000172

Time matters in brain health:

how can health systems respond to the growing demand for genetic testing?

Authors: Alastair J Noyce,[1]* Gavin Giovannoni,[2] Philip Scheltens,[3] Daniela Berg,[4] Laurie Brown,[5] Kris Dierickx,[6] Giovanni B Frisoni,[7] John Hardy[8] and Karl Heilbron[9]

Author affiliations: [1]Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK; [2]Blizard Institute and Wolfson Institute of Preventive Medicine, Queen Mary University of London, Barts and The London School of Medicine and Dentistry, London, UK; [3]Alzheimer Center Amsterdam, Amsterdam University Medical Centers, Amsterdam, Netherlands; [4]Department of Neurology, Christian-Albrechts University of Kiel, Kiel, Germany; [5]Institute for Governance and Policy Analysis, University of Canberra, Canberra, Australia; [6]Centre for Biomedical Ethics and Law, Catholic University of Leuven, Leuven, Belgium; [7]Centre de la Mémoire, University Hospitals and University of Geneva, Geneva, Switzerland; [8]Department of Neurodegenerative Diseases, University College London, London, UK; [9]23andMe, Inc., Sunnyvale, CA, USA

*Presenting author

BACKGROUND

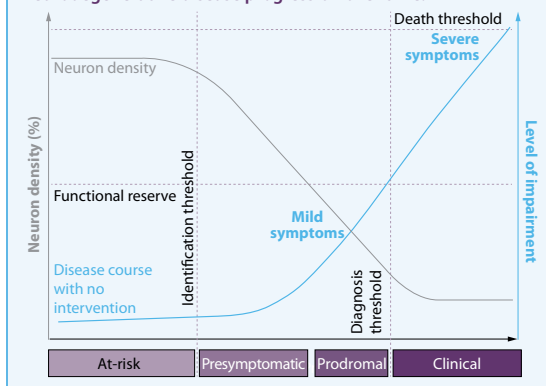
- Brain health is about making the most of your brain and helping to reduce some of the risks to its health as you age.
- The burden of neurodegenerative disease is increasing, but health systems are not equipped to manage the large numbers of people at risk of a neurodegenerative condition.
- Awareness of risk factors is rising, and more people are looking to find out about their individual risk through testing and consultation with healthcare professionals (HCPs).
- The *Think Brain Health* initiative is exploring the role of HCPs in helping individuals understand genetic and other risk factors for neurodegenerative diseases, and ensuring they are supported to meet this growth in demand for information and interpretation of test results.

KEY POINTS

- Parkinson's disease (PD) affects more than 6 million people globally.[1] As this number rises, a growing pool of individuals is keen to understand their level of risk of developing it.
- Neurodegeneration begins many years before symptoms of disease appear (**Figure 1**).[2] This means that PD and other neurodegenerative diseases are often not diagnosed clinically until relatively late in the disease course.[3,4]
- Some individuals may seek support from an HCP if they spot prodromal, early PD symptoms such as REM sleep behaviour disorder (RBD) or sense of smell loss. This presents ethical considerations and issues around disclosing risk, which may be challenging for HCPs.
- Engaging with those who have sought more information about their risk could increase the opportunities for early intervention or prevention.

Think **Brain Health**
ACT EARLY!

Figure 1. Simplified schematic representation of neurodegenerative disease progression over time.



Adapted from Giovannoni G *et al.*[5]

- Direct-to-consumer (DTC) genetic testing is available to the public without assistance from an HCP. However, a desire to understand the potentially complex results may prompt people to request explanations from an HCP.
- Many HCPs feel unprepared to discuss such results or to communicate risk appropriately, so how should they and health systems respond?

THE *THINK BRAIN HEALTH* REPORT AND NEURODEGENERATIVE DISEASE RISK

- A multidisciplinary, geographically representative group with expertise in dementia, PD, genetics, epidemiology, public health, patient advocacy and ethics developed evidence-based recommendations.[5] Two of these 18 recommendations focus on preparing a framework for a preventive approach to neurodegenerative diseases (**Figure 2**).

Figure 2. Key health promotion recommendations from *Time matters: a call to prioritize brain health.*

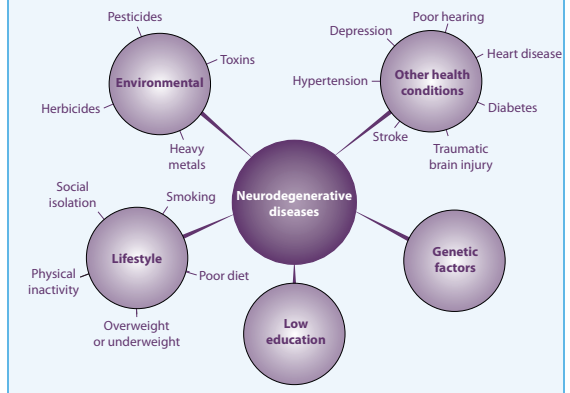
Provide a supportive environment, including guidance and legislation that empowers people to make important lifestyle changes

Prepare for likely growth in the demand for genetic testing from people who want to understand more about their own risk

Adapted from Giovannoni G *et al.*[5]

- Many things can influence an individual's risk of developing a neurodegenerative disease (**Figure 3**). Further research is needed to determine the focus for modifiable risk factors, as outlined in some of the report's research recommendations.

Figure 3. Risk factors associated with neurodegenerative diseases.



Adapted from Giovannoni G *et al.*[5]

DIRECT-TO-CONSUMER TESTING

- The most popular tests use common genetic variations to make predictions about:
  - physical traits like lactose intolerance and male pattern baldness
  - how a person might respond to specific medications
  - whether there is a higher-than-average risk of developing certain diseases like cancer or neurodegenerative disease
  - whether the person is a carrier of genetic alterations that are associated with several rare genetic conditions.
- The ability of the general public to understand DTC genetic test results depends on their ability to understand and interpret the complex risk values associated with the results.
- Misunderstanding of the results could have negative consequences, including unnecessary concern, false reassurance or unwarranted changes in behaviour.

RESPONDING TO THE GROWING DEMAND FOR DTC TESTING

- An HCP who is asked to advise on the results of a DTC genetic test may be aware of the challenges this presents, but there are also opportunities for positive action (**Table 1**).

Challenges	Opportunities
• Inadequate support or training to provide effective counselling after risk disclosure • Lack of oversight and inconsistent regulation of both direct-to-consumer companies and the use of data • The need to consider lifestyle factors as well as genetics • Lack of validation of such tests to provide a medical diagnosis	• Promotion of healthy lifestyle advice to all individuals from early adulthood onwards • Raising awareness of diseases that have a genetic component • Data sharing with responsible biomedical researchers, where consent is given

Table 1. Challenges and opportunities for healthcare professionals with direct-to-consumer genetic testing.

WHAT NEXT?

- Preparation for the likely growth in the demand for genetic testing by people who want to understand their risk of developing a neurodegenerative disease needs to start now.
  - Rigorous support systems and processes should be set up.
- Training resources are needed to help prepare clinicians for increased uptake of DTC genetic tests. Such resources might include:
  - guidance on identifying genetic contributions to health and disease
  - a framework for discussing the benefits and limitations of genetic testing
  - help with interpreting test results for individuals, in the context of personal and family history
  - summary of possible interventions or other actions.
- Are you interested in participating in further discussions on how to develop supporting resources for training? If so, contact us here: info@thinkbrainhealth.org.
- Find out more about Think Brain Health via our website: www.thinkbrainhealth.org.

Disclosures
Alastair Noyce is funded by the Barts Charity. He reports additional grants from Aligning Science Across Parkinson's (ASAP), Parkinson's UK, The Michael J Fox Foundation and Virginia Keiley Benefaction; grants and non-financial support from GE Healthcare; and personal fees from AbbVie Pharmaceuticals, Bial Pharmaceuticals, Biogen, Britannia Pharmaceuticals, F. Hoffmann-La Roche and Profile Pharmaceuticals. Gavin Giovannoni has received compensation for serving as a consultant or speaker for, or has received research support from, AbbVie, Actelion, Atara Bio, Biogen, Canbex, Celgene, EMD Serono, F. Hoffmann-La Roche, Genentech, GlaxoSmithKline, GW Pharma, Japanese Tobacco, Merck, Novartis, Sanofi-Genzyme, Synthon BV and Teva. Philip Scheltens has received consultancy/speaker fees (paid to the institution) from Biogen, Novartis Cardiology, People Bio and Roche (Diagnostics). He is Principal Investigator of studies with AC Immune, CogRx, EIP Pharma, IONIS, Probiodrug and Toyama. Daniela Berg has within the last year received compensation in the form of consultancies, honoraria or grants from AbbVie, Bial Pharmaceuticals, Biogen, Damp Foundation (Damp Stiftung), Desitin, European Union, GE Healthcare, German federal support (BMWi and BMBF), German Parkinson's Disease Association, Janssen Pharmaceutica NV, Lundbeck, Novartis Pharma, ParkinsonFonds Deutschland, UCB Pharma and Zambon. John Hardy has received funding and support from Dementia Research Institute, Dolby Family Fund, Medical Research Council, University College London Hospitals' National Institute for Health Research Biomedical Research Centre and Wellcome Trust. Karl Heilbron is an employee of and has stock, stock options, or both, in 23andMe. Laurie Brown, Kris Dierickx and Giovanni Frisoni have no disclosures to report. The authors acknowledge the expertise of Dr Nick Fahy, University of Oxford, in providing guidance about policy recommendations and processes.

Support for the development of this publication was provided by Oxford Health Policy Forum CIC, UK, funded by grants from Biogen, F. Hoffmann-La Roche and UCB Pharma SRL, who had no influence on the content.

References
1. Dorsey ER, Elbaz A, Nichols E *et al. Lancet Neurol* 2018;17:939–53. **2.** Noyce AJ, Lees AJ, Schrag AE. *J Neurol Neurosurg Psychiatry* 2016;87:871–8. **3.** Tinelli M, Kanavos P, Grimaccia F. 2016. Available from: http://www.lse.ac.uk/business-and-consultancy/ consulting/consulting-reports/the-value-of-earlydiagnosis. **4.** Cahill S. *Aging Ment Health* 2019:1–3. **5.** Giovannoni G, Noyce A, Scheltens P *et al.* 2019. Available from https://www.oxfordhealthpolicyforum.org/reports/brain-diseases/brain-diseases-report.