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Summary and Recommendations

Predictive Genetic Diagnostics as an Instrument of Disease Prevention

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Main Office: Emil-Abderhalden-Straße 37, 06108 Halle (Saale)
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acatech – DEUTSCHE AKADEMIE DER TECHNIKWISSENSCHAFTEN
Main Office: Residenz München, Hofgartenstraße 2, 80539 München
Berlin Office: Unter den Linden 14, 10117 Berlin

Berlin-Brandenburgische Akademie der Wissenschaften
Jägerstraße 22/23, 10117 Berlin

Union der deutschen Akademien der Wissenschaften
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Predictive Genetic Diagnostics as an Instrument of Disease Prevention

Summary and Recommendations

Preface

The early recognition of treatable illnesses is playing than ever-increasing role in modern medicine. Predictive genetic diagnostics, combined with rapidly developing analysis methods and the sequencing of entire genomes in this respect, represents new territory.

The central task of the Nationale Akademie der Wissenschaften is to deal with such themes and questions, with which the society is entering new territory, and point out science-based recommendations in order to answer them.

With this statement, Leopoldina - Nationale Akademie der Wissenschaften, acatech – Deutsche Akademie der Technikwissenschaften and the Berlin-Brandenburgische Akademie der Wissenschaften (for the Union der deutschen Akademien der Wissenschaften – Union of German Academies of Sciences and Humanities) is tackling a subject, which is extraordinarily relevant and controversially discussed in society.

The statement explores the wider field of predictive genetic diagnostics from various sites. In light of the current state of knowledge, opportunities and limits will be considered with as much care as the medical, ethical, economical and legal dimensions of predictive genetic diagnostics.

Prof. Dr. Jörg Hacker — *President of Leopoldina*

Prof. Dr. Reinhard F. Hüttl — *President of acatech*

Prof. Dr. Günter Stock — *President of BBAW and Akademienunion*

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Prof. Dr. Urban Wiesing	Institut für Ethik und Geschichte der Medizin,
	Universität Tübingen

The report was compiled with the collaboration of	
Dr. Christoph Engel	Institut für Medizinische Informatik, Statistik und
	Epidemiologie, Universität Leipzig
Dr. Sabine Herterich	Institut für Klinische Biochemie, Universitätsklinikum Würzburg
Prof. Dr. Bernhard Horsthemke	Institut für Humangenetik, Universitätsklinikum Essen
Dr. Poupak Javaher	Institut für Humangenetik, Medizinische Hochschule Hannover
Prof. Dr. Thomas F. Wienker	Institut für Medizinische Biometrie, Informatik und
	Epidemiologie, Universitätsklinikum Bonn

Academic Administration	
Dr. Ruth Raff	Institut für Humangenetik, Universitätsklinikum Bonn
Dr. Kathrin Happe	Leopoldina – Nationale Akademie der Wissenschaften, Halle (Saale)

The statement was adopted by the standing committee of the Nationale Akademie der Wissenschaften on 17th September 2010.

Review Panel	
Prof. Dr. Dr. Henning M. Beier	Institut für Molekulare und Zelluläre Anatomie,
	Universitätsklinikum Aachen
Prof. Dr. Jens Reich	Max-Delbrück-Centrum für Molekulare Medizin, Berlin-Buch
Prof. Dr. Otmar Schober	Klinik und Poliklinik für Nuklearmedizin, Universitätsklinikum
	Münster

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Summary and Recommendations

Preamble

Predictive genetic diagnostics are part of an individualised medicine. In connection with extraordinarily efficient analytical methods through to the sequencing of entire genomes, predictive genetic diagnostics represent new territory for society. They are subject to the largely accepted and, in many cases, stipulated ethical principles of medicine: predictive genetic diagnostics should help people remain healthy, to regain their health or, at least, to alleviate the consequences of illness. The person being examined must agree voluntarily to each diagnostic investigation after being provided with information and consultation.

The three academies responsible for this statement consider it necessary to inform society, politics, funders of research, the medical profession and health insurers about the chances, limits and risks of predictive genetic diagnostics. During the preparation phase of this statement, the Deutsche Bundestag adopted the Gendiagnostikgesetz (GenDG). Due to the fact that some regulations of this law concern predictive genetic diagnostics, these regulations will also be commented upon.

Self-Determination

1. The medical significance of predictive genetic diagnostics for individual people emerges especially when an illness is predicted with a high probability through a genetic examination and can be successfully prevented or treated through prevention or early treatment. In addition, predictive genetic diagnostics can be advantageous for the life planning of a person.

see chapters 3, 8, 9

Predictive genetic diagnostics must only be carried out at the request of and in the interests of individual people.

2. ***The Academy Group expressively rejects eugenic ideas, such as the aim of wanting to eliminate certain genes from individual genomes or wanting to systematically "improve" the human gene pool.***

see chapters 2, 3, 5, 8, 9

Responsible Handling of Information from Genetic Analyses

3. In the future, systematic analyses (array technology, high-throughput sequencing) will be available in genetic diagnostics. In doing this, more information will sometimes be generated than is necessary for the intended examination. If such an "excess of genetic information" is conceivable and generated with the informed consent of the person being examined, a decision must be made jointly with this person in advance as to whether this information should be a) immediately used in a specific manner, b) destroyed or c) saved for the time being in an unused state.

see chapters 5, 9

The problem of dealing with an excess of genetic information should be discussed appropriately with the person concerned and should bring about their "enlightened decision".

4. Longer-term storage of genetic information can be wise because the information can gain in importance for the health of the examined person in the future. Storage has both technical and legal aspects. Genetic information is subject to the power of disposition of the examined person. In order to be able to use new insights in genome research for the benefit of the examined person, the examined person should have the opportunity to undergo a secondary analysis of the saved sequence information at a later point in time.

see chapters 5, 9

The Gendiagnostikgesetz should take into account the aspects of long-term storage and subsequent analysis of the excess of genetic information. The medical files should only contain the genetic information and its interpretation, which relates to the indication for examination (primary genetic information). An excess of genetic information should not appear in the medical file or any doctor's letters.

5. In Section 14, the Gendiagnostikgesetz regulates the handling of genetic examinations and any data arising therefrom in the case of an incompetent person. A systematic genetic examination can be in the health interests of an incompetent person, for example to precisely diagnose a genetic illness. After the diagnostic aim has been achieved, the excess of genetic information should not be permitted to be interpreted in the case of a child or a temporarily incompetent adult because this would take the option of ignorance away from the examined person. However, the excess of genetic information should be saved in a restricted form to ensure that this group of people is not disadvantaged relative to an adult competent person. As soon as competency is bestowed, in the case of an examined child once he has reached his 18th birthday, the affected person should be able to decide of his own free will and after a genetic consultation whether the information a) is immediately used in a specific manner (primary information), b) destroyed or c) continued to be stored for the time being. If a person is deemed incompetent on a permanent basis due to a severe and non-reversible impairment to his intellectual abilities, the legal representative should decide according to No. 3.

see chapters 8, 9

The Gendiagnostikgesetz should accommodate for the considerations of genetic diagnostics in terms of longer-term storage of an excess of genetic information for an incompetent person and regulate the subsequent use. This recommendation presupposes that security against misuse is technically possible.

6. Samples from abroad are quite often sent to German laboratories for genetic examination. This is not regulated in the Gendiagnostikgesetz. If the law is applied strictly, de facto, the Gendiagnostikgesetz would transfer to foreign patients. The patient must be informed about the procedure in accordance with the detailed specification of Section 9. Alternatively, it would also be conceivable that a higher level of explanation, which is legally required abroad, would have to be "downgraded" to German law. Neither option is reasonable or practical.

see chapter 9

The genetic analysis of a sample acquired abroad by a German laboratory should be acceptable if the doctor that has sent the sample confirms that the person concerned has been provided with information about the being, scope and significance of the genetic examination in accordance with the legal regulations in the sample's country of origin and the person concerned has subsequently granted his consent. If the German laboratory has doubts about the assignment of the sample to the person concerned or a substantiated suspicion that there has been insufficient information provided or even misuse, then the laboratory must refuse to examine the sample sent.

Newborn Screening

7. In many countries, including Germany, newborns are systematically screened for genetically-caused and treatable metabolic disorders. The children concerned would become severely ill without the diagnostics but develop normally if treated correctly.

see chapters 1, 3, 9

The newborn screening is a successful example of the use of early recognition of illnesses using predictive diagnostics. Surveys for other genetic illnesses should be aligned with the newborn screening.

8. The Gendiagnostikgesetz considers the newborn screening as a genetic survey. Accordingly, since the Gendiagnostikgesetz came into force, the parents must be provided with a genetic consultation before blood is taken. Baby nurses and midwives, who previously took the blood, are no longer allowed to do this on their own responsibility. There are already indications that this is leading to the newborn screening not being carried out for some newborn babies. This can lead to life-long disability, which could have been avoided with early diagnosis and appropriate treatment.

see chapter 9

The Gendiagnostikgesetz should regulate the newborn screening separately and in accordance with the special circumstances. The person, who takes the blood sample as part of the newborn screening, e.g. the baby nurse or midwife, should be allowed to explain the aim of the examination to the parents. The examination should then be dependent on whether the parents provide written confirmation of their consent. If a normal result is provided, the parents would not need to be contacted again. If the findings, on the other hand, were abnormal, the parents should then be provided with extensive information and genetic consultation from the responsible doctor.

Monogenic Diseases

9. A series of genetically-caused and essentially treatable diseases, which have a high probability of occurring during the course of a life, can be predicatively diagnosed. These include, for example, hereditary forms of bowel cancer, breast cancer, ovarian cancer and thyroid cancer, the dominant hereditary hypercholesterolemia or the recessive hereditary haemochromatosis. In Germany, patients with these diseases have only been recorded in an unsystematic and incomplete manner to date. If the genetic diagnosis is not provided, the patients cannot be cared for appropriately.

see chapter 3

Organisational measures should be taken within the health system to more efficiently identify predicatively diagnosable illnesses, which are treatable, before the illness manifests, so that the patients concerned have the option of availing themselves of appropriate medical care. The Academy Group recommends appropriate research programmes should be set up in Germany.

10. The diagnostics, treatment and long-term care of patients with genetically-caused and essentially treatable illnesses and their families requires special knowledge and cross-sectoral care. To date, this structuring has not been sufficiently provided in the Federal and sectoral health system in Germany.

see chapters 3, 5

For the illnesses listed as examples in No. 9 and other illnesses, where particular expertise is required to care for the persons affected, more specialists in human genetics should be trained further, the genetic competence of specialists in the relevant clinical sectors should be improved and an adequate number of interdisciplinary and cross-regional centres of competence should be set up.

11. In the future, the technical development of genetic analytical procedures will make it possible to identify the risk of healthy people for treatable genetically caused and related illnesses through screenings along the same lines as the newborn screening test. The first experiences of this are available from abroad.

see chapters 3, 5

The Academy Group suggests research projects to identify the prerequisites and criteria that must be fulfilled in Germany in order to expand the range of genetic screenings on offer.

12. Before pregnancy, healthy people or couples can be interested in finding out whether they are genetic carriers of any recessive hereditary disease, even if there is no index case for such an illness in their family already. This is to assess the health risk of their own child. Such a heterozygote examination represents a new situation for our society with far-reaching ethical and social implications.

see chapter 5

For the time being, systematic heterozygote examinations with regard to the health risks for the children of the examined people should only be carried out as part of research projects. They should be embedded in secondary medical, ethical and social research in order to gain experience about the personal and social effects.

13. Before predictive genetic diagnostics can be integrated into the health system, evidence for their efficiency and cost effectiveness must be provided. This includes patient benefits, which arise from the diagnostics and connected prevention and care as well as the related costs.

see chapters 4, 5, 7

In parallel to the fundamental genetic research, evidence which verifies the effectiveness of predictive genetic diagnostics and takes into account the profitability should be compiled.

14. Without exception, the Gendiagnostikgesetz considers confidentiality for patients to be of a higher significance than the medical fiduciary duty towards relatives that have a high risk of developing a treatable, monogenic illness under certain circumstances. The doctor has no opportunity to verify whether the person affected by a genetic illness has passed on the information and medical recommendation of a consultation to his relatives. In individual cases, the doctor should weigh up which of the two legally protected interests should be categorised more highly: the duty of confidentiality or the medical fiduciary duty.

see chapters 8, 9

In very concrete cases and in cases of clear medical benefits, the doctor should consider appropriately indicating the risk of an at-risk person among the relatives of a patient with a treatable, hereditary illness and advising him to undergo a genetic consultation. The Academy Group recommends modifying Section 11, Paragraph 3 of the GenDG in this sense.

15. In Section 15, Paragraph 2, the Gendiagnostikgesetz prohibits the antenatal diagnosis of the embryo or foetus for an illness, which "will only appear after the 18th birthday of the child in accordance with the generally recognised state of medical science and technology". The formation of the law is incomprehensible. It is unwise to connect the appearance of an illness with "the general state of medical science and technology". Often, symptoms of a subsequent illness, which are discrete and not yet clinically relevant, can be determined before the 18th birthday. The formulation of Section 15, Paragraph 2 suggests that the legislator no longer wants to prohibit an antenatal genetic examination of a late manifesting illness as soon as more sophisticated analytical methods have succeeded in objectifying the appearance of the illness from very early on. From genetic consultation, the experience is that it is very rare for an antenatal genetic examination of a pregnant woman to be desired to test for the increased risk of a late manifesting illness.

see chapters 3, 9

Section 15, Paragraph 2 of the GenDG should be deleted due to the fuzzy definition of the age of onset.

16. In Section 12, Paragraph 1, Number 1, the Gendiagnostikgesetz stipulates that, in principle, the responsible medical person must destroy the results of genetic examinations and analyses ten years after the examination. However, before the expiration of the 10-year deadline, the significance of a certain genetic finding for an affected person at a later point in time cannot always be assessed. Genetic findings are often also relevant for family members. If the previously ill person (index case) died, they would be irretrievably lost. For the rest, it is a recurrent experience in human genetics that previously examined people and their family members inquire about their collected genetic findings long after 10 years because new viewpoints have arisen.

see chapter 9

It should be permitted to store the results of the genetic diagnosis without any concrete time limit, as was previously the case, in the interests of the person seeking consultation and their family members.

Multifactorial Illnesses

17. The majority of frequently occurring illnesses, such as diabetes mellitus, hypertension and arteriosclerosis, develop through a complex interplay of genetic factors and external influences. The development of these multifactorial illnesses can only be partially explained by genetic factors. Even if a series of gene variations, which contribute to the risk of illness, are already known, it must be ascertained that the scientific prerequisites for valid predictive genetic diagnostics are not currently fulfilled and the resulting clinical and health economical consequences are not yet sufficiently clarified.

see chapters 2, 3, 5

The complete sequencing of the genome of well-defined patient groups with genetically complex illnesses in comparison with healthy people opens up the opportunity of identifying all differences relevant to illness in the DNA sequence. This research strategy can help to cover the genetic contributions to multifactorial illnesses. The difficulty in the interpretation of such, extraordinarily extensive data records is in distinguishing differences relevant to illness from irrelevant differences. The Academy Group recommends intensively setting up appropriate, systematic research programmes.

18. It is a long path from the discovery of an association between genes and an illness and the improvement of health ("translation"). Before a wide use of certain predictive genetic diagnostics is suggested, effective prevention or treatment for the illness in question must exist and a reliable diagnostic procedure must be developed. The patient must be properly advised before the test and the presentation of the results and the result must be confirmed. Sufficient specialist capacities must be available for the entire procedure.

see chapter 5

The Academy Group recommends promoting translational research as well as basic research. In addition, medical guidelines for predictive genetic diagnostics should be developed.

„Direct-to-Consumer"-Tests (DTC)

19. Genetic tests, as they are currently offered directly over the internet – so-called DTC-Tests ("Direct to Consumer" tests) –, largely have an uncertain scientific basis and do not tend to fulfil the requirements of adequate genetic consultation. The examining laboratory is also unable to check whether the DNA samples sent actually come from the person, who has issued the investigation assignment.

see chapter 5

DTC tests ("Direct to Consumer" tests) should not be permitted because they do not fulfil the requirements of medical and ethically acceptable predictive genetic diagnostics.

20. In the case of DTC tests, the same risks exist as for prescription medications, which are prohibited outside the expert groups with good reason.

see chapter 5

As for prescription medications, a ban on advertising should be anchored in the law for predictive gene tests.

Information of the General Public and Further Medical Training

21. The opportunities of genetic analysis will gain in significance for an increasing number of people in the future, particularly in terms of the prevention of illness.

see chapters 2, 3, 5

The population should be informed properly and continually about the possibilities and limits of genetic medicine, including predictive genetic diagnostics. The new findings of inheritance research should be presented in schools, in particular.

22. In their past education and further training, doctors on a whole have not been made familiar enough with the significance of genetics in medicine. However, the treating doctor must be able to recognise family illness risks in his patients.

see chapters 3, 5

The Academy Group recommends providing doctors with further training in genetic medicine using special measures. They must be in the position to recognise high-risk people for treatable hereditary illnesses and refer them to specialists for consultation, diagnostics and care.

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Deutsche Akademie der Naturforscher Leopoldina - Nationale Akademie der Wissenschaften
Emil-Abderhalden-Straße 37
06108 Halle (Saale), Germany
Tel.: +49 (0)345 472 39-0
Fax: +49 (0)345 472 39-19
E-Mail: leopoldina@leopoldina.org

Berlin Office:
Reinhardtstraße 14
10117 Berlin, Germany

acatech - DEUTSCHE AKADEMIE DER TECHNIKWISSENSCHAFTEN
Residenz München, Hofgartenstraße 2
80539 München, Germany
Tel.: +49 (0)89 5 20 30 9-0
Fax: +49 (0)89 5 20 30 9-9
E-Mail: info@acatech.de

Berlin Office:
Unter den Linden 14
10117 Berlin, Germany
Tel.: +49 (0)30 20 63 09 6-0

Berlin-Brandenburgische Akademie der Wissenschaften
Jägerstraße 22/23
10117 Berlin
Tel.: +49 (0)30 20370-0
Fax: +49 (0)30 20370-0
E-Mail: bbaw@bbaw.de

Union der deutschen Akademien der Wissenschaften
Geschwister-Scholl-Straße 2
55131 Mainz, Germany
Tel.: +49 (0)6131 218528-0
E-Mail: info@akademienunion.de