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ORIGINAL ARTICLE

The promises of genomic screening: building a governance infrastructure. Special issue: genetics and democracy

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Abstract New screening possibilities become available at a high rate, both useful and unsound possibilities. All screening programmes do harm, and only few have more advantages than disadvantages at reasonable cost. Horizon scanning is needed to identify those few possibilities with more pros than cons. Attunement is needed between actors involved: scientists developing new high-throughput screening techniques and treatment, health care workers, patients and consumers and governmental agencies. The product of a process of attunement may be a quality mark as a norm for professional conduct, rather than legal measures, as the field is moving fast. As actors may have varying perspectives, a governance structure is needed to develop an agenda that is agreed upon by all or most actors involved. A standing committee might oversee the evaluation of benefits and disadvantages in an integrated approach, taking evidence, economics and ethics into account. A proactive role of governmental agencies is needed to facilitate agenda setting and attunement. Policy making has to be transparent and open to stakeholder engagement.

Keywords Genetic screening · Clinical utility · Governance · Stakeholder involvement · Quality mark

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Introduction

In 1957, the US Commission on Chronic Illness defined screening as

> The presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment (Commission on Chronic Illness 1957).

Screening in medicine differs from diagnostic health care, where patients come to a physician because they experience a health problem. High expectations exist on the increasing possibilities for screening, involving both early disease detection and early detection of avoidable disease risk. In the first half of this paper, we will briefly sketch the dynamics of the field in terms of technological developments (using newborn screening as an example), societal changes and conceptual challenges. In the second part, we will then discuss the need for a governance infrastructure to

attune the promises of technology, the needs of patients and citizens, the responsibilities of governmental agencies and the experiences and expectations of health care workers.

The paper is mainly based on a presentation given in Lund, Sweden in the Genetics and Democracy series on the 5th of October 2009. The main source of the presentation is a report of the Health Council of the Netherlands: Screening: between hope and hype (2008). Two of the authors (MC, WD) were involved in the preparation of this report, respectively, as a member of the committee and of the staff of the Health Council.

The dynamics of the field

The dynamics of the field is determined by several overlapping factors. These include technological developments (genomics, imaging and related technologies) that allow for improved testing possibilities both for diagnostics and screening, demographic changes emphasising the need for disease prevention in specific (e.g. ageing) populations, societal developments informing the way screening is perceived as a means of risk management and developments regarding how and to whom screening is offered that challenge the classical definition of screening and the delineation between care and prevention.

Technological developments allowing extended screening programmes

Genetic screening can be performed in the different phases of life, including shortly after birth. Newborn screening (NBS) is an example of a health care setting where recent changes took place in many countries. NBS programmes have been developed to identify infants in whom early diagnosis may avoid irreversible health damage. In the Netherlands, a national newborn screening programme started with phenylketonuria in 1974, followed by congenital hypothyroidism in 1981 and congenital adrenal hyperplasia in 2000. As in many other countries, the development of tandem mass spectrometry (MS/MS) made it possible to screen for several other diseases, especially metabolic conditions, and in 2007, 14 disorders were added to the programme. Apart from developments in diagnostics such as MS/MS, also medical research had improved the therapies for severe diseases that affect newborns. The promises of the fast developments in genomics, proteomics, metabolomics and bioinformatics make it relevant to reconsider NBS programmes in many countries. An important question is the governance of this dynamic field: Who sets the agenda for reconsideration, who scans the horizon, and who decides? Attunement is needed between researchers who develop new technology, physicians who treat the patients and public health authorities who organise screening programmes in many countries (Achterbergh et al. 2007). Also, nonprofit organisations (www.marchofdimes.com) and organisations of patients and parents (www.ncfs.nl/index.php?id=000184) have actively engaged in the agenda setting.

In the Netherlands, the decision to extend NBS from 3 to 17 diseases was made by the Minister of Health after the advice of the Health Council of the Netherlands (2005). The committee that prepared the advice included experts in the fields of paediatrics, gynaecology, biochemical chemistry, genetics, public health, ethics and legislation. Advisors from the Ministry of Health and patient and parents organisations attended (some of) the meetings. The committee defined three categories:

- Considerable, irreparable damage can be prevented (category 1)
- Less substantial or insufficient evidence of the prevention of damage to health (category 2)
- No prevention of damage to health (category 3)

For disorders in category 1, if a good screening test was available, inclusion in the NBS programme would be advised. For category 3, NBS would not be advised. For category 2, different advices are conceivable. More research was advised for cystic fibrosis, where especially the specificity of the test was considered unsatisfactory. A large-scale pilot study was performed since leading to a proposal for a four-step screening procedure, and in 2010, the inclusion of cystic fibrosis in NBS was advised (Health Council of the Netherlands 2010). The publication of a report including the argumentation and the use of the three categories make the decision process and the governance transparent to a high extent.

Societal developments: risk and responsibility

Scientific progress and technological innovation have made new and better tests possible, but that alone does not explain the dynamics in the area of screening (Health Council of the Netherlands 2008). Health care systems are changing in many countries. Traditionally, medical professionals exercised the power to decide what should be done, with government monitoring quality and costs. New parties, including commercial players, have emerged, and governments and insurance companies increasingly stress cost-effectiveness. Sometimes, as in the Netherlands, this is accompanied by a focus on market incentives leading to a redefinition of roles and responsibilities, also with regard to screening. According to the official philosophy behind the politics of current health care reform, the increasing involvement of the market is intended to lead to a better quality and greater response to

patients' needs. But a consequence is also that screening may be offered without proper validation or evidence-based advice, as in the case of the so-called whole-body scans (Al-Shahi Salman et al. 2007; Health Council of the Netherlands 2008). Moreover, as a logical consequence of addressing patients as 'health care consumers', there is a growing emphasis on the personal responsibility of individuals to stay healthy and make an optimal use of the opportunities for prevention (Schmidt 2007). From a wider perspective, the rise of predictive and preventive medicine fits in with what the German sociologist Beck has termed a 'risk culture', meaning that the development of a more secular society and the fading away of a deterministic world view have made managing uncertainty a structural element of our lives (Beck 1992). Companies selling genetic tests direct to consumers may appeal to and reinforce anxiety about potential risk through their advertisements, while insurance companies may offer health checks and preventive testing as a service to attract more clients. In this modern risk culture with its increasing emphasis on individual responsibility for health, many people are receptive for the reassurance that they expect from screening, with hardly any attention to the potential disadvantages that screening may also have (Ransohoff et al. 2002; Schwartz et al. 2004).

Redefining screening

The Health Council of the Netherlands report 'Screening: between hope and hype' (2008) redefines screening as:

> Screening (…) involves the medical examination of individuals who exhibit no health problems with the aim of detecting disease, or an hereditary predisposition to disease, or risk factors that can increase the risk of disease.

While screening has often been offered in public health programmes, neither in the definition from 1957 mentioned previously nor in this definition the 'systematic offer' is mentioned. In the described dynamic cultural changes, opportunities for (genetic) screening develop in new contexts. Apart from national population screening programmes, public health care may offer screening to specific groups at risk, private practitioners may offer health checks and commercial parties may offer both screening services direct to consumers and do it yourself testing kits. A proper evaluation of the benefits and disadvantages of screening possibilities has not always been performed before these screening tests and programmes are made available, while it is certain that disadvantages always also exist. Especially direct-to-consumer tests have raised concern (European Society of Human Genetics 2010).

Blurring boundaries of care and prevention

Genetic testing in individual client-focused health care is done for diagnostic purposes, or because of increased risk, for instance if a family member has a genetic condition. Family testing offered systematically to all individuals on a family tree that has been traced both vertically and horizontally is a form of screening (cascade screening) and is aimed at prevention (Health Council of the Netherlands 2008). Screening for familial hypercholesterolaemia, which is already carried out in the Netherlands, is an example of this approach. Several other monogenic subtypes of common disorders could profit from a systematic cascade screening approach, especially in cardiogenetics (hypertrophic cardiomyopathy, long QT syndrome, arrythmogenic right ventricular dysplasia), oncogenetics (breast and ovarian cancer caused by BRCA1 and BRCA2 mutations, familial adenomatous polyposis), hereditary nonpolyposis colorectal cancer and diabetes (MODY subtypes, hemochromatosis) (Van El and Cornel 2011). Newborn screening may start as a public health screening programme, but can only be successful if health care for the patients identified is well in place. These are but a few examples of the blurring boundaries of care and prevention. Funding in many countries differs between screening programmes (often collectively funded public health programmes) and diagnostic health care (insurance), unless there is a national health care system. Regulations and legislation may also differ. This makes extension of screening programmes a matter of policy change on various domains.

The need for a governance infrastructure

Given the dynamics of the field, there is an urgent need for a governance infrastructure to attune the promises of technology, the needs of patients and citizens, the responsibilities of governmental agencies, the aspirations of commercial parties and the experiences and expectations of health care workers. In this connection, we use the term 'governance' as referring to the idea of a non-traditional way of public policy making, involving coordination of responsibilities between government and societal stakeholder networks rather than through classical hierarchical control (Mayntz 2003; Bennett et al. 2009).

The role of the government

Both encouraging sensible screening and protection against unsound screening are the duties of the government. To ensure that worthwhile screening is available to the population, it can be decided to include certain screening

programmes in a national screening package. While the field is changing fast, legislation to regulate or ban certain forms of screening may not be the most suitable means of protection against unsound screening offers. A fresh approach may include

- A standing expert committee on a national level to perform horizon scanning to identify new and promising screening possibilities, and
- A quality mark for responsible screening, based on scientific assessments of new developments and aimed at promoting responsible provision and responsible choices

Standing committee

A standing committee of independent experts could oversee the entire sphere of screening, proactively assess new developments on their merits, pick up on hiatuses in the development of knowledge and identify the risks of screening and produce comprehensible and accessible public information (Health Council of the Netherlands 2008). It would have to follow an integrated approach, assessing evidence, economics and ethics (Grosse et al. 2010). Several frameworks of screening criteria have further elaborated the Wilson and Jungner (1968) criteria developed for the World Health Organization in 1968. Some of the elements need to be made more explicit, such as the definition of a 'good test'. An acceptable sensitivity (more than 95%?), specificity (more than 99.99%?) and positive predictive value (more than 1 in 4?) need cut-offs. Evidence needed for evaluation includes whether early treatment leads to less mortality, morbidity, loss of weight, days in hospital, pain, suffering, etcetera and better quality of life. Economical evaluation needs agreement on the most relevant aspects of cost (cost of the programme compared to all health care expenditure? Cost per QALY?). Ethical aspects need to be discussed and agreed upon between actors involved to help implement screening programmes in an ethically sound way (for instance, with regard to NBS, relevant aspects include informed consent, unintended findings, information on carrier status). The balancing of pros (longer and healthier life) and cons (false positives, identification of mild forms) has to be part of health technology assessment (Hofmann 2008). The application of these frameworks demands evaluation before a decision is made whether or not to screen, but also monitoring of the performance of the programme once installed. Genetic screening policies have often been determined by technological capability, advocacy and medical opinion rather than through a rigorous evidence-based review process (Grosse et al. 2010). Decision making should, however, take into account the principles of ethics and opportunity costs. It is imperative that screening policy development is transparent and open to stakeholder engagement, not only from a democratic point of view but also to be able to draw upon the relevant knowledge of stakeholders.

Quality mark

To guard citizens against health damage from risky or unsound forms of screening, it is a key to inform them adequately. Consumers who want to buy a product can inform themselves for instance by checking the Conformité Européenne (CE) marking. The CE marking certifies that a product has met EU consumer safety, health or environmental requirements. However, in vitro diagnostic tests used in health care presently often have to be assessed only by the manufacturer to get CE marking. A more informative quality mark would have to refer to the clinical validity and clinical utility of both screening products and services. It is very important that professional groups and their scientific associations are closely involved in the development and implementation of such a quality mark. This will not happen spontaneously, but will have to be actively encouraged by a powerful central body (Health Council of the Netherlands 2008). A quality mark would have to be based as much as possible on existing guidelines and standards, while in turn the development of such guidelines and standards could serve as a norm for professional conduct, or even a 'code of conduct'. The existing schemes of quality control, accreditation or certification, development of standards and recognition of competence are available in several health care and laboratory settings. Information to the public accompanied with education of professionals, together with exposure of both good and bad examples of screening practices, might lead to public trust. Examples of quality marks or similar developments can be found in the clinical utility gene cards (Schmidtke and Cassiman 2010), EGAPP evaluation (Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group 2011), the activities of the USA Food and Drug Administration to evaluate direct-to-consumer genetic tests (Vorhaus 2011) and UK Genetic Testing Network (Kroese et al. 2010).

Conclusion

A strong governance framework is needed to both guarantee that sound screening is available and accessible to the public, while citizens are protected against the risk of unsound screening. A proactive role of governmental agencies is needed to facilitate agenda setting and attunement. Policy development should be transparent and open to the engagement of all stakeholders involved.

Conflict of interest The authors declare that they have no conflict of interest.

References

Achterbergh R, Lakeman P, Stemerding D, Moors EHM, Cornel MC (2007) Implementation of preconceptional carrier screening for cystic fibrosis and haemoglobinopathies: a sociotechnical analysis. Health Policy 83:277–286

Al-Shahi Salman R, Whiteley WN, Warlow C (2007) Screening using whole-body magnetic resonance imaging scanning: who wants an incidentaloma? J Med Screen 14:2–4

Beck U (1992) Risk society: towards a new modernity. Sage, London

Bennett B, Gostin L, Magnusson R, Martin R (2009) Health governance: law, regulation and policy. Public Health 123:207–212

Commission on Chronic Illness (1957) Chronic illness in the United States, vol 1. Harvard University Press, Cambridge

European Society of Human Genetics (2010) Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes. Eur J Hum Genet 18:1271–1273

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group (2011) Recommendations from the EGAPP Working Group: routine testing for factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. Genet Med 13:67–76

Grosse SD, Rogowski WH, Ross LF, Cornel MC, Dondorp WJ, Khoury MJ (2010) Population screening for genetic disorders in the 21st century: evidence, economics, and ethics. Public Health Genomics 13:106–115

Health Council of the Netherlands (2010). Neonatal screening for cystic fibrosis. The Hague: Health Council of the Netherlands. Publication no. 2010/01E. Available at www.gezondheidsraad.nl/sites/default/files/201001E.pdf. Accessed 4 Jun 2011

Health Council of the Netherlands (2005). Neonatal screening. The Hague: Health Council of the Netherlands. Publication no. 2005/11. Available at www.gezondheidsraad.nl/sites/default/files/05@11E.pdf. Accessed 4 Jun 2011

Health Council of the Netherlands (2008). Screening: between hope and hype. The Hague: Health Council of the Netherlands. Publication no. 2008/05E. Available at www.gezondheidsraad.nl/sites/default/files/200805E_0.pdf. Accessed 4 Jun 2011

Hofmann BM (2008) Why ethics should be part of health technology assessment. Int J Technol Assess Health Care 24(4):423–429

Kroese M, Burton H, Whittaker J, Lakshman R, Alberg C (2010) A framework for the prioritization of investment in the provision of genetic tests. Public Health Genomics 13(7–8):538–543

Mayntz R (2003) New challenges to governance theory. In: Bang HP (ed) Governance as social and political communication. Manchester University Press, Manchester, pp 27–40

Ransohoff DF, McNaughton CM, Fowler FJ (2002) Why is prostate cancer screening so common when the evidence is so uncertain? A system without negative feedback. Am J Med 113:663–667

Schmidt H (2007) Personal responsibility for health-developments under the German Healthcare Reform 2007. Eur J Health Law 14:241–250

Schmidtke J, Cassiman JJ (2010) The EuroGentest clinical utility gene cards. Eur J Hum Genet 18(9):1068

Schwartz LM, Woloshin S, Fowler FJ Jr, Welch HG (2004) Enthusiasm for cancer screening in the United States. JAMA 291:71–78

Van El CG, Cornel MC (2011) Genetic testing and common disorders in a public health framework. Recommendations of the European Society of Human Genetics. Eur J Hum Genet 19:377–381, On behalf of the ESHG Public and Professional Policy Committee

Vorhaus D. Update: FDA taking another (public) look at DTC genetic tests. Genomics Law Report 2011. Available at www.genomicslawreport.com/index.php/2011/02/08/update-fda-taking-another-public-look-at-dtc-genetic-tests/. Accessed 4 Jun 2011

Wilson JM, Jungner YG (1968) Principles and practice of screening for disease. World Health Organization. Geneva, Switzerland. Available at whqlibdoc.who.int/php/WHO_PHP_34.pdf. Accessed 4 Jun 2011