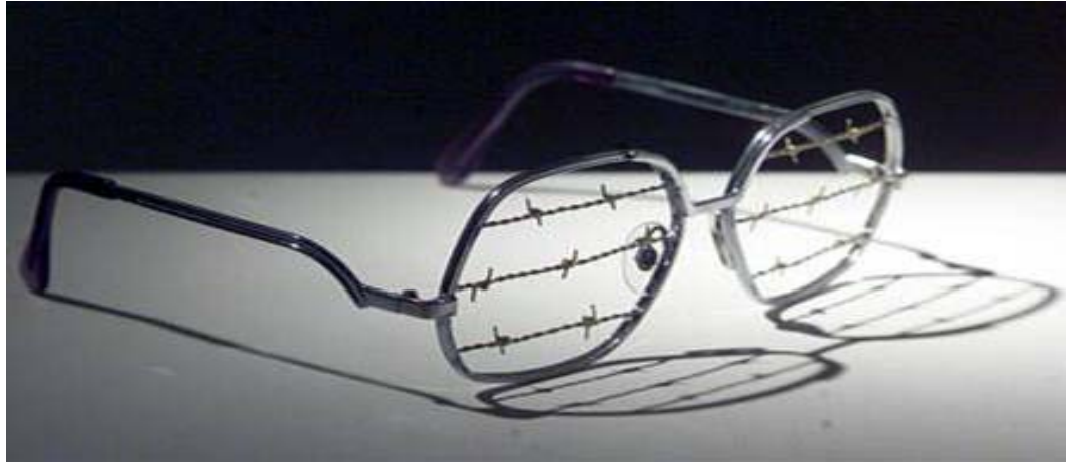

Genetics of Psychiatric Diseases and Insurances: the ethical challenge

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Summary



- The context
- The issue
- The challenge



THE CONTEXT



Definition of Mental Disorders

A mental disorder is an illness with psychological or behavioural manifestation associated with significant distress and impaired functioning caused by biological, social, psychological, genetic, physical, or chemical disturbances. It is measured in terms of deviation from some normative concepts (*Diagnostic and Statistical Manual of Mental Disorders IV Revisited- APA 2000*)

MD include many diseases and syndromes such as depressive disorders, substance use disorders, schizophrenia, epilepsy, Alzheimer's disease, mental retardation, and disorders of childhood and adolescence.



Psychiatric Genetics

Like other common conditions, all psychiatric disorders are driven by multiple genes (polygenics) in addition to environmental forces.

Until recently polygenic characters were believed to be too difficult to be investigated. Consequently psychiatric genetics was only of academic interest.

Moreover scientific misuse and lack of moral standards made psychiatric genetics a disreputable research area.

The renewed research interest was promoted both by the scientific progress and by the establishment of rigid ethical standards.



Contemporary Psychiatric Genetics

Complex disorders such as mental disorders result from the interaction of many susceptibility genes and environmental influences. Rather than rare mutations, the susceptibility genes involved are likely to be common variations (polymorphisms) in the population. Susceptibility genes do not act in a deterministic, all-or-nothing manner, but rather as a complex interaction of genes and environment that alter the risk of developing a disorder.

Today new molecular genetic strategies and new statistical techniques allow to detect genes which contribute, even modestly, to the variance of a behavioural trait, and many types of behaviour - from normal variations in personality to complex psychiatric disorders - are now under scrutiny.



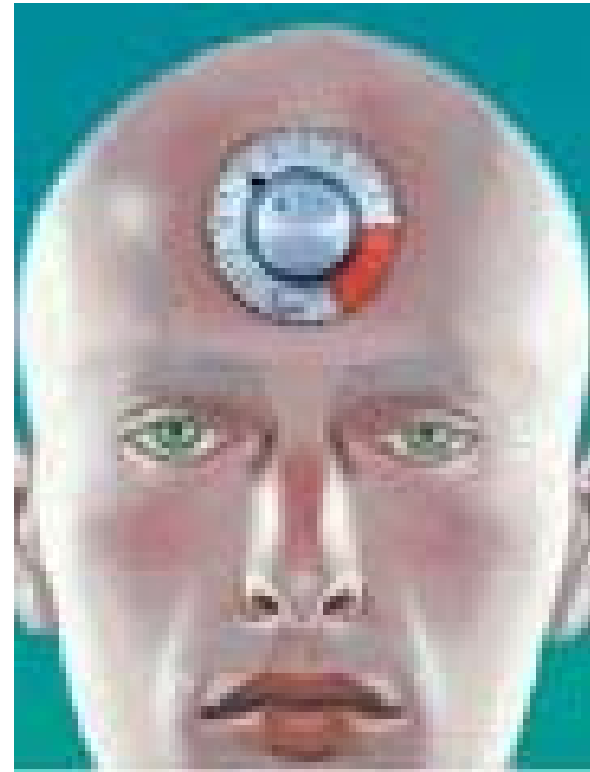
Current results

- To date only two susceptibility alleles, which directly increase the disease risk, have been identified:
 - 1) The ADH-2 and ALDH-2 genes in alcoholism
 - 2) The APOE4 in late onset Alzheimer's Disease



Major Psychiatric Disorders

- As far as major psychiatric disorders are concerned, there are some interesting results but with little explanatory power. Not a single susceptibility gene has been identified with certainty for major psychiatric disorders. Psychiatry is made up by clinical entities that are defined in psychopathological terms and are probably not emerging from direct gene effects. The mind is complex “object” that has complex relations with physical realities such as the brain. Yet it is unlikely that genetics research will lose of importance. The pressure towards more effective psychiatric diagnosis and care is indeed more and more imperative.



Positive implications

- There are a number of positive implications for the discovery of susceptibility genes for mental illness. An **improved understanding** of aetiological mechanisms is likely to lead to the development of improved classification systems and better, more targeted treatments.
- It is likely to be possible to **predict the response and side-effects of various treatments** based on an individual's genotype, so called 'pharmacogenetics'.
- **Preventative strategies** are likely to become better informed — for example, it may be possible to identify genotypes associated with an increased risk of acute psychotic episodes being precipitated through the use of illicit drugs.
- Genotype may also predict **prognosis** and influence decisions regarding the use of **prophylactic strategies**. Such developments have the potential to become a reality in the relatively near future for Alzheimer's disease.



The burden of mental diseases

The burdens of mental illnesses, such as depression, alcohol dependence and schizophrenia, have been seriously underestimated by traditional approaches that take account only of deaths and not disability. While psychiatric conditions are responsible for little more than one per cent of deaths, they account for about 25 per cent of disease burden worldwide



Global Burden of Disease Project

- The *Global Burden of Disease Project* – a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020 carried by the Harvard University and sponsored by the WB and the WHO - developed a single measure to allow comparison of the burden of disease across many different disease conditions by including both death and disability. This measure was called Disability Adjusted Life Years (DALYs).



GBD Results

Of the ten leading causes of disability worldwide in 1990, measured in years lived with a disability, five were psychiatric conditions: unipolar depression alcohol use, bipolar affective disorder (manic depression) schizophrenia and obsessive-compulsive disorder. Unipolar depression alone was responsible for more than one in every ten years of life lived with a disability worldwide.

Altogether, psychiatric and neurological conditions accounted for 28 per cent of all Years Lived with a Disability (YLDs), compared with 1.4 per cent of all deaths and 1.1 per cent of years of life lost.

The predominance of these conditions is by no means restricted to the rich countries, although their burden is highest in the Established Market Economies



The leading causes of years lived with disability, worldwide, 1990

	Total (millions)	Per cent of total
All causes	472.7	
1. Unipolar major depression	50.8	10.7
2. Iron deficiency anaemia	22.0	4.7
3. Falls	22.0	4.6
4. Alcohol use	15.8	3.3
5. Chronic obstructive pulmonary disease	14.7	3.1
6. Bipolar disorder	14.1	3.0
7. Congenital anomalies	13.5	2.9
8. Osteoarthritis	13.3	2.8
9. Schizophrenia	12.1	2.6
10. Obsessive compulsive disorders	10.2	2.2



Ten leading causes of DALYs in developed regions, 1990

	DALYs (thousands)	Per cent of total
All causes	160,944	
1. Ischaemic heart disease	15,950	9.9
2. Unipolar major depression	9,780	6.1
3. Cerebrovascular disease	9,425	5.9
4. Road traffic accidents	7,064	4.4
5. Alcohol use	6,446	4.0
6. Osteoarthritis	4,681	2.9
7. Trachea, bronchus and lung cancers	4,587	2.9
8. Dementia and other degenerative CNS disorders	3,816	2.4
9. Self-inflicted injuries	3,768	2.3
10. Congenital abnormalities	3,480	2.3



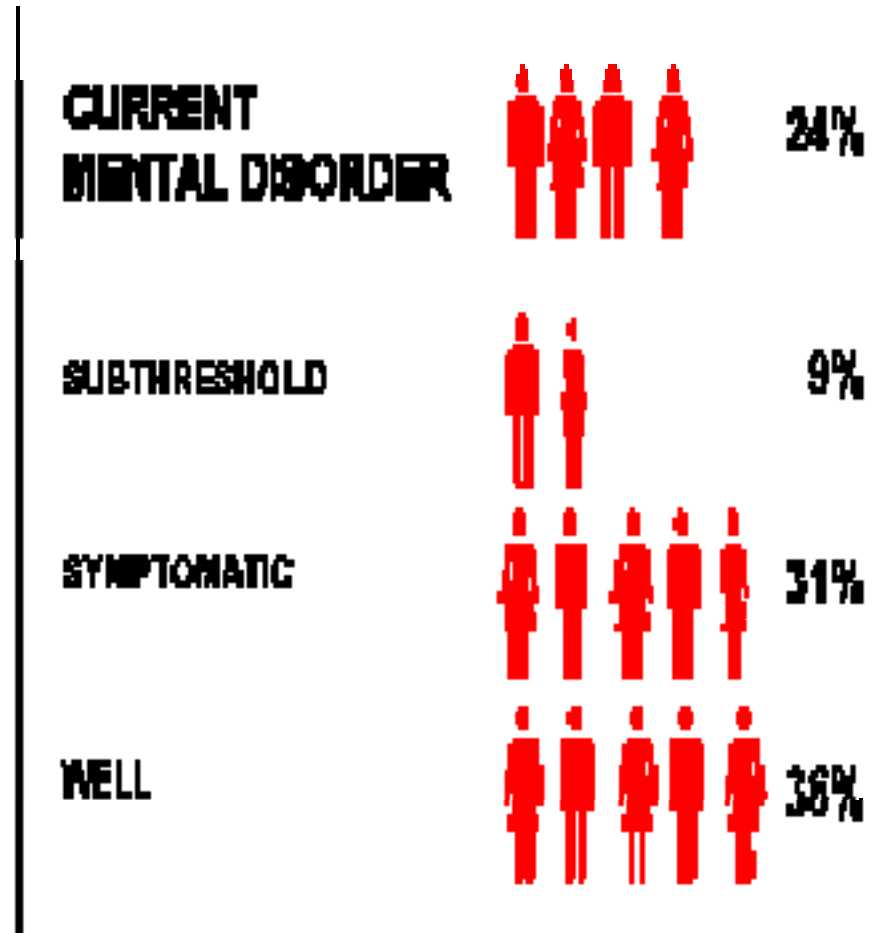
The leading causes of DALYs at ages 15-44 years worldwide, 1990

	Total (thousands)	Per cent of total
All causes	419,144	
1. Unipolar major depression	42,972	10.3
2. Tuberculosis	19,673	4.6
3. Road traffic accidents	19,625	4.7
4. Alcohol use	14,848	3.6
5. Self-inflicted injuries	14,645	3.5
6. Bipolar disorder	13,189	3.1
7. War	13,134	3.1
8. Violence	12,955	3.1
9. Schizophrenia	12,542	3.0
10. Iron-deficiency anaemia	12,511	3.0



Relevance of Mental Disorders

- Mental and behavioural disorders are common, affecting more than 25% of all people at some time during their lives. Mental and behavioural disorders are present at any point in time in about 10% of the adult population. Around 20% of all patients seen by primary health care professionals have one or more mental disorders. One in four families is likely to have at least one member with a behavioural or mental disorder.



Global Burden Diseases 2020



The projections show that with the aging of the world population, psychiatric and neurological conditions could increase their share of the total global disease burden by almost half, from 10.5 percent of the total burden to almost 15 percent in 2020. This is a bigger proportionate increase than that for cardiovascular diseases.

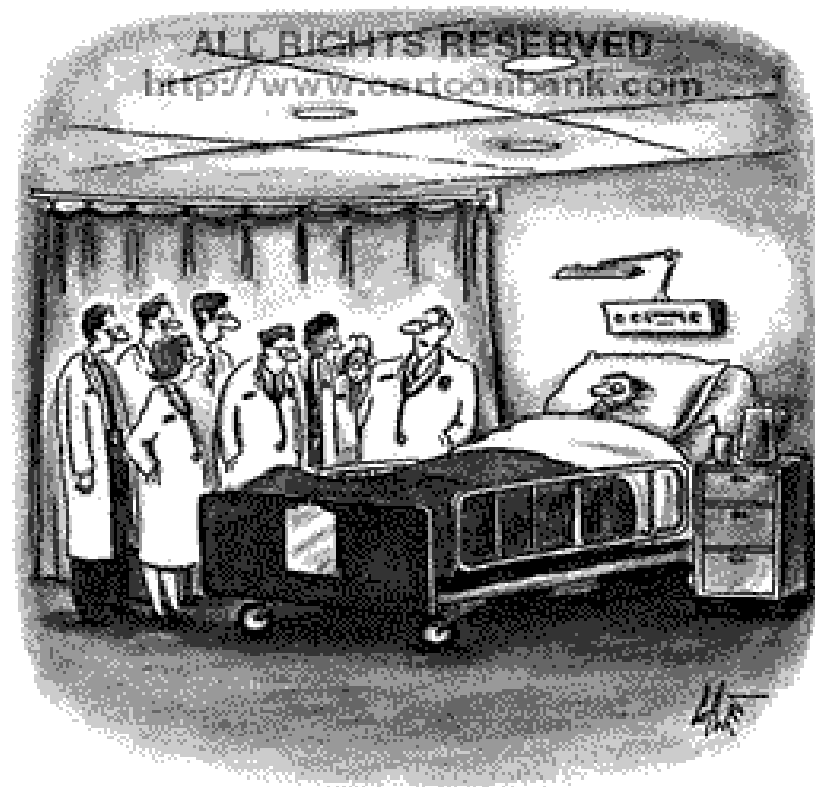


THE ISSUE



Psychiatric Disease and Insurance

Insurance provides a way of controlling risks. By pooling, and so transferring risks, those who turn out to suffer uncertain harms can be assured in advance that they will be helped if those harms arise. The impressive scenario of the current and future health impact of psychiatric diseases has obviously affected the world of insurances. The possibility to reduce uncertainty in dealing with risks of psychiatric diseases by using genetic information is certainly attractive.



"This patient has a rare form of medical insurance."



Today...

- Private insurances prefer to exclude, or to insure with many limitations, risks related to mental disturbances.
- Public health insurances cover only some major risks related to mental disturbances.



The reasons are:

- 1) Arguable diagnostic criteria and disease classification; poor capacity to discriminate between different diseases and syndromes;
- 2) Lack of elective treatments and difficulties in evaluating outcomes;
- 3) Blurred distinction between normal and abnormal behaviours, between medical and social deviance.



Tomorrow...

- Genetic information may lead to less uncertainty by allowing to identify groups genetically predisposed to develop specific mental disorders, by making diagnosis more certain, by indicating more targeted therapies, by providing effective prophylactic strategies.
- The genetically predisposed may be asked to carry more of the burden of health care since they carry more of the risk, provided that the public system based on the principle of solidarity can cover those genetically predisposed who are not able to pay for the extra premium. It could allow insurance company to cover risks related to mental disturbances.



Affymetrix via AP



THE CHALLENGE



Genetic Discrimination

- Current ethical debate has been centred on individuals, and thus on the issue of discrimination
- Should an insurance company be able to charge higher premiums to those genetically predisposed to disease? Should they even have access to a policyholder's genetic information? Do we want these private actors to have access to better information?
- Yet discrimination is not probably the main issue. Indeed each of these circumstances could be easily avoided by genetic privacy and anti-discrimination legislation.
- The crucial issue is the use of genetic information in the context of the overall health care debate.



Uncertainty as source of social ethics

- Uncertainty has become integral to our society. We depend on uncertainty for moral comfort, for social inclusion and for protection of human society. The rational use of genetic information will erode some of the layers of uncertainty that have surrounded us in the past, exposing vexing moral problems. As our knowledge of risk is focused from generic groups to individuals, the burden of mitigating risk will inevitably fall increasingly on individuals.



Insurance and Risks

Both publicly organized and commercial insurance provide standard ways of securing fundamental ethical values such as solidarity and mutuality. Commercially-based insurance, where the premiums depend on risk level, is chiefly based on mutuality, while public insurance is chiefly based on the principle of solidarity.



**"Don't even bother reading the fine print.
We've included it merely for the sake of tradition."**



Solidarity and Mutuality



- It is not only individual liberty that may be threatened by a shift in responsibility for reducing risk from society to individuals. By focusing so heavily on reducing risks to human health at the cheapest cost, we may be led to ignore other values, as those values of solidarity and mutuality that ethically justify the insurance system. Insurance corporations do not exist just to make profit for investors. They provide a service. Obviously they do so in order to make a profit, but their primary object is their function.



Corporate Ethics



- What will insurance corporation mission become in the genomic era? Uncertainty has forced human society to share; will we make the conscious choice to continue sharing societal burdens even as more of the uncertainty is cleared away?
- My point is thus that contemporary genetics has more to do with corporate and societal ethics rather than with standard bioethics.



Future Agenda



- Psychiatric Diagnosis (reliability and accountability)
- Treatment of mental disorders (cost-effective and elective treatments)
- Distinction between medical and social deviance (substance abuse, antisocial behaviours, suicide, etc.)



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