Journal of Risk Research

ISSN: 1366-9877 (Print) 1466-4461 (Online) Journal homepage: informahealthcare.com/journals/rjrr20

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To cite this article: Mats G. Hansson, Frederic Bouder & Heidi C. Howard (2018) Genetics and risk – an exploration of conceptual approaches to genetic risk, Journal of Risk Research, 21:2, 101-108, DOI: 10.1080/13669877.2017.1382562

To link to this article: https://doi.org/10.1080/13669877.2017.1382562

Published online: 24 Nov 2017.

Journal of Risk Research, 2018
Vol. 21, No. 2, 101–108, https://doi.org/10.1080/13669877.2017.1382562

EDITORIAL

Genetics and risk – an exploration of conceptual approaches to genetic risk

Many readers of the *Journal of Risk Research* may be aware of the surge in studies since the middle of the twentieth Century that have analysed different types of risks from nuclear energy to vaccines and from space travel to radon in homes. In recent years, scholars have become increasingly preoccupied with the need to better communicate 'dreaded', 'complex' and 'systemic' risks in post-trust societies where confidence in science and institutions has become fragile (Löfstedt 2005). Over the last decade, the so-called genomic revolution is raising new questions for risk research. Information about our personal genetic make-up may be perceived as opportunities to discover more about our risks of developing multifactorial diseases such as diabetes and cancers. Furthermore, genetic information is personal yet shared by many relatives and is multi-generational. The information is intimate in a way since it comes from our own body, yet it may also seem very unfamiliar and ambiguous for those who are unaware of the science of genetics and genomics and the ultimate meaning of the results. A more thorough attention to the relationship between genetics and the notion of risk is therefore pertinent at this time, in order to accompany the recent developments in human genetics, including the fields of genomics and epigenetics. This special issue provides a multi-disciplinary view of different concepts of genetic risk and genetic risk information. It regroups the work of scholars from the social and medical sciences as well as humanities who share a common purpose: exploring conceptual approaches and advancing empirical investigations about genetic risk as a way to better understand its different meanings and uses in different domains.

Dealing with situations of risk is a characteristic of modernity (Beck 1992). The notion of risk here is related to special risks of technological progress, and the use of technology such as nuclear power as well as the use of legal, socio-economic and technical concepts to manage the risk (Slovic 1987, 1993, 2010; Behrens, Pigeot, and Ahrens 2009). In a risk society, everybody can be affected by adverse events and as such, society evolves measures for risk management. Genetic risk has a double structure, with individual health risk connected to genetic information as well as individual health behaviour on the one hand and social aspects of public health on the other hand. The individual meaning ascribed to such events as well as the (normative) evaluation can vary broadly. Individual interpretation doesn't necessarily match scientific risk assessment (Hansson 2004; Möller 2012). The evaluation of risk varies between persons but also with regard to time and place; anticipating a possible future event can differ significantly from the evaluation of the same event that has already taken place. Furthermore, cultural and social factors have an impact on the evaluation of adverse events and risk and need to be taken into account when discussing risk communication (Fischhoff 1995; Renn 2008a, 2008b; Bennett et al. 2010).

The complexity of genetic risk and its communication

Information about risk(s) and the understanding of risk are an intrinsic part of medical practice as there is no medicine, treatment or intervention that involves only benefits. The interpretation and communication of risk information are complex tasks in traditional clinical settings and this is accentuated with the recent development of high-throughput approaches in genetics and genomics, which allow for the generation of large volumes of sequencing data and consequentially, a potentially large volume of genetic risk information. This development contributes to the hopes and development of individualized genetic- or genomic-based health advice and the selection of optimal treatment and prevention. However, with the use of genetic or genomic data, there are also concerns: public understanding and the support of autonomy when making decisions, stigmatization, the provision of risk information that is not actionable, and the fact that such information may give rise to unrealistic expectations, misunderstanding and/or anxiety. There are several concrete examples about this rapidly emerging problematic situation including the potential misunderstanding of consumers purchasing genetic testing from a direct-to-consumer genetic testing company; the problems stemming from biomarkers that do not completely explain the risk of developing a disorder or the usefulness of a treatment for all patients; the complexities of supporting probands at increase risk of developing a disorder to discuss the implications for family members; the ethical, legal, social and logistical problems surrounding the return of results, including incidental findings and variants of unknown significance when using whole genome or whole exome sequencing.

Traditionally, genetic testing was confined to specialist medical genetic services, focused on relatively rare, inherited diseases caused by highly penetrant causal mutations (e.g. Mendelian disorders such as Tay-Sachs, Huntington Disease or Cystic Fibrosis). In contrast, common complex disorders such as heart disease, diabetes, arthritis and cancer are usually the result of variations in different genes, each contributing some portion of the genetic susceptibility, acting in concert with environmental, including epigenetic factors. Some of the environmental factors might be changeable (e.g. smoking, nutrition, exercise, alcohol intake) while others are less able to be changed (such as environmental pollution or psychosocial stress). The complexities (and current uncertainties) of identifying and understanding the interplay between (multiple) genetic and environmental factors also contribute to the difficulties of risk assessment and communication in genetics.

Ethical and psycho-social issues of genetic risk information

There is extensive research on the psychosocial effects and ethical implications of genetic testing, both for pre-symptomatic individuals and for different disease groups, e.g. (i) how individuals and patients understand their risk of disease after testing and genetic counselling (Nordin et al. 2002; Berglund et al. 2003; Lidén et al. 2003); (ii) their emotional responses to the information (Arver et al. 2004); (iii) the effects of the information on aspects related to quality of life (Liljegren et al. 2004); (iv) their uptake of recommended risk-reducing strategies (Gahm, Wickman, and Brandberg 2010); and (v) ethical implications (Hansson 2010; Hansson et al. 2006; Pinxten and Howard 2014). Furthermore, recent reviews are available regarding psychosocial effects of testing in general (Vansenne, Bossuyt,

and de Borgie 2009; Collins, Wright, and Marteau 2010), for different diseases (Hamilton, Lobel, and Moyer 2009), for developmental disorders (Willcutt et al. 2010), for cardiomyopathy (Skrzynia, Demo, and Baxter 2009), for hereditary cancer syndromes (Shulman 2010), and regarding the effects on children and the family (Wiseman, Dancyger, and Michie 2010).

Particularly relevant psychosocial implications of genetic risk information from this literature include:

- Patient estimates of relative risk are at odds with what clinicians believe patients to have understood. Genetic counselling may improve understanding of risk information, yet a significant proportion of patients still misunderstand the meaning of risk information returned to them.
- Numeric probabilities are interpreted differently in different contexts such as family history, aetiology, environmental factors, stress and worry.
- The nature of the outcome will influence risk perception and understanding. For example, the severity of the disease and the lack of effective treatment may lead to risk estimates being described by patients as considerably higher compared with outcomes less severe even when objective risks are the same.
- Descriptors of risk such as 'likely' or 'unlikely' and 'high', 'moderate' or 'low chance' may not be related to objective risk estimates ('likely' may imply perception of probabilities between 0.5 to 0.99 and 'low chance' is conceptualized differently by doctors and probands). There is an asymmetric loss of information content in that the more undesirable an outcome is, the more costly are underestimates for the patient or the proband (Austin 2010).
- Affective outcomes of genetic information and counselling, e.g. satisfaction, being at ease, need to be taken into account in risk information strategies.

Currently, there is no evidence that information from genetic tests about health risks will lead to a change of behaviour (Marteau et al. 2010). Further, cultural and social factors have an impact on the evaluation of adverse events and risk and need to be taken into account when discussing risk communication, as well as affective elements (Fischhoff 1995).

The need for conceptual analysis

Given the aforementioned issues and complexity, the communication of genetic risk information to different publics must be well informed; it should include consideration for the ethical issues and psychosocial effects of receiving risk information as well as the abilities, attitudes and preferences of those receiving the information. Before conducting such studies, conceptual clarifications including notions related to (genetic) risk, uncertainty, harm, loss and responsibility are crucial to properly inform, delineate and support the research questions and research methodologies. The *Mind the Risk* project (http://www.crb.uu.se/mind-the-risk/publications/) is an international research project funded by the Swedish Foundation for Humanities and Social Sciences lead by the Centre for Research Ethics and Bioethics at Uppsala University (Sweden, http://anslag.rj.se/en/fund/46205). Through a multi-disciplinary research programme, with increasing trans-disciplinary input from researchers working at internationally recognized academic centres throughout

Europe, the aims of the project all revolve around the further understanding of genetic risk information from different academic and user-specific perspectives. These overarching aims include: (i) providing a rich philosophical and conceptual framework (including historical, sociocultural and psycho-cultural analyses) of (genetic) risk information; (ii) conducting empirical investigations to obtain the perceptions and preferences of different stakeholder groups about genetic risk information; (iii) conducting continuing ethical analyses of risk in genetics and genomics. The work involved in achieving these aims may guide regulation and management of genetic risk (and other related risk) information in various settings including public health-based research and clinical services as well as commercial settings (i.e. direct-to-consumer genetic testing).

Beside the analysis of factors influencing the individual perception of risk, potential psychosocial–ethical impacts and possible coping strategies, a philosophical analysis of risk and risk communication also needs to take the different theoretical perspectives of risk into account. Risk and uncertainty are distinctly different. One approach to differentiate the two concepts is to define risk as linked to a known probability of possible outcomes whereas with uncertainty the probability is unknown. However, in medical contexts, there is rarely a thorough knowledge of probabilities assigned to the different outcomes (Palmboom and Willems 2010). The term risk is often used even when probabilities are unknown, and the distinction between risk and uncertainty becomes unclear. Risk communication in clinical settings has to deal not only with the already complex statistical information of probabilities and different ways to calculate risk (Behrens, Pigeot, and Ahrens 2009) but also with the problem of uncertainty and trust (or mistrust) in scientific knowledge about these probabilities, as well as the trust in the clinical practice of handling risks that may be at stake. The relationship between risk and uncertainty is important, and as such, it is discussed in several papers of this issue. They map out the broad variety of possible perspectives on the meanings and distinction between risk and uncertainty. Authors discuss the applicability of the different theoretical approaches to the field of genetic risk information and analyse strength and weaknesses of different definitions of risk and uncertainty when dealing with genetic risk information. One of the most relevant discussions in this field is whether uncertainty is inherent to risk and therefore risk analysis is fundamentally about the appraisal of uncertainty and its management (Morgan 1990) or whether risk is a distinct form of uncertainty. In Han's concept of uncertainty (Han, Klein, and Arora 2011) which was developed for the medical field, the authors understand risk as a (sub)case of uncertainty open to probabilistic assessment. They stress that many aspects of uncertainty are inherent to medicine and will persist even with new research results and routines and thus cannot be transformed into risk (as per their definition of it). This is in contrast to other contributions in this issue where risk and uncertainty are used to mark different levels of available information for risk communication.

Moreover, new insights from social epistemology problematize not only the already mentioned problem of social construction of risk, but also how competing forms of knowledge production and value assessment are being considered (Renn 2008a, 2008b). This is especially true in the field of health care, where not only single agents are acting, but also social groups such as professions, patient collectives, political stakeholders or companies. Risk is not only assessed in different ways but there are various coping strategies individuals apply to deal with risk

(information). They range from insurance and other safety measures to integrating risk as a source to escape the 'ennui' of a modernized, controlled world or simply ignoring risk. Whereas some risks are part of individual risk behaviour—like smoking—some risks can potentially affect anybody. Traditionally diseases—especially common diseases like cancer, but also infectious pathogen borne diseases—have been conceptualized as the later and a potential risk for anybody. New research on genetic disposition to develop a certain disease changes the idea of how diseases and risk are connected (Lemke 2004).

Exploring the conceptual approaches

The academic articles of this special issue represent a broad variety of approaches to genetic risk information; they discuss theoretical approaches from fields of risk research, sociology and philosophy of risk as well as medical risk. This is supplemented by empirical views on concepts of genetic risk information prevalent in medical practice both from the perspective of professionals and the perspective of patients. Furthermore, the papers discuss the applicability of the different concepts on a variety of conditions for which genetic tests are offered using examples ranging from Mendelian to common complex disorders. They also consider different contexts for testing including the diagnostic testing of adults and the preconceptional testing (or screening) of (potential) parents before conception or pre-natally. While these articles show the heterogeneity of what is often subsumed under the—seemingly uniform—term 'genetic risk', they also show common features that need further exploration in order to fully assess genetic risk information.

The special issue begins with an editorial by *Inthorn*, which offers a basic map of the different uses and meanings of the term risk in medicine and in genetics. She describes different areas where genetic testing can be used and what the 'risk' involves in each scenario.

Howard and Iwarsson use the taxonomy of uncertainty developed by Han and colleagues (2011) to analyse and describe where different notions of uncertainty (including risk) arise in genetics and genomics. They take a closer look at whole genome sequencing (WGS) and show how uncertainty is inherent to the use of this high-throughput approach. They identify the complexity of the technology and the process of WGS, as well as the unprecedented large amounts of data and the unknowns surrounding their meaning as a large contribution to uncertainty

From this conceptual analysis of uncertainty in genomics, Falahee and colleagues as well as Bayliss and colleagues provide empirical data on different stakeholders' perspectives on genetic risk and predictive testing. *Falahee et al.* provide a qualitative meta-synthesis of health care professionals' views on risk from genetic testing for the prediction of chronic disease. Results show that experts struggle (among others) with the utility of genetic risk information, misunderstanding of risk information by patients, as well as the psychosocial impacts and ethical issues of risk information. Complementing this work, *Bayliss et al*. offer a meta-synthesis of qualitative research to explore patient and public perceptions of predictive testing for chronic inflammatory diseases. The study identified a number of barriers to predictive testing including concern about a lack of confidentiality around the use of risk information; a lack of motivation for change; poor communication of information; and a possible (negative) impact on emotional well-being. The authors also offer guidance on how to overcome these barriers by using a patient-centred approach.

Bouder addresses the concept of risk tolerance in relation to genetic information. By drawing on theoretical approaches from the field of risk research, his inquiry looks at key concepts such as 'individual' and 'societal' risk, 'risk acceptability' and 'risk tolerability'. He also offers a first attempt to hypothesize how key elements of individual and societal risk analyses may influence genetic risk tolerance. As a conclusion, Bouder suggests some guiding principles to support forthcoming policy-making in the area of genetic risk.

Hansson offers an ethical analysis focussed on four problematic issues in genetic risk assessment and management: (1) the tensions between individual and societal risk-benefit analysis; (2) consideration for the protection of sensitive groups; (3) measures to handle risks associated with teratogenic, embryotoxic and foetotoxic agents; and (4) new issues relating to equity and to group-based risk assessment in the context of genomic medicine. In his ethical analysis, he also points at possible societal change and issues of justice and thus goes beyond the idea of individual risk assessment in doctor–patient communication, linking ethical thoughts to the conceptual work on risk.

Discussion of risk-benefit analysis already touches upon normative aspects of risk that are further explored and analysed more in depth by two papers:

Kihlboom takes a closer look at the relationship between risk and values and discusses different theoretical understandings of values (welfarism and capability approach) and their contribution to a concept of risk. A theoretical understanding of how values are integrated into the concept of risk may help to get a better understanding of risk-benefit assessment and underlying normative assumptions.

Based on a historical overview on the growing importance of the concept of responsibility in genetic medicine, *Schicktanz* presents a concept of responsibility as an analytic tool. She presents how this can facilitate the understanding of the problem of uncertainty as well as the temporal dimension of genetic risk.

Finally, Oliveri and Pravettoni explore whether hermeneutic phenomenology and methodology could provide a deeper understanding of an individual's experience of having an inherited predisposition. Drawing on the data from a literature study, the authors found that an Interpretative Phenomenological Analysis could be a good methodology to gain access to an individual's lived experiential world.

Funding

This work was supported by the Riksbankens Jubileumsfond [grant number M13-0260:1].

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