysiological turbulence and entanglement leading to dysautonomic, autoimmune, arrhythmic pathologies and also pleasure/pain dysfunctions.

This resource constitutes an Inteligence Information Domain (IID) in the contextual framework of the OASIS architecture and its implementations. The PHEBR includes:

- diagnostic history data of several types (e.g., EKG, echocardiography, and pertinent other imaging and recording, as well as histories of hypertension, temperature flux and arrhythmia, equilibrium and balance episodes, and other quantitative and qualitative parameters over life-history, as much as possible)
- patient and family behavioral and lifestyle data (both specific, as known and accessible, and through computational inferences) such as nutrition, exercise and fitness, exposure to and ingestion of toxins and stressors of chemical nature (e.g., air, water, food) and particularly psychological and social stress (e.g., abuse, anxiety, depression, trauma, PTSD).

Research and clinical studies, globally, provide the rock-solid basis for the assertion that what are termed neuroelectrochemical stressors – within the range of sources indicated above – are a major contributing factor – even beyond genetic factors – leading to subsequent disorders and diseases of the types indicated above. These pathologies commence particularly in adolescence and middle age and the outcomes are almost universally of only two types:

- extraordinary complications, disabilities and comorbidities, reducing the potentials for a normal lifestyle (including employment and a professional life) and for an average-length lifespan
- early and often sudden death

Building the PHE Bioinformatics Resource (PHEBR)

The database(s) and the synthetic ("AI") intelligence components are straightforward, non-complex, and principally based upon existing, proven, accepted technologies. There are collaborative partners at other institutions worldwide in all aspects of PHEBR implementation and use (as summarized below).

The focus of the PHEBR begins with large-scale population health data acquisition (as indicated above) and analysis capabilities. Along with the capabilities mentioned above, there are two critical components of data acquisition that are viewed within the research/clinical community as major positives:

- incidents and probabilities of epidemic or pandemic type diseases (e.g., influenza and COVID-type viral infections; e.g., Long-COVID), with a focus upon early detection of infection cases, attention to variants, and prediction of transmission & distribution through the general population

- pregnancy and first months after childbirth – these are significant risk-periods for certain demographic segments of the female population, and minority groups in particular.

The PHEBR will include computational (modeling, simulation, and dissemination) capabilities for:

- analysis of deficits and development of methods (mechanisms, procedures) for removing deficits in diagnostics and early detection of disorders and diseases:
  - cardiovascular and dysautonomic disorders as the primary focus
  - autoimmune diseases including multiple sclerosis (MS), Alzheimer's, Parkinson's, Lupus, which are particularly challenging to detect, particularly in early-onset or pre-onset stages, in general, among any and all populations, and for which many minority populations are receiving inadequate diagnostic and preventive medical care including education as well as prophylactic/therapeutic treatments.

- analysis of deficits and development of methods for improving day-to-day and long-term care of patients afflicted with such disorders (i.e., removing deficits in long-term care of persons with physical and mental disabilities that prevent or reduce dramatically the person's ability for self-mobility (e.g., walking), self-care (e.g., household, personal), and social interactions).

Within the PHEBR there is extensive employment of synthetic intelligence ("SI", aka "AI") algorithms, and the primary applications are in:

- decisions regarding authenticity and usability of data elements
- inferences where data is incomplete, sketchy, and unambiguous
- natural language understanding for data originating as text descriptions
- inferences regarding sources for new data on patients and patient group types that should be obtained
- inferences including forecasts for symptoms and specific pathologies to be targets of examination and diagnostics including by empirical, instrumental forms of measurement and evaluation

The central component of the SI technology used within the PHEBR is known as Seldon. This is a composite of pattern recognition, inference and predictive software developed over a period of years by members of the TETRAD collaborative research team. Seldon has been designed for large datasets with high degrees of uncertain, incomplete and conflicting data.

The PHEBR includes data pertinent to the following (which constitute the focus of a current, long-term, multi-institutional, international consortium in which M J Dudziak and TETRAD are involved, serving as principal investigator and institution ("Neuroplex-C"):

- Cardiomyopathies[1] including but not limited to progressed development of arrhythmias such as tachycardia and AFIB
- Myocarditis and percarditis, and consequent cardiomuscular disorders linked with infectious diseases and/or other forms of inflammatory disease, including but not limited to COVID-19
- POTS (postural orthostatic tachycardia syndrome)

1 Dilated (DCM), hypertrophic (HCM), restrictive (RCM and left-ventricular non-compaction (LVNC), with particular attention to the other conditions, disorders and diseases referenced above in this proposal context

- MALS (median arcurate ligament syndrome)
- EDS and hyperelasticity within the arterial network and particularly the aorta
- Hypertension, atherosclerosis and myocardial infarction
- Gastrointestinal disorders (such as IBS, POI and Crohn's) linked with the above, particularly POTS
- Dysautonomic disorders which are viewed as being related in causal and/or concomitant relations with one or more of the cardiac dysfunctions listed above
- Psychological disorders linked with several of the above conditions, particularly PTSD and depression)
- Special attention to disorders with both neurophysiological components that are associated with the following areas of investigation:
  - chronic pain
  - post-surgical trauma including development of adhesions affecting cardiovascular, gastrointestinal and urological organs
  - psychological reactions including development of dependencies upon addictive substances

[2.4]
The PHEBR meets clear and consensus-agreed needs expressed within the medical communities focused upon these categories of disorder and disease. PHEBR provides new, systematic, thorough, and large-scale bioinformatics and supports the subsequent development of useful large-population medical databases, covering precisely the disorder and disease topics listed above. PHEBR can be used within academic, public-sector, and corporate (e.g., pharmaceutical industry) sectors for:

- healthcare planning by all types of provider professionals and institutions
- pharmaceutical design and development
- medical device design and development
- pregnancy and postpartum healthcare
- long-term healthcare
- social services for the disabled
- public health education for the general population, especially youth

The diagrams on subsequent pages illustration core purpose, design and functionality of the PHEBR.

4 - Integral importance of large-scale population-based bioinformatics:

Significance of Population Health Equity and Diversity Biometrics for Improved Early Diagnostics and Proactive Treatment and Positive, Sustainable Survival

Issues:

► Incomplete Data being collected from virtually all patients at risk

► More people than ever at risk due to:

♦ COVID-19 and PASC

♦ Massive Stress, Anciety, Passive/Active Abuse, *Social Deconditioning*

♦ Variances between Racial and Ethnic Groups – Not Understood, Not Examined, Not Considered

♦ Social / Institutional / Professional Prejudices toward Most-At-Risk Population Sub-Groups for many dysautonomic/autoimmune conditions

► Need for Massive Biometrics including Behavioral & Genetic Data in order to:

♦ Ascertain genetic etiology and amplification factors

♦ Understand the psychosocial, nutrition, lifestyle factors

♦ Develop personalized plans for individuals at risk and in general

♦ Overcome medical/healthcare prejudices and discrimination which result in misdiagnosis and ignoring problems until Too Late

More Issues that Demand Population Health Equity and Diversity Satisfaction:

This is about BOTH
♦ Inequities in diagnostic and therapeutic medicine AND
♦ The GAP in understanding the variances between multiple genotypes and beahavior/lifestyle types which is Required in order to Answer the many questions raised and implied by this Project and many others in related fields

► Massive Statistics of a different "order" than what are typically queried or discussed by healthcare providers – particularly in USA
► Yes, anonymity and privacy can be preserved and protected – including for critical data pertaining to lifestyle including mobility functions
► COVID-19 and PASC must be addressed head-on because This is a Large and Multi-Generational Problem we now face
► Psychological Dynamics including parent-child, adult-adult, and societal factors of abuse, bullying(!) and other discrimination – spanning indeed all races and demographics and arguably intensifying in the 2020s – this must be included in the Data Collection and the Biometric Resources to be assembled
► This must Not be yet-another-exercise in building a huge database and then it sits there and is used by (maybe) only a handful of researchers
► **Population Health Equity Biometrics Resource (PHEBR) can and must be a Tool for Social Health Change including Policy and Practice (not only "research")**

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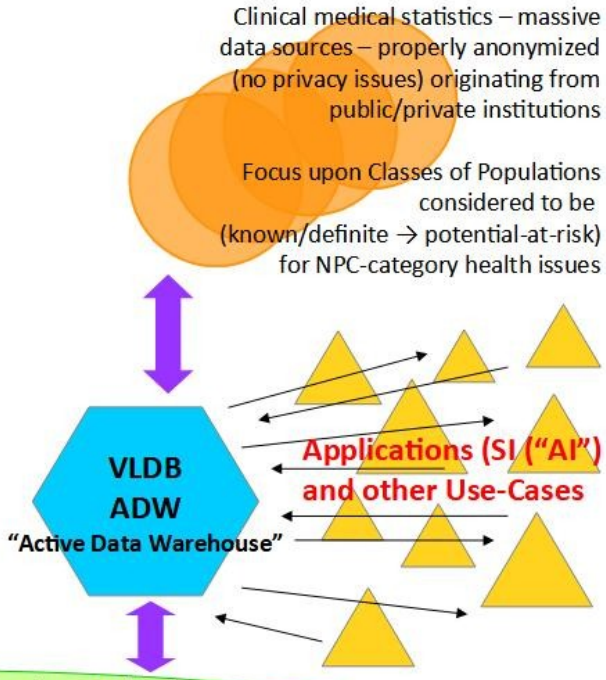
What is and how to build the PHEBR

Prime Objectives:
[1] Resource for Identifying and Reducing Health Inequities (Inequialities) for Affected, Vulnerable, and Ignored Minorities and Population Sub-Groups
This, of course, pertains to many (all) aspects of healthcare

[2] Assist genomics-focused research "across the board"

[3] Assist in the challenge of identifying "earlier than later" the at-risk populations for "neuro-cardio-plus" disorders, including other autoimmune types

[4] Other objectives include the benefits to healthcare industry entities: pharmaceutical, medical device, hospital, insurance, others



Human-Machine Users (Agents) – different use-cases, objectives, applications
- Genomics, genetic engineering, diagnostics, therapies, pharma, devices
- Public health (equity/inequality problem; pandemic prevention/containment)
- Identifying and refining relations and etiologies of NpC-type disorders and diseases

The PHEBR is a kind of "New Genesis" for studying links between poorly-understood and syndrome-categorized disorders and diseases ---- What better way to do this than to "couple" together ADAM and EVE? 😊😄

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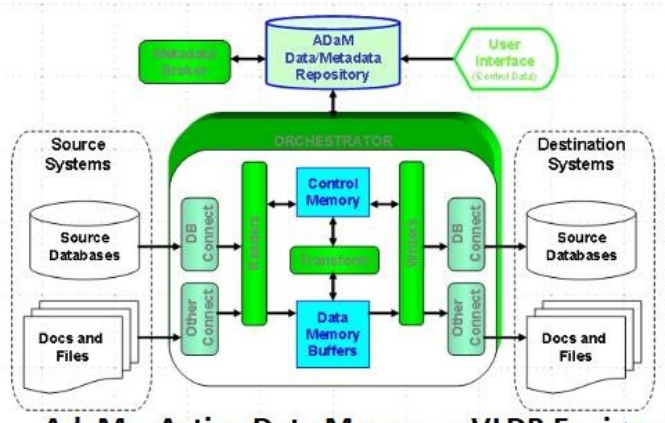
ADAM and EVE

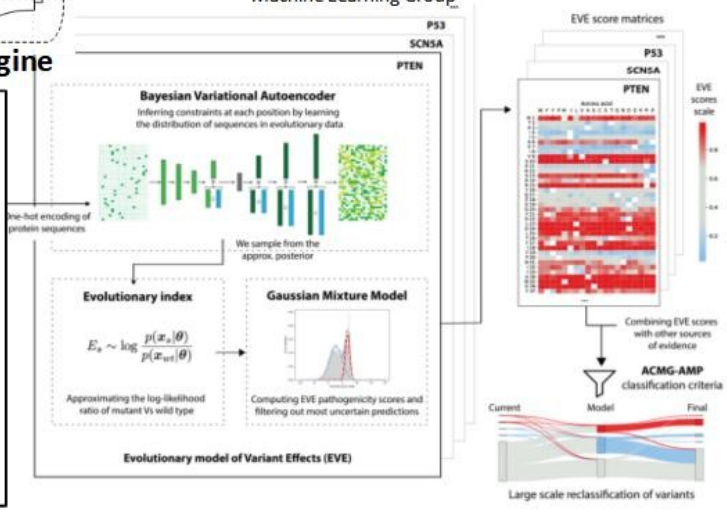


AdaM – Active Data Mover – a VLDB Engine

eve

evolutionary model of variant effect

Marks Lab - Harvard Medical School
OATML - Oxford Applied and Theoretical
Machine Learning Group



GOAL with PHEBR:
Adapt EVE logic (Bayesian + NN pattern detection) to task of seeking and identifying patterns within massive data streams of clinical-origin patient medical histories for:

- ♦ Indicators of risk conditions and causal relations on the basis of acquired data sets in PHEBR
- ♦ Missing-gaps - types of data to pursue and collect through future clinical measurements (e.g., behavioral, lifestyle)
- ♦ What-Ifs and Hypotheticals pertinent to NpC for investigation and evaluation and linkage with genetic modeling systems like EVE (HMS/OATML)

More coming soon...

