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Translating genetics beyond bench and bedside: A comparative perspective on health care infrastructures for 'familial' breast cancer

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ABSTRACT

Developments in genomics research are considered to have great potential for improving health care – making genomics an urgent site for translational efforts. Yet while much emphasis is put on the technical challenges of translation, there is less scholarly attention for the social infrastructures through which novel medical interventions may be delivered to patient populations. Reflecting the idea that cancer is at the frontier of genomic applications in health care, this paper explores how the assessment of familial breast cancer risks was 'translated' into routine health care in Germany, the Netherlands and the United Kingdom. The paper identifies regulation, institutionalization and standardization as key mechanisms of translation that find distinct expression in particular sociocultural contexts and shape both the social and technical making of genomics into routine clinical practice. Translation is therefore an area of social as well as technical concern, and therefore requires collective decision-making.

1. Introduction

Recent achievements in basic genomic science are widely heralded as carrying great clinical potential – and therefore in need of translational support. Knowledge on the molecular mechanics and pathways of disease should contribute to more tailored forms of individual medical care, but it is widely acknowledged that this cannot happen without considerable investment in bringing advances from the laboratory 'bench' to the clinical 'bedside' (Niederhuber, 2010). In particular, the detailed understanding of human biological complexity at the molecular level is expected to contribute to further patient stratification and the delivery of care tailored to biologically differentiated patient groups. Rooted in genomics and systems biology, the future of medicine is often sketched in terms of the *preservation* of individual health, rather than *treating disease* in the aggregate population (Hood and Friend, 2011). Yet to arrive there, various technical and social challenges to translation need to be addressed to 'bridge the gap' between bench and bedside.

In recent years, the intricate complexity of such 'bridging' has increasingly been recognized, and translation reconsidered as a two-way road (Marincola, 2003) that should involve broader communities around bench and bedside (Cohrs et al., 2015). The challenge of making scientific knowledge beneficial for overall population health has consequently been defined as a continuum of various translational phases – especially in the context of genomics (Khoury et al., 2007; Schully and Khoury, 2014). For translation to proceed through the various phases, medical researchers call for investments in all of them, ranging from translation of basic science to clinical application (T1); on to evidence based practice guidelines (T2); evaluation in practice (T3); and population level evaluation of health outcomes (T4), respectively. Yet even while this approach to translation acknowledges the work that remains to be done for novel diagnostics or therapeutics to contribute to population health, the multi-phase model of translation remains attached to a technical (i.e. evidence-based) understanding of the problem (for a broader critique around this point, see (Van der Laan and Boenink, 2015)). Research in the social sciences, by contrast, has shown how translation efforts are always closely entangled with a broader social context that shapes how medical innovation, its application and its integration in health care delivery arrangements take shape (Vignola-Gagne and Biegelbauer, 2013). Moreover, the various phases of translation may relate and unfold very differently considering both the social configuration of research and clinical care and the specific domains of genomic research and medicine in which these efforts unfold (Gardner and Webster, 2016; Merriman and Molina, 2015). A more detailed understanding of specific sociocultural understandings of health and diseases and social preferences vis-à-vis the incorporation of particular novel (genomic) technologies in health care distribution is therefore required to fully understand how translation may benefit population health (Aarden et al., 2010).

This paper aims to contribute to a more detailed understanding of the intersections between social and technical dimensions of translation by investigating how genomic advances are delivered to populations in different health care contexts. It explores this question through a comparison of services available for risk assessment and follow-up for

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familial breast cancer predispositions in Germany, the Netherlands and the United Kingdom. Applications of genomics in the oncological domain are at the forefront of translating genomics from research to medical care (Dolsten and Soegaard, 2012; Bombard et al., 2013), both in terms of genomic approaches to cancer risks (related to germline mutations) and the development and characteristics of tumors (somatic mutations). While germline and somatic approaches to cancer genomics are different, they share certain characteristics of interest from the viewpoint of translation. Both (should) allow more sophisticated classification of disease (risk) into distinct subcategories and earlier intervention more tailored to affected sub-populations (Bydoun et al., 2014). At the same time, a focus on familial cancer risks allows us to see how uses of genomics are established as routines, how the limits of molecular technologies are confronted (since only around 30% of familial breast cancers has a known genetic background (Shiovitz and Korde, 2015; Foulkes, 2008)), and how technicalities of risk stratification intersect with the social dimensions of health care infrastructures to bring genomics to the population. Approaching translation of genomic technologies to patient care from this vantage point provides insight into the mutual influence between risk classification and health care delivery infrastructures and the social and technical dimensions of translation in distinct contexts.

2. The importance of health care infrastructure

The technocratic nature of much of the translation discourse – particularly in the domain of bench-to-bedside (Woolf, 2008) – reflects a 'technological imperative' that suggests that new technologies will by definition reshape health care. Yet various studies of the development of technologies in health care and beyond have shown how these commonly develop in close interaction with their social environment, with both technology and society coproducing each other (Jasanoff, 2004). In the context of complex health care environments that both shape and are shaped by advances in medical technology, a framework that understands the roads new technologies travel to become available to patients in particular clinical settings may be fruitfully understood in terms of *health care infrastructures.* This notion of infrastructure expands on Parthasarathy's study of 'architectures' for genetic testing for breast cancer in the United States and the United Kingdom (Parthasarathy, 2005). While she helpfully notes how structures of regulation, technology development and health care delivery influence how genetic tests are delivered in distinct forms to different segments of the population in these countries, the notion of infrastructure more explicitly considers the wider context of genetic tests and the more extensive range of issues that characterize 'translation'. These issues include culturally specific responses to how medical knowledge is made and incorporated in health care, which configurations of actors and mechanisms are involved in evaluating new diagnostics and therapeutics, how they are distributed, etc. (Daemmrich, 2004). These diverse socio-cultural elements collectively shape an infrastructure for translating genomics to patient care, a process that involves a balancing act between full development of technological possibilities and improving health for as large a part of the population as possible (Aarden et al., 2011).

The infrastructures that shape the translation of genomic technologies to health care delivery are highly context-specific. A powerful way to gain insight into the role of infrastructures in the later phases of translation is therefore to compare between different infrastructural environments. The comparison in this paper includes three Western-European countries – Germany, the Netherlands, and the United Kingdom – that are similar in many ways, but differ in several respects that are important to our purpose here. In particular the organizational structure of health care delivery and sociopolitical responses to advances in medical applications of genomics color the ways familial understandings of breast cancer have been adopted in health care delivery. We will encounter some of these differences in detail when discussing the infrastructures for delivering familial breast cancer diagnostics below, yet in broad terms we may identify two axes of difference. On the one hand, health care delivery in Germany and the Netherlands is based on (social) health insurance, where individuals pay a premium to an insurance company that purchases medical services on behalf of their collective membership. In the UK health care is funded through general taxation, with funds for the National Health Service (NHS) redistributed to regional purchasing authorities (Van der Zee and Kroneman, 2007). These different structures affect how financial resources are distributed, how decisions about reimbursement are made, and who is involved in making health care policies (Van Hoyweghen, 2014). At this structural level, Germany may further be distinguished from the other two countries by having a so-called 'double structure' of physicians employed by hospitals and those that are self-employed (a differentiation that roughly overlaps with the delivery of inpatient and outpatient care). Where it comes to political responses to the advent of genomics, the Netherlands and the United Kingdom may be grouped together as well, since in both countries the health ministries developed elaborate strategies for integrating genomics in health care. For various reasons, no strategy of that sort was developed in Germany. As we will see, these and more specific characteristics constitute the infrastructures that give shape to the translation of genomics to routine medical interventions – affecting both the social and technical configuration of genomics' contributions to population health.

3. Developing a comparative perspective

This paper deliberately takes a step back from the frontier of developments in cancer genomics to focus on the assessment of hereditary breast cancer risks and genetic testing for BRCA mutations in three European countries. It thereby seeks to answer a question that has received relatively little attention in discussions on how the translation of genomic knowledge can contribute to the improvement of population health. While various social scientists have pointed to the changes that affect research communities, clinical practitioners and the relations between genomics research and the attribution of meaning to genomic findings in the clinic (Rabeharisoa and Bourret, 2009; Harvey, 2011), the broader infrastructures for health care delivery, access and reimbursement of genomic technologies remain more obscure (Aarden, 2016). To address this void, the paper neither seeks to address only the cutting edge of advances in the field, nor does it seek to be comprehensive with regard to contributions genomics has made to understanding the complexity of breast cancer predispositions and progression of disease. The paper instead provides empirical evidence for the complex intersections between social and technical dimensions of how diagnostics are distributed. On that basis it proposes a way to explore the social dimensions of translation from, as it were, bedside to health care infrastructures. We may thereby gain insight into the establishment of health care delivery routines and how some of these routines may affect further incorporation of genomics in health care delivery in the future.

The paper focuses on the establishment of routines for the delivery of diagnostics and follow-up services for familial breast cancer risks in the first decade of the present century. Empirical material was primarily collected between 2005 and 2010, complemented with a short literature reviews to assess whether guidelines and standards for risk assessment have changed to a significant degree since the initial data collection was completed. While this should not imply that no important developments in breast cancer genomics have taken place since, medical evidence suggests that no radical change has taken place in the main risk categories (based on family history and identifiable gene mutations; (Shiovitz and Korde, 2015)). Moreover, taking a few years of distance allows us to clarify the origins of routines in specific contexts, without having them obscured by 'incomplete' evidence from recent and experimental approaches that are highly prevalent in health care systems' attempts to grapple with the significance of genomics for the future of medicine.

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