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Legal and social aspects on Personalized Medicine research.

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Implementation Research in Personalized Medicine: Ethical, Legal and Social Aspects
Perspective.

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COI disclosure.

- GOCUR receive research funds from pharmaceutical companies. MC is Chief Operator Office.
- Roche and Bayer advisory.
- Research funds from IARC. Horizont 2020.

Predictive Medicine. 4P

- Predictive
- Personalized
- Preventive
- Participative

Personalized Medicine complexities.

- **Increased amount of health information.**
- **Exacerbation of existing health disparities.**

Legal Aspects in PM

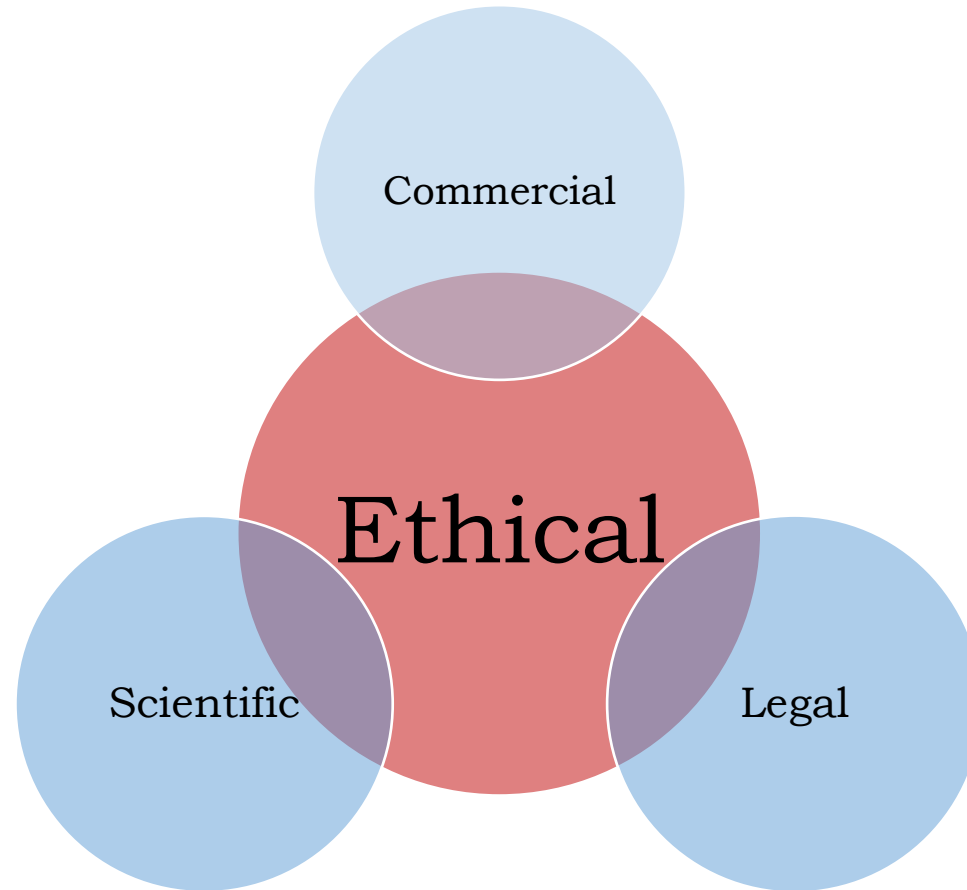
- Special legal requirements
- Intellectual property
- Reimbursement
- Informed consent
- Privacy

Legal Aspects in PM.

- Countries regulate isolated aspects of precision medicine without harmonizing.
- Precision medicine include rules around human subjects research, privacy, antidiscrimination, informed consent and trade, among others.
- Some mechanisms can vary widely from state to state and how they are established (by statute or court order or court rules).
- Laws must keep pace with the continually evolving realms of science and technology.
- As precision medicine advances and becomes further incorporated into clinical practice, it's essential to consider these important ethical, social and legal issues as precision medicine continues to evolve.

Impact on the current system for valorizing research

Determinants of the value of research



Intellectual property of PM

Diagnostic tests in this context cannot be patented, as they are based on purely natural principles or phenomena.

- BRCA1 and BRCA2 are the genetic loci relating to certain forms of breast and ovarian cancer. Myriad Genetics has extracted a series of consensus sequences on the two genes and requested the relative patents. The products of these genes are key proteins that contribute to DNA repair.
- **The Myriad patents have been revoked (USPTO) or strongly limited in their scope (EPO).**

Laws of nature cannot be patented...

- *Laboratory Corporation of America vs. Metabolite Laboratories* (2006)
 - Patent on the **evaluation of homocysteine levels for the diagnosis of vitamin deficiencies**. The patent covered the inference mechanism, by reading the level of homocysteine upon the diagnosis of cobalamin and folate deficiencies. The judges evaluated the correlation between biomarkers and vitamin levels to be a natural phenomenon, and therefore not patentable.
- *Mayo Collaborative Services vs. Prometheus Laboratories* (2012)
 - Patent on the **correlation between thiopurine levels and the treatment of autoimmune diseases**. The patent covered the method for adjusting the dose of the drug on the basis of a measurement of the thiopurine levels in the patient's plasma. The judge laid down a sentence to withdraw the patent as a "mere set of instructions to the physician on how to aggregate data from which to be able to infer the best treatment".
- *Association for Molecular Pathology vs. Myriad Genetics* (2012)
 - The patents covered **the use of BRCA1 and BRCA2 to predict the development of breast and ovarian cancer**, through a process of analysis and comparison of the sequences of patients with "normal" sequences to make a diagnosis. The patent was denied as it essentially described the mental method for comparison and analysis.

Informed consent

- future use of data
- disclosure of results
- the discovery of new information and considerations regarding genetic information.

Informed consent

- As precision medicine research relies on large quantities of data, it may not be possible to anticipate all future uses of data and information.
- Is it necessary for researchers to go back to participants whenever their data or specimens are used? (Biobanks)
- Issues relating to disclosing research results to patients.
- How should researchers address incidental findings, which may become more frequent as technology progresses

Data Sharing

- Data sharing has important implications for individual and group privacy and confidentiality. For example, in the context of inherited cancers is there a duty to warn family members who may develop a genetic disease. Law does not provide a clear answer.
- Data sharing is necessary to advance research and develop new tests and therapies. Range of barriers: from protecting patient data and other legal risks to technical difficulties and institutions' reluctance to collaborate.

Direct-to-consumer genetic testing.

- Direct-to-consumer genetic testing, a product of precision medicine, also raises important concerns, conferring both risks and benefits.
- The potential for patient empowerment must be weighed against risks such as spotty oversight of at-home tests.
- The importance of clinically advised care.
- False positive and negative results and incorrectly reported data.

Health disparities

- Danger that advances in science and technology may solidify and worsen health disparities.
- Factors contributing to health disparities in precision medicine:
 1. Cost
 2. Access to new services cannot be reimbursed by many payers, limiting the provision of care to those who can afford it.
 3. Access is more than money: health literacy and medical training.

Underrepresentation in research.

- Lack of diversity in research contributes to health disparities in precision medicine.
- Minorities
- Structural racism

Millions of black people affected by racial bias in health-care algorithms

Study reveals rampant racism in decision-making software used by US hospitals – and highlights ways to correct it.

An algorithm widely used in US hospitals to allocate health care to patients has been systematically discriminating against black people, a sweeping analysis has found.

The study, published in *Science* on 24 October¹, concluded that the algorithm was less likely to refer black people than white people who were equally sick to programmes that aim to improve care for patients with complex medical needs. Hospitals and insurers use the algorithm and others like it to help manage care for about 200 million people in the United States each year.

Racism and PM

- According to *Oxford English Dictionary*, the word “racism” is defined as “prejudice, discrimination, or antagonism directed against someone of a different race based on the belief that one’s own race is superior” or “the belief that all members of each race possess characteristics, abilities, or qualities specific to that race, especially so as to distinguish it as inferior or superior to another race or races”.
- Given the influence that racism still has in healthcare, the marginalization of racial and ethnic minorities might not be the only reason why PM does not stand up to its promise of providing equal chances for all.

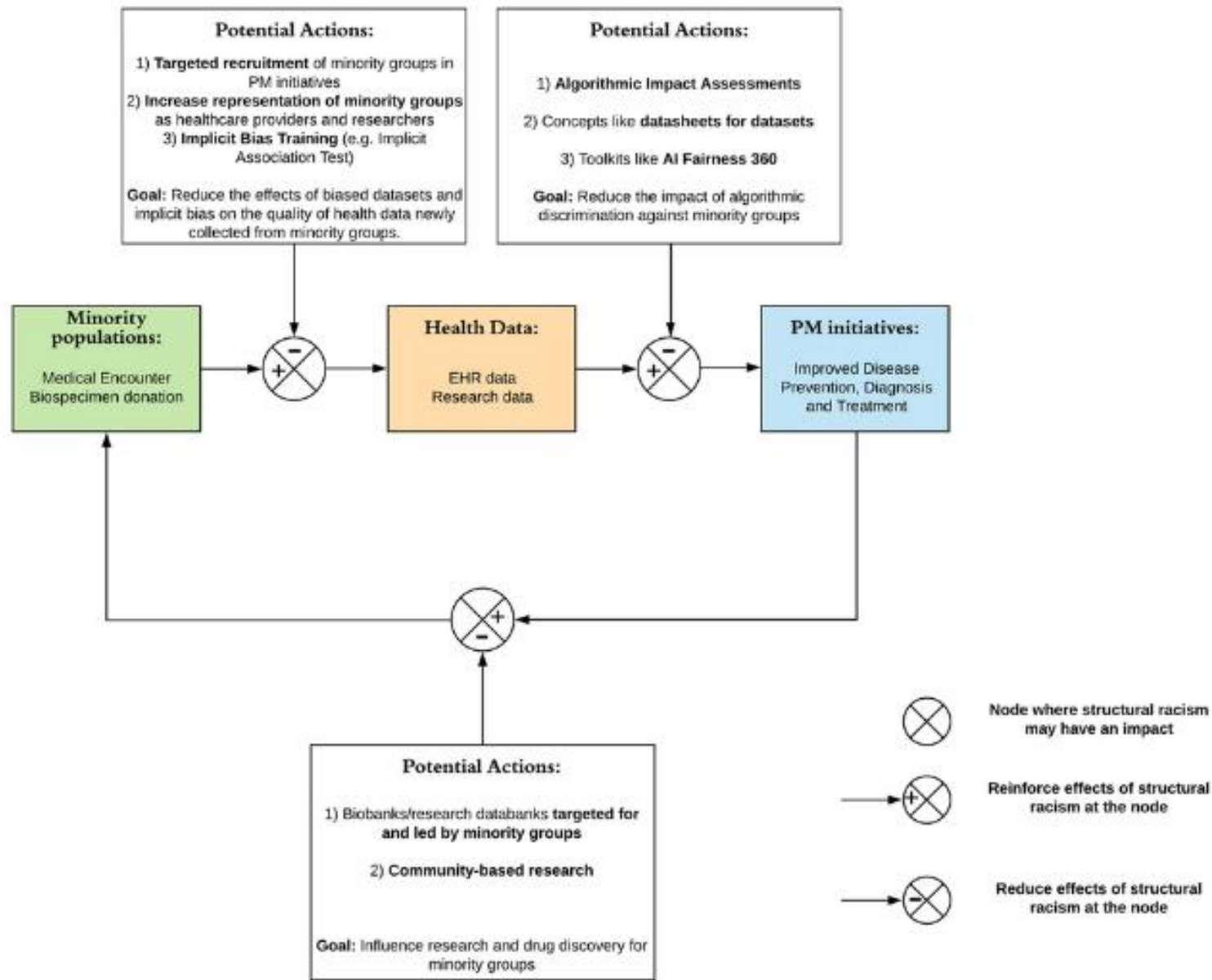
PM and structural racism

Three nodes of a process flow where structural racism can affect PM

- The collection of biased health data during the initial encounter of minority groups with the healthcare system and researchers.
- The integration of biased health data for minority groups in PM initiatives.
- The influence of structural racism on the deliverables of PM initiatives for minority groups.

The scientific racism threat.

- Perpetuation of inaccurate notions of human populations.
- Scientific racism advances the mistaken notion that phenotype is equivalent to genotype.
- Scientific racism overlook the well documented fact that 99,9% of humans are genetically identical.
- Confusion gene frequency with gene expression.
- Simplification: behavior and physiology are merely biological causes
- Redirection of policies and research resources away from interventions that might eradicate health inequalities.



Potential actions to reduce the cascading effects of structural racism on the quality of health data collection, integration and deliverables in precision medicine initiatives

Personalized Medicine need trust construction

- Without a trusting relationship between minority groups and PM initiatives, these are unlikely to succeed in their research objectives, as representative collection and integration of health data (from EHRs, tissue samples, etc.) will be compromised.
- PM initiatives need to be implemented with the aim of ensuring ethnic diversity and appropriate ethno racial representation in their cohorts.



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