



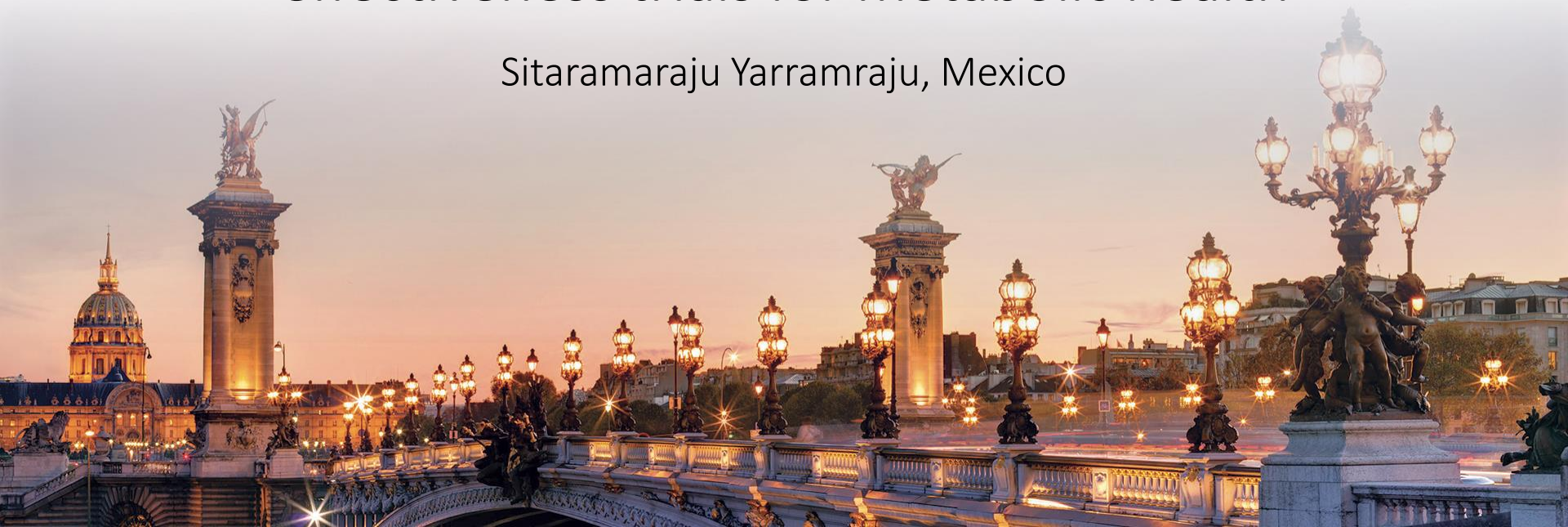
Paris
NASH
Meeting

September 8 & 9, 2022

8th edition

Creating a global infrastructure for efficacy to effectiveness trials for metabolic health

Sitaramaraju Yarramraju, Mexico





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Conflict of interest disclosure

- Founder & CEO of Avant Santé Research Center SA de CV
- Founder & CEO of ETCURAE
- Avant Santé and VCU Health have formal collaboration agreement research
- Dr. Arun Sanyal is formal advisor for the Metabolic health excellence centers of Avant Santé & EtCurae in Latin America

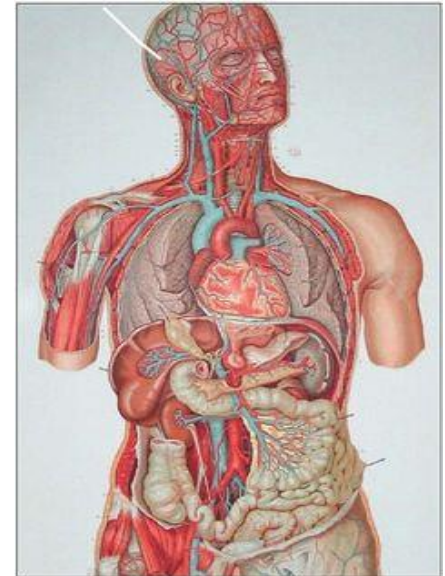




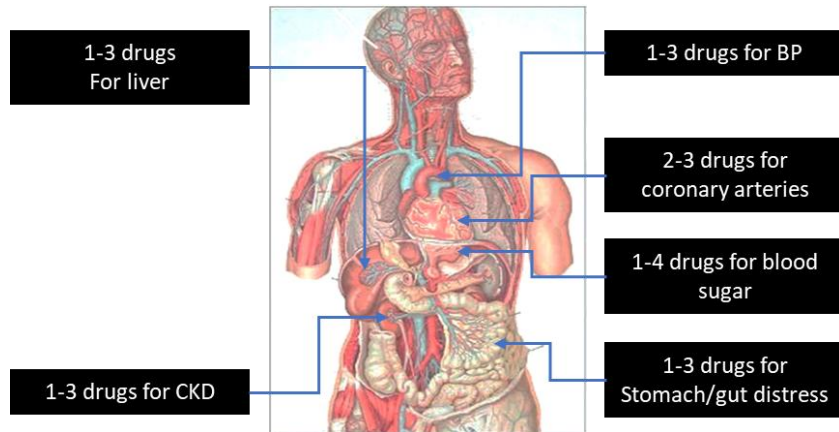
Metabolic health

- *Physical conditions that involve metabolic functions and its associated health impacts.*
- *Metabolism involves harmonious signaling between multiple organs. One of the central metabolizing organs is the liver.*
- *More than one third population has Metabolic health related diseases. It continues to grow.*

One human Body &
multiple interacting organs



Care - Metabolic health



- Fragmented
- Organ-centric approach.
- Long-term impacts on meaningful clinical outcome is unknown.
- Patient & system health care burden
- Risk of Drug-drug interactions
- Not patient-centric.

The disease burden continues to grow... Current approaches not Effective



Care - Metabolic health

- Research:** Multi-centric views on disease understanding, interventions developments and care path ways (great discussions yesterday – clearly there is need for better integrated approaches, better understanding of disease and effective interventions).
- Practice:** Organ-centric treatment approach in attending patient under current standard of care: leading to no effective outcomes and possibly compromising patient safety.
- Gap:** Huge gap in growth rate between disease burden, effective interventions/ care pathways development, and the knowledge of care providers.



Efficacy

Randomized controlled Trials:

- Evaluate the therapeutic benefit in ideal conditions
- Internal validity
- Homogeneous population
- Controlled conditions
- Treatment selection is driven by design

Effectiveness

Real world evidence studies:

- Evaluate the therapeutic benefit in real world conditions, clinical setting
- External validity
- Heterogeneous population
- Conditions as inclusive as real world
- Treatment defined by provider as per standard of care.



Metabolic health – Stakeholders in efficacy & effectiveness trials

- Undiagnosed or Confused **Patients** with disease progression
- **Providers** with knowledge gaps both in patient/disease identification & management
- **Researchers** with organ specific view on disease and intervention development
- **Drug developers:** Execute the efficacy & safety trials faster to attend the immediate need of disease burden and demonstrate effectiveness of their interventions successfully.



Metabolic health – Implication in efficacy trials

- Increased burden of project specific investment on execution infrastructure and control
- Longer duration for patient recruitment: small sample size
- Challenges in patient adherence to treatment
- Uncontrollable placebo effect: under or over estimation of outcomes
- Challenges in long-term patient retention: under or over estimation of outcomes especially safety outcomes.

Increased chances of failure in Phase III trials



Effectiveness data demand is growing

- Growing regulations about need for effectiveness data
- Effectiveness data is critical in decision making for payers and policy makers
- Given the difference between the conditions of the efficacy and effectiveness trials, current stand of care, evolving knowledge on metabolic health related diseases care pathways, there is high possibility:

An intervention with proven efficacy can be observed ineffective.



Factors that can influence Effectiveness data negatively

- Awareness (disease & treatment benefits)
- Gaps in knowledge of Provider in real clinical environment
- Ineffective communication between provider & patient
- Poor acceptance by the patient/provider
- Poor adherence by patient
- Poor implementation



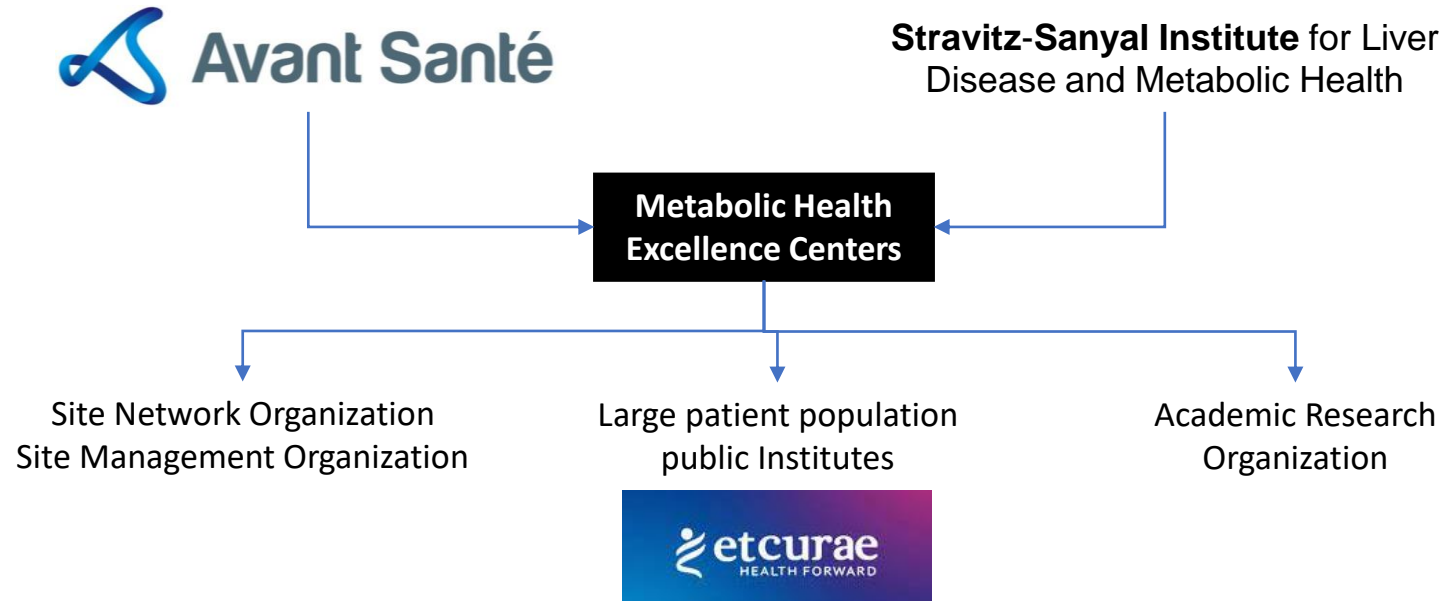
Need for integrated infrastructures to address the challenges:

Integrated Infrastructures that offers:

- Reliable and efficient way to Conduct retro and prospective studies to better understand the disease, progression and risks.
- Continuous awareness, education and training to patient, providers.
- Harmonized case definitions and data collection
- Patient engagement and data collection over longer periods.
- Test interventions efficacy & effectiveness efficiently



Our efforts in integrated infrastructure development:





Our efforts in integrated infrastructure development:

Metabolic Health Excellence Centers is a global program aim to establish integrated infrastructure in the following regions:

- LATIN AMERICA (2020 – 2023)
- USA (Q1 2023)
- Europe (2023 - 2024)
- Middle East (Q4 2023)



What we aim to develop in this infrastructure:

- Continuous training & education tools – Providers, patients
- Hybrid patient engagement & data collection
- Harmonized case definitions & data collection
- Long –term observational studies
- Life-style impact studies
- Care pathways testing platform
- Bio-markers & novel diagnostics testing platform
- Fast-track proof of concept study platform
- Seamless efficacy & effectiveness trail platform



What we aim to develop in this infrastructure:

- Global cohort with 100,000 patients for metabolic disorders.
- 400 clinical research sites including public institutions.
- Total access of 42 million population.



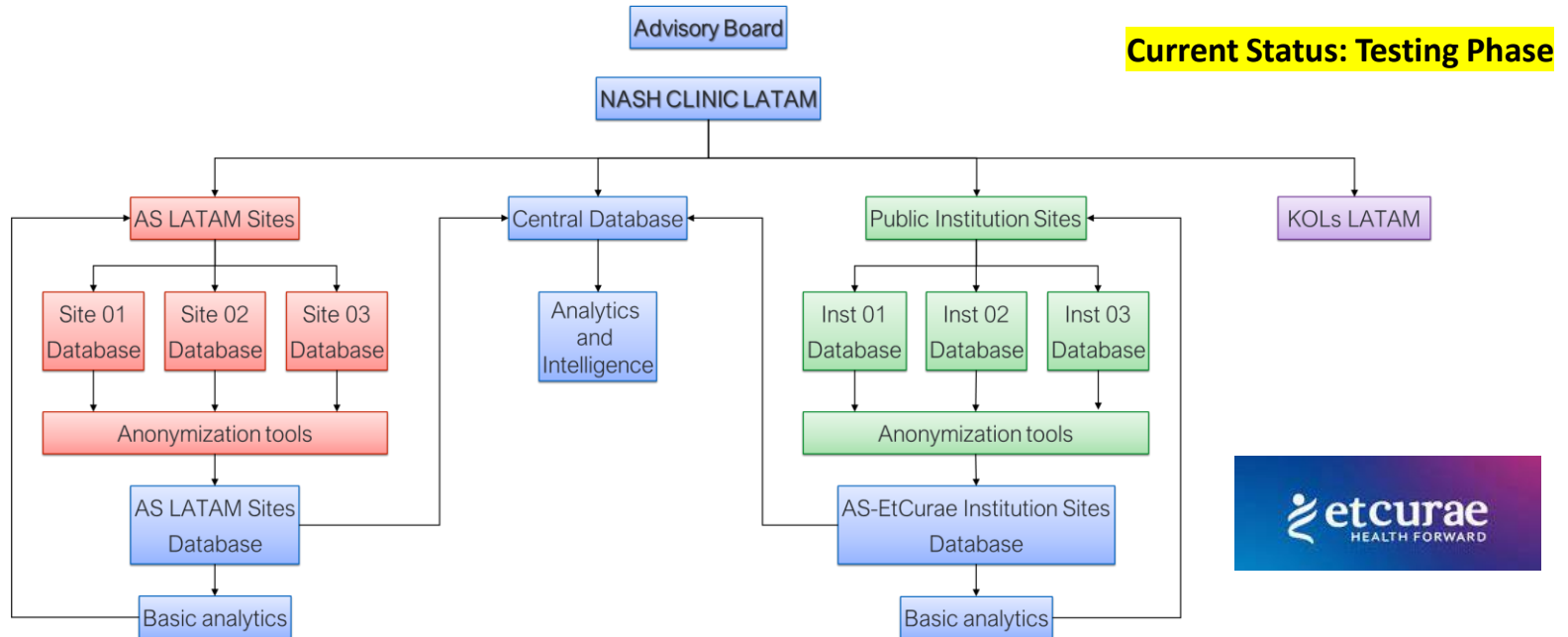
Our efforts in Latin America:

- We have deployed three metabolic health research centers in Mexico
- We have created sustainable access to 13,700,000 patients for the following 25 years
- This population has metabolic disorders incidence little above 50%

- We are in process to deployed 6 more metabolic health research centers in LATIN AMERICA before Q2 2023.
- This will create sustainable access to 39,000,000 patients including Mexico.
- This population has average metabolic disorders incidence little above 40%



Our efforts in Latin America:





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Our efforts in Latin America:



Lead : Dr. Jorge Guerrero Aguirre.Cirujano Gastro, Exdirector Medico Medico Nacional ISSSTE



Global Cohort for Metabolic Health:

- 100,000 patient cohort
- 20% USA, 55% Latin America, 10% Europe & 5% Middle East
- Standard labs, Fibro scan, MRI, Biopsy data (MRI & Biopsy for a sub-set)
- Biobank for blood, nasal swab and imaging
- Patients recruitment start date in Mexico: Q1 2023



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Thank you!