

Using Circadian Heart Rate to assess the Impact of Chronic Stress and Mental Health

March 2016



We believe individuals, families and carers affected by mental health can live full, happy & healthy lives.

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Company Summary

- Medibio's Digital Mental Health Platform will transform the assessment and management of mental health
- Defensible IP/technology based on 20 years of research into the relationship between the autonomic nervous system and mental health
- Support of notable research partners- Johns Hopkins University, Mayo Clinic, Emory University, Ottawa University, BMRI
- Endorsement from corporate partners- Medtronic, Bupa, Preventice, others
- FDA submission this year and existing reimbursement codes to pave the way for clinical and corporate acceptance
- Multiple commercialisation routes – Clinical, Pharma, B2B and B2C represent multi-billion dollar market opportunities
- B2B product on market now and in use with key strategic partners

“It is critical to realise that we cannot succeed if we use DSM categories as the gold standard. We need a quantitative method for diagnosing depression.”

(U.S. National Institute of Mental Health - 2013)

“The Single Greatest Illness that Affects Mankind” *

- Neuropsychiatric disorders are the leading cause of disability in the U.S.
- WHO estimates the global cost of mental illness as \$2.5T in 2010 (est. \$6T in 2030)

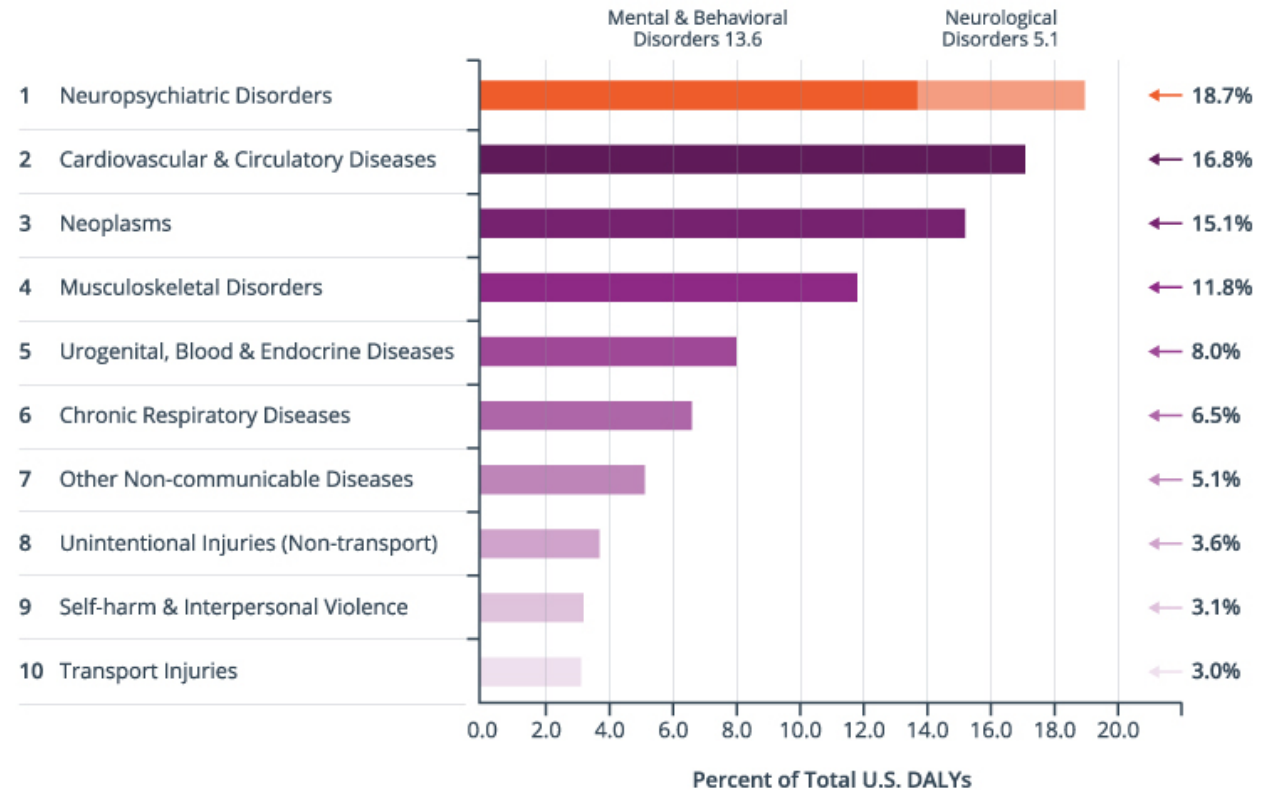
References

- NIMH [article](#)
- World Health Organization. (WHO 2011a). *Global status report on non-communicable diseases 2010*. Geneva: WHO

* World Mental Health Day 2015
Professor [Stephen Lawrie, Head of Psychiatry at Edinburgh](#)

Data courtesy of WHO

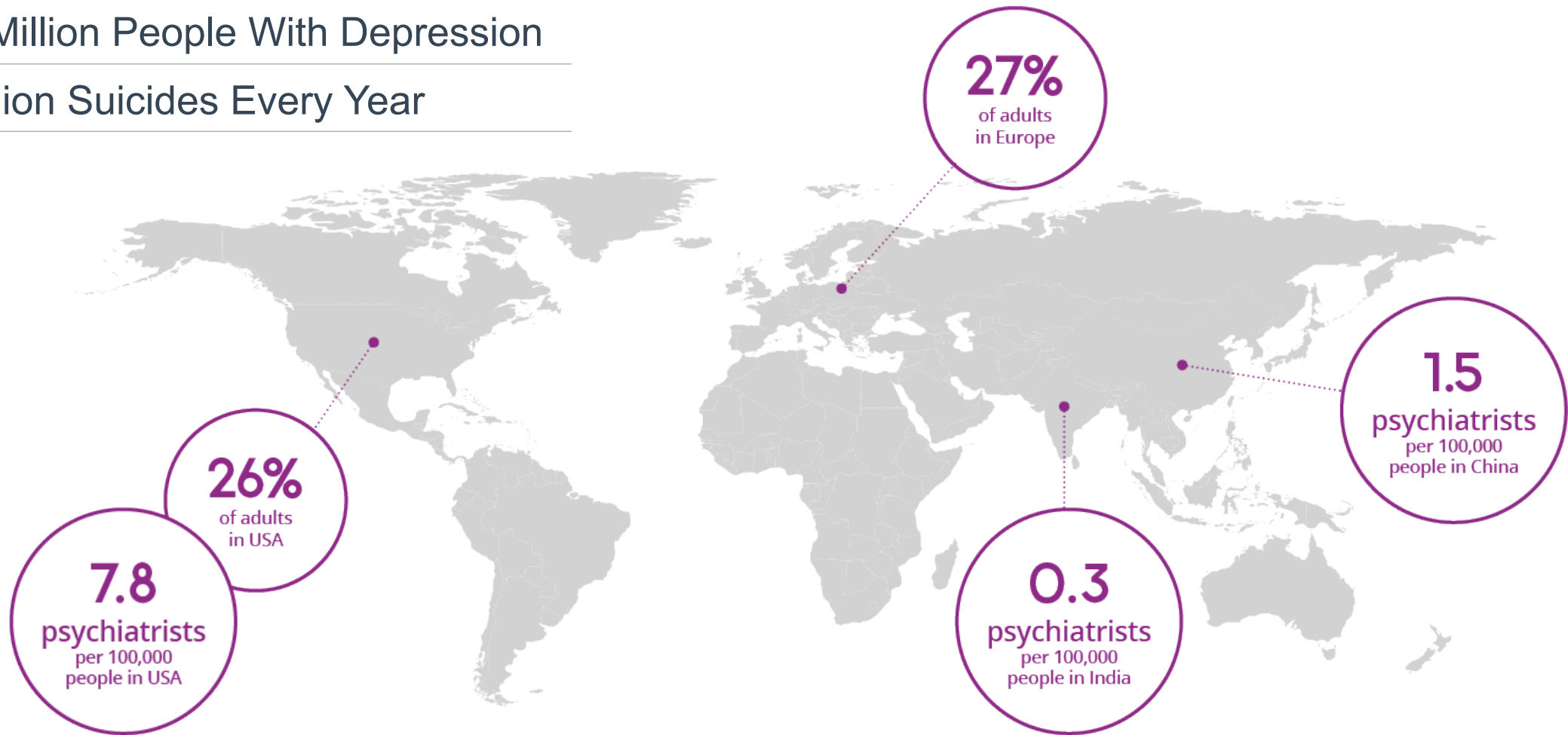
Top 10 Leading Disease/Disorder Categories Contributing to U.S. DALYs (2010)



A Global Crisis of Access & Management

350 Million People With Depression

1 Million Suicides Every Year



Snowball Effect of Depression

Patients diagnosed with MDD are far more likely to develop serious co-morbidities.



The Need for Objectivity

“The economic costs of mental illness will be more than cancer, diabetes & respiratory ailments put together.”

Thomas Insel, MD – Former Director National Institute of Mental Health

Current Pain Points

- No objective test for mental illness.
- The diagnostic “gold standard” is a clinical/expert opinion.
- Diagnostic agreement between clinicians can vary considerably – concordance rates near 70%.
- Current assessments are subjective which can lead to inadequate or incorrect diagnosis.
- Misdiagnosis of depression (and other mental illness) places a huge cost burden on the healthcare system and the workplace.

Medibio's Solution

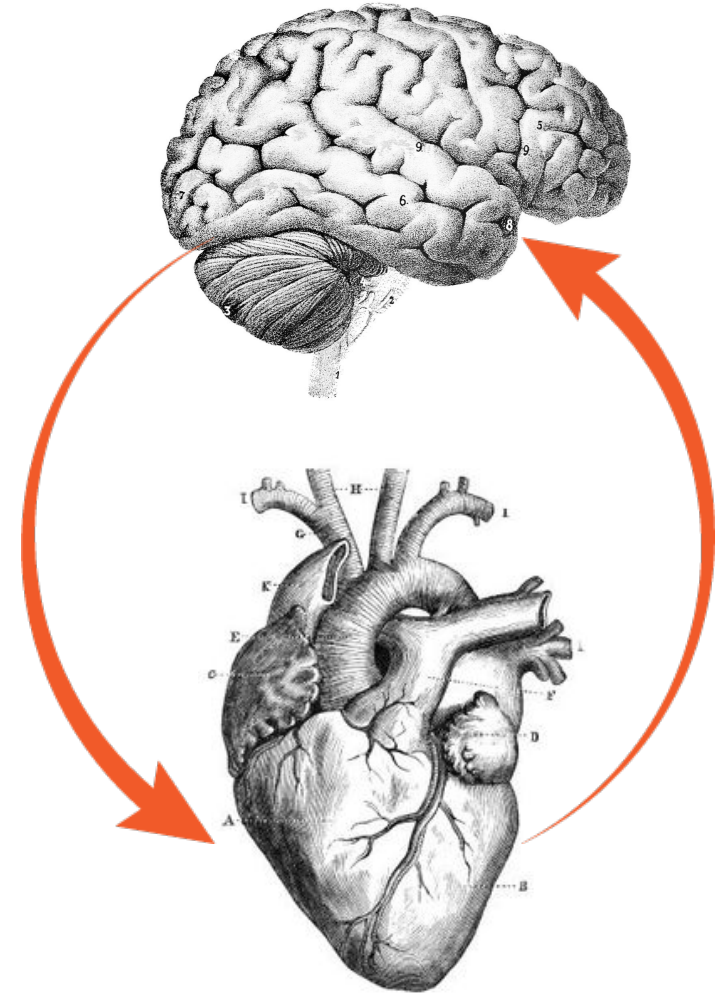
- Quantitative, objective test.
- Diagnosis based on patient's biometric data (circadian heart rate waveform).
- Repeatable, reliable test with classification accuracy of >80%.
- Provides objective indication of treatment efficacy along with medication compliance and adherence.
- Savings to the health system and better patient outcomes.

**Medibio's
Digital Mental Health Platform
will transform the assessment
and management of mental health
by:**

- Enabling access to care
- Providing objective, quantifiable diagnosis
- Confirming the effectiveness of therapies
- Driving optimal disease management

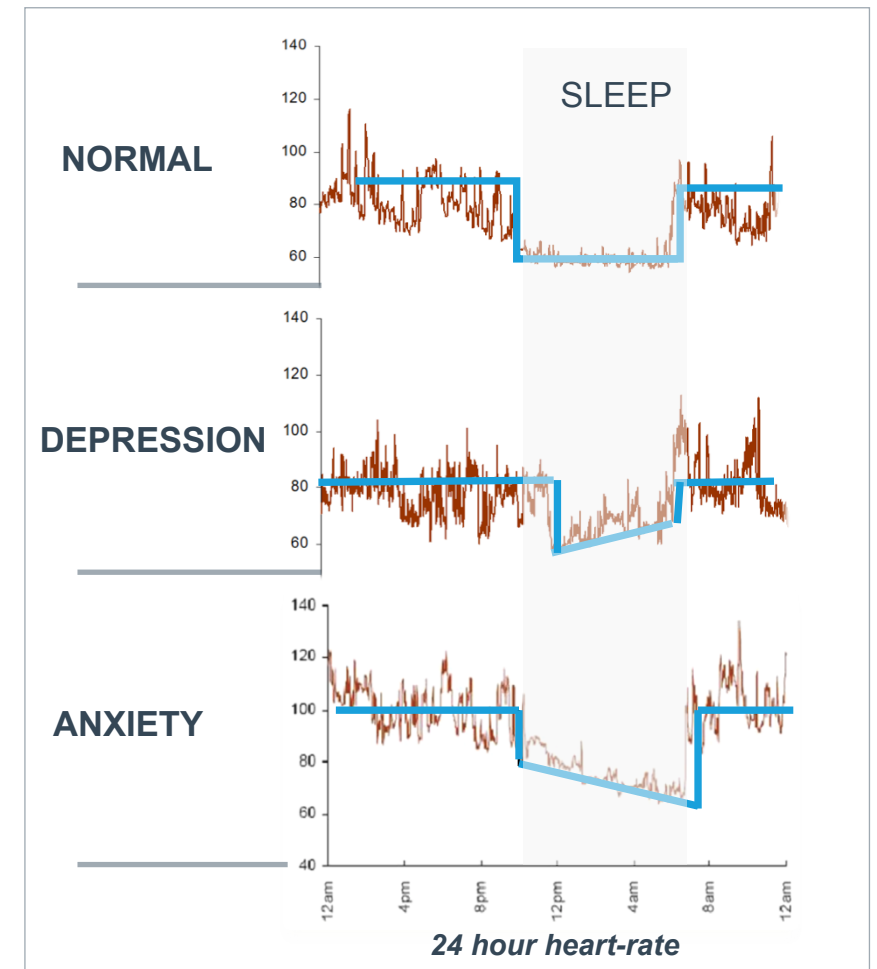
The Mind-Heart Link

- The psychosomatic link between the heart and emotion has been recognized since antiquity and is embedded in language ('made my heart skip a beat... heart broken... cold hearted')
- 5000 years ago, Ayurvedic physicians diagnosed mental illness by feeling a person's pulse!
- The heart is not merely a pump. It has a neuronal circuitry of around 40000 neurones, secretes hormones [A&B natriuretic, norepinephrine & dopamine (ICA cells), oxytocin], has endocrine receptors and has dense interconnections with different parts of the brain.
- The autonomic nervous system (ANS) plays a key role in circadian sleep-wake regulation which includes heart rate.
- All serious mental illness (SMI) are associated with ANS and wider neuroendocrine dysregulation (especially affective disorders) and abnormalities in circadian regulation.



Insights Based on 20 years of Clinical Experience

- Research initiated 20 years ago at University of Western Australia to test the theory that mental state linked ANS disturbance could be observed via the cardiovascular system.
- Mental state-linked ANS disturbance is observed via the cardiovascular system during sleep when external influences are absent.
- Morphologic analysis of circadian heart rate waveforms (CHR) gives objective indications of 'core' physiological differences between different forms of mental illness such as anxiety, depression, and stress.
- Serial monitoring of patients under psychiatric treatment showed that effective intervention is associated with normalisation of CHR, providing a tool for determining treatment effectiveness.



Assessing the Impact of Chronic Stress

Using stress specific algorithms Medibio's technology provides objective indications of the stress. Based on the type and degree of deviation of their CHR waveform individuals are classified into one of three distinct categories.

- **GREEN** – mild (no immediate action needed)
- **AMBER** – moderate (the impact of stress on wellbeing is approaching unhealthy levels)
- **RED** – serious (the impact of stress may have an unhealthy impact on wellbeing recommend lifestyle changes)

Initial target market is the **Corporate Wellness** market where Medibio provides an end to end solution for Corporates.

We provide the first objective measure of stress, a series of corporate dashboards, and can plug into our wellness partners interventions.

ASSESSMENT



- Enable employees to check their stress levels
- Personal early warning system for people at risk
- Prevention is better than cure

SUPPORT



- Provide education, support, and intervention based on stress level
- May recommend discussion with PCP
- Provide the ability to conduct on-going monitoring to check progress

EMPLOYER BENEFIT

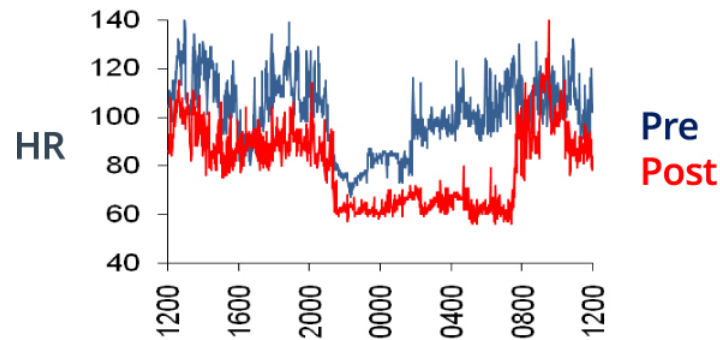


- Metrics on stress levels for job classes/types
- Reduced absenteeism and increased productivity
- Reduced claims and pressure on the health care systems

Objective Assessment of Therapy Effectiveness

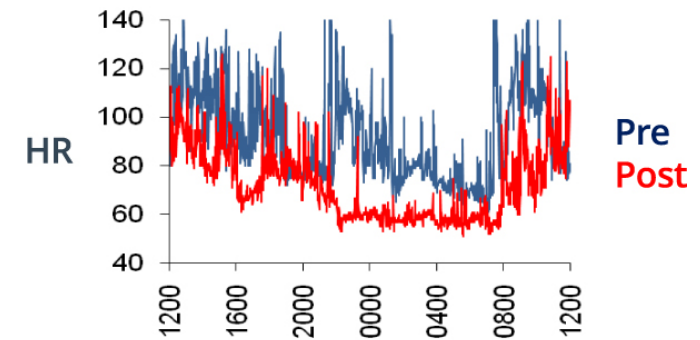
Case Study 1

- Depressed individual upon initial diagnosis
- Treated for 18 days with:
 - Olanzapine – 10mg (night)
 - Mirtazapine – 60mg (night)



Case Study 2

- Individual diagnosed with Generalized Anxiety Disorder (GAD)
- Re-evaluated 10 days following effective treatment



Significant Validation Supporting Technology

CLASSIFICATION ACCURACY	STUDY OUTLINE	REFERENCE
98%	32 controls (normals) and 28 with either an affective disorder or a psychotic disorder	International Congress on Schizophrenia – 2003
78%	50 across the mental health continuum	Psychiatric Quarterly, Vol. 73, No. 3, Fall 2002 (2002)
80%	98 patients, mixed psychopathology and normals	Diligence by UNSW and Newcastle University independent researchers
82%	200 patients, 30 normals, 30 depression, 30 GAD, 110 other mixed psychopathologies	Australian & New Zealand Journal of Psychiatry 1998; 32; 187-198

Defensible Position Based on Decades of Research



Comprehensive suite of patents around CHR & technology:

- Medical diagnostics including assessment of treatment efficacy
- Stress assessment



Patent suite for medical diagnostics includes:

- Method for Diagnosing Psychiatric Disorders
- Method and System for Monitoring Stress Conditions covering the use of CHR for stress assessment
- Method and System for using CHR to Diagnose Psychiatric Disorders



Proprietary data set required is the natural protection:

- 10,000+ 12 hour ECG files with a corresponding psychiatric diagnosis
- This data set would take 5 years and cost \$20 million to replicate

Validation Trial with Johns Hopkins University

Study Objective

- To validate the use of Medibio's CHR technology to differentiate between depressed and non-depressed individuals
- Designed to provide clinical data to support FDA certification of Medibio's proprietary depression test

Study Timeline

- Anticipated data collection completed Q4 2016
- Simple, quick, powered to only need 80-100 participants
- 50 subjects with MDD, 50 Normal Controls

Johns Hopkins University (JHU)

- Ranked number one in the U.S. by US News & World Report for 22 years of the survey's 25 year history

Principal Investigator

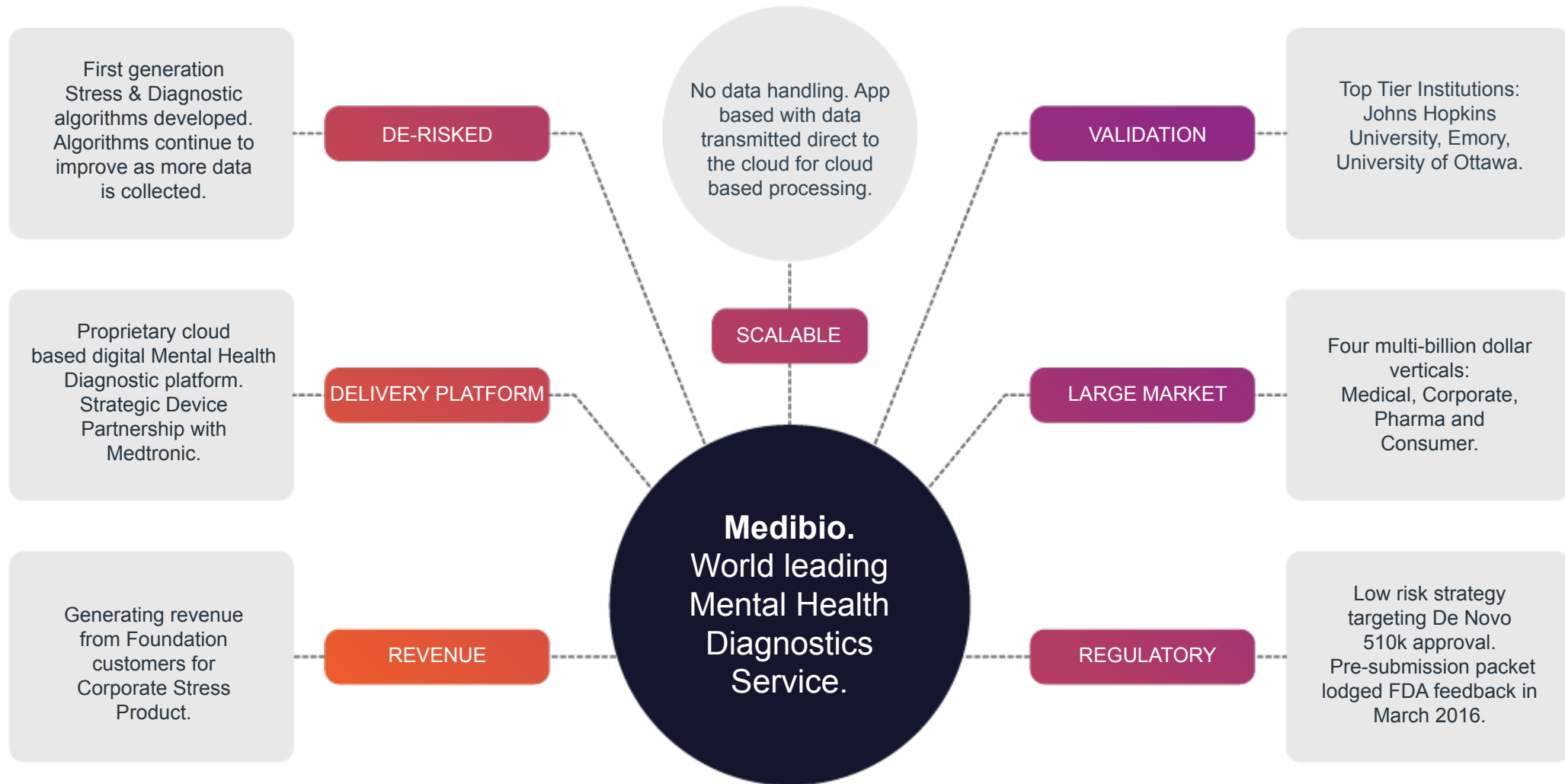
Dr Naresh Punjabi

Professor of Medicine and Epidemiology in the Division of Pulmonary and Critical Care Medicine Associate Director of Graduate Training Program in Clinical Investigation at JHU. Published more than 100 research papers.



Dr Naresh Punjabi

All the building blocks are now in place:





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