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The Ethics of Global Psychiatric Genomics: Multilayered Challenges to Integrating Genomics in Global Mental Health and Disability

A Position Paper of Oxford Global Initiative in Neuropsychiatric GenEthics (NeuroGenE)

Summary

Psychiatric genomics has the potential to radically improve prevention and early intervention of serious mental and neurodevelopmental disorders worldwide. However, little work has been done on the *ethics* of psychiatric genomics – an oversight that could result in poor local uptake, reduced practical / clinical application, and ethical violations in this rapidly developing area of scientific research. As part of the Global Project of the Stanley Center for Psychiatric Research, the Global Initiative in Neuropsychiatric GenEthics (NeuroGenE) based at the University of Oxford aims to embed ethical inquiry within scientific investigation and engage with fundamental ethical questions around a psychiatric genomic approach to mental and neurodevelopmental disorder. This position paper sets out the core aims of the NeuroGenE research programme and explores the importance of a cross-cutting research orientation using multidisciplinary methodologies to ensure efforts to translate and apply global psychiatric genomics in public policy and clinical practice are ethically grounded.

Introduction / Rationale

Psychiatric genomics research has accelerated rapidly in recent years and now forms a core pillar of major scientific and mental health research programs. Through population wide association studies, psychiatric genomics examines the biogenetic causes for neurological traits underlying major psychiatric disorders, with the goal of generating a more nuanced psychiatric nosology and improve preventative and targeted treatments within a precision-medicine framework.^{1,2} Thus far, genome-wide association studies have mainly targeted samples from European populations. Recognising the need to diversify representative populations, the Global Project of the Stanley Center for Psychiatric Research at the Broad Institute has embarked on an ambitious initiative to broaden sample collections of populations within sub-Saharan Africa, (Kenya, Ethiopia, Uganda, South Africa), Asia (China and

Japan), and eventually South America, in order to probe the underlying biological mechanisms for mental and neurodevelopmental disorders (such as ADHD and autism).

In theory, psychiatric genomics presents a potentially transformative approach that could rapidly advance precision medicine in the field of psychiatry in the global context. As laudable as this aim is, there are significant concerns in terms of how its goals and aspirations are to succeed in the global context: first, psychiatric genomics will not be practically applicable if there is little engagement with a range of ethical issues that are raised in this approach; second, there is a risk that ethical violations could occur in research and application if these issues are not examined carefully. The ethics of psychiatric genomics from local and global perspectives has garnered little attention thus far but the very limited literature which exists has focused on potential implications of this approach to mental health in deepening or alleviating genetic essentialism and stigma, as well as individualising patients to the detriment of social and relational contexts.^{3,4,5} Yet such a research agenda is urgently needed to ensure that pressing ethical considerations remain foremost in practical and clinical applications, utilising interdisciplinary bioethical research strategies to explore the mechanisms which lead to genetic essentialist views.^{6,7}

This position paper sets out the core aims of the NeuroGenE research programme through a review of key debates within global mental health, genomics, and disability studies. We also explain the project's methodological approach, guiding principles, and expected outputs.

Aims of NeuroGenE

NeuroGenE is a multilayered research and training programme focused on the ethics of psychiatric genomics within the global context. The ultimate goal of the programme is to ensure the responsible conduct and uses of scientific research, such that the research contributes to improvements in the treatment of and respect for persons facing mental health challenges, their families and their carers. An equally important, parallel goal is to identify how scientific research on psychiatric genomics can

best respect and benefit local communities including local stakeholders, practitioners, and scientific infrastructures.

The NeuroGenE project is structured along three related levels of research: (i) pragmatic inquiry; (ii) substantive inquiry; and (iii) policy / practice application. *Pragmatic inquiry* examines the ethical questions embedded within scientific investigation of psychiatric genomic data, including issues related to data collection and ownership, biobanking, and research procedure. *Substantive inquiry* critically examines deeper questions around the conceptual grounding, cultural translation, and normative implications of a psychiatric genomics lens to mental health within the global setting. These two levels of inquiry will feed into investigations on *policy / practice application*, exploring how an ethically grounded approach to psychiatric genomics should inform national and international policies in public health, as well as local practices of community mental health treatment.

Current Status of Research

The ethics of psychiatric genomics intersects with the existing fields of research within genomics, global mental health, and disability studies, each of which are motivated and informed by specific practical concerns and normative orientation. Alongside scientific research into the genomics of physical conditions, ethical discussions have explored core procedural issues around the protection of research participants (e.g. community consent and consultation) and scientists in low-income countries (e.g. data-sharing and capacity-building), as well as the regulatory mechanisms of international collaborations (e.g. sample storage and ownership).^{8,9,10} Questions of genetic identity, responsibility, and the ethics of return of results have also been part of substantive bioethical discussions within the clinical context.^{11,12,13}

Meanwhile, global mental health discussions readily identify the urgent need for collective action, investment, and innovative solutions to address chronic inequality and poor delivery of mental health care in the global context.^{14,15} Gaps in treatment and care, both within and across countries – remain foremost in these debates. Other strands of global mental health focus on the justification of a global

mental health framework to local cultural contexts, beliefs, and social practices around mental disorder, sometimes questioning the portability of standard diagnostic tools and treatment recommendations.^{16,17}

Recent research in disability studies echoes this scepticism towards standard diagnostic tools, both for treatment and research, and highlight instead the systemic structures (i.e. public policy, laws, societal norms) that discriminate against and inhibit the full respect of persons with disabilities – including those with mental and neurodevelopmental disorders. Increasingly important in disability studies is the co-production of knowledge by persons with disabilities and survivors of psychiatry in alignment with a human rights lens that recognises their right to equal participation and structural accommodations.^{18,19,20}

On one hand, critical engagement with relevant discussions internal to genomics, global mental health, and disability studies is necessary in order to clarify the role of psychiatric genomics in improving mental health care and advancing advocacy efforts to promote the rights of individuals with mental and neurodevelopmental disorders. On the other hand, each field of inquiry in isolation captures only a partial picture of the complex ethical challenges facing the research and practical application of psychiatric genomics. Overcoming these challenges will ultimately depend on detecting where the ethical faultlines lie in the first instance. This demands an original cross-cutting approach that generates dialogue between these debates rather than a singular research orientation (Fig.1).

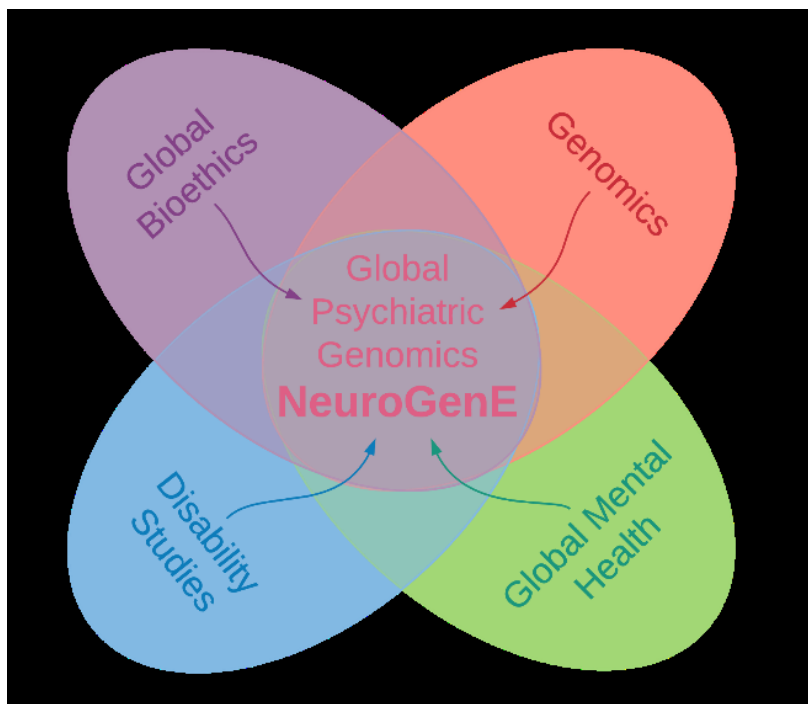


Figure 1: NeuroGenE Programme of Research

Importantly, these different areas of research have yet to be bridged in a single programme of inquiry. As it stands, the existing literature in each respective field of study has failed to detect the need for such a cross-cutting approach in order to address the fundamental ethical issues at stake as global psychiatric genomics rapidly advances. A broadened intellectual orientation is necessary if innovative ethical inquiry and solutions are to be developed and as we discuss below, three major ethical faultlines are brought into sharp relief once a cross-cutting approach is adopted.

Dimensional Approaches of Mental Disorder and Disability

One major faultline in psychiatric genomics revolves around the concept of mental health and possible tensions with a disability rights ethos. Psychiatric genomics tracks important conceptual changes in mental health, moving away from dichotomous classifications of ‘health’ and ‘disease/illness’ and towards a more dimensional understanding which accommodates a spectrum of experiences between mental health to disorder and disability.²¹ Psychiatric genomics reveals a symptom spectra: risk alleles for mental disorders can be present in both affected and unaffected people, whilst multiple disorders have common genetic aetiology and environmental risk factors.^{22,23,24}

Not only do these findings invite greater nuance to diagnostic classifications of mental disorder, but the range of interventions is also broadened to encompass prevention and early intervention strategies in addition to treatment and rehabilitation.^{25,26,27}

At first glance, this dimensional approach appears consistent with recent changes to classifications of disability. The World Health Organization's International Classification of Functioning, Disability and Health (ICF) similarly charts health and disability along a multidimensional continuum based on a taxonomy of body functions, corresponding body structures, and contextual, environmental, and personal factors that impact on components of body functioning.^{28,29} Functioning and disability are conceived as universal phenomena that all people experience over the life-span. Echoing this spectrum view is the UN Convention of the Rights of Persons with Disabilities (CRPD), a potentially transformative human rights framework that articulates the rights and obligations owed to individuals with disabilities, to accommodate a diverse range of bodily and intellectual functionings. Recent disability studies and advocacy work have therefore focused on securing crucial protections for persons with disabilities based around an ethos of respect for bodily difference, protection of autonomy, participation in all areas of life, and non-paternalism.³⁰⁻³³

Fundamental tensions between the dimensional approaches to mental health and disability are nonetheless revealed once a cross-cutting perspective is adopted. First, within a dimensional approach to mental health, the criterion of functional impairment continues to be used as a threshold measure by which a person can be diagnosed with a disorder that *prima facie* warrants clinical treatment and rehabilitation. From the perspective of disability studies, however, this threshold concept of functional impairment might be viewed as discriminatory and prejudicial, where it is used to presume the loss of decision-making competence, question the authenticity of a person's deliberation and choices, or justify (coercive or non-coercive) interventions. Indeed the ICF's concept of functionality has little to do with setting a threshold to separate 'prevention' from 'treatment', but instead provides the foundation for a tool to collect more accurate population-based disability statistics (via census and national survey) as a means of monitoring the international implementation of the CRPD.³⁴

The second tension touches on even more profound ethical issues around the putative justifiability of prevention / early intervention in mental health care and the role of psychiatric genomics. Improved scientific understanding of underlying genetic mechanisms could help develop early biomarkers and precision medicine in psychiatry, focused mainly on the early detection (and prevention) of mental disorder and disability. But this aspiration of psychiatric genomics may be ethically problematic through the lens of disability activism and research, where neurological difference is increasingly recognised as identity difference, and efforts to ‘fix’ the individual’s traits that are typically associated with the disability can be viewed as discriminatory.³⁵ This view welcomes support and may even advocate for appropriate treatment, yet also critically challenges the concept of the individual being considered ‘abnormal’ with the expectation that they should immediately adjust to societal norms, either voluntarily or through coercive means.^{36,37,38}

The dimension of cultural context adds further complexity to these tensions. For example, though various African countries are signatories of human rights conventions which expressly support a disability rights paradigm, such as the CRPD,³⁹ cultural perspectives on disability vary, often resting on the extent to which traditional or religious conceptual frameworks and healing practices can support and accept individuals with mental and neurodevelopmental disorders.^{40,41}

In sum, the aspiration to facilitate prevention and early intervention strategies means psychiatric genomics raises core questions around the societal and clinical acceptance of neurological disorders in different cultural contexts, see Box 1.

Box 1: Core Ethical Questions on the Impact of Psychiatric Genomics on the Approaches of Mental Disorder and Disability

- Does the early intervention prism of psychiatric genomics imply (i) the pathologisation of certain behavioural conditions and (ii) the aspiration to cure the individual or prevent the individual from developing certain disorders? How can the prevention and early intervention lenses of psychiatric genomics balance the imperative towards better life outcomes for people with mental and neurodevelopmental disorders on one hand, with respect for and acceptance of such individuals on the other?
- Would genomic responsibility suggest individuals and their family members are obligated to engage in preventative or early intervention strategies?
- How does psychiatric genomics affect notions of personhood and personal identity amongst individuals with mental and neurodevelopmental disorders?

The Dilemma of the Global and the Local

Another major ethical faultline clusters around the dilemmas of navigating the *global* and the *local* at multiple levels of psychiatric genomics. These range from culturally specific issues around informed consent procedures, to questions of translation and cultural understanding of genomics and mental disorder, to fundamental issues around global equity and distributive justice. Here we focus on the latter two issues to highlight the importance of our cross-cutting approach.

The Stanley Initiative seeks to expand genetic samples to accurately represent a global population, with the recognition that genomics research requires contextualised data and the involvement of non-

Western stakeholders in lower- and middle-income settings. The ‘global’ nature of psychiatric genomics discourse itself, however, needs to be questioned more carefully. The wide variation between local belief systems around mental disorder,^{42,43,44} indicates that the biogenetic assumptions underlying psychiatric genomics research may have little resonance at both the conceptual level (frameworks of descriptive and normative concepts and beliefs) and the practical level (existing and normative practices and rituals). Additional contextual realities of different LMIC sites, such as the wide range of dialects / languages, low literacy levels – especially amongst those with mental and developmental disorders,^{44,45} – contribute to the substantial and bi-directional translational challenges of psychiatric genomics.

The claim that translation and dissemination moves in a single direction, from ‘global’ scientific knowledge to ‘local’ beliefs, needs to be critically challenged if psychiatric genomics is to function as an asset to existing tools at the local and individual level. Collaboration between biomedical knowledge and indigenous perspectives, neither of which are static,⁴⁶ may be necessary to improve cross-cultural translation and cultivate mutual understanding around mental health and psychiatric genomics.^{43,47} A major area of work in the NeuroGenE programme therefore explores ways in which the learning and translational process of psychiatric genomics is *multidirectional*, so that global psychiatric genomics engages seriously with local knowledge systems and beliefs around mental disorder in a reciprocal fashion. Core research questions are shown in Box 2a.

Box 2a: Core Research Questions on the Impact of Psychiatric Genomics on the Global and Local

Dilemma

- To what extent can global psychiatric genomics become ‘localised’?
- What does ‘translation’ mean in this project? To what extent can cultural / indigenous views be reconciled with biogenetic explanations of mental / neurodevelopmental disorder? Should ‘reconciliation’ be a goal of respectful scientific translation?
- How can these local conceptual frameworks and tools potentially enhance, not just the practical, clinical implementation of psychiatric genomics research, but Western frameworks of mental disorder and mental health practices?

Issues concerning justice and equity reveal the global-local dilemma in a different form. Significant attention has been paid to the structural and systemic challenges facing global mental health in recent years.^{14,48–51} Although mental health provision can be unequal *within* HIC settings, the most extreme disparities exist between HIC and LMIC countries. The barriers to equity in global mental health care are especially daunting, ranging from poor infrastructure and lack of investment in community-based services, training programmes, and public mental health campaigns,^{49,50,52} to socio-economic and environmental factors of poverty physical and sexual abuse / exploitation, gender-specific issues,^{53,54} to restricted civil economic, political, and social rights, and institutionalisation.⁴⁸ Despite multinational support to alleviate such barriers,⁵⁵ the lack of tangible inroads in this area indicates two shortcomings: first, there is little consensus in terms of priority-setting with regards to where scarce funds can improve the lives of people with mental disorder, with solutions ranging from investment in human rights and regulatory frameworks,⁵⁶ community-services,⁵⁷ and government initiatives.⁵⁸ Second, the language of equity, global justice, and global health is often distilled through the prism of liberal rights-based language,⁵⁹ but whether it has sufficient normative power to express individual entitlements, empower advocacy work and motivate systemic change in different cultural contexts is debatable.^{17,60,61}

Questions of justice and equity are also deeply relevant to issues of global research collaboration, specifically around the practices of collaboration amongst stakeholders, which psychiatric genomic research will have to navigate so that benefits accrue for local academic centres and individual researchers. Global scientific research programmes often encounter tensions between the pragmatic, cost-benefit interests of research and the imperative to include local expertise and knowledge. Funder expectations, government initiatives, familiarity with legal processes and existing collaborators, as well as the influence of scientific clusters (i.e. prominent academic researchers or centres) often justify why certain collaborators are favoured as opposed to others.⁶² Yet the legitimacy and credibility of global health research often comes through the inclusion of less recognised stakeholders within LMICs, particularly given the increasing importance of local understanding and expertise in research design. This tension can mean the disproportionate benefit to high-income countries and research centres through inequitable practices of collaboration,⁶³ which evokes deeper questions around the necessary mechanisms for a fair and ethically-grounded global research collaboration that encourages mutual respect, reciprocity, and shared ownership.⁶⁴

These pressing political, economic, and social challenges in global mental health policies and research draw attention to three fundamental issues within the ethics of psychiatric genomics. First are concerns of distributive justice and fairness: in the face of scarce resources in global and local mental health programs, critical reflection on the putative justification of financial investment in psychiatric genomics, particularly within LMIC settings, is essential. Second are concerns around the ethical appropriateness of liberal rights-based language. Indeed, a genomics approach raises difficult questions as to *who* is the rights-holder and *whose* rights should be protected: the scientific research depends on population-wide samples to generate tangible findings, whilst the reciprocal benefits to individuals may be inconsequential or non-existent in the first instance. Finally, the nature of international scientific collaborations in the name of equity and social justice needs further scrutiny to better understand how diverse stakeholders interpret and enact these concepts from their different perspectives. These tensions are ripe for further bioethical research, as detailed in Box 2b.

Box 2b: Ethical Questions on the Impact of Psychiatric Genomics on the Global and Local Dilemma

- What are the cultural and political realities in LMICs and what does equity and justice mean to different communities and various stakeholders within these communities and in scientific collaborations?
- Are there general principles of equity and justice in relation to global psychiatric genomics research and what obligations are generated out of these principles?
- How should equity and justice be expressed in psychiatric genomics and mental health practices and policies?
- Does international scientific collaboration drive or hinder equity and justice; does it promote better outcomes and for whom? What mechanisms or procedures can be used to ensure global collaboration on psychiatric genomics itself is equitable and inclusive?

Further research into the ethical challenges of navigating the global and local will be vital to ensure psychiatric genomic research reflects an approach that balances respect for different cultural values and local conceptual frameworks,^{65,16} with the pursuit of a just, equitable distribution of global mental health resources.

Combating Stigma

Persons with mental and neurodevelopmental disorders are likely to experience stigma from multiple, intersecting angles: from the angle of mental disorder, they can be viewed as dangerous, uncontrollable, and unpredictable;^{66,67} from the angle of disability, they can be perceived as helpless, less than human, and dependent.⁶⁸ There is also significant self-stigma.^{69,70} Whatever the angle, they can be labelled outsiders and are often subject to discriminatory or even inhumane treatment. But the complex, divergent anti-stigma strategies used in mental health and disability advocacy respectively

reveal a third major ethical faultline that psychiatric genomics will need to navigate, and depending on the approach adopted, this lens could potentially mitigate or worsen the problem of stigma facing those with mental and neurodevelopmental disorders and disabilities.

Anti-stigma public health strategies often emphasise the physiological or neurological basis of mental disorder to help reduce attributions of individual voluntariness and personal weakness, and in turn, social exclusion and rejection.⁷¹ However the evidence that this is a helpful approach is mixed, with some studies indicating heightened perceptions of dangerousness and immutability accompany such explanations.^{72,73} By contrast, anti-stigma campaigns in disability advocacy typically focus on the social construction of diagnostic labels and disability and downplay biological causes of impairment to confront discriminatory attitudes and empower individuals to advocate for their human rights and equal participation.^{74,75}

Different cultural and religious beliefs further complicate this existing tension between social construction and biogenetic explanation within the context of global psychiatric genomics.^{38,76} From one standpoint, psychiatric genomics could have a substantial role in mitigating the stigma of persons with mental and neurodevelopmental disorder in non-Western contexts: emphasis on the inheritance of traits and genetic risks might displace indigenous explanations based on individual and/or familial moral failure, supernatural causes or being cursed.^{17,44,77} Equally, a psychiatric genomics lens could potentially exacerbate essentialist stereotypes and perceived differences among racial groups,^{78,79} where the racial distribution of certain disorders may negatively influence public perceptions⁸⁰ or appear to validate racial prejudices.⁸¹ A cross-cutting approach promises to generate original research around stigma in the context of psychiatric genomics, of which questions include those given in Box 3.

Box 3: Key Ethical Questions on the Impact of Psychiatric Genomics in Addressing Stigma

- Can genomic explanations of mental disorder help mitigate these stigmatising views?
Can these help mitigate the subjective effects of stigma?
- Is there a danger that notions of genomic responsibility / citizenship could perpetuate essentialist understandings of race / disability / mental disorder?
- What does an ethically grounded strategy to combating stigma in LMIC contexts look like, particularly in the context of psychiatric genomics?

Methodologies

NeuroGenE takes an expansive view about the methodologies that are needed to undertake this ambitious cross-cutting research agenda. Different stages will deploy a variety of methodologies, gradually building up an empirical and theoretical evidence base that will function as a vital resource for developing future practical and policy recommendations. These stages build on one another, but are not necessarily chronologically ordered and may be simultaneously undertaken; different ethical questions may also involve vacillating between the methodologies of early and later stages. However, the overall NeuroGenE strategy ensures that the final stage of policy recommendations and guidelines is substantively informed by prior stages.

Stage 1 involves literature reviews and thematic analyses of existing research in the areas of genomics, global mental health, and disability studies in order to survey, systematise, and evaluate the regulatory, legal landscape as well as ethics research in these respective areas as they bear on the issues within psychiatric genomics. Systematic reviews will synthesise relevant global and country-specific statistical data that will be used for purposes of comparison as well as provide a contextual survey of each potential site for fieldwork in Stage 2.

Building on the identified areas of intersecting ethical concerns from the literature / thematic analyses and relevant statistical data within systematic reviews, *Stage 2* uses ethnographic, qualitative, and participatory methodologies to explore various perspectives of key stakeholders of global psychiatric genomics. These include local practitioners, individuals affected by mental and neurodevelopmental disorders, family members, and local advocacy groups, to explore (i) local knowledge systems, beliefs, and cultural meanings around mental health practices; (ii) the portability and translational challenges of global mental health and psychiatric genomics concepts; (iii) the perceived interests and priorities in mental health care by local stakeholders; (iv) lived experience of stigma. Case studies will be developed and a comparative analysis of this data will indicate relevant points of converging and diverging interests.

Stage 3 draws on the examination of cultural beliefs and indigenous conceptual frameworks in Stage 2 and deploys cultural and normative theorising to facilitate critical engagement with biomedical concepts and methodological assumptions underlying psychiatric genomics. Even within Western contexts, the presumed scientific objectivity of psychiatric concepts and diagnostic classifications remain contested. The global context complicates this even further, where issues of power, particularly in post-colonial and LMIC settings, warrant careful consideration. Hence, Stage 3 uses cultural and normative theorising to critically examine points of contestation and open points of dialogue between cultural and scientific meanings. This is of particular importance if psychiatric genomics is to play an active role in combating stigma in future applications.

Stage 4 utilises philosophical and conceptual analysis to probe the underlying ethical concepts, obligations, and principles (around distributive justice, equity, and human rights) which should guide global psychiatric genomics research and its application, taking as its point of departure the phenomenological, empirical, and conceptual data generated out of Stages 2 and 3, to engage in ethical theorising that reflects the nexus of local-global, cultural-scientific perspectives.

Together these different stages will provide a crucial evidence base for practicable recommendations at Stage 5, facilitating efforts to address the gap between scientific translation and clinical practice and public health policy,⁸² through ethically grounded and context-sensitive strategies. Such policy recommendations will take both a short and long term perspective, as some research will be relevant for immediate ground level change for persons with neurological disorders, whilst other aspects of research will support the development of future policy and practice.

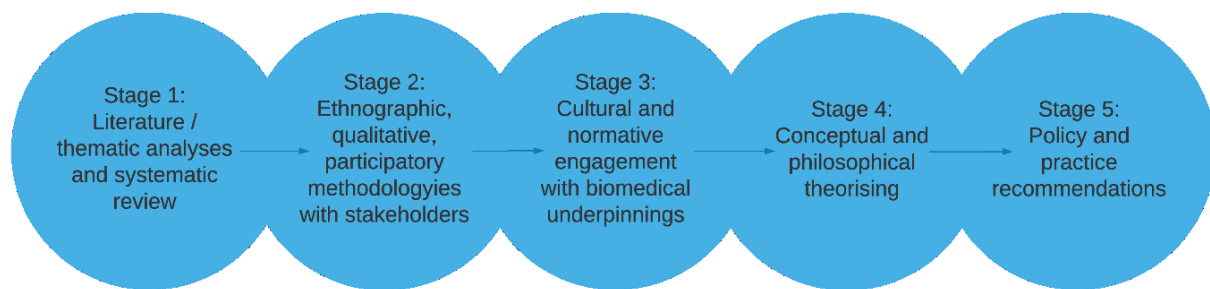


Figure 2: NeuroGenE Methodologies

Guiding Principles and Expected Outputs

Four core principles guide the NeuroGenE research programme: (i) reciprocity; (ii) collaboration; (iii) accountability; and (iv) capacity-building. These principles are operationalised at both procedural and substantive levels:

- (i) the process of developing and generating research questions;
- (ii) the practical ethos and virtues of researchers involved in NeuroGenE;
- (iii) the obligations embedded within the overarching NeuroGenE research strategy and organisational structure.

The principle of *reciprocity* is an adaptation of deliberative practices of ‘mutual reason-giving’,⁸³ but we understand the term to work inseparably with the principle of *collaboration*. These principles not only denote the equal status of stakeholders, but demand an equitable, mutually respectful, and trusting space for deliberation on the values, reasons, and motivations of different conceptual frameworks. This is crucial to mitigate the colonialism that can inadvertently shape the intellectual sphere: Western, medical and scientific frameworks or normative concepts assume their portability

and tend to ignore the reality of non-Western beliefs, traditions and practices related to human identity, health and wellbeing.^{84,85,86} The principles of reciprocity and collaboration embed multi-directional knowledge production to facilitate the kind of cultural exchange that is demanded by a truly global orientation towards mental health and psychiatric genomics.

Reciprocity and collaboration with local stakeholders and service-users are also vital to avoid the exclusion and discrimination of persons with mental disorder and intellectual disability. Persons with mental disorder and intellectual disability are too often treated as subjects or objects of research,⁸⁷ yet they may have something fundamentally at stake with the widespread application of psychiatric genomics within a precision medicine framework. Direct engagement and dialogue with disabled persons organisations (DPOs), mental health advocates, and service-users is necessary so as to probe how *they* believe their lives can improve through the research. Psychiatric genomics is unlikely to have little or no buy-in from local communities, or have practical relevance for different cultures or local stakeholders, unless reciprocity guides the entire process of learning, knowledge production, and practical translation.

The principle of *accountability* denotes interactions and processes where persons / entities are held to account for their choices, reasons, and justifications through a transparent and fair process. Accountability is applied in both vertical and horizontal senses: *vertical* accountability denotes responsibility to hierarchical decision-making bodies, such as NeuroGenE's Advisory Group that will be comprised of leading experts in relevant disciplines and strategic partnerships. But more important are the mechanisms of *horizontal* accountability within regional working groups and research partners, designed to encourage project collaborators to operate with transparency and mutual answerability, and exercise collective oversight of the research programme.

Capacity-building forms the fourth core principle of the NeuroGenE research programme. This includes mechanisms to strengthen capacity in bioethical research, collaborative structures, and policy and practice expertise. Mentorship and training for local researchers will be provided to develop,

conduct, analyse, and publish their work. Other capacity-building activities include the formation of a global network of multidisciplinary researchers, within and across institutions. NeuroGenE is developing institutional research capacity through partnerships with different organisations, such as the African Mental Health Research Initiative (AMARI) and University of Ghana, as well as through the provision of postdoctoral training. Meanwhile, the programme provides support for enhancing research capacity of individual researchers who participate in the project's local working groups, such as the African Ethics Working Group (AEWG) comprised of early and mid-career individual academics from Moi University, Addis Ababa University, University of Cape Town, and Makerere University. Support mechanisms include core research, training and grant funding to enable the pursuit of individual and collaborative research projects at various levels of inquiry of the ethics of psychiatric genomics that will eventually feed into initiatives to enhance capacity within institutional review boards and amongst public health policy makers.

The expected outputs of the NeuroGenE programme of research include:

- The establishment of a diverse, interdisciplinary, and sustainable research network devoted to the ethics of psychiatric genomics and regional centres of training, capacity-building, and academic research;
- Cutting edge bioethical research papers and reports;
- The development of policy guidelines and recommendations to address the prospective application of psychiatric genomics in public health and clinical practice;
- Sustainable relationships with DPOs and service user organisations which feed into future research and policy initiatives.

Conclusion

Global psychiatric genomics is at the forefront of scientific research and has the potential to transform psychiatric nosology, public health policy, and the nature of clinical interventions. We have drawn on the literatures of global mental health, bioethics and disability studies to frame a set of reasons why

the *ethics* of global psychiatric genomics will form a necessary part of genomic programmes of research in mental health. The NeuroGenE project establishes a cross-cutting, interdisciplinary programme which embeds ethics research within the science and establishes a proactive agenda of work around the ethical implications and challenges of psychiatric genomics in the global context.

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Author Contributions

Camillia Kong developed the literature review and led the first draft and subsequent revisions of the paper.

Iina Singh contributed to the literature review, read and contributed to revisions and drafts of the paper.

Declaration of Interests

The authors declare no conflicts of interest.

Search Strategy and Selection Criteria

References for the ethics papers in this article were identified through searches of PubMed and Google Scholar for relevant articles published between 2002-2018 by the use of terms “ethics”, “psychiatric genomics”, “global mental health”, “stigma”, “disability rights”. Relevant articles from bioethics, genomics, disability studies and global mental health were identified through the authors’ professional networks; searches through the authors’ personal databases; and in Google Scholar and PubMed. Articles resulting from these searches and relevant references cited in those articles were reviewed. Only articles published in English were included.

References

1. Cross-Disorder Group of the Psychiatric Genomics Consortium. 'Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis'. *Lancet* 2013; **381**(9875): 1371–79.
2. Sullivan PF, et al. Psychiatric Genomics: An Update and an Agenda. *American Journal of Psychiatry* 2017; **175**(1):15–27.
3. Kong C, Dunn M, Parker M. Psychiatric genomics and mental health treatment: Setting the ethical agenda. *The American Journal of Bioethics*. 2017; **17**(4):3–12.
4. de Vries J, Stein DJ, Kamuya D, Singh I. Psychiatric genomics: Ethical implications for public health in lower-and middle-income countries. *The American Journal of Bioethics*. 2017; **17**(4):17–9.
5. Viaña JN, Bueno RJ, Gilbert F. Beyond genomic association: Ethical implications of elucidating disease mechanisms and genotype-influenced treatment response. *The American Journal of Bioethics*. 2017; **17**(4):24–6.
6. Lázaro-Muñoz G. Responsible translation of psychiatric genetics and other neuroscience developments: In need of empirical bioethics research. *The American Journal of Bioethics*. 2017; **17**(4):33–5.
7. Hyman SE. A Valuable New Direction in Ethical Analysis of Psychiatric Genetics. *The American Journal of Bioethics*. 2017; **17**(4):13–5.
8. de Vries J, et al. Ethical issues in human genomics research in developing countries. *BMC medical ethics*. 2011; **12**(1):5–15.
9. Kaye J. The tension between data sharing and the protection of privacy in genomics research. *Annual review of genomics and human genetics*. 2012; **13**:415–31.
10. Parker M, Kwiatkowski D P. The ethics of sustainable genomic research in Africa. *Genome biology*. 2016; **17**(1):44–6.
11. Novas C, Rose N. Genetic risk and the birth of the somatic individual. *Economy and society*. 2000; **29**(4):485–513.
12. Easter MM. "Not all my fault": Genetics, stigma, and personal responsibility for women with eating disorders. *Social Science & Medicine*. 2012; **75**(8):1408–16.
13. Phelan JC, Yang LH, Cruz-Rojas R. Effects of attributing serious mental illnesses to genetic causes on orientations to treatment. *Psychiatric Services*. 2006; **57**(3):382–7.
14. Collins PY, Saxena S. Action on mental health needs global cooperation: as threats to populations transcend national boundaries, it is crucial that responses to mental-health problems do too. *Nature*. 2016; **532**(7597):25–8.

15. Patel V, Belkin GS, Chockalingam A, Cooper J, Saxena S, Unützer J. Grand challenges: integrating mental health services into priority health care platforms. *PloS medicine*. 2013; **10**(5):e1001448.
16. Sax W. Ritual healing and mental health in India. *Transcultural Psychiatry*. 2014; **51**(6):829–49.
17. Read UM, Adiibokah E, Nyame S. Local suffering and the global discourse of mental health and human rights: An ethnographic study of responses to mental illness in rural Ghana. *Globalization and Health*. 2009; **5**(1):13–8
18. Charlton JI. *Nothing about us without us: Disability oppression and empowerment*. University of California Press; 1998.
19. UN Committee on the Rights of Persons with Disabilities. Equal Recognition before the Law, UN Doc. No. CRPD/C/GC/1, adopted at the 11th Session. 2014.
20. Dhanda A. Legal capacity in the disability rights convention: stranglehold of the past or lodestar for the future. *Syracuse J. Int'l L. & Com*. 2006; **34**:429–62.
21. Patel V, Saxena S, Lund C, Thornicroft, G. et al. The Lancet Commission on Global Mental Health & Sustainable Development. *The Lancet*, Under review.
22. Kavanagh DH, Tansey KE, O'Donovan MC, Owen MJ. Schizophrenia genetics: emerging themes for a complex disorder. *Molecular psychiatry*. 2015; **20**(1):72–6.
23. Doherty JL, Owen MJ. Genomic insights into the overlap between psychiatric disorders: implications for research and clinical practice. *Genome medicine*. 2014; **6**(4):29–42.
24. Mullins N, et al. Polygenic interactions with environmental adversity in the aetiology of major depressive disorder. *Psychological medicine*. 2016; **46**(4):759–70.
25. Merikangas KR, et al. Comorbidity of physical and mental disorders in the neurodevelopmental genomics cohort study. *Pediatrics*. 2015; **135**(4):e927–38.
26. Woodberry KA, Shapiro DI, Bryant C, Seidman LJ. Progress and future directions in research on the psychosis prodrome: a review for clinicians. *Harvard review of psychiatry*. 2016; **24**(2):87–103.
27. Guloksuz S, van Os J. The slow death of the concept of schizophrenia and the painful birth of the psychosis spectrum. *Psychological medicine*. 2018; **48**(2):229–44.

28. World Health Organization (WHO). Towards a Common Language for Functioning, Disability and Health. The International Classification of Functioning, Disability and Health: ICF. Geneva: WHO, 2002.
29. Kostanjsek N. Use of The International Classification of Functioning, Disability and Health (ICF) as a conceptual framework and common language for disability statistics and health information systems. *BMC Public Health*. 2011; **11**(4):S3–4
30. Bach M. Inclusive citizenship: Refusing the construction of “cognitive foreigners” in neo-liberal times. *Research and Practice in Intellectual and Developmental Disabilities*. 2017; **4**(1):4–25.
31. Goodley D. *Dis/ability studies: Theorising disablism and ableism*. Routledge; 2014.
32. Flynn E, Arstein-Kerslake A. The support model of legal capacity: Fact, fiction, or fantasy. *Berkeley J. Int'l L*. 2014; **32**:124–43.
33. Mulvany J. Disability, impairment or illness? The relevance of the social model of disability to the study of mental disorder. *Sociology of Health & Illness*. 2000; **22**(5):582–601.
34. Oliver M, and Sapey R. *Social work with Disabled People*. Fourth Edition. Palgrave Macmillan; 2012
35. Harpur P. Embracing the new disability rights paradigm: the importance of the Convention on the Rights of Persons with Disabilities. *Disability & Society*. 2012; **27**(1):1–4.
36. Oliver M. *Understanding disability: From theory to practice*. St Martin's Press; 1996.
37. Baker DL. *The Politics of Neurodiversity: Why Public Policy Matters*. Boulder: Lynne Rienner; 2011.
38. Norbury CF, Sparks A. Difference or disorder? Cultural issues in understanding neurodevelopmental disorders. *Developmental Psychology*. 2013; **49**(1):45–58.
39. Fernandez EL, Rutka LJ, Aldersey HM. Exploring Disability Policy in Africa: An Online Search for National Disability Policies and UNCRPD Ratification. *Review of Disability Studies: An International Journal*. 2017; **13**(1):1–12.
40. Hussey M, MacLachlan M, Mji G. Barriers to the implementation of the health and rehabilitation articles of the United Nations convention on the rights of persons with disabilities in South Africa. *International journal of health policy and management*. 2017; **6**(4):207–18.
41. Bayat M. The stories of ‘snake children’: killing and abuse of children with developmental disabilities in West Africa. *Journal of Intellectual Disability Research*. 2015; **59**(1):1–10.

42. Foster GM. Disease etiologies in non-western medical systems. *American Anthropologist*. 1976; **78**(4):773–82.
43. Keikelame MJ, Swartz L. ‘A thing full of stories’: Traditional healers’ explanations of epilepsy and perspectives on collaboration with biomedical health care in Cape Town. *Transcultural psychiatry*. 2015; **52**(5):659–80.
44. Deribew A, Tamirat YS. ‘How are mental health problems perceived by a community in Agaro town?’ *Ethiopian Journal of Health Development*. 2005; **19**(2):153–9.
45. Owusu-Ansah FE, Mji G. African indigenous knowledge and research. *African Journal of Disability*. 2013; **2**(1):1–5.
46. Greene S. The shaman's needle: development, shamanic agency, and intermediality in Aguaruna Lands, Peru. *American Ethnologist*. 1998; **25**(4):634–58.
47. Kane JC, et al. Challenges for the implementation of World Health Organization guidelines for acute stress, PTSD, and bereavement: a qualitative study in Uganda. *Implementation Science*. 2015; **11**(1):36–51.
48. Drew N, et al. Human rights violations of people with mental and psychosocial disabilities: an unresolved global crisis. *The Lancet*. 2011; **378**(9803):1664–75.
49. Saraceno B, et al. Barriers to improvement of mental health services in low-income and middle-income countries. *The Lancet*. 2007; **370**(9593):1164–74.
50. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. *The Lancet*. 2007; **370**(9590):878–89.
51. Jacob KS et al. Mental health systems in countries: where are we now?. *The Lancet*. 2007; **370**(9592):1061–77.
52. Chappell P, Johannsmeier C. The impact of community based rehabilitation as implemented by community rehabilitation facilitators on people with disabilities, their families and communities within South Africa. *Disability and rehabilitation*. 2009; **31**(1):7–13.
53. Belle D. Poverty and women's mental health. *American psychologist*. 1990; **45**(3):385–89.
54. Patel V, Rodrigues M, DeSouza N. Gender, poverty, and postnatal depression: a study of mothers in Goa, India. *American journal of Psychiatry*. 2002; **159**(1):43–7.
55. WHO Commission on Social Determinants of Health, and World Health Organization. *Closing the gap in a generation: health equity through action on the social determinants of health: Commission on Social Determinants of Health final report*. World Health Organization; 2008.

56. Burns JK. The mental health gap in South Africa: A human rights issue. *The Equal Rights Review*. 2011; **6**(99):99–113.
57. Alem A, Jacobsson L, Hanlon C. Community-based mental health care in Africa: mental health workers' views. *World Psychiatry*. 2008; **7**(1):54–7.
58. de-Graft Aikins A, Unwin N, Agyemang C, Allotey P, Campbell C, Arhinful D. Tackling Africa's chronic disease burden: from the local to the global. *Globalization and Health*. 2010; **6**(1):1–7.
59. Daniels N. Justice, health, and healthcare. *American Journal of Bioethics*. 2001; **1**(2):2–16.
60. Flikschuh K. The idea of philosophical fieldwork: Global justice, moral ignorance, and intellectual attitudes. *Journal of Political Philosophy*. 2014; **22**(1):1–26.
61. Gostin LO, Gable L. The human rights of persons with mental disabilities: a global perspective on the application of human rights principles to mental health. *Medical Law Review*. 2004; **63**:20–121.
62. Hennemann S, Rybski D, Liefner I. The myth of global science collaboration—Collaboration patterns in epistemic communities. *Journal of Informetrics*. 2012; **6**(2):217–25.
63. Engels A, Ruschenburg T. The uneven spread of global science: Patterns of international collaboration in global environmental change research. *Science and Public Policy*. 2008; **35**(5):347–60.
64. Parker M, Kingori P. Good and bad research collaborations: researchers' views on science and ethics in global health research. *PloS one*. 2016; **11**(10):e0163579.
65. Munsaka E, Charnley H. 'We do not have chiefs who are disabled': disability, development and culture in a continuing complex emergency. *Disability & Society*. 2013; **28**(6):756–69.
66. Crisp AH, Gelder MG, Rix S, Meltzer HI, Rowlands OJ. Stigmatisation of people with mental illnesses. *The British journal of psychiatry*. 2000; **177**(1):4–7.
67. Phelan JC, Link BG. The growing belief that people with mental illnesses are violent: the role of the dangerousness criterion for civil commitment. *Social Psychiatry and Psychiatric Epidemiology*. 1998; **33**(1):7–12.
68. Fine M, Asch A. Disability beyond stigma: Social interaction, discrimination, and activism. *Journal of social issues*. 1988; **44**(1):3–21.
69. Corrigan PW, Watson AC, Barr L. The self-stigma of mental illness: Implications for self-esteem and self-efficacy. *Journal of social and clinical psychology*. 2006; **25**(8):875–84.

70. Link BG, Struening EL, Neese-Todd S, Asmussen S, Phelan JC. Stigma as a barrier to recovery: The consequences of stigma for the self-esteem of people with mental illnesses. *Psychiatric services*. 2001; **52**(12):1621–6.
71. Angermeyer MC, Holzinger A, Carta MG, Schomerus G. Biogenetic explanations and public acceptance of mental illness: systematic review of population studies. *The British Journal of Psychiatry*. 2011; **199**(5):367–72.
72. Read J, Haslam N, Sayce L, Davies E. Prejudice and schizophrenia: a review of the ‘mental illness is an illness like any other’ approach. *Acta Psychiatrica Scandinavica*. 2006; **114**(5):303–18.
73. Schomerus G, Matschinger H, Angermeyer MC. Causal beliefs of the public and social acceptance of persons with mental illness: a comparative analysis of schizophrenia, depression and alcohol dependence. *Psychological medicine*. 2014; **44**(2):303–14.
74. Duffy RM, Kelly BD. Rights, laws and tensions: a comparative analysis of the Convention on the Rights of Persons with Disabilities and the WHO Resource Book on Mental Health, Human Rights and Legislation. *International journal of law and psychiatry*. 2017; **54**:26–35.
75. Green S, Davis C, Karshmer E, Marsh P, Straight B. Living stigma: The impact of labeling, stereotyping, separation, status loss, and discrimination in the lives of individuals with disabilities and their families. *Sociological Inquiry*. 2005; **75**(2):197–215.
76. Marsh VM, Kamuya DM, Molyneux SS. ‘All her children are born that way’: gendered experiences of stigma in families affected by sickle cell disorder in rural Kenya. *Ethnicity & health*. 2011; **16**(4–5):343–59.
77. Gureje O, Lasebikan VO, Ephraim-Oluwanuga O, Olley BO, Kola L. Community study of knowledge of and attitude to mental illness in Nigeria. *The British Journal of Psychiatry*. 2005; **186**(5):436–41.
78. Phelan JC, Link BG, Feldman NM. The genomic revolution and beliefs about essential racial differences: A backdoor to eugenics?. *American sociological review*. 2013; **78**(2):167–91.
79. Foster MW, Sharp RR. Race, ethnicity, and genomics: social classifications as proxies of biological heterogeneity. *Genome Research*. 2002; **12**(6):844–50.
80. Duster T. Buried Alive. In *Genetic nature/culture: Anthropology and science beyond the two-culture divide*. 2010; **23**:258–77.
81. Condit C, Bates B. How lay people respond to messages about genetics, health, and race. *Clinical Genetics*. 2005; **68**(2):97–105.
82. Insel TR. Translating scientific opportunity into public health impact: a strategic plan for research on mental illness. *Archives of general psychiatry*. 2009; **66**(2):128–33.

83. Gutmann A, Thompson D. Deliberative democracy beyond process. *Journal of Political Philosophy*. 2002; **10**(2):153–74.
84. Kleinman A. *Patients and healers in the context of culture: An exploration of the borderland between anthropology, medicine, and psychiatry*. University of California Press; 1980.
85. Kleinman A, Benson P. Anthropology in the clinic: the problem of cultural competency and how to fix it. *PLoS medicine*. 2006; **3**(10):e294.
86. Kirmayer LJ. Cultural competence and evidence-based practice in mental health: Epistemic communities and the politics of pluralism. *Social science & medicine*. 2012; **75**(2):249–56.
87. Kachaje R, Dube K, MacLachlan M, Mji G. The African Network for Evidence-to-Action on Disability: A role player in the realisation of the UNCRPD in Africa. *African Journal of Disability*. 2014; **3**(2): 86–91.