Second Consultation on Translation of Genomic Advances into Health Applications

The Impact on Advances in Genomics on Health Care

WHERE ARE WE AND WHERE ARE WE GOING?

March 6-8, 2014

Why this Consultation?

THE INCREASING PREVALENCE and the long-term implications of autism and related developmental disorders have made them a growing global public health concern. Major investments made by governments in scientific research are at the cusp of returning health and economic benefits. New scientific discoveries and rapidly evolving technologies for genetic analysis are now beginning to be used in clinics and hospitals. Other new technologies are just around the corner and rapidly making their way into health systems. Building on a previous workshop held in Toronto in 2010, our consultation, held in Cambridge (Ontario) on March 6-8, 2014, brought together experts from a range of disciplines to continue dialogue around health-systems and policy options that will support effective and ethically-sound translation.

Who attended?

A group of 50 basic, clinical and social scientists, health practitioners, ethicists, economists and community stakeholders from the UK and Canada attended the consultation including several world-leading experts. Complementarity of expertise was advantageous for covering the depth and breadth of complex issues surrounding genetic testing and for promoting dialogue across traditionally isolated disciplines, sectors, and geographies.

What did we learn from the consultation?

We focused on four contexts relevant for the impact of genomic advances on health care for autism and related conditions: advances in research; impact and utility within diagnostic services; clinical genetics and genetic counseling; ethics, public policy and health economics.

Advances in Research

A number of scientific and technological advances in genetics and genomics have high potential impact on health care. Very recent studies suggest that a relevant genetic finding can be identified in a subgroup of affected individuals. Improved genetic analysis enhances our ability to detect more genetic changes on a lower level of resolution, but they also result in greater volume of complex genetic information.

A key challenge in to understanding clinical significance of genetic changes is the lack of direct mapping between the genotype and individual outcomes, which are influenced by the environment as well as by the process of development itself. Similar

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genetic changes can lead to a variety of neurodevelopmental and psychiatric disorders, not only ASD; moreover such changes can sometimes be found in typically developing individuals. Importantly, long term outcomes in terms of the individual's symptom profile and their skills cannot be readily predicted from genetic changes. Therefore, current research is focusing on furthering our understanding of the underlying mechanisms at play and constructing a more coherent picture of how genetic risk interacts with other factors to lead to autism over development.

Key messages in moving forward

- To enhance the impact of existing discoveries, the field needs to shift from highly controlled laboratory experiments towards more inclusive and representative community samples, albeit without compromising data quality.
- A greater focus on the role of genes over the course of neurodevelopment is needed and could ultimately be achieved using robust phenotype-genotype databases from real-world healthcare settings.
- Given the current integration of genetic testing in many clinical settings, future studies could be designed with the goal of addressing the needs of families affected with autism and related developmental disorders while simultaneously building larger data repositories.

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Genomics within diagnostic services

The fast pace of scientific advances has made genetic testing accessible for hospitals, clinics and families. Despite many challenges, genetic testing is currently used for the clinical management of individuals with ASD and related developmental disorders. Enhancing the impact of genetic testing in diagnostic services relies on having a clearly defined concept of clinical utility. In contrast, the emerging genetic complexity of autism and related developmental disorders greatly complicates this endeavour. Clinical utility differs across various clinical settings and populations. Utility is also influenced by many real-world factors: the tests' ability to provide long-term prognostic information for an individual or a family, families' expectations and response to testing, clinicians' knowledge and understanding of genomics in general and genetic testing for autism in particular, the availability of services or programs, and health systems' response to testing more generally.

Key messages in moving forward

- Diagnostic services utilizing genetic testing need to consider motivation of families to seek genetic testing or their expectations when testing is offered. Informed and comprehensive methods for obtaining consent for genetic testing are needed to ensure that expectations are adequate and relevant for clinical care.
- There need to be clearly defined uses for genetic results within clinical care as well as for research, e.g. building clinically-relevant data banks. Involvement of diagnostic centers in research is very valuable in the long run.
- Diagnostic services need to take into consideration the impact of genetic results on families in various contexts such as clinical care, family planning, personal understanding of a disorder and insurability.
- Physicians involved in the diagnostic process need to be supported through education on methods of genetic testing, clinical utility and applicability and need to contribute to a national and/or international clinical database.

Medical Genetics and Genetic Counseling

Genetic testing has the potential to lead to significant improvements in clinical care, where specialized services and clinical capacity are available. In this case, genetic testing can identify associated health problems and co-morbidities, reveal biological pathways responsive to medications, and offer a recurrence risk for family planning. The extent to which genetic testing can support or aid identification of autism in community based settings is less clear. The lack of standardization for result reporting among genetic laboratories impacts the relevance of genetic information that is provided to primary care physicians. Moreover, reporting of genetic findings back to families currently lacks clear guidelines, but efforts to develop such guidelines are underway. The rapid pace of development and utilization of new molecular genetic methods, such as whole exome sequencing, will add an additional level of complexity to these issues as more genetic information becomes available.

Key messages in moving forward

- There is a need for a stronger collaboration between geneticists/genetic counselors and other specialists as well as with primary care community physicians. Such collaboration needs to focus on improving informed consent, interpretation and sharing of genetic results, and access to genetic counseling as a result of testing.

- Development and adoption of common standards among genetic laboratories for reporting test results, as well as clinical guidelines for reporting these to families can enhance the utility of current testing.
- Education around genetic literacy in health settings is of paramount importance in order to improve the impact of genetic testing.

Ethics, public policy, and health economics

Research advances and clinical practice interact with the wider ethical, economic and societal issues. Understanding and balancing the best interests of the family and the best interests of the affected child with the goals of research, clinical care and society as a whole is paramount for successful translation of discoveries. Despite many perspectives, much work is still needed to understand how genetic information impacts personal experience of the disorder and the extent to which it increases or reduces societal stigma. Moreover, the specific context of application including health systems and legal frameworks modifies the impact of genetic testing.

Key messages in moving forward

- In both research and clinical care, genetic information must always be used in meaningful ways for improving lives of people affected by autism and their families, through considering each individual's understanding, values and perspectives.
- Establishing cost-effectiveness of genetic testing in health systems is needed to understand current impact and inform future service planning and policy.
- Utility of genetics in the management of autism requires a holistic approach that integrates science and medicine with relevant social, economic and legal frameworks.

How did we involve the community?

The consultation activities were designed to allow for input from various stakeholders across multiple tailored activities. A number of our sponsors and community partners (listed below) have been active in shaping the objectives and activities. The expert consultation on March 6-7 centered around scientific/clinical knowledge, experience and evidence. Consensus from the expert group was immediately shared and discussed with the local community during a public event on March 8 entitled: "Straight Talk with Experts on Genetics and ASD." The event included a range of interactive and educational activities where affected individuals and their families engaged in conversations with the expert group and with other community stakeholders.

What was the feedback from the participants?

Feedback from 60 percent of participants was very positive, averaging 89 percent satisfaction with the event, including the goals, format and potential for wider impact. In qualitative feedback, participants highlighted that the caliber and broad representation of attendees across disciplines and sectors, as well as richness of discussion within a convivial atmosphere, to be the strongest aspects of the consultation. Participants suggested that including experts from the neurosciences as well as policy representatives would further improve the value of future activities related to the topic.

What next?

There was much interest among participants in continuing the conversation and in pursuing a range of potential collaborations emerging from the consultation. Some of the next steps are to:

- Share our consultation findings with other scientists and clinicians through journals and web-based tools.
- Work with our partner organizations – Autism Ontario, Autism Speaks Canada and the Sinneave Family Foundation to share the findings with the wider community.
- Continue to work towards outlining more detailed practice- and policy-options and solutions to improve the impact of advances in genomics on health systems. This includes how to enhance current impact and prepare for new technologies that are right around the corner.
- Plan a follow-up meeting in 2016.

Organizing Committee

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Ilina Singh, Professor of Science, Ethics and Society, King's College, London

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We are thankful to our sponsors and community partners for their support.