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VIEWPOINT

Rethinking biobanking and translational medicine in the Netherlands: how the research process stands to matter for patient care

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Biobanking has been identified as one of the key components of translational medicine, and while current models for translation tend to focus their attention on how the *products* of research projects are fed back into health-care practices, we suggest that in addition to that *the research process itself* can have beneficial effects on the delivery of high-quality health care by streamlining diagnostic and follow-up protocols, reduced patient waiting times, and facilitating data comparison across patients. This Viewpoint is based on experiences with, and observations of, the neurodegenerative component of a clinical biobanking initiative in the Netherlands called the *Parelsnoer Institute* (PSI), which links all eight of the University Medical Centers for harmonized and standardized collection and storage processes for multiple disease conditions.

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MODELS OF TRANSLATIONAL MEDICINE AND THE ROLE OF BIOBANKING

Since the completion of the Human Genome Project, considerable attention has been given towards the translation of genetic research and evidence-based practices into routine health care. This can take the form of new diagnostic protocols or assays,[1] and on rare occasions even new treatments.[2] Whereas these are evidently worthwhile outcomes of medical research, it is often the case that the translational expectations of research are not met, or in other cases take years – or even decades – to be achieved.[3–5] These challenges have led to the development of new initiatives such as the American National Center for Advancing Translational Sciences (NCATS),[6] as well as new umbrella disciplines such as translational science and medicine,[7,8] translational research,[9–11] and even subdisciplines such as translational bioinformatics[12,13] that report on new outlooks, translational successes, and failures. Recent research in the EJHG has also argued that biobanking – or the collection, storage, and use of biological materials for research purposes – 'can have a pivotal role in elucidating disease etiology, translation, and advancing public health'.[14] Within these institutional and epistemic developments, various models have been developed to facilitate the process and overcome translational challenges. For instance, in the case of genomic medicine a four-phase translational model has been advanced in which the discovery of a candidate health application (that is, translational research phase one, or T1) is developed into a evidence-based guideline (T2) that is disseminated and taken up in health practice or Phase IV clinical trials (T3), which are then monitored at the population level for 'real world' health impact (T4).[15] Whereas models similar to this have been influential in steering research and care, they tend to focus their attention on how the products of research projects (that is, health applications, guidelines, and so on) are – or can be – fed into health-care practices. In this Viewpoint, a different perspective on the benefits of translational medicine and biobanking is forwarded. We suggest that it is not simply the products – or outcomes – of research that stand to improve medicine, but, in addition to that, *the research process itself* can have beneficial effects on the delivery of high-quality health care. What our experiences with, and observations of, the collaborative Dutch clinical biobanking initiative called the *Parelsnoer Institute* (PSI) have shown is that improvements in patient care are also being gained through the establishment of the research infrastructure and its associated collection practices. The harmonization and standardization of collection requirements across all of the university clinical centers in the Netherlands have not only been mandatory for the construction of a high-quality biological research resource, but those same harmonization and standardization processes have also meant that clinical care has been ratcheted-up across all of the centers so that best practice becomes the standard practice.

THE *PSI* FOR CLINICAL BIOBANKING IN THE NETHERLANDS

The *PSI* was first established in 2007 with the goal of collecting high quality and standardized health data and biological material in a clinical setting from patients suffering from a set of originally eight (now 13 and counting) conditions such as diabetes, ischemic stroke, neurodegenerative diseases (especially Alzheimer's), hereditary colorectal cancer, and others, in all eight of the University Medical Centers (UMCs) in the Netherlands.[16,17] The idea is to integrate standardized data and biomaterial collection processes into routine care of each of these conditions in a harmonized way within and across all eight UMCs. Each patient visiting an UMC who suffers from a disorder associated with the PSI has biomaterial and health data included into the biobank – after consent – by default and without any extra burden. As such, PSI is the

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ultimate research infrastructure for all clinical research processes in the UMCs and has consequently been endorsed by the Federation of UMCs in the Netherlands. By capitalizing on the vast number of patients who are treated in these centers, the various disease-based collections can be strung together to create a resource for researchers within the UMCs – as well as others – to utilize, which is complete with sample populations that are well characterized, consented, and have tissue and data ready-to-use. The PSI is distinguishing itself from practices in oncology or rare diseases that have regularly integrated research in care settings by increasing the scope of conditions that are being collected, and through their ability to do all of this in care settings on a massive scale involving thousands of patients. Whereas collections of this nature are framed as important components in the process of translational medicine and the pursuit of personalized medicine,[9–11] it can be instructive to examine other positive patient benefits that *precede the results* of translational research. The PSI is an ideal location to explore the prospects for multiple patient benefits that can be associated with translational research because of its direct integration within all of the university hospitals in the Netherlands, and its organizational goals concerning translational work. What follows here are our some of our experiences derived from coordinating the PSI (that is, Scheltens), and from qualitative social science research with participants across the organization (that is, Douglas). The focus here is on how standardized and harmonized data and tissue collection processes – specifically within the neurodegenerative component of the PSI – have worked to increase the quality of neurodegenerative patient care across all eight of the UMCs.

HOW THE RESEARCH PROCESS STANDS TO MATTER FOR PATIENT CARE

Collection protocols were established within the PSI to standardize data and tissue from the diverse UMCs across the Netherlands. Whereas such protocols can be standard practice in multicentered studies, their imposition into the clinical setting has demanded alterations to clinical practices in many of the treating neurodegenerative centers within the UMCs. Often such impositions can be met with resistance because of disruptions in the routine clinical practices through which care is delivered; however, doing so as a part of establishing the PSI research infrastructure has led to positive alterations in both the diagnostic procedures for patients suffering from memory complaints, as well as their standardized follow-up care.

The process of harmonizing PSI research collection protocols (that is, defining the minimal data set) across the eight UMCs has required the harmonization of diagnostic work-ups.

The two centers that are jointly leading the neurodegenerative component of the PSI are the recognized centers of excellence for neurodegenerative care in the Netherlands. They had data and tissue collection practices for research purposes before the PSI, and as a result not many alterations in their diagnostic processes were needed. However, for the other UMCs, harmonizing data and tissue collection for the PSI have meant making numerous changes to their clinical routines, which have subsequently worked to streamline and improve their diagnostic procedures. For example, there is now a reduced number of visits needed for diagnostic procedures for any patient seeking help for memory complaints at any of the UMCs, and the entire process takes much less time than before. Other examples of positive changes included adopting a standard protocol for MRI in all centers in which all scans are sent to a central storage facility for future research. What is more, harmonized collection and diagnostic procedures mean that UMCs can more easily compare patient data with refine their diagnosis even before any research using the PSI biobank is conducted. Evidence that the establishment of the biobanking infrastructure has helped to improve the care process can be seen by most UMCs continuing to use the diagnostic protocol instituted by the PSI even after having satisfied their patient-recruitment commitments that were agreed upon at the start of the project.

The neurodegenerative component of the PSI concentrates its efforts in collecting data and material (that is, clinical, cerebrospinal fluid, blood, and MRI) over the course of the patients' disease development. Doing so has consequently meant structured and routinized follow-up clinical visits across all eight of the UMCs. To be sure, all of the UMCs conducted follow-up care on their patients; however, rarely was it performed in a methodological manner in which patients are seen at specified times, over a specified period of time, and re-examined in a thorough and verifiable way.

It is true that the harmonization of the PSI's neurodegenerative collection process, and concurrently its diagnostic work-up and follow-up procedures, is forcing some of its participating clinicians to adhere to specific standards of care by imposing actions that may not have been undertaken routinely (for example, conducting MRI or drawing cerebrospinal fluid). That being said, this is not just harmonization for the sake of collection; rather, it is an acknowledgment of a high standard of care and then raising other practices around the country to that standard. This has been confirmed by adoption of diagnostic procedures by other Dutch hospitals that are not participating in the PSI.

REFRAMING THE BENEFITS OF TRANSLATIONAL MEDICINE GOING FORWARD

The PSI has been established as infrastructure to facilitate translational research and medicine;[16] however, whereas conventional notions of translational medicine fixate on prospective beneficial impacts of integrating *research findings* into clinical practice, what has been stressed here is that the *research process itself* also has an important and beneficial role for patient care through its standardization of best practice across clinical centers. Whereas it is well known that other forms of research can lead to improvements in patient care through more regular visits, increased monitoring, and access to experimental interventions, these are often temporary or impermanent benefits that last only as long as the research project or clinical trial. Within the PSI we have seen alterations in routine clinical practices across treating neurodegenerative departments within the UMCs through their participation in this clinical biobanking initiative. In this case the establishment of a research infrastructure, and its associated collection protocols, has led to diagnostic and follow-up best practices in neurodegenerative care becoming standard practice within UMCs and beyond. When improvements in care resultant from these kinds of biobanking processes are taken into consideration, we can begin to reframe the expected benefits of translational endeavors and expand what we understand the role that the research process can have in the delivery of health care. What is more, the care benefits derived from the research process are more immediately observed than those derived from the findings of research projects, which can take considerable time to implement or commercialize. Being able to immediately demonstrate tangible care benefits to research participants is an important component of maintaining the trust of biobank donors, and demonstrating the value of research investments to funders.

To be sure there is widespread recognition of the importance of standardization in the

collection of biobanking samples for there to be success in translation of such biomaterial and data into health applications.[18] Furthermore, the PSI is not the only initiative that is uniting clinical sites for establishing research infrastructures for translational medicine. For instance, in the United States the Electronic Medical Records and Genomics (eMERGE) network was established in 2007 by the National Human Genome Research Institute (NHGRI) as consortium 'to explore the utility of DNA repositories coupled to Electronic Medical Record (EMR) systems for advancing discovery in genome science'[19] and has 'the ultimate goal of returning genomic testing results to patients in a clinical care setting'.[20] With that in mind, the PSI is an important example of how such standardized collection processes can not only work to create a high-quality research infrastructure, but also improve patient care.

COMPLIANCE WITH THE ETHICAL GUIDELINES

The social science research that was conducted as the basis of this manuscript was approved by the Medical Ethics Committee (Medisch Ethische Toetsingscommissie) of the VU UMC Amsterdam on 9 August 2010 as a part of the 'A wealth of data? Blurring boundaries and user-roles at the interface of genetic, medical, and personal information'.

CONFLICT OF INTEREST

PS is the Director of the Parelsnoer Instituut upon which this work is based. CMWD declares no conflict of interest.

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AUTHOR CONTRIBUTIONS

Both authors contributed to the writing of this work, whereas CMWD led in the literature review and data collection.

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