Human genetics and health

Ethical, legal and social issues in research and clinical practice

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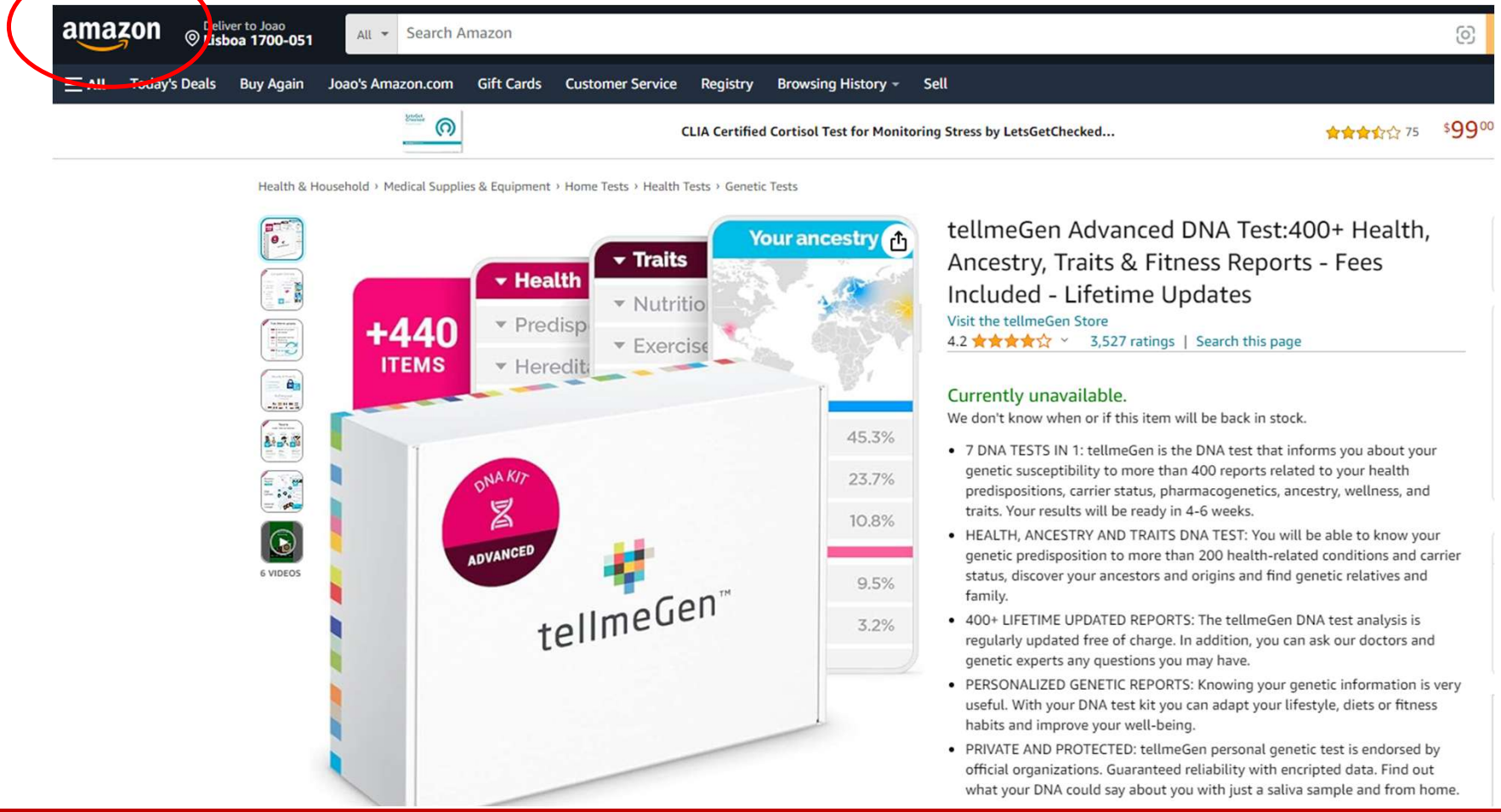
XXIV JORNADAS CIENTÍFICAS DE ANÁLISES CLÍNICAS E DE GENÉTICA HUMANA

Temas abordados nestas jornadas* relacionados com genética humana (cuidados de saúde, I&D)

- ✓TENDÊNCIAS ATUAIS EM SEQUENCIAÇÃO GENÓMICA
- ✓MICROBIOMA HUMANO: EXPLORANDO O ECOSSISTEMA DO NOSSO CORPO
- ✓A GENÉTICA NO CAMINHO DA MEDICINA PERSONALIZADA
- ✓BIOMARCADORES DA DOENÇA VASCULAR
- ✓HIPERCOLESTEROLEMIA FAMILIAR
- ✓FARMACOGENÓMICA: DESAFIOS E OPORTUNIDADES
- ✓TERAPIAS DIRIGIDAS EM HEMATOLOGIA

*XXIV Jornadas de Análises Clínicas e Genética Humana. Ordem dos Farmacêuticos. Lisboa,15 e 16.02.2025.

Direct-to-consumer genetic testing



Health predispositions, monogenic disorders carrier status, pharmacogenetics, ancestry, wellness (lifestyle), and physical and personality traits. Source: https://www.tellmegen.com/en/results

Excecionalismo genético na

Lei n.º 12/2005

de 26 de Janeiro

Informação genética pessoal e informação de saúde

Artº 6º (Informação genética)

4 — A informação genética que não tenha implicações imediatas para o estado de saúde actual, tal como a resultante de testes de paternidade, de estudos de zigotia em gémeos, e a de testes preditivos — com a excepção de testes genéticos para resposta a medicamentos —, de heterozigotia, pré-sintomáticos, pré-natais ou pré-implantatórios não pode ser incluída no processo clínico, salvo no caso de consultas ou serviços de genética médica com arquivos próprios e separados.

5 — Os processos clínicos de consultas ou serviços de genética médica não podem ser acedidos, facultados ou consultados por médicos, outros profissionais de saúde ou funcionários de outros serviços da mesma instituição ou outras instituições do sistema de saúde no caso de conterem informação genética sobre pessoas saudáveis.

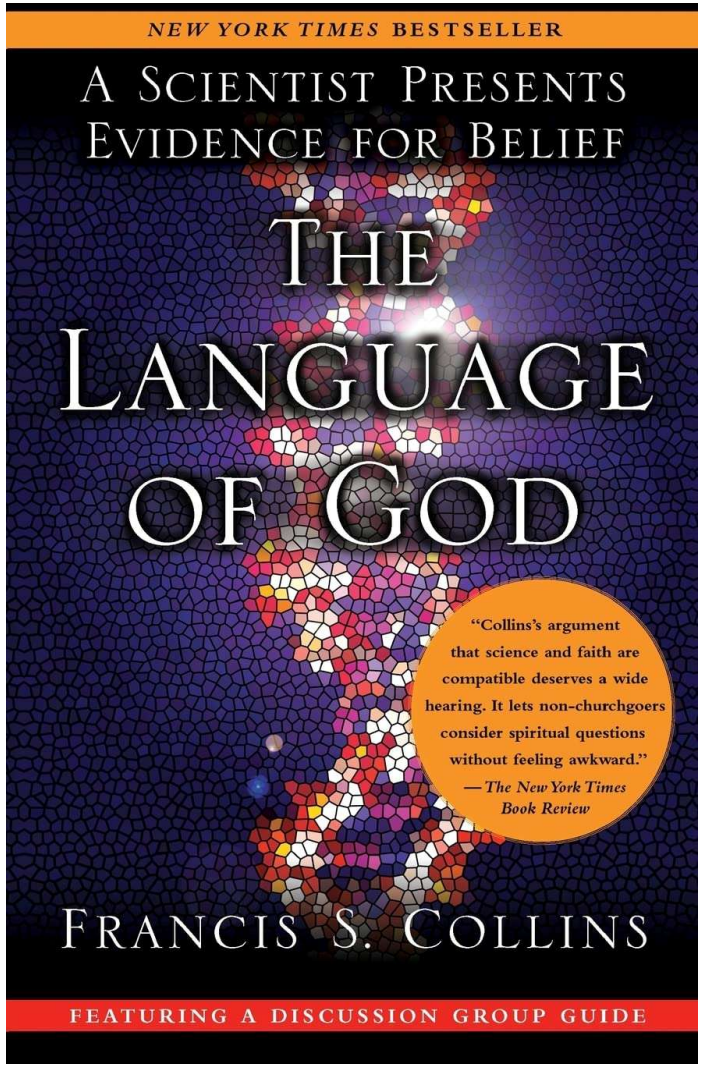
6 — A informação genética deve ser objecto de medidas legislativas e administrativas de proteção reforçada em termos de acesso, segurança e confidencialidade.

Separação entre os profissionais responsáveis por assegurar os melhores cuidados de saúde aos doentes e os que transmitem a informação, ao doente e seus familiares, sobre prevenção de nascimento de mais pessoas com a mesma doença (Ordem dos Médicos, 2024).	Incomplete patient charts? "Shadow" files? Such practices sound as fishy as two sets of account books (Lagay, 2001).

E ainda…

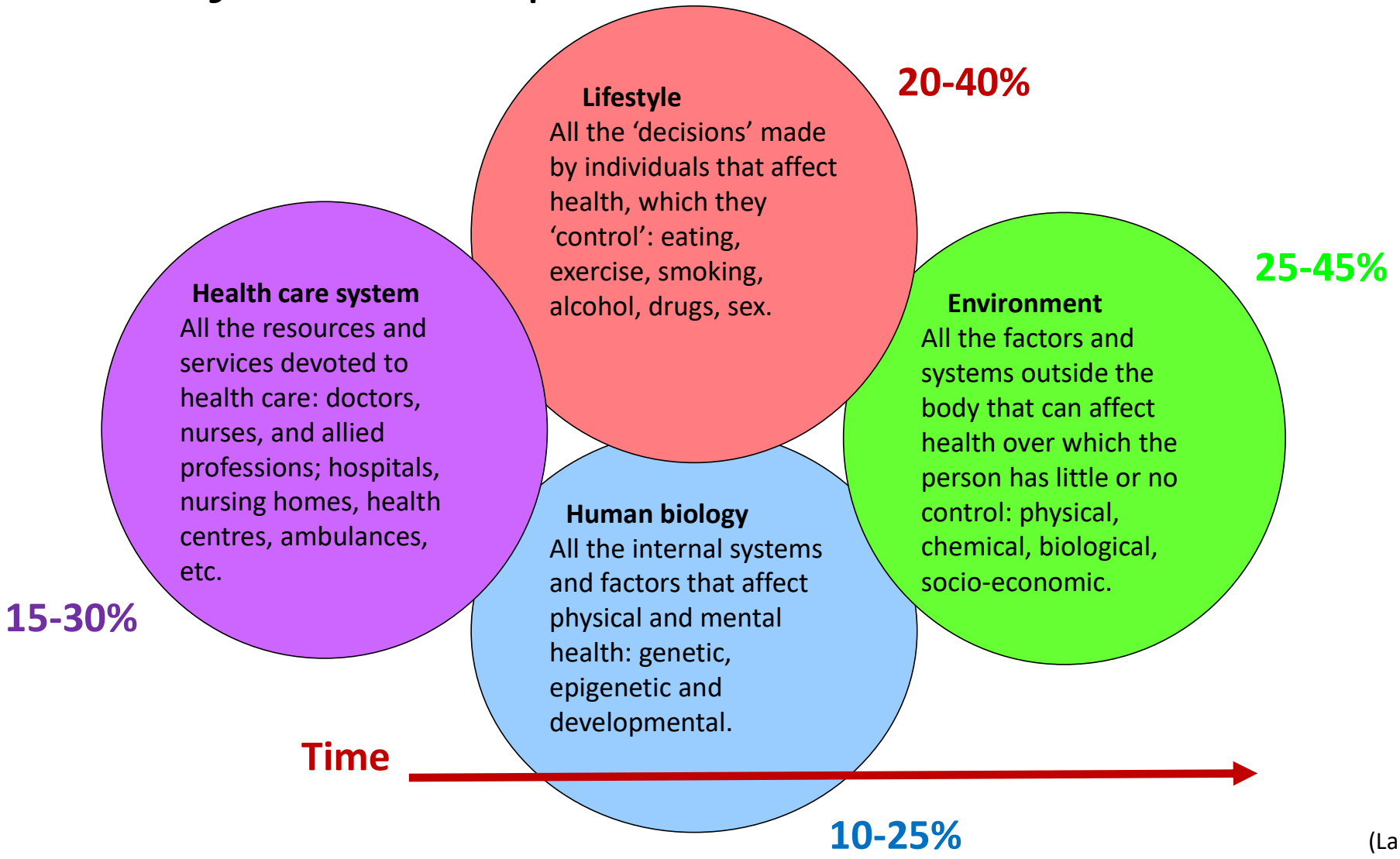
… Artºs 9º (Testes genéticos), 12º (Testes genéticos e seguros), 13º (Testes genéticos no emprego), 17º (Dever de proteção), 19º (Biobancos), etc.

2024 PT general election:
“O seu ADN é o nosso ADN.”
“Vota no teu ADN!”



From the book synopsis: [Collins, 2006] "offers an inspiring tour of the human genome to show the miraculous nature of God's instruction book"

The *health field* concept and the determinants of health



(Lalonde 1974)

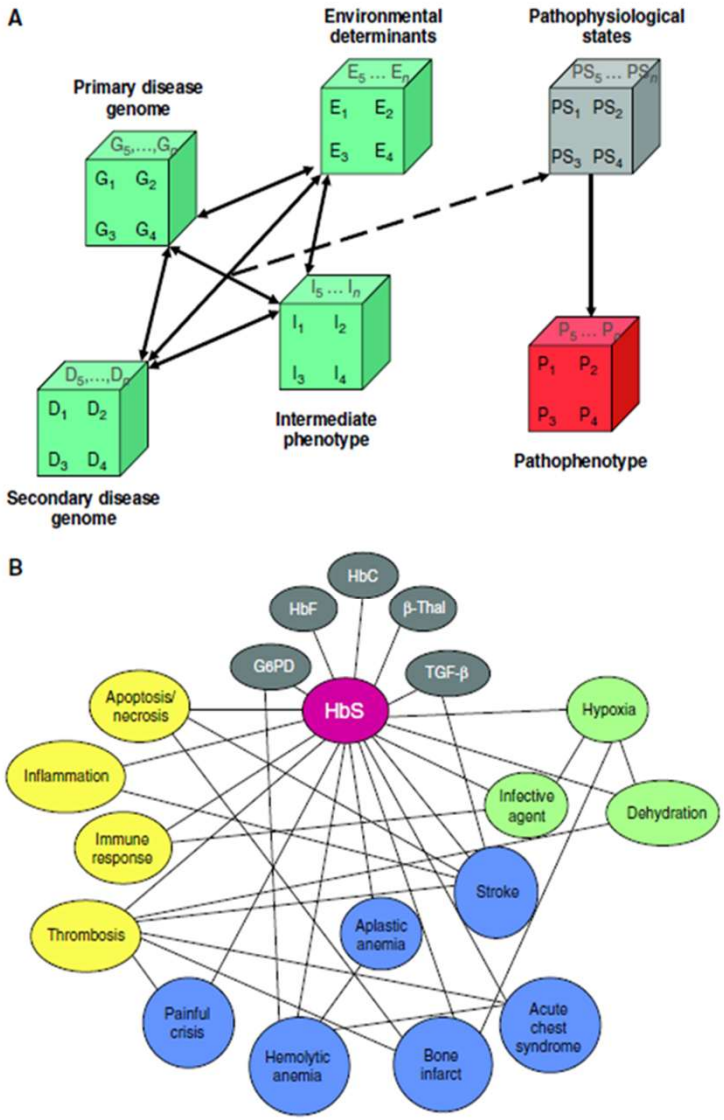


Figure 2 (**A**) Theoretical human disease network illustrating the relationships among genetic and environmental determinants of the pathophenotypes. Key: G, primary disease genome or proteome; D, secondary disease genome or proteome; I, intermediate phenotype; E, environmental determinants; PS, pathophysiological states leading to P, pathophenotype. (**B**) Example of this theoretical construct applied to sickle cell disease. Key: red, primary molecular abnormality; gray, disease-modifying genes; yellow, intermediate phenotypes; green, environmental determinants; blue, pathophenotypes.

Network medicine:

All disease phenotypes reflect the consequences of defects in a complex genetic network operating within a dynamic environmental framework

(Loscalzo et al, 2007)

Most drug responses are multifactorial

Drug efficacy and safety result from a complex network of interactions between many (human and microbial) **genes** and **environmental factors** (e.g., nutrition, microbiomes, co-medication, general health status, lifestyle, education, socio-economic and cultural situation, …) evolving in time, thus subject to (intrinsic and extrinsic) **stochastic factors**.

Clarification of geneticizing terms

Genetic determinism

- **Genetic determinism:** A phenotype is governed by genetic determinism if, and only if, given a specified genotype, the way the phenotype develops thereafter is fixed as a matter of natural law: If one knows the genotype, then one can foretell the phenotype with a very high degree of certainty, regardless of social or environmental context (Harden, 2023).

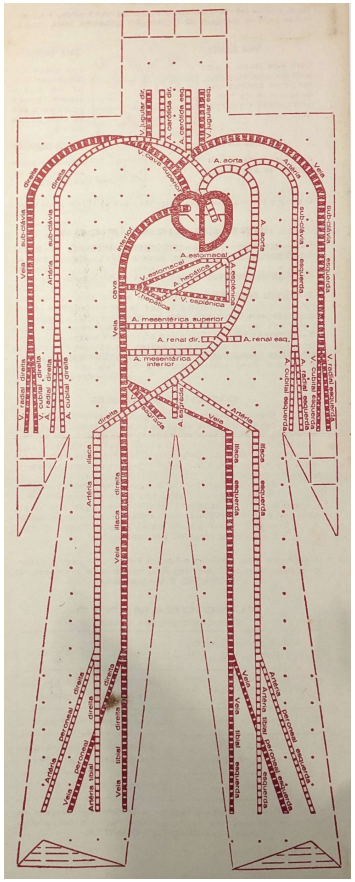
Elis-Van Creveld syndrome (mutated *EVC1, 2*)

Ref: Naqash et al, 2018.

Genetic reductionism*

Knowledge about genes [genotype] and genetic processes could ever be sufficient to explain higher-level phenomena [phenotype], or that these phenomena are best studied using genetic tools and methods. E.g., pharmacogenetic tests.

Reductionism versus holism:
From a components approach to a systems approach.



*Other types of reductionism: physiological, psychological, socio-cultural, climatic…

Genetic essentialism

A particular type of essentialist thinking, where the essence that constitutes what a thing or person ‘really’ is, or that links various individuals to a single category, is some DNA sequence (Harden, 2023).

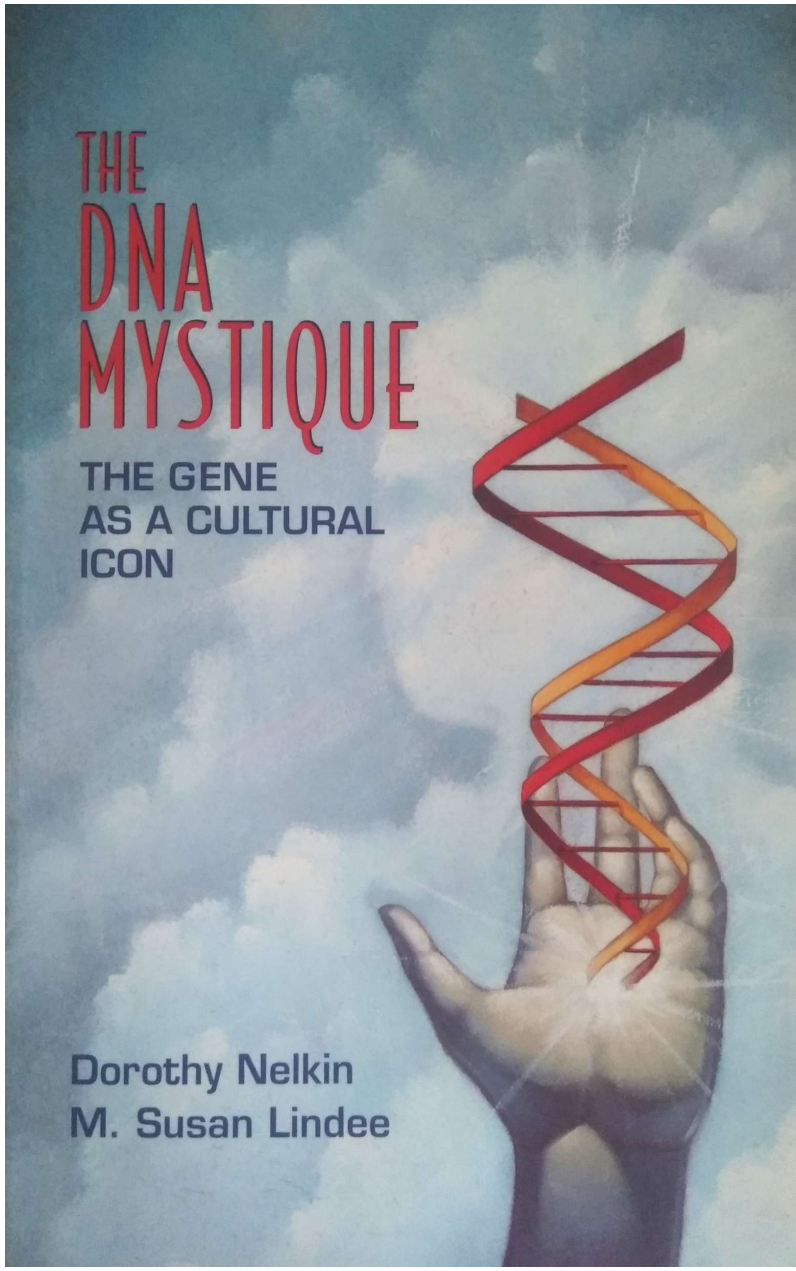
The individual’s genome is taken not only to cause characteristics and typical behaviors, but to represent the very essence of the individual’s identity (Tabb et al, 2019).

The gene has an a-historical and discrete essence that is closely tied to biological determinism of traits and diseases (Mannette, 2021).

Genetic fetishism: the God-like agency of the genome

- **Fetishism:** (i) the worship of some object or idea for its alleged magical powers or (ii) the excessive attachment or attention given to some object or idea. In this case, the object of such veneration is the genome.
- **Genetic fetishism** obfuscates the various ways in which genes are necessarily dependent and embedded in biological contexts of various interacting actors. The embeddedness is required for the genome to function (Haraway, 1997; Gilbert, 2018): “Fallacy of Misplaced Concreteness” or the “Fallacy of Reification” (Marx, Freud).

(Nelkin & Lindee, 1995)



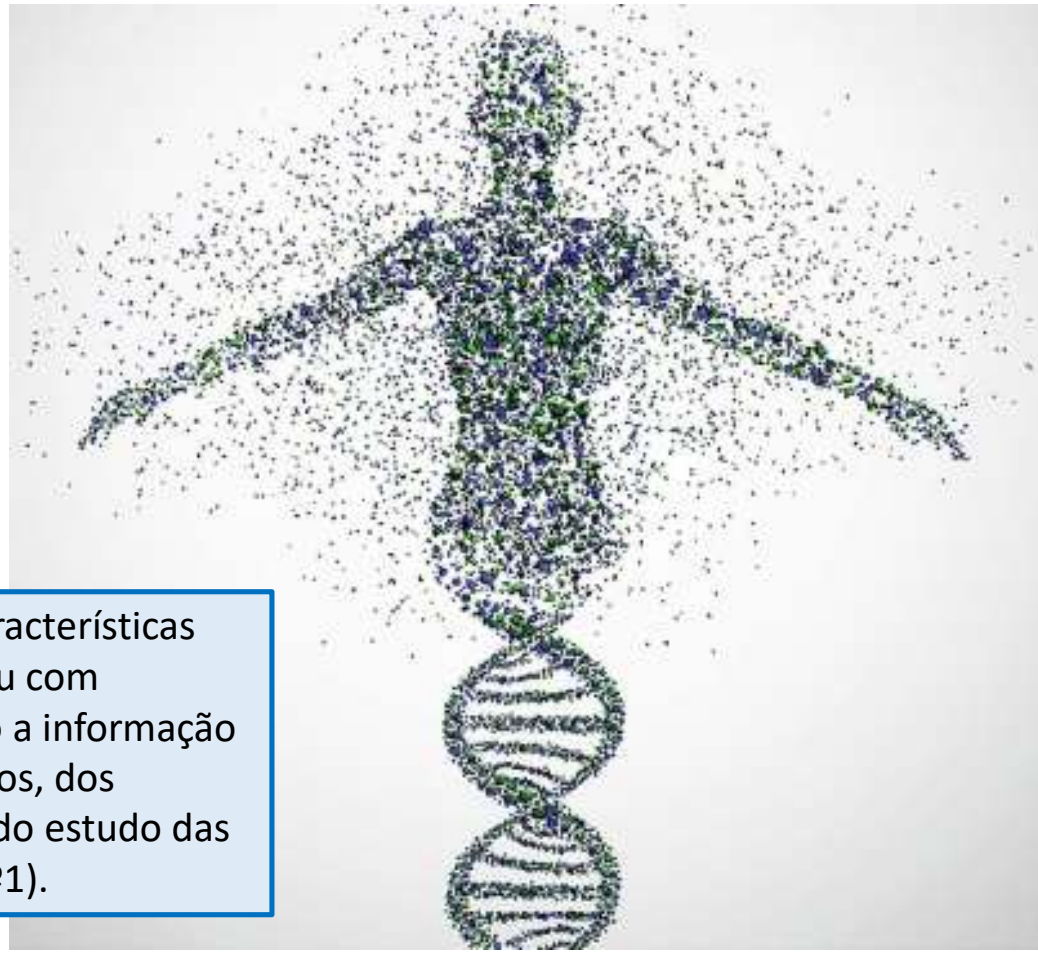
Genetic fatalism/horoscope

'Genetic fate' [genetic horoscope] implies that a person's phenotype is knowable given the knowledge of their genotype, rather than being dynamically responsive to environmental conditions and subject to developmental variability (Harden, 2023).

(Cocca & Haasen, 2018: https://webinars.csmls.org/genetics-and-society/)

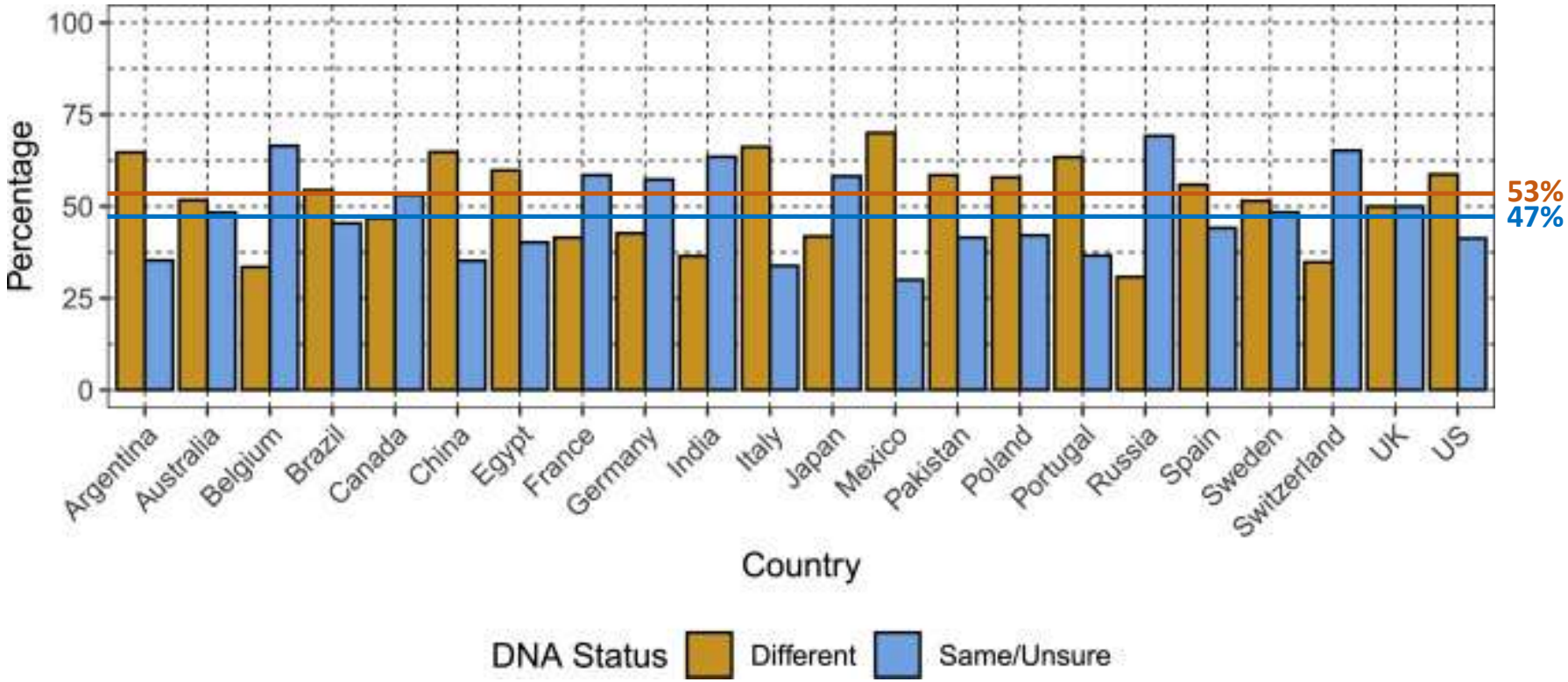
Genetic exceptionalism

Genetic information* is unique, fundamentally differing from other kinds of health information, and – compared to non-genetic health information – should *per se* be protected in a special way to prevent misuse.



*A informação genética é a informação de saúde que verse as características hereditárias de uma ou de várias pessoas, aparentadas entre si ou com características comuns daquele tipo, excluindo-se desta definição a informação derivada de testes de parentesco ou estudos de zigotia em gémeos, dos estudos de identificação genética para fins criminais, bem como do estudo das mutações genéticas somáticas no cancro (Lei 12/2005, artº 6º, nº1).

Your DNA, your Say: Main results - I



Perception of DNA as being different from other medical information (genetic exceptionalism) versus DNA as being the same (or unsure)

(Middleton et al, 2017, 2020)

92% of participants in another study felt that Social Security numbers deserved extra protection, compared to 44% for genetic test results (Kaufman et al, 2009).

Article 4 (Special status)

(a) Human genetic data have a special status because:

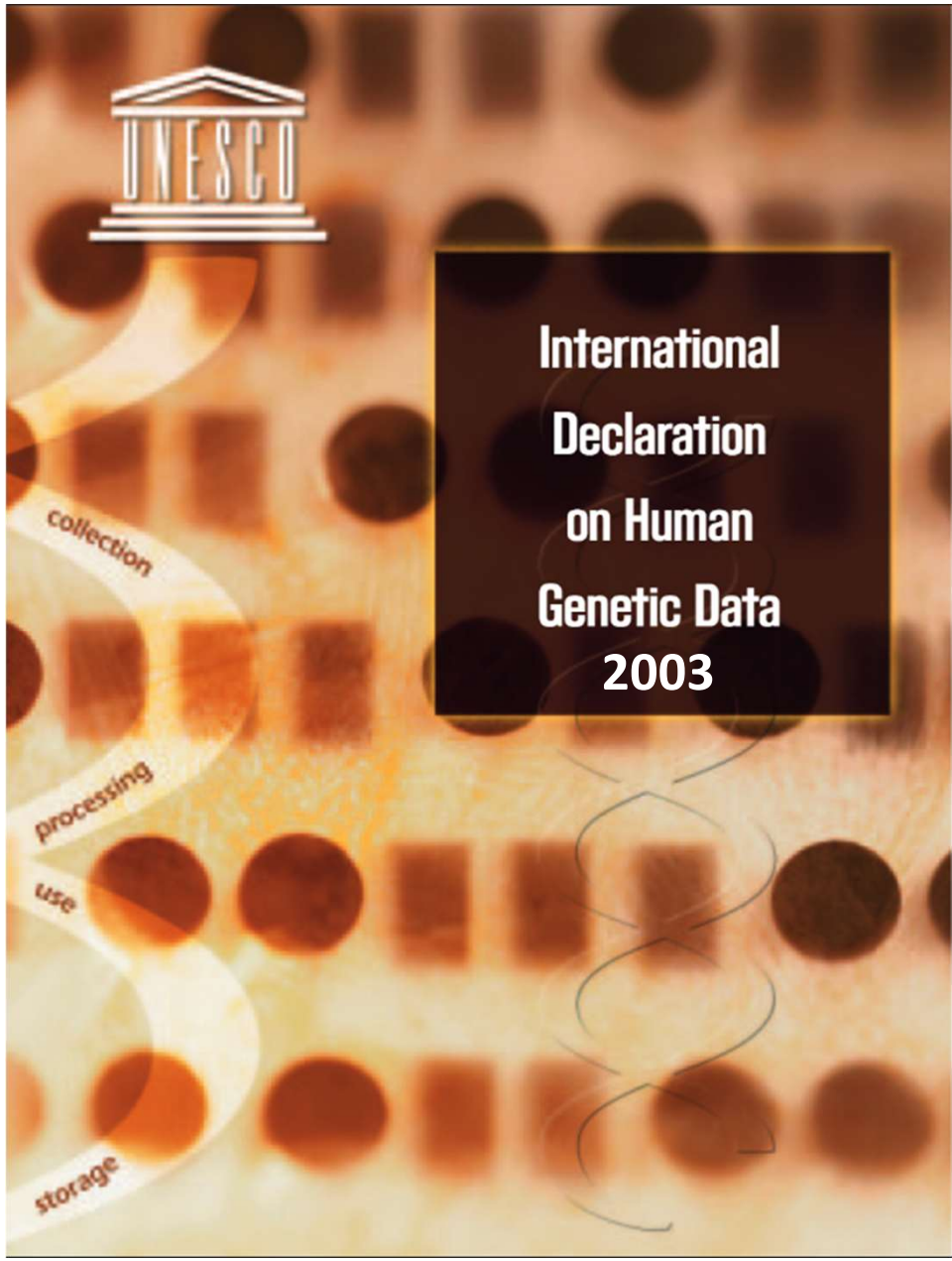
(i) they can be predictive of genetic predispositions concerning individuals;

(ii) they may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs;

(iii) they may contain information the significance of which is not necessarily known at the time of the collection of the biological samples;

(iv) they may have cultural significance for persons or groups.

(b) Due consideration should be given to the sensitivity of human genetic data and an appropriate level of protection for these data and biological samples should be established.



Genomic contextualism: a possible synthesis between geneticization and de-geneticization

- The **scientific features** of genetic information alone do not suffice as a basis for an ethical evaluating of its uses. What is decisive is the **application** of such information and the associated consequences for those involved [genetic information should be put in context] (Ilkilic, 2009).
- **Genomic contextualism:** Genomic tests both share characteristics with other types of medical tests and represent a combination of features that make them distinct (Garrison et al, 2019).
- Different **predictive value** of the tests (for monogenic versus polygenic or multifactorial conditions): ~100% (predictive-deterministic gene tests); ~0% – 80% (predictive-probabilistic gene tests).
- The importance of a genetic test in the context of a **hiring** or **insurance** procedure differs from that of a **medical** test.
- Genomic contextualism recognizes that the contexts where genomic information will be used will determine what qualities of genomic information [similarity or difference regarding other health information] are salient to the case at hand.
- A consensus is needed around genomic contextualism to account for the multiple distinguishing features of genetics, the features it shares with other domains, and the importance of context in deciding when similarities and/or differences matter.

Some ethical implications… for policy and practice

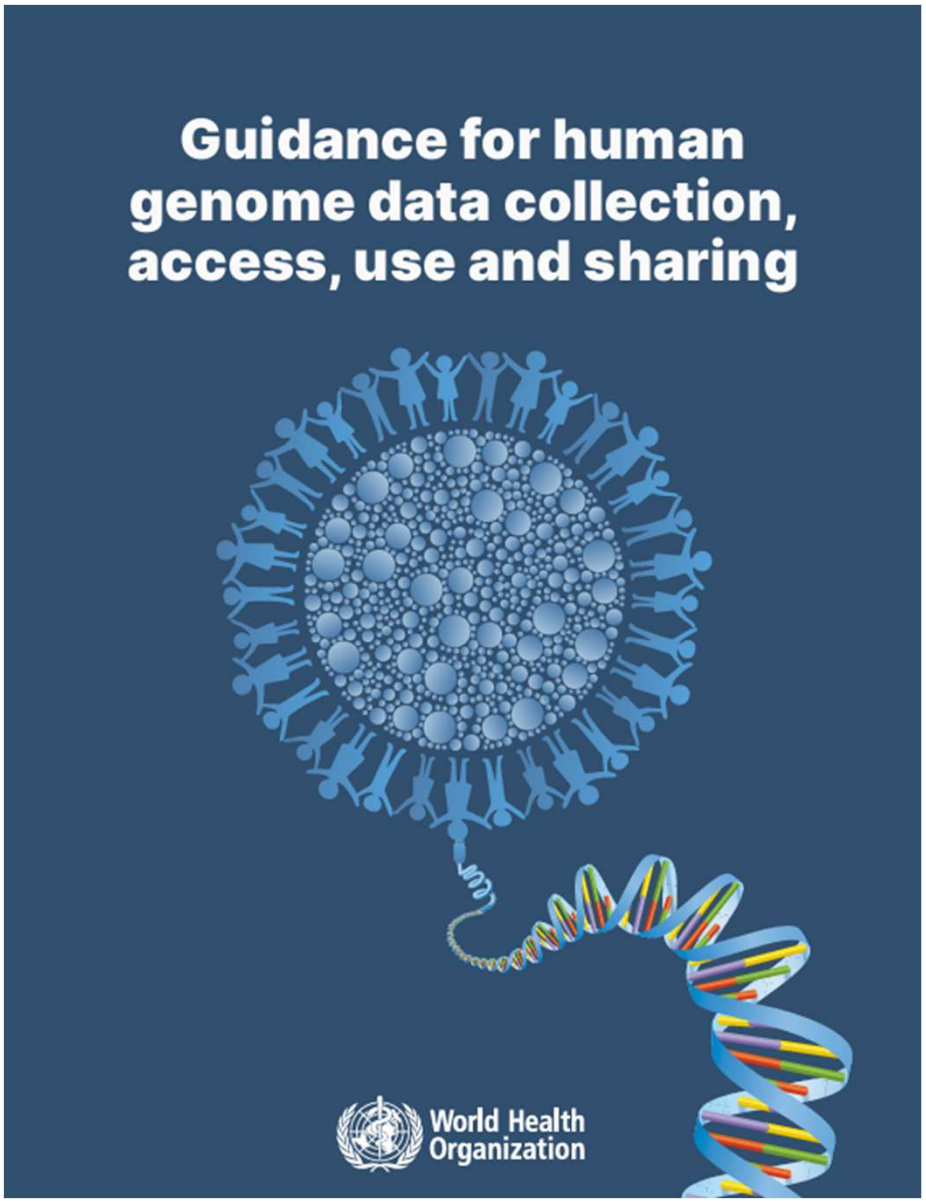
- Genetic determinism: (i) social and economic inequalities [justice] between people are fixed and immutable, (ii) environmental interventions, social policies or structural changes will be ineffective, (iii) people have no moral or political responsibilities to address inequalities, (iv) concerns about agency, free will [autonomy] and moral responsibility.
- Genetic essentialism: the genome does not limit what a person can do or become but, rather, constitutes who a person 'really' is.

Blameworthiness or praiseworthiness: Determinism ↘ Essentialism ↗

- Genetic essentialism can be seen in the legal field [justice], in particular, in defining parentage of children, e.g., Fasano *versus* Perry-Roger case (2000).
- Genetic reductionism redirects resources disproportionately [justice] to genetic or other biological testing/research/therapies, at the expense of understanding and ameliorating the social determinants of poor health.
- Genetic fetishism may negatively impact scientific research and could possibly lead to overspending [justice in resource distribution] and overdiagnosis [non-maleficence].
- Genetic exceptionalism would give preferential protection [justice] to someone who contracts a disease from so-called genetic causes (e.g., rare disease programs). Scientific consistency, individual values acknowledged, historical reflection.
- The context and manner in which it is appropriate to return incidental/secondary findings to patients: ACMG policy (97 genes; Miller et al, 2023) *versus* the patient's perspective and preference [beneficence, autonomy].

- ✓ Weighing the potential benefits and harms of genomics initiatives, such as biobanks and research programmes.
- ✓ What needs to happen to ensure that patients and participants are able to provide informed consent for genomic and genetic testing and screening and make decisions about this testing in children and people who are not able to give consent themselves.
- ✓ Deciding what findings should be returned to patients and participants and their families, how to do this and whose responsibility it is.
- ✓ Resolving the tension between respecting data privacy and facilitating the sharing and use of data for research and diagnosis.
- ✓ Addressing inequalities in how people experience and benefit from genomic healthcare and research and mitigating the potential for genetic discrimination.
- ✓ Understanding and aligning genomics initiatives with public values, for example in response to changing societal perceptions of disability and impairment.
- ✓ Managing the expectations of participants and patients and avoiding hype around genomics.
- ✓ Considering the implications of genomics beyond health, such as in the field of education and employment.

Many of the ethical considerations identified are not dissimilar to those across other areas of healthcare and research.



WHO (Geneva), 2024

Principles for human genome data **collection**, **access**, **use** and **sharing**:

- ✓ To affirm and value the rights of individuals and communities to make decisions
- ✓ Social justice
- ✓ Solidarity
- ✓ Equitable access to and benefit from human genome data
- ✓ Collaboration, cooperation and partnership
- ✓ Stewardship of human genome data
- ✓ Transparency
- ✓ Accountability

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