Advancing Parkinson's Disease Research in Africa: A Strategic Training Framework of the Global Parkinson's Genetics Program

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Parkinson's disease (PD) is a neurodegenerative disorder with diverse motor, nonmotor, and neuropsychiatric symptoms. Genetic and environmental factors contribute to its development.[1] However, PD research has predominantly focused on individuals of European descent, with over 80% of genome-wide association studies (GWAS) centered on this group.[2] This lack of diversity limits our understanding of disease mechanisms and creates disparities, preventing the equitable implementation of personalized medicine.[2-4] Collaborative efforts are underway to enhance diversity in PD genetic research.

Africa is the second most populous continent and is expected to host 26% of the global population by 2050.[5] Despite exhibiting the highest genetic variation and complex admixture, African populations are significantly underrepresented in PD research, with only a fraction of their extensive genetic diversity being surveyed,[6] primarily focusing on Mendelian genes associated with monogenic PD.[2,7,8] Genetic studies have characterized a limited number of Africa's 2000 ethnolinguistic groups, mainly using genotyping arrays with variants common in Europeans, leaving the distribution of novel, rare, and medically relevant variations largely unknown.[8] For instance, although the *LRRK2* p.G2019S variant is present in 1% to

2% of Europeans PD patients,[9] 29.7% of familial Ashkenazi Jewish PD patients,[10] and 40% of North African Arabs,[11] it has not been identified in Black Africans to date.[12] Given Africa's ethnic and genetic diversity, including these populations is crucial for understanding novel genetic determinants underlying PD risk, onset, and progression.[13]

Research capacity and research infrastructure in Africa remain limited, with PD genetic research facing challenges, including political and economic instability, a predominant focus on infectious diseases, limited medical personnel, and insufficient funds and infrastructure.[12]

Challenges Encountered in the Region

Health System Disruptions and Instability

Africa has a long history of political instability, characterized by military coups, armed conflicts, uprisings, and displacement, which negatively impact sectors like health care, medical education, and research.[14] Conflict disrupts economic productivity by discouraging investment, destroying infrastructure, and reducing government spending.[15]

Additionally, African health-care systems face significant pressure from infectious diseases such as tuberculosis, malaria, and HIV, and outbreaks like Ebola.[16-18] For this reason, many African countries allocate limited funding with insufficient prioritization, resources, and infrastructure for neuroscience research. Essential funding is necessary for sustainable training programs, technology acquisition, stable research personnel positions, and effective research administration. Research outputs are relatively few compared to high-income countries,[12] with a focus on communicable diseases.

However, the burden of noncommunicable diseases, such as PD, is rapidly increasing due to population aging, lifestyle, metabolic risk factors, and increased environmental exposures.[19] PD ranks as the 10th and 11th most prevalent nervous system disorder in North Africa and sub-Saharan Africa, respectively.[20] Despite its growing prevalence, African health-care systems, government stakeholders, and research priorities remain predominantly focused on infectious diseases.

Shortage of Neurology and Neuroscience Expertise

The number of neurologists is severely limited in many African countries, with an even greater shortage of movement disorder specialists. The World Health Organization recommends one neurologist per 100,000 people[21]; however, Africa has only 0.03 neurologists per 100,000, compared to 8.45 per 100,000 in Europe.[22,23] Previous research underscores this disparity, with two African nations having more than 200 neurologists, six nations having 31 to 200 neurologists, and 36 nations having 1 to 30 neurologists. The distribution remains highly uneven, with North Africa, notably Egypt and Algeria, having the highest numbers, and southern, eastern, and western Africa facing severe shortages, with 13 countries lacking any neurologists.[22] The shortage of movement disorder specialists is more severe. As of 2020, Mali had 2 movement disorder specialists for 20 million people, Nigeria had 40 for 206 million, and South Africa had 17 for 59 million.[12] To date, there is evidence of only one movement disorder specialist in Zambia, with no data available for other African countries. This uneven distribution underscores the critical need for neurologists, movement disorders specialists, and neuroscientists with expertise in genomics and bioinformatics across Africa.

Over the past decade, more international programs and fellowships have become available for African researchers seeking training in genetics and genomics abroad, although the challenges persist. Students often lack early exposure to neuroscience, and medical training programs offer inadequate exposure to neurology.[23,24] Mentorship opportunities are scarce, hindering the development of future researchers. Financial constraints and visa issues also pose challenges for attending international training (eg, fellowships, internships, rotations), conferences, and workshops.[25] Language barriers exacerbate the situation, as many African countries are Francophone or Lusophone, whereas neuroscience courses are primarily conducted in English.[26]

Clinical Research and Participant Recruitment

Limited awareness of the disease, cultural beliefs, and misconceptions about its causes, symptoms, and treatments hinder effective participant recruitment efforts.[27] Limited health care access and the lack of disease registries also hinder patient recruitment and follow-up. Leveraging community engagement, local health-care networks, and educational initiatives can enhance participation. By involving local stakeholders and tailoring recruitment strategies to address specific regional needs, researchers can build trust and foster collaboration. Ensuring ethical practices is also crucial, particularly in protecting individuals' autonomy, dignity, and informed consent in all aspects of data and sample usage.[28]

Limited Bioinformatics and Genomics Capacity

In addition to global challenges in genomic research, Africa faces specific struggles. Genomic research requires solid infrastructure, including well-equipped facilities and robust computational networks, reliant on stable power supply and internet access. However, 30 African countries experience regular electricity outages, and only 23% of East Africa has access to reliable energy sources.[29] Furthermore, some governments impose

internet shutdowns, as observed in Sudan, Chad, and Zimbabwe.[30]

Another significant challenge is inadequate training in genomic research.[31] Many researchers trained abroad opt not to return to their home countries, exacerbating Africa's brain drain. Additionally, shipping biological samples is problematic due to unreliable courier services, high costs, and inadequate local infrastructure for sample processing and preparation. These factors collectively impact the quality and quantity of genomic research in Africa.

Efforts from the Global Parkinson's Genetics Program in Addressing These Challenges

A recent global effort, the Global Parkinson's Genetics Program (GP2, www.gp2.org), supported by Aligning Science Across Parkinson's (ASAP), aims to address the need for diversity in PD research. GP2 is expanding to include at-risk populations and patients with "atypical" parkinsonism. The principal aims of GP2 extend beyond enhancing our understanding of the genetic factors in PD across global populations; it also seeks to transform this knowledge into practical applications. Achieving this vision entails creating a unified network of collaborators; conducting large-scale data collection, analysis, and harmonization; and training analysts worldwide. To achieve this, GP2 allocates funds and resources to support PD genetic research and capacity building in underrepresented regions, with a focus on retaining local scientists to ensure a lasting impact.[32]

Collaboration to Genotype and Sequence African Cohorts

As of September 2024, 34 study cohorts from 14 African countries are contributing samples to GP2, with an expected total of 10,450 patients, 11,369 neurologically healthy controls, and 23 "other" phenotype samples, including nonaffected family members and patients with atypical parkinsonism (Fig. 1A). In the standard procedure, sporadic PD patients and controls were genotyped using the Illumina NeuroBooster Array,[33] whereas suspected monogenic PD patients and their affected and nonaffected family members underwent both whole-genome sequencing (WGS) and genotyping.[32] We are currently transitioning to ensure that all GP2 samples will exclusively undergo WGS. After analysis, the resulting data are returned to the respective groups for further investigation and interpretation, with GP2 providing support and expertise in data analysis, interpretation, and dissemination of results.

To date, GP2 has genotyped 2633 African, 1107 African admixed, and 824 participants with complex admixture history (CAH),[34] with 1806 samples having undergone WGS. The CAH ancestry group was introduced in response to a large number of samples with South African and other highly admixed individuals being incorrectly predicted as Central Asian ancestry. These samples are too highly admixed to be included in analyses with other GP2 ancestry groups.[35] DNA isolation and genotyping of African participants are facilitated through collaborative efforts.[32] For instance, GP2 has funded the establishment of a DNA extraction laboratory at the University of Lagos to support local DNA extraction and biobanking. This initiative reduces shipping costs and addresses a major barrier in the region, where sequencing facilities are limited and extremely costly. This improved infrastructure has enabled WGS of 1786 Nigerian samples. Furthermore, GP2 has initiated an incentive for newly recruited large families with unsolved monogenic forms of the disease.[36] This incentive allows principal investigators to further invest in local PD research.

Many African researchers experience "helicopter research," where researchers from high-income countries visit lower-income areas to recruit participants and collect samples. In this scenario, laboratory work and data analysis occur outside the region, and published results often lack involvement from local researchers.[37] However, GP2's approach ensures local scientists are involved throughout the research process, providing opportunities for skill development and capacity building. GP2 ensures that genotyping and sequencing data generated are returned to the study sites. Additionally, GP2 investigators are encouraged to propose projects that align with GP2 objectives. These proposals are reviewed by the Project Proposal, Approval, and Execution Working Group to ensure efficient implementation. To date, GP2 has published 29 research articles, 10 of which were coauthored by African collaborators (Table S1).

The success of GP2's collaborative efforts is exemplified by the largest GWAS of PD in African and African admixed ancestry to date.[38] The novel African-ancestry variant GBA1 c.1225-34C > A (rs3115534) was found in 39% of patients studied, demonstrating its significant impact on PD risk compared to common variations identified in previous GWAS. The study integrated data from the International Parkinson's Disease Genomics Consortium—Africa (IPDGC Africa) and GP2 and summary statistics from 23andMe, Inc., emphasizing the importance of including underrepresented populations in genetic research to understand the genetic basis of PD.

Training and Capacity Building

To address the shortage of neurologists and PD researchers, GP2 is building a network of researchers to promote collaboration in genetic research. Training clinicians and researchers is a key priority for GP2, led by
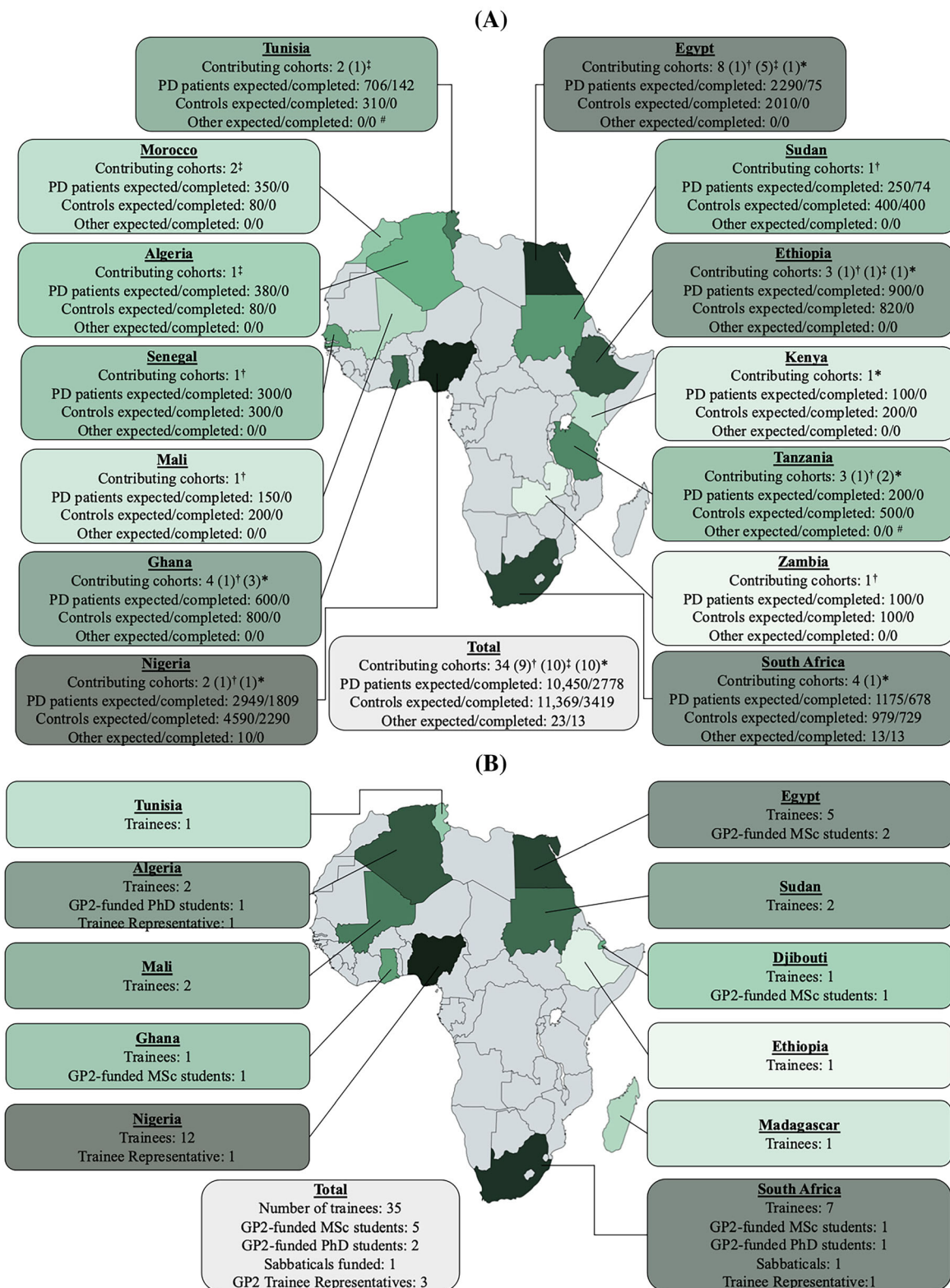
FIG. 1. (**A**) Map of Africa showing the number of cohorts contributing samples from 14 African countries to the Global Parkinson's Genetics Program (GP2), including the number of cohorts from the Transforming Parkinson's Case in Africa (TRaPCAf-GP2) collaboration (*), the International Parkinson's Disease Genomics Consortium—Africa (IPDGC Africa) (†), and AfrAbia-GP2 (‡). The map includes the expected and completed numbers for Parkinson's disease (PD) patients, controls, and "other" individuals (nonaffected family members and patients with atypical parkinsonism). Countries expected to expand to recruit patients with atypical parkinsonism are indicated by a hashtag (#). (**B**) Map of Africa showing the 11 countries with GP2 trainees, trainee representatives, and GP2-funded students in Africa. The darker the color, the higher the number of participants. All values are accurate as of September 12, 2024. PD, Parkinson's disease; MSc, master of science. [Color figure can be viewed at wileyonlinelibrary.com]

the Training and Networking group (TN-WG), to dedicate resources and efforts providing both general and tailored training for researchers and clinicians. The GP2 Trainee Network currently consists of 260 members worldwide, with 35 trainees and 3 trainee representatives in Africa.

As part of the TN-WG training resources, the web-based GP2 learning platform (https://training.gp2.org/) had over 1110 registered users as of September 2024 (6.3% from Africa).[39] This platform offers free virtual training, in multiple languages, through a user-friendly, accessible interface. Additionally, the TN-WG provides tailored training programs designed to meet the needs of GP2 researchers, particularly underrepresented collaborators. These training opportunities include short courses, workshops, regional training initiatives, master's and PhD programs, visiting fellowships, placements, and sabbaticals (Fig. 1B), and equip local researchers with bioinformatics expertise, enabling them to conduct analyses using GP2 data. These initiatives address challenges related to mentorship, guidance, and funding for underrepresented clinicians and researchers, fostering capacity building in their regions and strengthening partnerships within the GP2 network.

Conclusion and Future Directions

In collaboration with GP2, the Transforming Parkinson's Case in Africa (TRaPCAf-GP2) study is underway across seven African countries and is expected to contribute 1000 PD patients and 2000 controls to GP2.[40] Furthermore, IPDGC Africa plans to expand its recruitment to 12 French-speaking countries to enhance GP2's coverage across Africa. GP2 is committed to performing WGS on all African PD patients to aid in identifying novel PD variants. As of June 2024, GP2 has 55 active projects, 22 involving African trainees and collaborators, emphasizing the contribution from both early-career and established researchers. The TN-WG is actively developing new training resources for African PD researchers, including in-person bioinformatics workshops, with one scheduled for Morocco in November 2024.

Upon completion of GP2, we anticipate a significant increase in professionals skilled in clinical research, genetics, and bioinformatics, along with strengthened collaborations among these experts, which will drive substantial progress in PD research in Africa. Ultimately, building strong partnerships with African institutions and encouraging their active involvement are crucial for the long-term sustainability of the initiative. ∎

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

References

1. Lim S-Y, Klein C. Parkinson's disease is predominantly a genetic disease. J Parkinsons Dis 2024;14:467–482.

2. Schumacher-Schuh AF, Bieger A, Okunoye O, et al. Underrepresented populations in Parkinson's genetics research: current landscape and future directions. Mov Disord 2022;37:1593–1604.

3. Elsayed I, Martinez-Carrasco A, Cornejo-Olivas M, Bandres-Ciga S. Mapping the diverse and inclusive future of Parkinson's disease genetics and its widespread impact. Genes 2021;12:1681.

4. Ben-Joseph A, Marshall CR, Lees AJ, Noyce AJ. Ethnic variation in the manifestation of Parkinson's disease: a narrative review. J Parkinsons Dis 2020;10:31–45.

5. Galal S. Population of Africa as a Share of Global Population 2020–2050; https://www.statista.com/statistics/1224632/population-of-africa-as-a-share-of-global-population/ 2024.

6. Milanowski LM, Oshinaike O, Broadway BJ, et al. Early-onset Parkinson disease screening in patients from Nigeria. Front Neurol 2020;11:594927.

7. Okubadejo NU. An analysis of genetic studies of Parkinson's disease in Africa. Parkinsonism Relat Disord 2008;14:177–182.

8. Choudhury A, Aron S, Botigué LR, et al. High-depth African genomes inform human migration and health. Nature 2020;586:741–748.

9. Zabetian CP, Hutter CM, Yearout D, et al. LRRK2 G2019S in families with Parkinson disease who originated from Europe and the Middle East: evidence of two distinct founding events beginning two millennia ago. Am J Hum Genet 2006;79:752–758.

10. Thaler A, Ash E, Gan-Or Z, Orr-Urtreger A, Giladi N. The LRRK2 G2019S mutation as the cause of Parkinson's disease in Ashkenazi Jews. J Neural Transm 2009;116:1473–1482.

11. Lesage S, Dürr A, Tazir M, et al. *LRRK2* G2019S as a cause of Parkinson's disease in North African Arabs. N Engl J Med 2006;354:422–423.

12. Dekker MCJ, Coulibaly T, Bardien S, Ross OA, Carr J, Komolafe M. Parkinson's disease research on the African continent: obstacles and opportunities. Front Neurol 2020;11:512.

13. Bentley AR, Callier SL, Rotimi CN. Evaluating the promise of inclusion of African ancestry populations in genomics. NPJ Genom Med 2020;5:5.

14. Mekolle JE, Tshimwanga KE, Ongeh NJ, et al. Political instability and hiv/aids response in the south west and north west regions of Cameroon: a qualitative study. BMC Public Health 2023;23:2155.

15. Le T-H, Bui M-T, Uddin GS. Economic and social impacts of conflict: a cross-country analysis. Econ Model 2022;115:105980.

16. Onohuean H, Aigbogun EO, Igere BE. Meta-synthesis and science mapping analysis of HIV/HPV co-infection: a global perspective with emphasis on Africa. Glob Health 2022;18:36.

17. Alegana VA, Macharia PM, Muchiri S, et al. *Plasmodium falciparum* parasite prevalence in East Africa: updating data for malaria stratification. PLOS Glob Public Health 2021;1:e0000014.

18. Moyo S, Ismail F, Mkhondo N, et al. Healthcare seeking patterns for TB symptoms: findings from the first national TB prevalence survey of South Africa, 2017-2019. PLoS One 2023;18:e0282125.

19. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019;18:459–480.

20. GBD 2021 Nervous System Disorders Collaborators. Global, regional, and national burden of disorders affecting the nervous system, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Neurol 2024;23:344–381.

21. Bower JH, Diop AG, Gouider R, Schmutzhard E. Addressing neurologic needs in sub-Saharan Africa: an opportunity for multisociety cooperation. Neurology 2014;83:1207–1209.

22. Kissani N, Liqali L, Hakimi K, et al. Why does Africa have the lowest number of neurologists and how to cover the gap? J Neurol Sci 2022;434:120119.

23. Aderinto N. Meeting the neurology demand: the impact of early exposure and mentorship on African medical students. Egypt J Neurol Psychiat Neurosurg 2023;59:164.

24. Yusuf S, Baden T, Prieto-Godino LL. Bridging the gap: establishing the necessary infrastructure and knowledge for teaching and research in neuroscience in Africa. Metab Brain Dis 2014;29:217–220.

25. Massi DG. The real barriers for neurology education in Africa and future directions. J Neurol Sci 2021;429:117881.

26. Brock-Utne B. Language of instruction in Africa - the most important and least appreciated issue. Int J Educ Dev Afr 2014;1:4–18.

27. Mshana G, Dotchin CL, Walker RW. 'We call it the shaking illness': perceptions and experiences of Parkinson's disease in rural northern Tanzania. BMC Public Health 2011;11:1–8.

28. Tiffin N. Tiered informed consent: respecting autonomy, agency and individuality in Africa. BMJ Glob Health 2018;3:e001249.

29. Agoundedemba M, Kim CK, Kim H-G. Energy status in Africa: challenges: progress and sustainable pathways. Energies 2023;16:7708.

30. Nyokabi DM, Diallo N, Ntesang NW, White T, Ilori T. The right to development and internet shutdowns: Assessing the role of information and communications technology in democratic development in Africa. Glob. Campus Hum. Rights J (2019);3:147–172.

31. Adebamowo SN, Francis V, Tambo E, et al. Implementation of genomics research in Africa: challenges and recommendations. Glob Health Action 2018;11:1419033.

32. Global Parkinson's Genetics Program. GP2: the global Parkinson's genetics program. Mov Disord 2021;36:842–851.

33. Bandres-Ciga S, Faghri F, Majounie E, et al. Neurobooster array: a genome-wide genotyping platform to study neurological disorders across diverse populations. Mov Disord 2024. https://doi.org/10.1002/mds.29902

34. Leonard H, Nalls MA, Vitale D, et al. The Components of GP2's Seventh Data Release; https://gp2.org/the-components-of-gp2s-seventh-data-release/ 2024.

35. Leonard H, Nalls MA, Vitale D, et al. The Components of GP2's Sixth Data Release; https://gp2.org/the-components-of-gp2s-sixth-data-release/ 2024.

36. GP2 Monogenic Network. Large family incentive. *Monogenic Network: a project of GP2*; https://monogenic.gp2.org/LargeFamilyIncentive.html 2024.

37. Minasny B, Fiantis D, Mulyanto B, Sulaeman Y, Widyatmanti W. Global soil science research collaboration in the 21st century: time to end helicopter research. Geoderma 2020;373:114299.

38. Rizig M, Bandres-Ciga S, Makarious MB, et al. Identification of genetic risk loci and causal insights associated with Parkinson's disease in African and African admixed populations: a genome-wide association study. Lancet Neurol 2023;22:1015–1025.

39. Global Parkinson's Genetics Program. GP2 Learning Platform; https://gp2.org/training/ 2024.

40. Walker R, Fothergill-Misbah N, Kariuki S, Ojo O, Cilia R, Dekker MCJ, et al. Transforming Parkinson's Care in Africa (TraPCAf): protocol for a multimethodology National Institute for Health and Care Research Global Health Research Group Project. BMC Neurol 2023;23:373.

Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique

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E.E.: 3A
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