



## EDITORIAL

## Next Generation Sequencing and the Child and Youth Psychiatrist

In this issue, Ungar comments on the clinical utility of genome-based diagnostic testing. This is a must-read article for practitioners who wish to stay abreast of current developments in genomics as psychiatry enters the genomic era. Although Ungar's attention is focused on autism spectrum disorder (ASD), her comments can easily be generalized to all mental health disorders.

Canadian scientists are at the forefront on genomic research into the nature of ASD. Next generation sequencing (NGS) is a novel approach that can potentially detect de novo mutations in the sequence of genes coding for proteins that may be present in children with ASD and absent in others. Even though the costs of NGS are rapidly dropping, does it add value for money? Should the health care sector, insurance plans, institutions and families be investing resources, institutional space and time to make NGS available? What opportunities are being missed because of massive investment in a single approach to understanding and diagnosing ASD? Ungar brings the perspective of health technology assessment (HTA) to the question of the social, legal, ethical and economic consequences of emerging technologies such as NGS. The HTA approach focuses on cost-effectiveness analysis which examines and quantifies the additional costs associated with a new technology compared to standard care and weighs those costs against established benefits. The story is a cautionary tale of rising cost and missed opportunities when funds are directed into technologies of questionable benefit. Ungar makes several suggestions for optimizing the information needed to conduct such cost-benefit analyses.

Currently, NGS is not able to explain the majority of variance in ASD and leads to a limited number of clinically useful interventions only. But NGS holds promise for a vastly better understanding of the cause of ASD which in turn will advance diagnostics and therapeutics. It is that vision that we are buying into with the current investment in genomics in mental illness. In order to maximize our understanding of how genetic variants are expressed phenotypically, it is critical to have access to an extensive data base of cases. Provision of NGS more broadly will support clearer understanding of the value of NGS.

Although the true benefits of NGS cannot yet be assessed, Lionel and colleagues demonstrated the value and promise of access to large-scale data bases of genomic information

for microarray (i.e. not NGS) data. In a study of ADHD and ASD children, Lionel et al (2011) found that deletions of the neuronal *ASTN2* and the *ASTN2*-intronic *TRIM32* genes yielded the strongest association with ADHD and with ASD. This initial discovery was found in 248 ADHD, 349 ASD and several controls. However, it was not until Lionel et al (2014) screened *ASTN2/TRIM32* and *ASTN1* (1q25.2) for exonic CNVs in clinical microarray data from 89,985 individuals across ten clinical sites, including 64,114 subjects with neurodevelopmental disorders that they were able to estimate the true extent of the associated risk. This data was available because several jurisdictions have introduced limited access to clinical testing.

Genomics is the most exciting opportunity that we have for breakthroughs in mental illness. Presently, Canadians are developing new methods for analyzing genomic information and for collecting the extensive clinical data that will be required to fully comprehend the meaning of these new findings. These discoveries will lead to additional technological discoveries that will further the understanding of ASD and other conditions. Collectively, these approaches afford an opportunity to place diagnosis and intervention for mental illness on a firm biological footing which will in turn provide insight into environmental influences that interact with genetic risks. Despite this enthusiasm, we should at all times remain aware of the costs and of the choices that expensive technologies place in front of us.

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### References

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