

# Evidence-based coverage decision making of genetic tests: an experience from the Brazilian Private Health Insurance Sector

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# Molecular Genetic Tests

- The Human Genome Project: rapid identification and characterization of genes associated with human diseases.
- OMIM:  $\approx 2500$  single-gene (Mendelian) phenotypes with known molecular basis, out of a total of  $>4000$  described Mendelian phenotypes or loci.
- Molecular genetic tests available for the identification of disease-causing inherited mutations (USA, GeneTests)
  - $\approx 1800$  inherited diseases
    - $\approx 1500$  tests available from clinical laboratories
    - $\approx 300$  tests available only from “research” labs

# Objective

- To evaluate the appropriateness of incorporating in the private health insurance mandatory coverage the genetic tests that are currently offered by health services in Brazil based on their ability to improve health outcomes of affected individuals and families.

# National Health System and Private Health Insurance



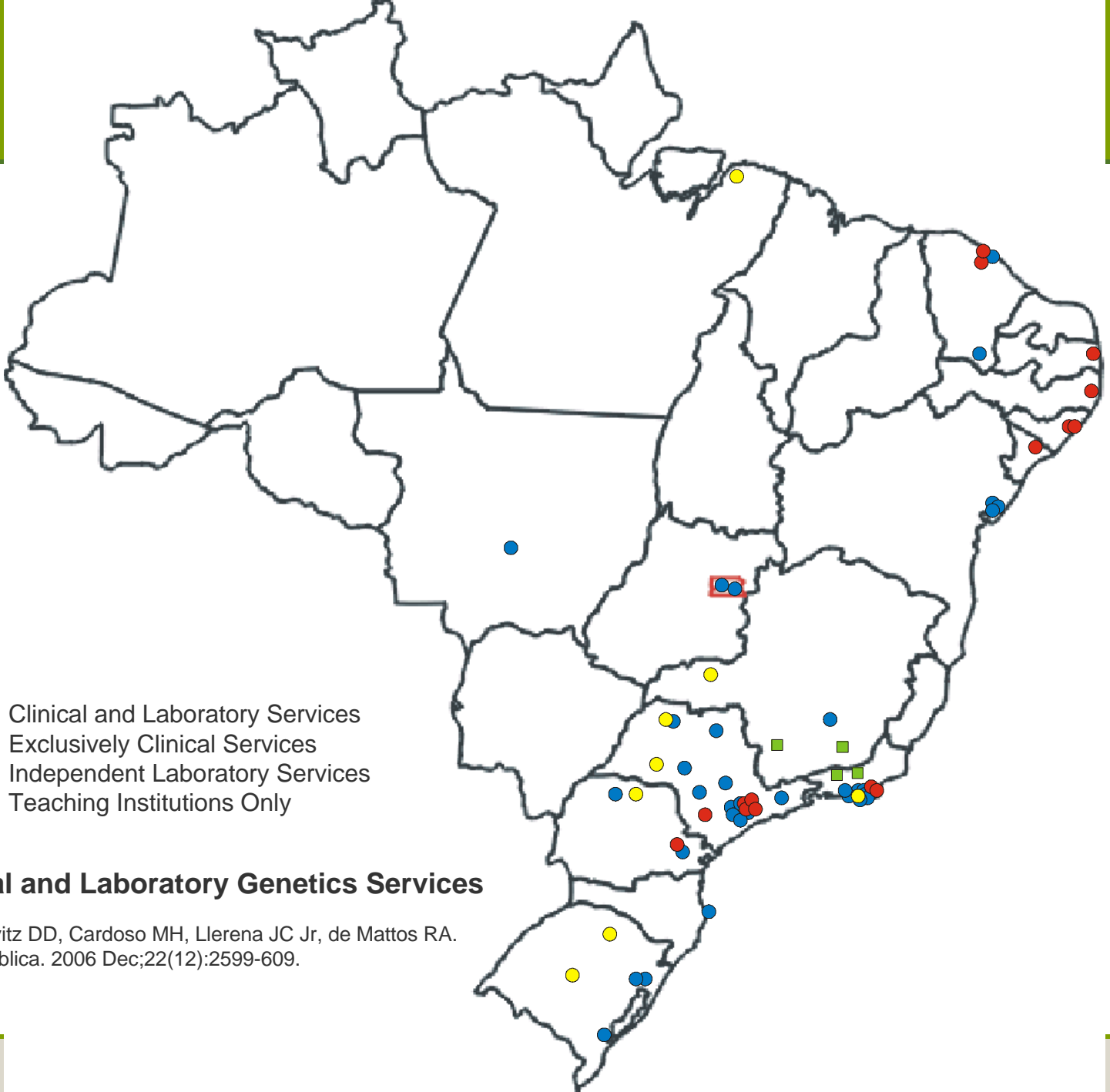
- Largest country in Latin America: 8.5 million km<sup>2</sup>;
- Fifth most populated country in the world: 194 million (2008 est.);
- National Health System (NHS – SUS, in Portuguese): universal and comprehensive health care;
- Private Health Insurance (PHI): 40.9 million people insured (21.6% of the population; Dec 2008)
- Total expenditure on health as % of GDP: 7.0% (2006)
  - Public: 47.4% (3.4% of GDP)
  - Private: 52.6%
- PHI: 51.3% of private expenditure on health.

# National Private Health Insurance Agency (NPHIA – ANS)

- Mandatory coverage by PHI is regulated by ANS.
- Considerable limitation in the range of genetic tests available in Brazil.
- Mandatory coverage by PHI:
  - Inherited primary disorders of muscles (Duchenne-Becker muscular dystrophy; dystrophia myotonica [Steinert's disease]),
  - Inherited neurodegenerative diseases (Huntington's disease; spinocerebellar ataxia type 1, 2, 3 – Machado-Joseph disease, 6 and 7; Kennedy's disease; **Friedreich's ataxia; spinal muscular atrophy**),
  - Thalassaemia, alpha and beta,
  - Gaucher's disease,
  - Cystic fibrosis,
  - Fragile X syndrome,
  - Multiple endocrine neoplasia, type 2,
  - Factor V Leiden thrombophilia.

# National Health System (SUS) Programmes on Genetic Diseases

- Newborn Screening:
  - PKU, Congenital Hypothyroidism, Hemoglobinopathies, Cystic Fibrosis
- Guidelines for the Clinical Management of Hereditary Diseases
  - Wilson's Disease, Gaucher's Disease, Congenital Adrenal Hyperplasia, Turner Syndrome, Osteogenesis Imperfecta
- Clinical and Laboratory Genetics Services, mostly based in universities and research institutions



- Clinical and Laboratory Services
- Exclusively Clinical Services
- Independent Laboratory Services
- Teaching Institutions Only

### 61 Clinical and Laboratory Genetics Services

Source: Horovitz DD, Cardoso MH, Llerena JC Jr, de Mattos RA. Cad Saude Publica. 2006 Dec;22(12):2599-609.

# The access to genetic tests in Brazil

- Several tests are offered on a research setting by institutions located in the more developed states (South and Southeast Brazil).
- Private genetic clinics located in large urban centres offer a diverse menu of molecular genetic tests. However, they send a significant number of samples across national borders for testing.

# Methods

- Genetic tests offered by a national reference research centre – Centre for Studies of the Human Genome, University of São Paulo: proxy of the maximum availability of these tests in Brazil.

Friedreich's ataxia	Spinocerebellar ataxias
Spinal muscular atrophies	Craniosynostosis syndromes
Dystrophia myotonica (Steinert's disease)	Facioscapulohumeral muscular dystrophy
Duchenne-Becker muscular dystrophy	Kennedy's disease
Cystic fibrosis	Charcot-Marie-Tooth disease
Rett syndrome	Fragile X syndrome
Factor V Leiden thrombophilia	Hereditary non-syndromic sensorineural deafness

# Selection of the Tests for Evaluation

- We selected seven tests that were not included in the mandatory coverage of PHI.

<b>Friedreich's ataxia</b>	Spinocerebellar ataxias
<b>Spinal muscular atrophies</b>	<b>Craniosynostosis syndromes</b>
Dystrophia myotonica (Steinert's disease)	<b>Facioscapulohumeral muscular dystrophy</b>
Duchenne-Becker muscular dystrophy	Kennedy's disease
Cystic fibrosis	<b>Charcot-Marie-Tooth disease</b>
<b>Rett syndrome</b>	Fragile X syndrome
Factor V Leiden thrombophilia	<b>Hereditary non-syndromic sensorineural deafness</b>

# Domains Considered in the Evaluation of Genetic Tests

- Clinical Utility:
  - Diagnostic advantage of the genetic test over other standard methods – impact on diagnostic thinking [Grosse SD, Khoury MJ. Genet Med. 2006 Jul;8(7):448-50]
- Prevalence of the disease:
  - Rare diseases:
    - Diseases affecting < 1 per 1300 to 1 per 2000 people (Stolk, Willemen, Leufkens, 2006),
    - Cut-off: > 1 per 50,000 people – the prevalence of very rare diseases.
- Diffusion of the test in Brazil.

# Results

- Fulfilled the domain of clinical utility:
  - To establish definitive diagnosis in patients that met clinical diagnostic criteria
    - Friedreich's ataxia (FXN)
    - Spinal muscular atrophies (SMN1 , SMN2)
    - Rett syndrome (MECP2)
  - Add-on to electrophysiological studies (electromyography [EMG] and nerve conduction velocity [NCV]), and sural nerve biopsy:
    - Charcot-Marie-Tooth disease type I (PMP22, MPZ)

# Discussion

- The performance of all the evaluated tests seemed to be dependent on the capacity of attending physicians to select patients that fulfilled established clinical criteria.
- The diagnostic pathways necessarily included other conventional tests like electromyography and biopsy.
- Most of the genetic tests were still restricted to a research setting in Brazil.
- The access to genetic tests without the simultaneous availability of reference centres, where patients could receive the appropriate medical guidance, could bring more harm than benefit.

An aerial photograph of a large park in Rio de Janeiro, Brazil. In the foreground, there is a large, ornate fountain with several water jets. The park is filled with green lawns, trees, and walking paths. In the background, a large body of water is visible, with a prominent, pointed mountain peak (Sugarloaf Mountain) rising in the distance. Several white buildings are visible on the right side of the image. The sky is overcast with grey clouds.

Obrigado!

Thank you!

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