Genetics in Public Health

The role of public health is to ensure that the basic conditions required for people to be healthy are present.

Until recently, public health focused mostly on environmental causes and risk factors for disease, such as infections, cigarette smoking, diet, etc.

Since the sequencing of the human genome has been completed, high hopes rest on the potential to prevent the impact of genetic risk factors or susceptibilities to disease.

Advances in genetic knowledge and technology could be used to try to prevent disease and improve population health.

The perceived role of genetics in public health is changing, as is the definition of what is a genetic disease. The role of genetics in public health is broadened if we consider all the diseases for which genetics might play a role, either by the presence of a genetic susceptibility for the development of this disease or for response to treatment, or by the presence of protective genetic factors, such as in resistance to infection.

Genetics and Public Health

I - Introduction

II - Populations targeted by public health genetics interventions

1. Genetic screening
2. Direct to consumer genetic testing

III - Ethical, legal, and social implications of public health genetic interventions

1. Use of genetic information: confidentiality and discrimination
2. DNA banks
3. Prenatal diagnosis, assisted reproduction, embryo selection
4. Genome editing

IV - Transition from genetics to genomics

V - Examples of the role of public health in genetics

1. Folic acid and neural tube defects
2. Newborn screening
3. Carrier screening in the context of reproductive decisions
4. Prenatal screening for aneuploidy and neural tube defects
5. Screening for genetic susceptibilities in adults
6. Pharmacogenetics and ecogenetics
7. Personalized Health Care and Genetic Information

II - Populations targeted by public health genetics interventions

Public health considers the overall health of the population as a group.

Resources for public health interventions are limited

Priorities need to be established

Screening should change the impact of the disease on the affected individuals or its burden on society.

Target a population at higher risk of disease, often the families of affected cases.

The community is in favor of screening and that it does not become a source of stigmatization for the community.

Public health considers the overall health of the population as a group, and not the health of each individual.

Since resources for public health interventions are limited, priorities need to be established to determine which interventions will be most beneficial to the population as a whole. These priorities will be based on the characteristics of the disease, such as its prevalence, its severity, and treatment availability, as well as the amount of resources needed for the intervention.

Monogenic diseases are rare. Is it justifiable to implement population-based interventions to identify a few rare cases of a particular genetic disease? There is no single right answer to this question. It depends on the burden these rare cases represent for society, on our ability to act to attenuate this burden, and on the value we place on obtaining an early diagnosis, compared to the complexity of detecting these cases and the amount of resources needed to detect them. For example, newborn screening for phenylketonuria is considered beneficial because it makes it possible for the children identified through screening, who would otherwise have developed severe mental retardation, to develop normally by following a special diet. In the majority of developed countries, all newborns are screened for phenylketonuria to detect a handful of cases, because the impact of treatment on these children's potential ability to contribute to society is so great. On the other hand, similar newborn screening for Huntington disease is not being considered, because it is a late-onset disease for which there is no treatment and no clear benefit to an early diagnosis. Screening would not change the impact of the disease on the affected individuals or its burden on society.

To improve the yield of a screening program for a genetic disease, one option is to target a population at higher risk of disease, often the families of affected cases. This approach limits the amount of resources needed for screening and increases the yield of screening. It unfortunately is limited by the fact that many new cases of genetic disease occur in individuals with no family history who would not be identified by family-based screening. In some cases, ethnic groups can be the target population of screening programs, when prevalence of the disease in questions is particularly high in that ethnic group. For example, Ashkenaze Jewish populations are screened for Tay-Sachs disease. In programs targeted at specific communities, it is important to ensure that the community is in favor of screening and that it does not become a source of stigmatization for the community.

Direct to Consumer Genetic Testing
Problems

Tests may not be available for the health conditions or traits that interest you.

This type of testing cannot tell definitively whether you will or will not get a particular disease.

Unexpected information that you receive about your health, family relationships, or ancestry may be stressful or upsetting.

People may make important decisions about disease treatment or prevention based on inaccurate, incomplete, or misunderstood information from their test results.

There is currently little oversight or regulation of testing companies.

Unproven or invalid tests can be misleading. There may not be enough scientific evidence to link a particular genetic variation with a given disease or trait.

Genetic privacy may be compromised if testing companies use your genetic information in an unauthorized way or if your data is stolen.

The results of genetic testing may impact your ability to obtain life, disability, or long-term care insurance.

Direct-to-consumer genetic testing provides only partial information about your health. Other genetic and environmental factors, lifestyle choices, and family medical history also affect the likelihood of developing many disorders. These factors would be discussed during a consultation with a doctor or genetic counselor, but in many cases they are not addressed when using at-home genetic tests.

Use of genetic information: confidentiality and discrimination

Why is the issue of confidentiality of genetic information important?

The issue of confidentiality of genetic information is frequently raised.
Genetic information is different from other types of personal information found in a medical chart.

First, genetic information does not change over time: the presence of a mutation or a polymorphism in an individual is immutable.

Second, genetic information about one individual has implications not only for the individual in question, but also for his/her family members,
since the genetic abnormalities are heritable in most cases.

In some cases, genetic information is used to confirm a clinical diagnosis,
but it is increasingly used to confer a level of risk or susceptibility for the development a specific condition.

In that context, it is not surprising that some are worried that information about a specific genetic susceptibility
might be used by insurers or employers as a source of discrimination.

DNA banks

- Collection of DNA samples
- Obtainable from research projects or from blood samples collected for newborn screening
- Who do they belong to?
- How long will they be kept?
- How is a researcher granted an access? For what purpose?
- What are the rights of the owners of the DNA samples?

UK **Biobank** recruited 500,000 people aged 40-69 years in 2006-2010 from across the UK. They have provided detailed information about themselves, provided a wide range of physical measures, provided blood, saliva and urine samples for future analysis and gave consent for their health to be followed-up through linkage to electronic health records.

Genetic research often requires the collection of DNA samples.

Many DNA banks were formed from DNA samples collected for specific research projects or from blood samples collected for newborn screening.

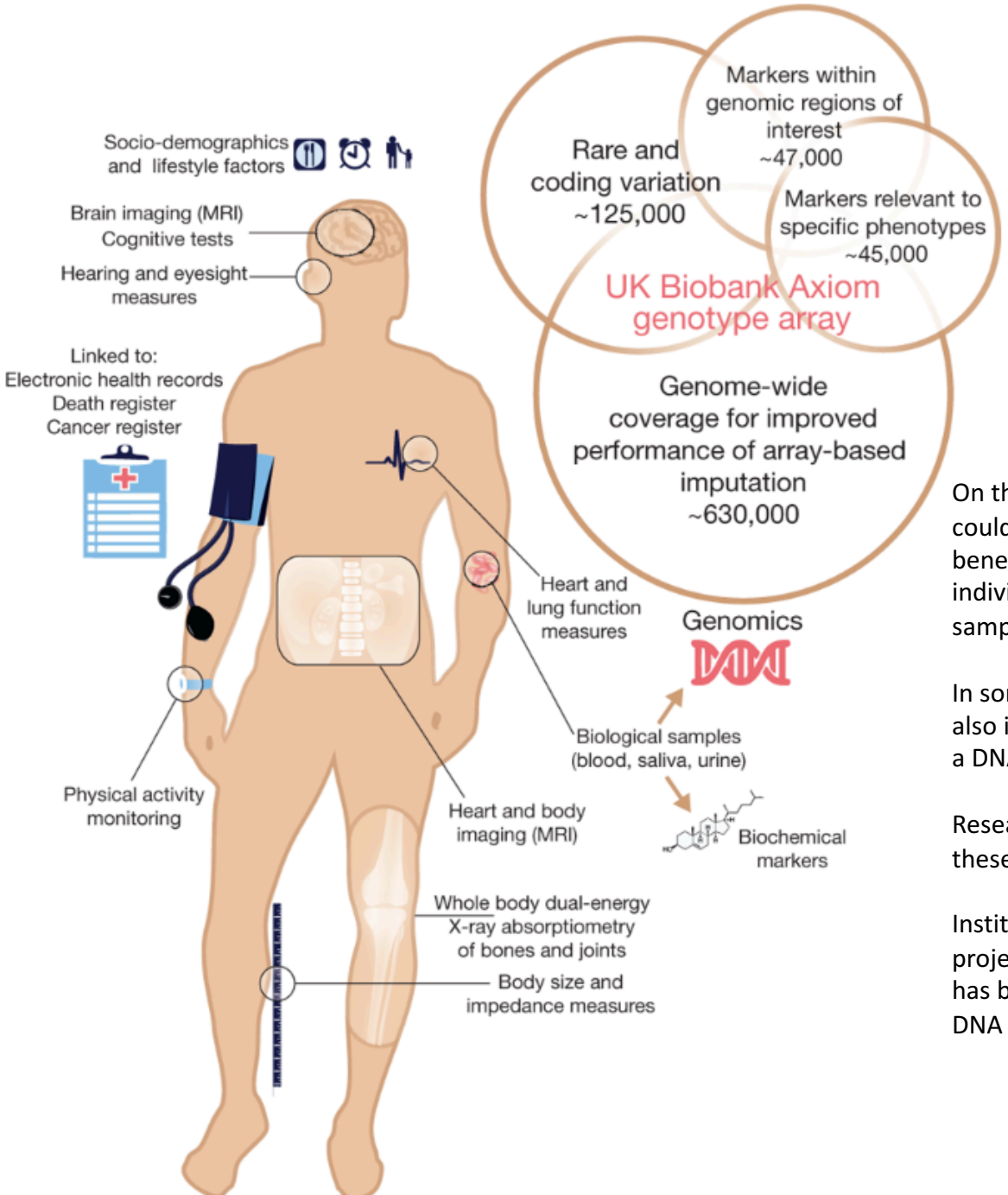
Once they have served their intended use, what should now be done with these samples? Who do they belong to?

Can the researcher use them for other purposes without the consent of those who gave these samples?

Can he only do it if he anonymizes the samples first?

Or does the researcher need to contact each individual to renew his/her consent?

To respect the autonomy of individuals who participated in previous research projects, it would be necessary to contact them again to obtain renewed consent before using their samples for other research projects.



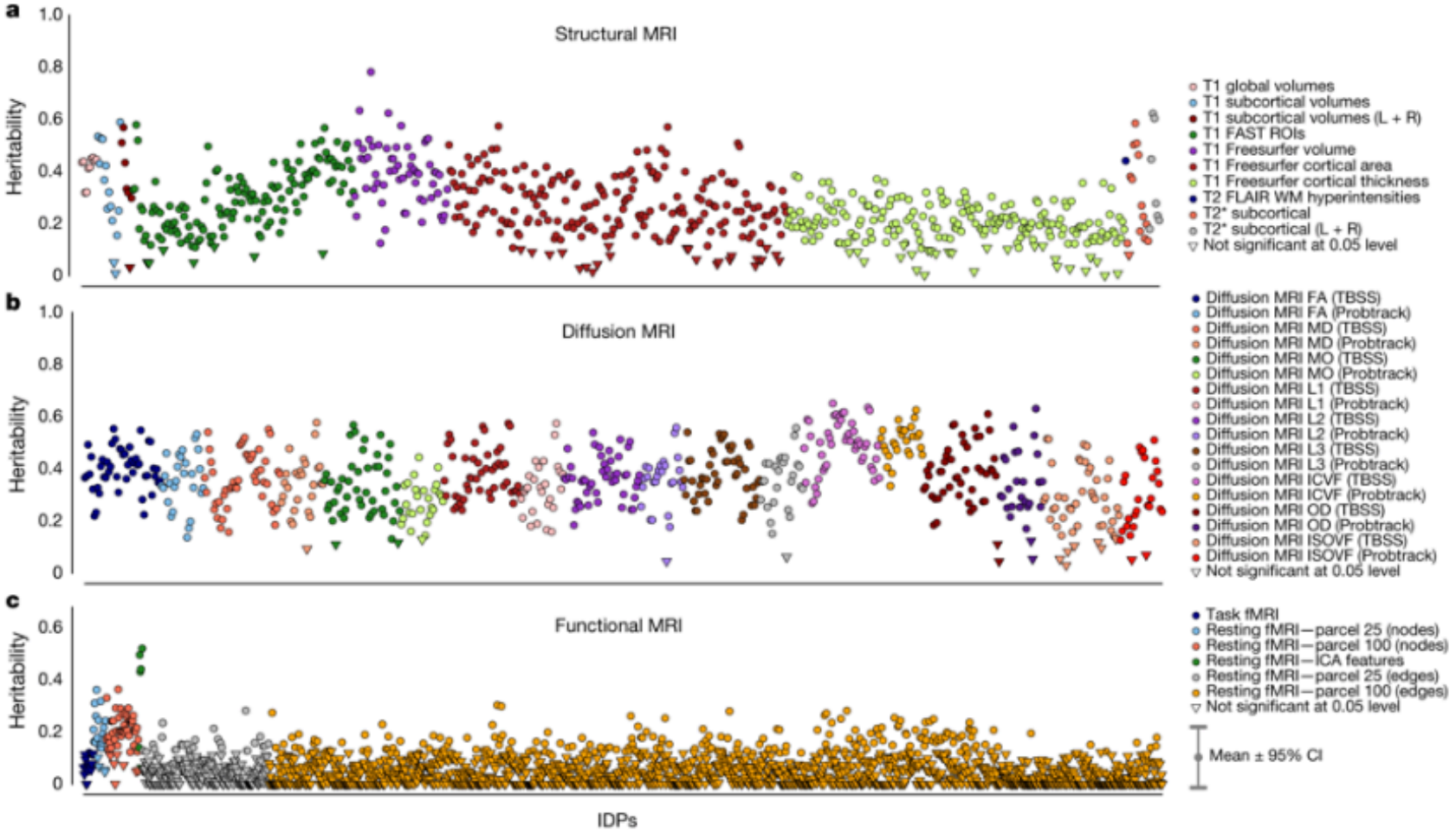
On the other hand, these samples are easily accessible and could be used to further scientific knowledge for the benefit of society without major negative impact on the individual who provided the sample, especially if the samples are anonymized.

In some cases, the nature of the prospective research will also influence the decision to use or not use samples from a DNA bank.

Researchers and ethicists all over the world are faced with these issues.

Institutional review boards are assessing each research project based on its specific context, because no consensus has been reached for now on procedures for the use of DNA banks in research.

From: Genome-wide association studies of brain imaging phenotypes in UK Biobank



Estimated heritability (*y*-axis) of all of the IDPs analysed (n = 8,428 subjects; see Methods for heritability calculation details). IDPs were split into three broad groups. **a**, Structural MRI. **b**, Diffusion MRI. **c**, Functional MRI. Points are coloured according to IDP groups. Circles and inverted triangles, respectively, are used to identify IDPs that do and do not have heritability significantly different from 0 at the 5% significance level. The mean 95% confidence interval (CI) error bar size is indicated at the bottom right.

Why GENOMICS not Genetics

- Genomics is a new evolving term
- Comes largely from knowledge emanating from the Human Genome Project

Genomics and Public Health

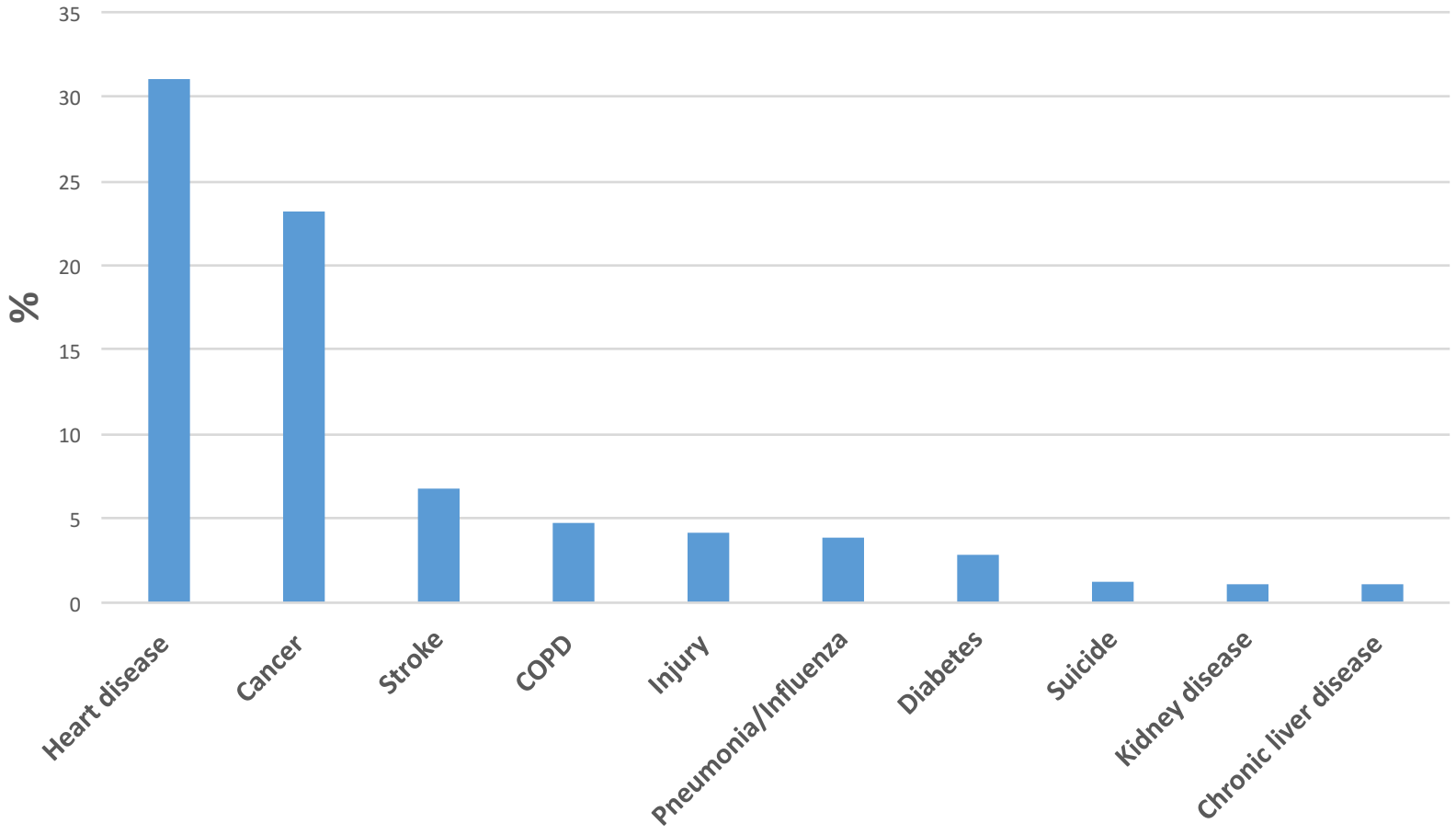
• Human diseases result from gene-environment interaction

• Public health leadership needed to translate gene discoveries

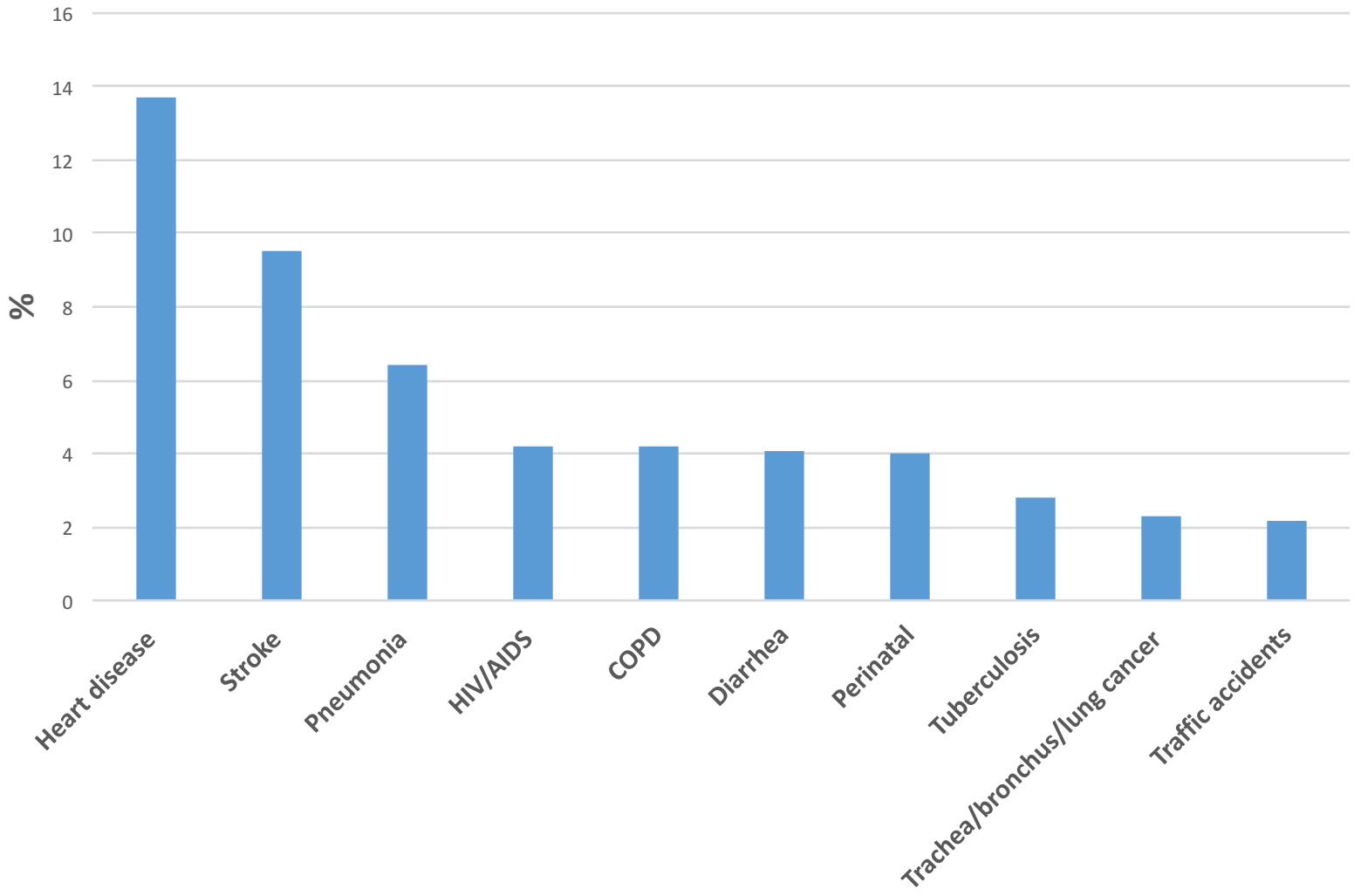
• Genetics affects allpublic health functions: assessment, policy development and assurance

• Public health must plan to train the work force in order to build genetics capacity across programs

9 of the CDC's 10 Leading Causes of U.S. Deaths Have Genetic Components



9 of the WHO's 10 Leading Causes of Global Deaths Have Genetic Components



Applications of genetic knowledge in medical practice

Pharmacogenomics

• The study of how an individual's genetic make up affects the body's response to drugs

– by combining traditional pharmaceutical sciences with annotated knowledge of genes, proteins, and single nucleotide polymorphisms (DNA sequence variations)

Pharmacogenomics will allow:

• individualized medication use based on genetically determined variation in effects and side effects

• use of medications otherwise rejected because of side effects

• new medications for specific genotypic disease subtypes

Applications of genetic knowledge in medical practice (cont.)

Genetic Testing

- DNA-based tests examine the DNA molecule itself
- Obtained from any tissue,or from blood
  - Biochemical tests examine enzymes and other proteins
  - Microscopic examinations look at stained or fluorescent chromosomes
  - Pre-implantation genetic diagnosis (PGD) screens for genetic flaws among embryos used in vitro fertilization

Pros of Genetic Testing

- Genetic testing can clarify diagnosis and enable appropriate treatments (e.g. cancer cell characterization)

- Information for families weighing their risks for familial genetic diseases

- People with high risk for preventable illness could improve lifestyle or environment

- Used in newborn screening

- Forensic/identity testing

Cons of Genetic Testing

- Costs can range from hundreds to thousands of dollars and insurances rarely cover them

- Commercialized gene tests for adult-onset disorders (Alzheimer's disease and cancers)

- Companies are targeting healthy people

- Results give only a probability of developing the illness

- Issue of Regulation.

Gene therapy

- Somatic gene therapy

(treatment of certain genetic diseases and types of cancer by manipulation of certain genes in body cells outside the germ line)
falls into the wide field of medical therapy

- It has little impact on public health policy

Potential Impact of Molecular Genetics on Medicine and Public Health

- Prenatal screening / Diagnostic testing
- Gene therapy
- Define susceptibility to common disease
- Drug discovery / Predicting drug response
- Explain health disparities

Potential Areas of Concern in the Application of Genomics

- Stigmatization of individuals and populations
- Intense commercialization
- Limited applicability in poor countries
- Promotes genetic determinism
- Poses technology as a solution to social problems

https://www.geneticsandsociety.org

TOPICS

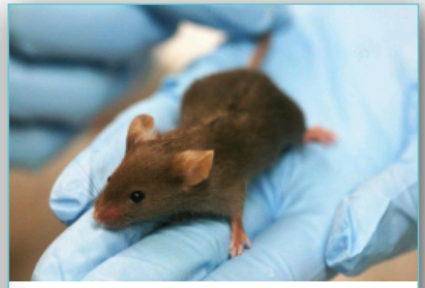
Technologies

A Consumer DNA Testing Company's Alarming New Marketing Pivot

By **Elizabeth Joh,** *Slate* | 03.29.2019

Sometimes a marketing pivot serves a truth-telling function. A **new television ad** for the consumer DNA database FamilyTreeDNA asks the...

Technologies



Genome engineers made more than 13,000 CRISPR edits in a single cell

By **Antonio Regalado,** *MIT Technology Review* | 03.26.2019

Since its invention, CRISPR has let scientists introduce DNA changes at specific locations in a genome. Often these precise changes...

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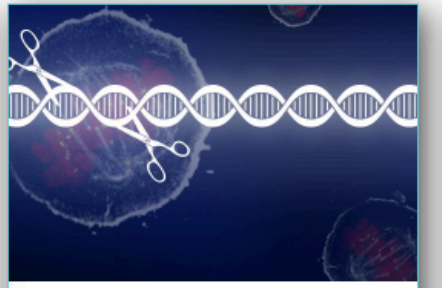


What Is the World to Do About Gene-Editing?

By **Stephen Buranyi,** *The New York Review of Books* | 03.21.2019

When the journal *Science* chose the radical gene-editing technology CRISPR as its 2015 breakthrough of the year, the editorial team...

Technologies

One Week Later: Reactions to the Proposed Moratorium on Human Germline Editing

By **Katie Hasson** | 03.20.2019

Has a **commentary** in *Nature* shifted the landscape of the debate about editing the genomes of future children? Or will...

Technologies

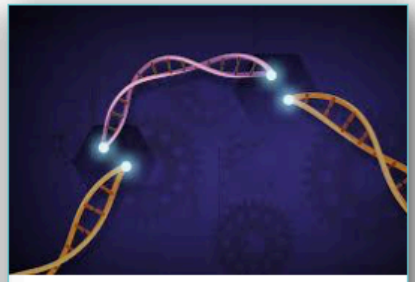
Policies

Don’t Buy California’s Callous Attempt to Ignore People’s DNA Privacy Rights, EFF Tells Court

By **Karen Gullo,** *Electronic Frontier Foundation [cites CGS]* | 03.29.2019

Analyzing and indefinitely keeping the DNA profiles of thousands of Californians arrested for felonies, but never charged with a crime,...

Genomics

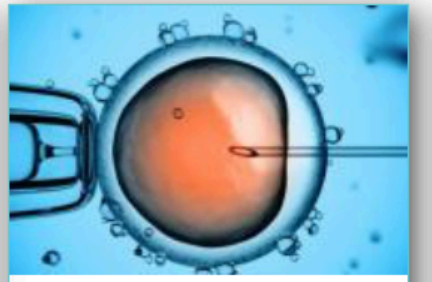


Call For Global Moratorium On Creating Gene-Edited Babies

By **Rob Stein ,** *National Public Radio [cites CGS' Marcy Darnovsky]* | 03.13.2019

A group of prominent scientists and bioethicists is calling for a global moratorium on any new attempts to bring gene-edited...

Technologies



Adopt a moratorium on heritable genome editing

By **Eric Lander, Françoise Baylis, Feng Zhang, Emmanuelle Charpentier, Paul Berg et al.,** *Nature* | 03.13.2019

We call for a global moratorium on all clinical uses of human germline editing — that is, changing heritable DNA...

Technologies

Heartbreak, anxiety, lawsuits: The egg-freezing disaster a year later

By **Rich Gardella and Erika Edwards,** *NBC News* | 03.04.2019

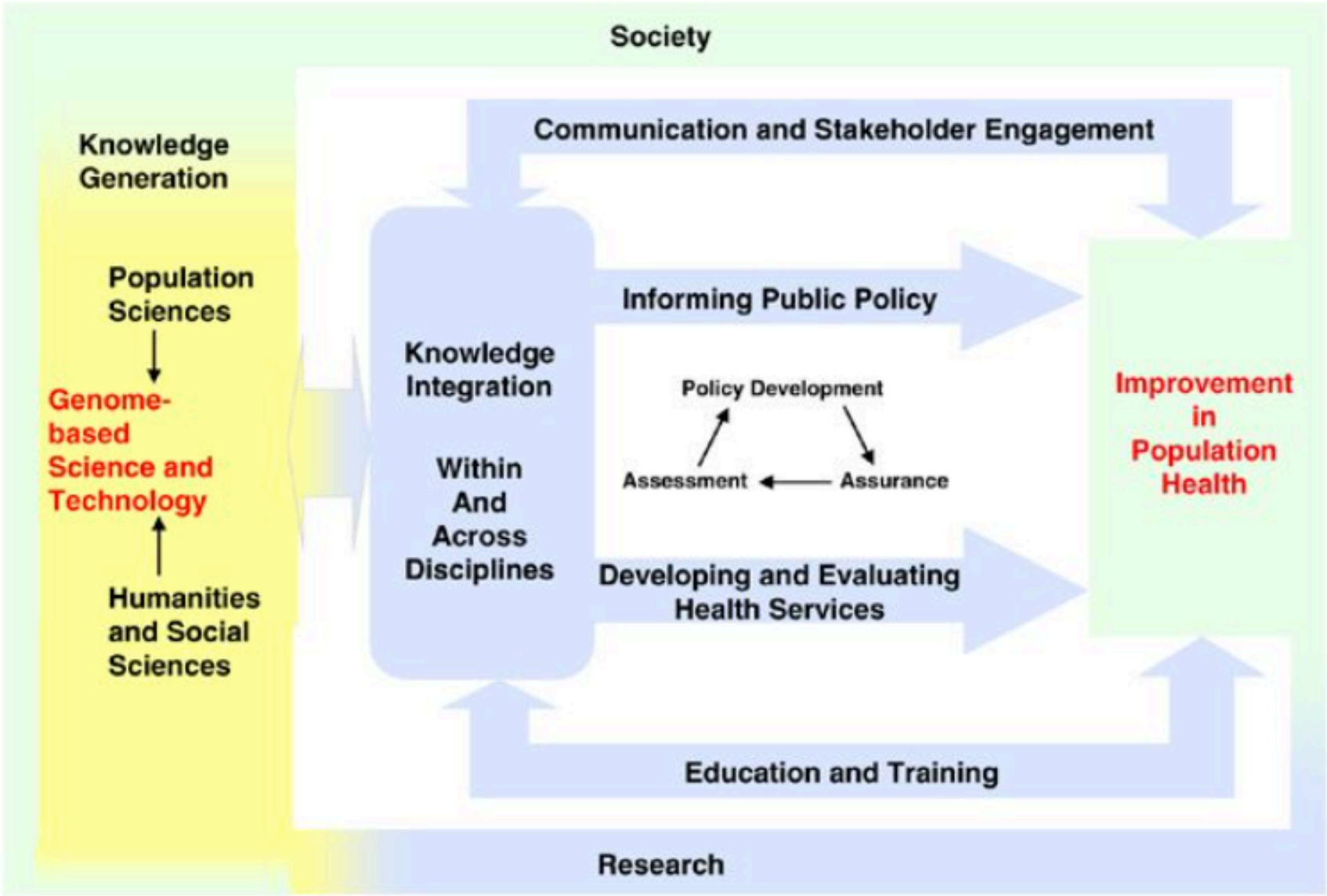
A Facebook post was what alerted Katelynn Gurbach to **a massive tank malfunction** at University Hospitals Fertility Center near Cleveland...

Assisted Reproduction

Social Measures

- Health Promotional Measure
  - Eugenics
  - Euthenics
  - Genetic Counseling

Impact of Genetics and Genomics on Public Health



Three Core Public Health Functions and Genetics

1) Assessment

To improve health, it is important to understand how genetics interacts with other factors. Therefore, it is necessary to regularly collect, analyze, and share information, including genetic information and environmental interactions related to health conditions, risks, and community resources. The surveillance is needed to determine:

•the population frequency of genetic variants that predispose people to specific diseases, both common and rare;

•the population frequency of morbidity and mortality associated with such diseases; and

•the prevalence and effects of environmental factors known to interact with the given genotypes in producing disease.

2) Policy development

Public health policies also provide members of the public with objective guidance and information to empower them in decision making regarding the use of genetic technologies. Issues such as health insurance discrimination, population screening, and privacy and confidentiality require guidance from State Health Officials to ensure the public's health and minimize potential harm.

3) Assurance

Agencies may collaborate with other public and private entities and educate public health staff and private health-care workers about the use of genetic information to improve health. Programmatically, the incorporation of up-to-date genetic information in areas such as maternal and child health, occupational health, and disease prevention programs will improve outcomes by providing better prevention information.

Ten Essential Public Health Services and Genetics

1) Monitor health status to identify community health problems

2) Diagnose and investigate health problems and health hazards in the community

3) Inform, educate, and empower people about health issues

4) Mobilize community partnerships at the state and local levels to identify and solve health problems

5) Develop policies and practices that support individual and community health efforts

6) Enforce laws and regulations that protect health and ensure safety

7) Link people to health services, including genetic services, and assure the provision of health care when otherwise unavailable

8) Assure a public health and personal health care workforce competent in genetics

9) Evaluate effectiveness, accessibility, and quality of personal and population-based health services, including genetics

10) Research for new insights and innovative solutions to health problems

Genetics in Public Health -2

The role of public health is to ensure that the basic conditions required for people to be healthy are present.

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Since the sequencing of the human genome has been completed, high hopes rest on the potential to prevent the impact of genetic risk factors or susceptibilities to disease.

Advances in genetic knowledge and technology could be used to try to prevent disease and improve population health.

The perceived role of genetics in public health is changing, as is the definition of what is a genetic disease. The role of genetics in public health is broadened if we consider all the diseases for which genetics might play a role, either by the presence of a genetic susceptibility for the development of this disease or for response to treatment, or by the presence of protective genetic factors, such as in resistance to infection.

Examples of the role of public health in genetics

1. Folic acid and neural tube defects
2. Newborn screening
3. Carrier screening in the context of reproductive decisions
4. Prenatal screening for aneuploidy and neural tube defects
5. Screening for genetic susceptibilities in adults
6. Pharmacogenetics and ecogenetics
7. Personalized Health Care and Genetic Information

Examples of the role of public health in genetics

There are already many examples of the role of public health in genetics. Better known examples deal with reproductive technologies (prenatal screening, carrier screening) and newborn screening. More recent examples in the adult setting concern genetic susceptibility screening and pharmacogenetics.

Folic acid and neural tube defects (NTD)

NTDs account for an important part of birth defect-related infantile mortality and morbidity.

Folic acid acts to prevent NTD.

Because the neural tube closes during the fourth week of gestation, it is recommended to start folic acid supplementation before conception.

Folic acid fortification has been established at the end of the 1990s in many developed countries, most often in flour.

Studies done since fortification seem to show a significant reduction in the incidence of NTD in the population.

Neural tube defects (NTD) account for an important part of birth defect-related infantile mortality and morbidity. Their incidence tends to be decreasing over time (secular trend). During the 1980s, studies have shown a decrease in the recurrence of NTD in subsequent pregnancies with the use of folic acid for women having already had a child with a NTD. Since then, studies done in women with no family history of NTD have also shown lower incidence rates of children born with NTD in women who took folic acid supplements. Even though the way in which folic acid acts to prevent NTD has not been elucidated, these observed findings have led to the hypothesis that folic acid supplementation would be beneficial to all women planning a pregnancy, to prevent the birth of a child with a NTD.

Because the neural tube closes during the fourth week of gestation, it is recommended to start folic acid supplementation before conception. The minimal dose needed to obtain an effect has not been established, but the usually recommended daily dose is 400 micrograms in women with no specific risk factor, and should be started at least 3 months before conception. However, supplementation often does not occur, either because women are not aware of the benefits of folic acid supplementation or because pregnancy was not planned.

To address this problem, some countries have decided to add folic acid to the food supply, most often in flour. This type of public health intervention has occurred in the past to prevent other diseases: iodized salt to prevent goiter, and vitamin D in milk to prevent rickets.

Folic acid fortification of flour has not been done without controversy. Some fear that folic acid fortification will mask vitamin B12 deficiency and delay its diagnosis. Others worry about long-term effects of a folic acid-fortified diet or about potential interactions between folic acid and prescribed drugs. No study has shown that this fortification strategy would be sufficient to reduce the incidence of NTD in the population. In spite of all that, many professional organizations have declared themselves in favor of fortification. Folic acid fortification has been established at the end of the 1990s in many developed countries, most often in flour. Studies done since fortification seem to show a significant reduction in the incidence of NTD in the population, even when accounting for the secular trend.

Newborn screening

Phenylketonuria (PKU) is the first example of population-based genetic screening.

A technique allowing the measurement of blood phenylalanine levels using blood samples collected on filter paper was developed by Dr Robert Guthrie and put in place in the U.S.A. in the early 1960s.

Newborn screening for PKU is now performed by the state in most developed countries.

Since the 1960s, other diseases have been added to newborn screening panels.

List varies but it almost always includes congenital hypothyroidism, and often includes galactosemia, tyrosinemia, sickle cell anemia, and/or congenital adrenal hyperplasia.

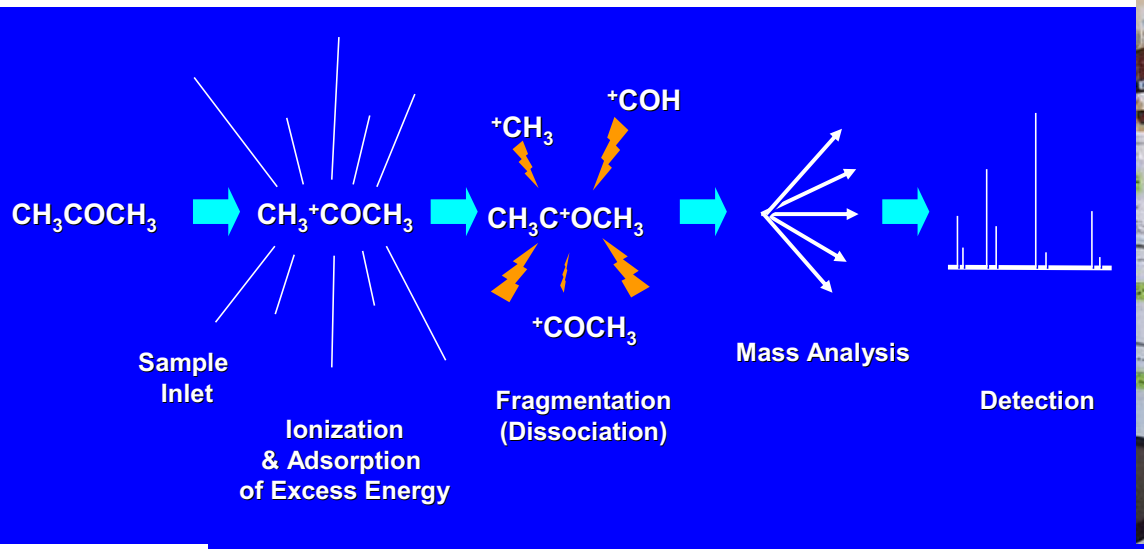
Phenylketonuria (PKU) is the first example of population-based genetic screening. It was put in place in the U.S.A. in the early 1960s, thanks to the development by Dr Robert Guthrie of a technique allowing the measurement of blood phenylalanine levels using blood samples collected on filter paper. Samples collected in this way are easy to store and ship, and can be preserved for extended periods of time.

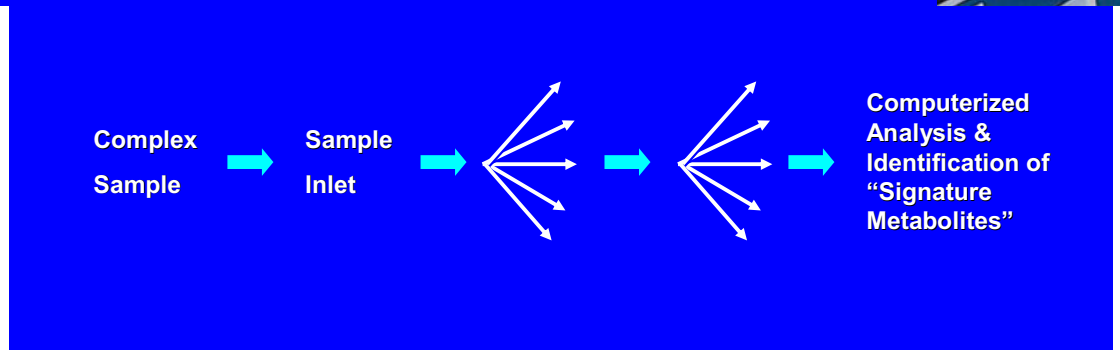
The technique itself is cheap and easy to perform. These characteristics have made it possible to develop large-scale screening programs. Newborn screening for PKU is now performed by the state in most developed countries.In the wake of newborn screening tests, a screening “system” was developed.

Today, a newborn screening system includes sample collection and shipment to screening facilities, performance of the screening test in the laboratory, diffusion of test results to parents and referring physicians, and, for newborns with abnormal results, rapid access to specialized evaluation and appropriate care. In parallel, severe quality control criteria have been established and voluntary laboratory quality control programs are managed by government agencies, such as the Center for Disease Control in the U.S.A.

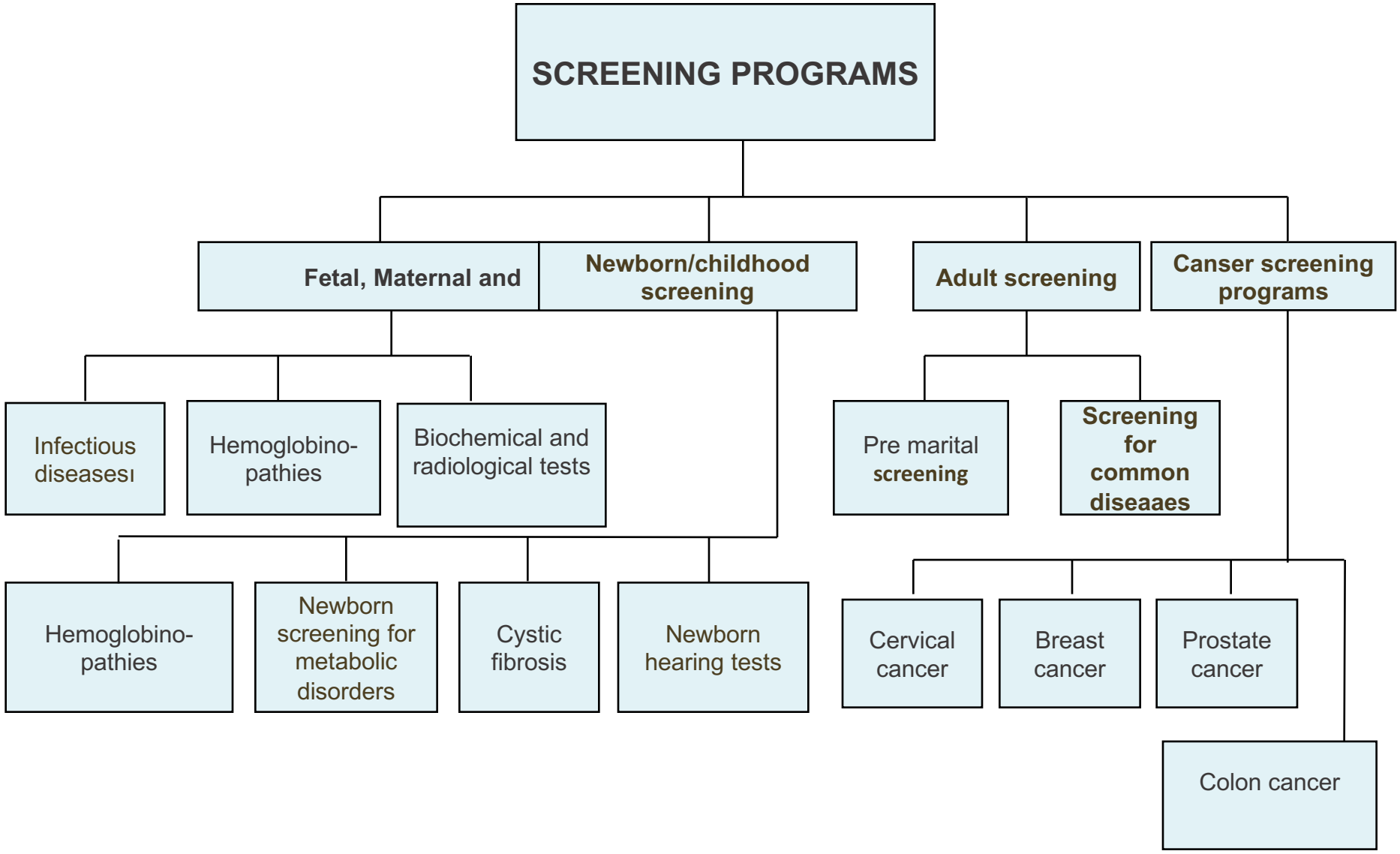
Since the 1960s, other diseases have been added to newborn screening panels. The list varies by region, but it almost always includes congenital hypothyroidism, and often includes galactosemia, tyrosinemia, sickle cell anemia, and/or congenital adrenal hyperplasia. For all these diseases, a dietary-based or drug-based treatment is available to prevent the effects of the disease or attempt to control their progression, and it seems preferable to start these treatments as early as possible.

Tandem Mass Spectormetry (MS/MS)





The main newborn screening criteria, as defined by the World Health Organization, state that an effective treatment must be available and that the early application of that treatment must improve the health outcome of the child.


SCREENING PROGRAMS
Fetal, Maternal and
Newborn/childhood screening
Adult screening
Canser screening programs
Infectious diseasesı
Hemoglobino-pathies
Biochemical and radiological tests
Pre marital screening
Screening for common diseaaes
Hemoglobino-pathies
Newborn screening for metabolic disorders
Cystic fibrosis
Newborn hearing tests
Cervical cancer
Breast cancer
Prostate cancer
Colon cancer

Carrier screening in the context of reproductive decisions

The first carrier-screening program for recessive diseases was developed in the Ashkenazi Jewish communities in New York and Washington, D.C., in the U.S.A. With the support of the community and religious officials, a carrier-screening program for **Tay-Sachs** disease was established in the early 1970s, shortly after the discovery of the enzyme whose deficiency is the cause of the disease.

Tay-Sachs disease then had a relatively high prevalence in the Ashkenazi Jewish community. This disease causes progressive neurodegeneration starting in the first year of life and inevitably leading to the child's death, usually by four years of age. Both the community members and the health professionals involved agreed that this disease is so severe that it would be preferable to take measures to avoid the birth of affected children. The screening strategy has been adapted to the needs and realities of the different communities: in orthodox communities where selective abortion was not acceptable, premarital screening is performed and results are taken into account in the rabbi's decision to bless the marriage or not, which has been deemed acceptable by the community. Carrier screening programs for Tay-Sachs disease now exist in Ashkenazi Jewish communities around the world. Thanks to these programs, the incidence of the disease has decreased by over 90% in these communities. In the wake of this success, other diseases with relatively high prevalence in Ashkenazi Jewish communities have been added to carrier screening panels, such as Canavan disease and Gaucher disease, to name a few. In response to the success of Tay-Sachs carrier screening in Ashkenazi Jewish communities, similar programs have been developed in other communities where an autosomal recessive disease was highly prevalent in children, such as carrier screening for beta-thalassemia in Cyprus and Sardinia. These programs have also led to drastic reductions in disease prevalence in these communities. Carrier screening programs for sickle cell anemia in African Americans in the U.S.A. in the 1970s have not had the same success, partly because the distinction between being a healthy carrier and having the disease was not made clear. This had led to discrimination against carriers. Recently, the American College of Obstetrics and Gynecology has recommended that all pregnant women be offered carrier screening for cystic fibrosis. This recommendation has been questioned by some, because screening is routinely offered when pregnancy is already ongoing and because cystic fibrosis is not considered as severe as Tay-Sachs disease.

Prenatal screening for aneuploidy and neural tube defects

In terms of population health, it is of note that prenatal screening for chromosomal abnormalities and neural tube defects is offered to pregnant women in many countries. These screening programs may be targeted at women with specific risk factors (i.e. according to maternal age), or to all pregnant women. In most cases, newborns with chromosomal abnormalities or neural tube defect are born of mothers with no specific risk factors.

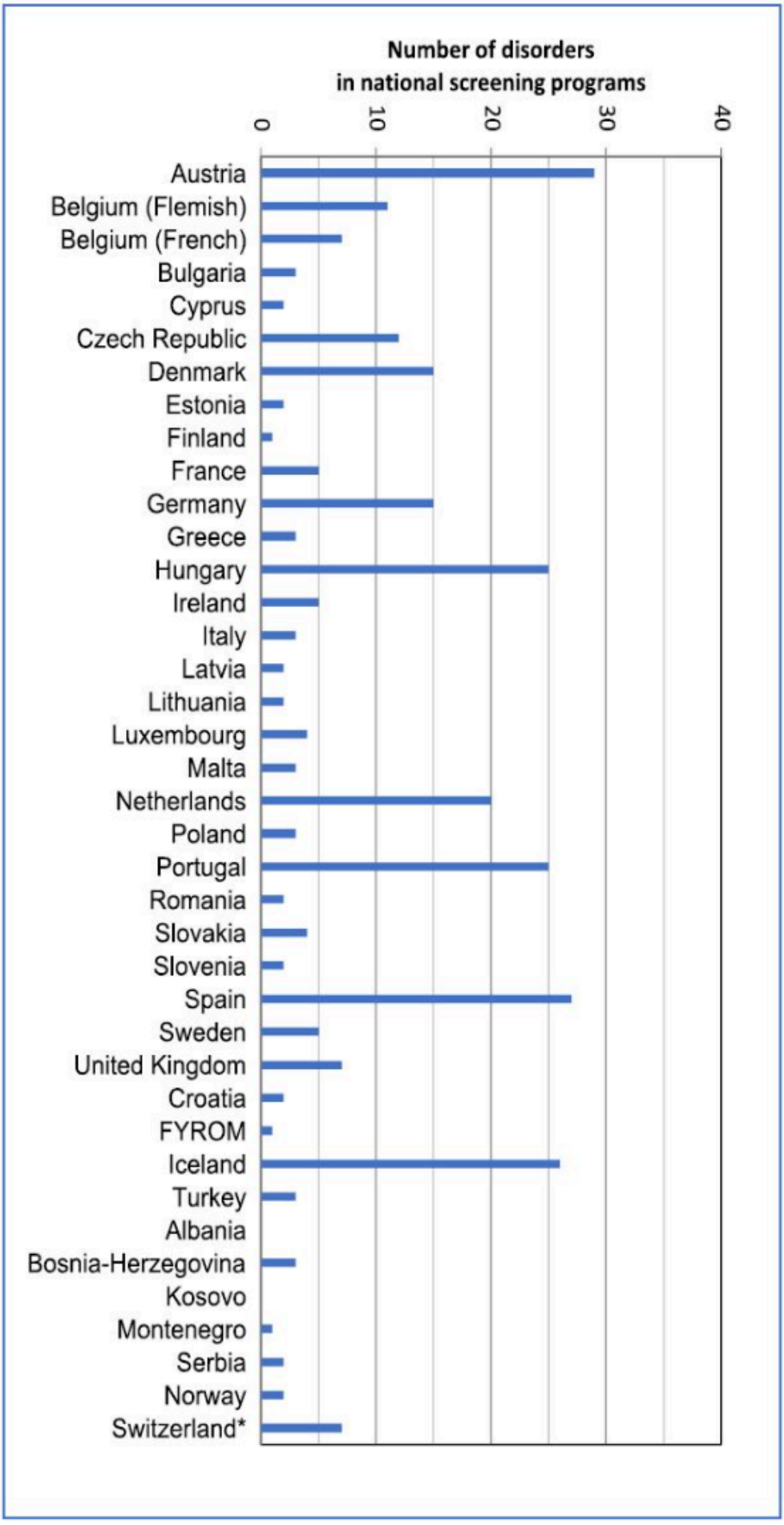
A screening test done during pregnancy can identify those women at higher risk of carrying a fetus with one of these conditions. This blood test, which measures a combination of serum and/or ultrasound markers, is not a diagnostic test: like all screening tests, it tends to be highly sensitive, but not necessarily very specific. The role of a screening test is to detect all cases of the targeted condition, at the expense of a certain amount of false positive results.

For prenatal screening, the test result is usually given as the probability that the fetus is affected, and the result is considered “positive” when this probability is higher than a specific threshold, usually between 1/400 and 1/200. Since this threshold is relatively low, there is inevitably a high proportion of false positive results, i.e. pregnancies with test results above the threshold and considered at high risk of having an affected fetus, but whose fetus is actually not affected. In a screening context, we tolerate a certain amount of false positive results that will have to undergo definitive diagnostic testing through amniocentesis and incur the associated risk of miscarriage. It is the price to pay to reduce as much as possible the rate of false negative results, i.e. a result placing the risk below the threshold when the fetus is actually affected.

These screening programs have been developed to give women the possibility of terminating the pregnancy if the fetus is found to be affected. In general, this option is considered acceptable because most people consider these conditions to be severe enough and prevalent enough to justify a population-based screening program. Those who consider termination to be unacceptable can select out of the screening process.

Screening for genetic susceptibilities in adults

Since the sequencing of the human genome, advances in genetic knowledge has led us to consider the potential use of genetic information to assess individual susceptibilty to disease. Although this is not widely possible yet, there are some examples of the use of genetic tests for that purpose. These examples raise questions about the real clinical utility of that type of information at the individual level. Hereditary hemochromatosis is an autosomal recessive disease. Individuals who suffer from this disease can develop cirrhosis of the liver, diabetes, and cardiomyopathy. Symptoms are caused by a defect in iron metabolism, which leads to iron deposition in tissues. Two main mutations in the hemochromatosis gene have been identified, C282Y and H63D. Most cases are C282Y homozygotes. Regular phlebotomies reduce iron deposition and can help prevent or reduce symptoms. For that reason, hemochromatosis is considered an ideal target for population-based screening. The use of a genetic test as a screening test for hereditary hemochromatosis is justified if we assume that penetrance of the disease is high, i.e. that most C282Y homozygotes will develop symptoms of hemochromatosis in their lifetime if untreated, and that they would benefit from early diagnosis and preventive treatment. Unfortunately, penetrance seems lower than previously thought: it seems that only a minority of C282Y homozygotes actually develop symptoms of hemochromatosis in their lifetime. The value of population-based genetic screening for hemochromatosis is being questioned. It is currently recommended to use transferrin saturation level as a screening test for hemochromatosis. This is a biochemical index of iron overload, and is closer to the phenotype of hemochromatosis than the genetic test. Factor V Leiden (FVL) is a variant of factor V, a coagulation factor. This variant is associated with an increased risk of thrombosis. Even though the presence of FVL in an individual with a history of thrombosis can help explain the cause of the thrombosis, it does not usually change immediate treatment or long-term management of that individual, who will be treated as any other individual with a personal history of thrombosis. On the other hand, not all individuals who have FVL will develop thrombosis. It is difficult to justify population-based screening for FVL, and especially to submit them to long-term prophylactic anticoagulation treatment, which is associated with significant risks of bleeding. Other factors also influence the risk of thrombosis in these individuals, such as smoking and hormonal therapy, and make it difficult to predict risk of thrombosis on an individual basis. As our knowledge of gene-environment interactions increases, it might be possible to improve our assessment of individual disease susceptibility by using predictive models based on combinations of genetic and environmental risk factors. For now, the impact of genetic susceptibility is difficult to assess, especially on an individual basis.


Number of disorders
in national screening programs
0
10
20
30
40
Austria
Belgium (Flemish)
Belgium (French)
Bulgaria
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Ireland
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Poland
Portugal
Romania
Slovakia
Slovenia
Spain
Sweden
United Kingdom
Croatia
FYROM
Iceland
Turkey
Albania
Bosnia-Herzegovina
Kosovo
Montenegro
Serbia
Norway
Switzerland*

Screening Programs in Turkey

- 1986 **PKU** in seven provinces; in 1990 26 were added. Now extended nation wide
- In 1992 1st of June is announced as National PKU Day
- 2004 newborn hearing screening
- 2006 **congenital hypothyrody** was included and a new act was employed under the name of “Neonatal Screening Program” by the Ministry of Health.
- 2008 **Biyotidinase deficiency**
- 2010 Congenital disclocation of the hip **(CDH)**
- 2015 **Cystic Fibrosis**
- 2017**-Congenital adrenal hyperplasia** as pilot screening in several provinces

Pharmacogenetics and ecogenetics

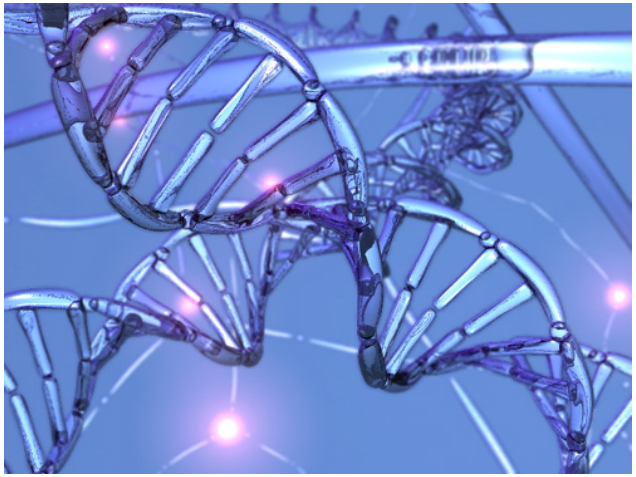
- Prediction pharmacologic response of an individual to a specific drug based on the presence or absence of a genetic polymorphism, allow adjusting dosage accordingly.
- Related with metabolism or elimination of drugs
- Polymorphisms might accelerate or slow drug metabolism or drug elimination.
- Ecogenetics is similar to pharmacogenetics, but focuses on the role of genetics in explaining the individual variability of response to environmental factors (carcinogens, pesticides, food products, industria pollutants, etc.),

Pharmacogenetics is a field of genetics focusing on the role of genetics in individual variability of drug response and side effect occurrence. If we can predict the pharmacologic response of a given individual to a specific drug based on the presence or absence of a given genetic polymorphism, we could adjust dosage accordingly.

Most genetic polymorphism studied until now have been in genes involved in the metabolism or elimination of drugs. It is thought that these polymorphisms might accelerate or slow drug metabolism or drug elimination.

Ecogenetics is similar to pharmacogenetics, but focuses on the role of genetics in explaining the individual variability of response to environmental factors (carcinogens, pesticides, food products, industria pollutants, etc.), instead of response to drugs. This information could be used in the workplace to identify individual workers at risk of developing complications related to occupational exposure to specifc agents. There is the danger that this might be used to discriminate against those with genetic susceptibility to develop complications, who might be refused employment.

On the other hand, workers at low-risk of complications might be exposed to higher levels of the agent in question if it gives them a false sense of security and protective measures are lessened, which would paradoxically put them at higher risk of actually developing complications.



Genetic Testing in high volumes

Practice of Personalized Medicine

- **Current Medical Practice:**

- Unexpected, sudden clinical conditions emerge

- Chronic disorders do not present them selves as emergencies. Complications of the disorders require prompt action

Personalized/Precision Medicine

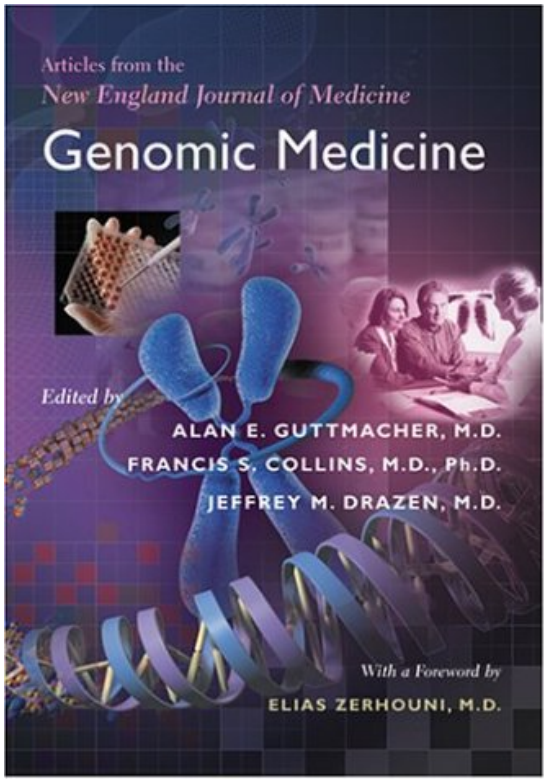
- Predictive
- Preventive

In addition to genomic sequence phenotypes are correlated with

modifier genes

gene X environment

epigenetic effects



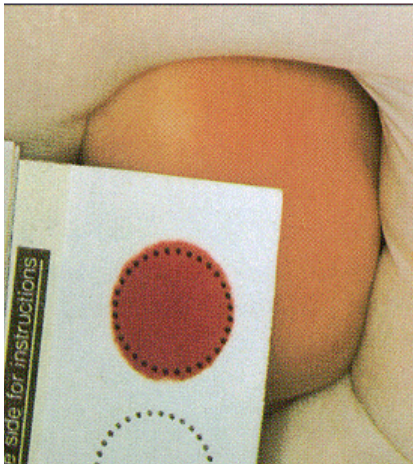
Precision Medicine

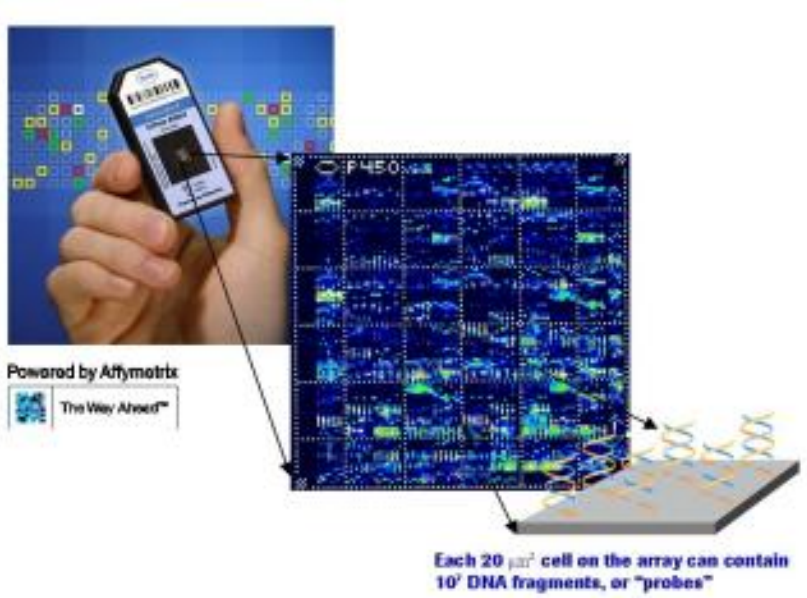
- Large scale population studies
  - Individual variations
  - Disease susceptibility and resistance
  - Course and progression of diseases
- High throughput bioinformatic capacity
  - Genome analysis, proteomics and metabolomics integrated


Whole Genome Analysis
of the Newborn

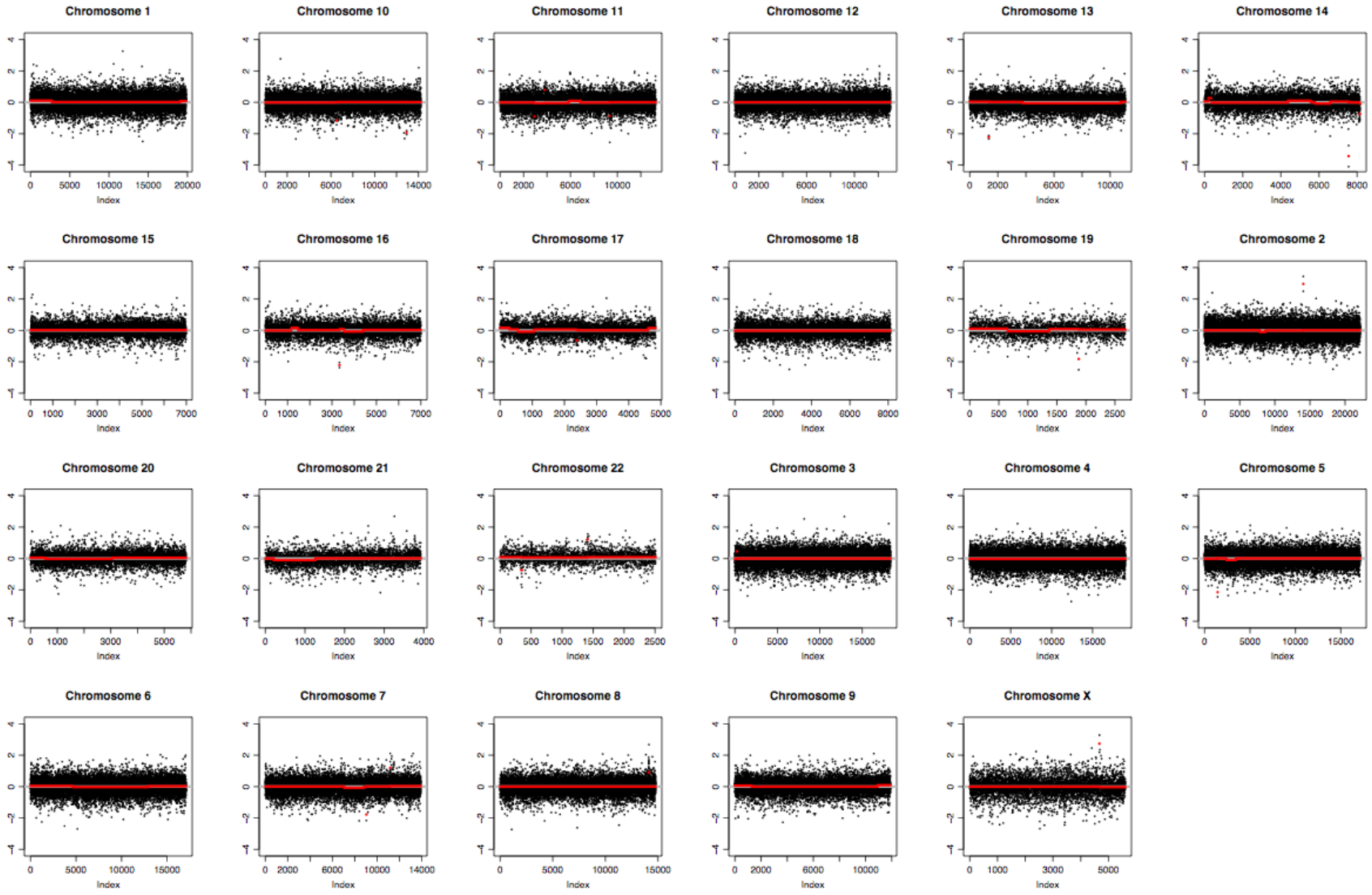
Microarray-based tesing

- AmpliChip CYP450
- FDA approved (2005)
  - 250K SNP chips
  - FDA approved (1MB patented)
- DNA molecule endures. Blood absorbed on filtre paper can be kept, transfered and tested.
- Single nucleotide polymorphisms (SNP) and copy number variations (CNVs) can be detected.

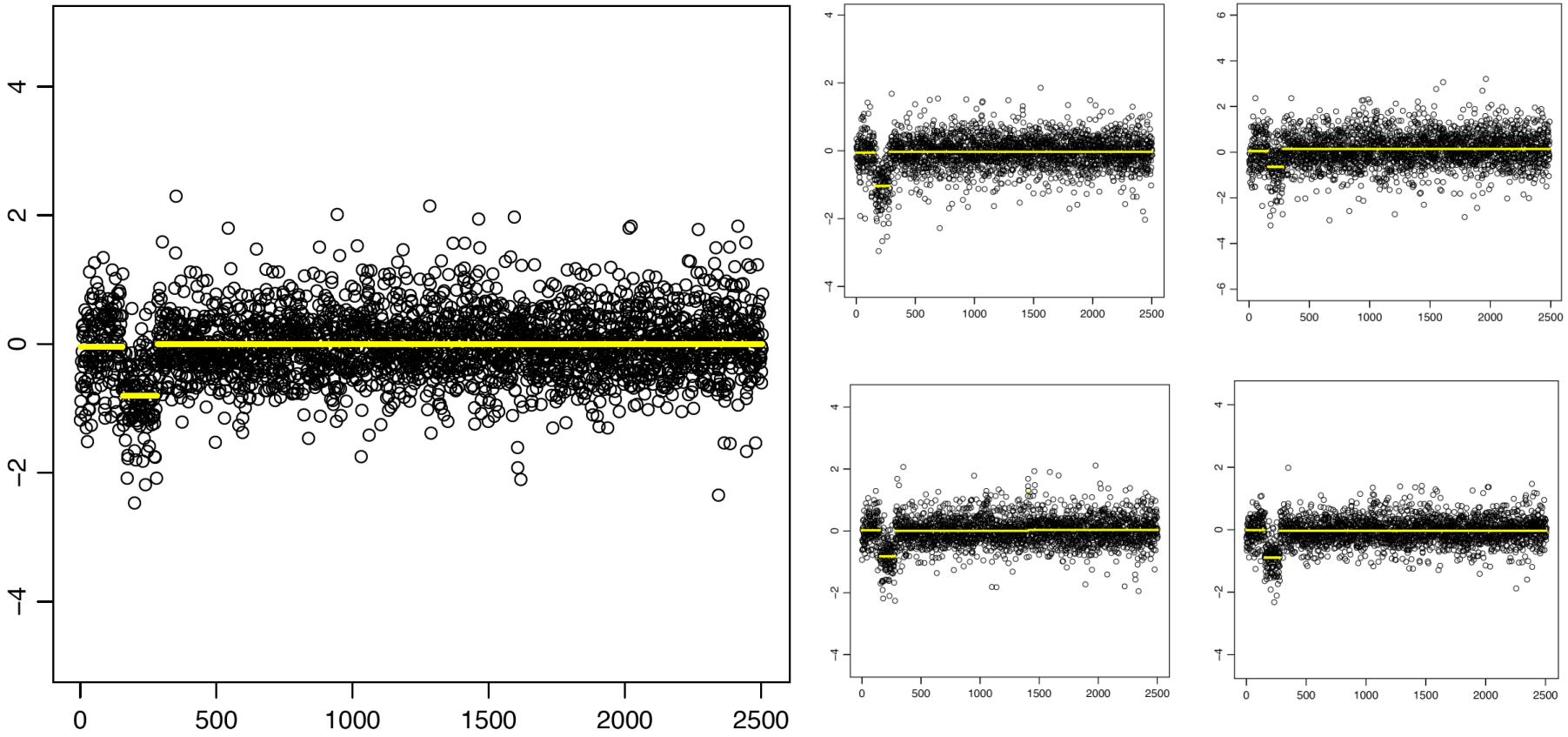


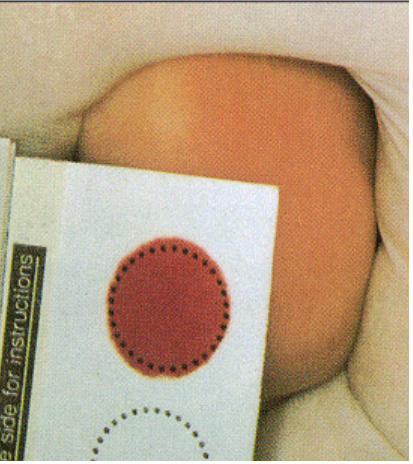


Molecular Cytogenetics (comperative genomic hybridization = CGH)



del 22q11.2 Syndrome





The impact of genetics in public health is still limited, but is expected to grow in the near future, as genetic knowledge rapidly increases. Current examples of the use of genetics in public health can serve as lessons for the future.