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Balancing Benefits and Burdens in Precision Medicine

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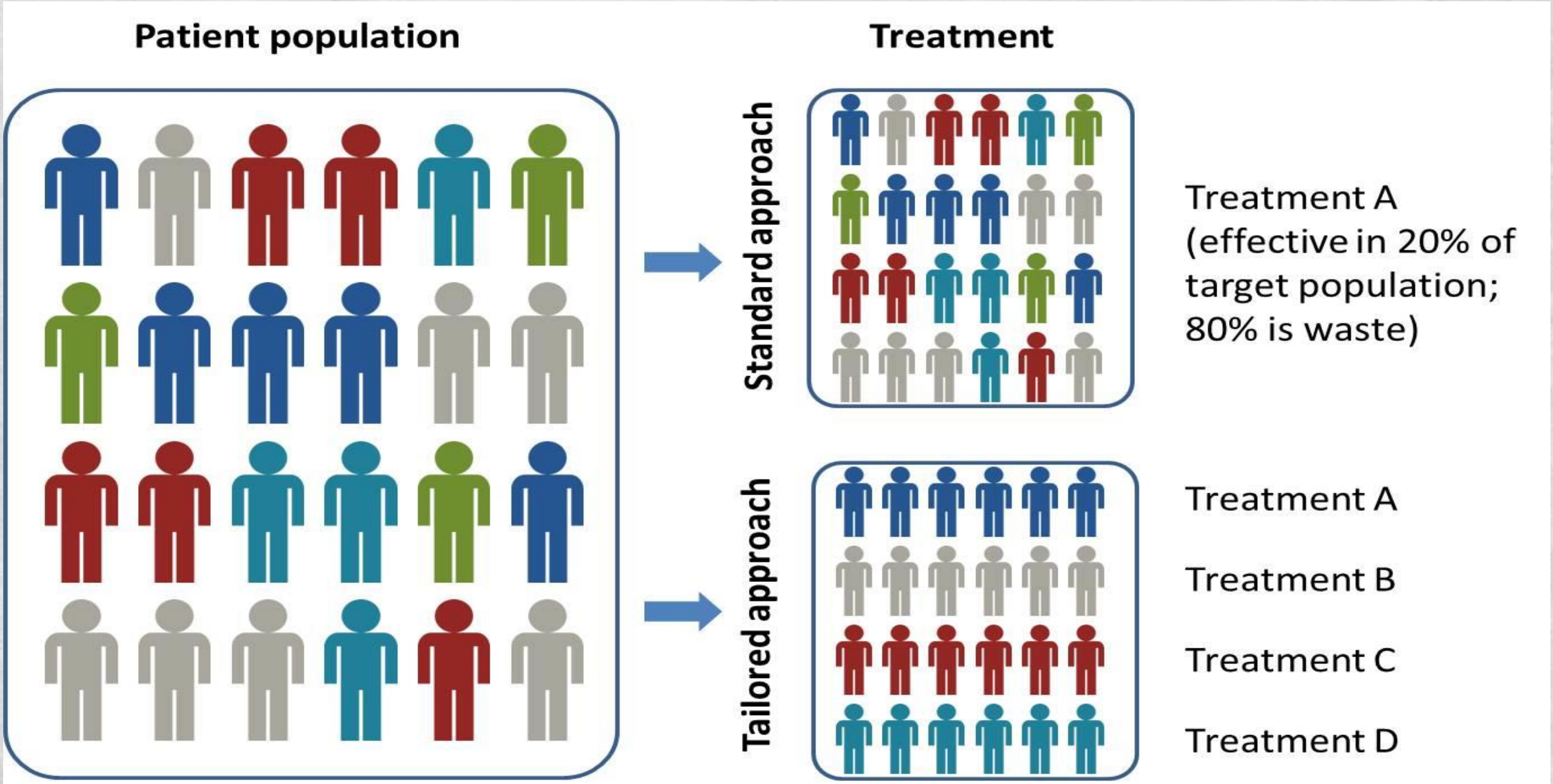
Concept of precision medicine

- The IOM's report titled "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease.
- PM is defined as aiming at the research and development the methods of prevention, diagnosis and treatment of diseases tailored to individual characteristics for individual patients through understanding the role of genome, environment and life styles as well as their interaction played in individual health and disease.
- Precision medicine=personalized medicine?

PM: how precision it is?

- PM as an attempt to correct the imprecision of current medicine.
- Current medicine seems to make medicines for average patients, just as tailors make clothes with free size.
- PM tries to make medicines tailored to individual characteristics.
- The term “personalized medicine” seems to likely lead to a misconception of making a unique medicine to individual patient.
- What PM could and would do is to categorize a group of patients into subgroups, and the medicines would be made tailoring to the subgroups with specific interaction between their genome, environment and life styles.
- With PM we can buy clothes with different sizes, and each individual can choose the clothes with size suitable to her/his length and body weight. However, the difference within a subgroup still exists.
- In brief, the precision is relative in PM.


Patient population
Treatment
Standard approach
Tailored approach
Treatment A
(effective in 20% of target population; 80% is waste)
Treatment A
Treatment B
Treatment C
Treatment D

National Key Projects of Precision Medicine (2016)

- R & D of omics technologies applied in clinics of new generation, such as sequencing, identifying, analyzing in genomics, proteomics or metabolomics etc;
- Large scale (million people) health research cohorts, including northeast, southeast, south, southwest an northwest areas;
- Major diseases research cohorts, including immunological diseases, diseases of nervous system, mental and psychological diseases, lung cancers, prostate cancers, liver cancers, colon-rectal cancers, gastric cancers etc.
- Building a platform to integrate, store, use and sharing of PM big data;
- Research in precision prevention, diagnose and treatment projects;
- Building a model system to integratively apply PM.
- **ELSI and public engagement project (5 millions)**

- The state will invest CNY 642 millions in PM project. (USD 210 millions in

Allocation of resources in setting priority

- A high priority for public policy: promoting public well-being and prioritizing the public good
  - **Public funding review and disclosure**
  - **Support for promising research**
    - realizing economic opportunities
    - Intellectual property and the sharing of scientific knowledge (overly broad vs. narrow patents)
    - Data sharing requirements: the 2007 NIH Public Access Policy; US Congress's provision for public distribution of research results; the Howard Hughes Medical Institute and the Wellcome Trust; US Public clinical trial disclosure requirement;
  - **Innovation through sharing**

- How society and its members-individually and collectively-can provide an environment for PM to flourish for the benefit of as many people and communities as possible?

How to make cost-effectiveness analysis (CEA)?

- CEA focuses on evaluating the ratio between cost and health-related outcomes, including the number of lives saved, life years saved, survival period of time without diseases (such as after the treatment of cancer), the reduced number of mortality or of the circle of acute diseases.

- CEA is an attempt to determine a ratio of aggregated costs of health intervention and produced change of health outcomes, in order to provide advice to decision-makers when they have to make decision how to use limited resources to maximize health benefits.

- What should be included in the effectiveness, such as disability-adjusted life years (DALYs), quality-adjusted life years (QALYs), or alternatively cost-utility analysis etc.

- In brief, utility and justice should be both taken into account in allocating resources.

Options

- What I emphasize is that before the government decided to invest CNY 426 millions in PM, did it make any evaluation? Has the government estimated that the investment in PM would reduce how much disease-burdens and bring about how much health benefits?

- In mainland China it is urgently needed to establish a system of accessible, available, affordable and high-quality primary health care, but precision medicine, even though successful, may be provided affordably only in tertiary care.

- Alternatively, if we invest the same public funds in expanding health coverage and improving primary health care and in preventing and treating substance disorders, especially nicotine and alcohol addictions which impose highest disease burdens on our society, would it bring about much more health benefits to our people?

Gattaca argument

- People worry about undesirable social consequences caused by the use of genetic engineering or genome editing.
- Can the use of genetic engineering results in genetic divide among the population, that is, part of the population became perfect human beings after genetically modified, they are superior and qualified to do the work sophisticated, complicated and thus admirable, and in a higher social status; but others who are genetically unmodified have to do the work unskillful in their whole life, and thus in an inferior social status.
- The Noble Literature laureate in 2017, Kazuo Ishiguro also worries that gene editing would lead to the society dividing into two classes: The upper class became elite citizens who are smarter, healthier and enjoy longer life years; but the lower class who are not modified by gene editing are physiologically laymen.

A "Social Contract" in research?

- The *public* agrees to support research with public money and to consider volunteering as research subjects, but only if they know that…
- *Scientists* have formulated strict scientific and ethical standards, and are being monitored to ensure that they are compliant with these standards.

International Research Ethics

- Nuremberg Tribunal
  - **Nuremberg Code**
- World Medical Association
  - **Declaration of Helsinki**
  - Focus: *physicians'* duties
  - professional control of research enterprise
  - Advisory only, but recognized in national legislation and WHO practices.
  - 32 short clauses, no elaboration
  - Adopted 1964; amended 1979, 1983, 1989, 1996, 2000.

International Research Ethics

- CIOMS
  - NGO created by WHO and UNESCO
  - "Elaboration" of Declaration of Helsinki
  - 15 Guidelines with extensive explanations
  - First version: 1993
  - Revised version 2002,2016
- ICH(International Commission on Harmonization)

Changes in the context of research

New roles for human subjects

- Access to experimental treatment:
  - participation is viewed as a privilege(HIV/AIDS research)
- Industrialization of Health Research: participant as employee
- Large-scale trials: experimentation as social policy
- International research: relations among people

Just distribution of risks vs. Just distribution of benefits

Changes in the context of research

New issues, old principles

- Placebo-controlled trial (Helsinki Paragraph 29)
- Standard of care (CIOMS revision)
- Post-trial benefit sharing (Helsinki Paragraph 30)
- Responsibilities to the community
- Internationally collaborative research
- **Genetic/genomic research and application**
- **Emerging technologies**: SynBio, **Gene editing**, **PM**, Xenotransplantation, etc.
- Population-based research

Exaggerating existing inequality and inequity

- Although not all people can envision such scenario caused by genetic engineering or gene editing, but the application of cutting-edge biomedical technologies would cause or exaggerate existing health and social inequality or inequity, it is a reality.
- Human genome project including mapping and sequencing promises personalized medicine. But who can afford the costs?

Structural issues

- The fundamental problem is: Research and development of medicine and science need the participation from private sectors including those who are profitable. Chinese PM project also promotes the participation from private sectors and the ratio of the investment from these sectors and that from the government should be 2:1.
- The profitable private sectors need returns for their investment. It is natural and reasonable. Now can we balance between enterprises pursuing profits and the poor enjoying the results of scientific research?

Can we prevent the widening health and social inequality in the application of PM?

- It is crucial to prevent the widening health and social inequality in the application of PM, because otherwise the original intention of developing PM would not be achievable: Improving health and life of quality of hundreds of million people.
- The issues involved include:
  - Who controls the access to the results of PM project?
  - It is medical professionals or the government who/which decides whom getting access to precision prevention, diagnosis and treatment?
  - Whether the access to the results of PM project depends on patient's health need or her/his buying power?
  - How to input the community values ?
  - How to integrate the respective regulations of different government agencies into one governance framework?
  - How to reform the health care and insurance system?

Thank you very much for your attention