How internal medicine is impacted by the overrepresentation of Nigeria in African North American ancestral genetic databases.

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Abstract

The genetics of African North Americans are complex amalgamations of various West and Central African peoples with modest gene flow from specific European and Amerindian peoples. The recently reported overrepresentation of Nigerian lineages in African North Americans reflects pronounced limitations in the African genomic database, the artificiality of the colonial maps of Africa, the contributions of multiple African empires and kingdoms into the transatlantic trade in enslaved Africans, and the overrepresentation of Yoruba peoples in the existing limited representation of West Africans in public genomic databases. For internal medicine, this overrepresentation reinforces the use of long held cultural stereotypes in clinical and didactic presentations. It encourages "short cut" assumptions that may not be biologically or sociologically sound. Additionally, this overrepresentation supports existing unconscious biases that harm holders and recipients of the biases and increases the magnitude of unintentional harm done to Legacy African North American patients.

Keywords: Genomic database, Stereotypes, Yoruba peoples.

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Introduction

Legacy African North Americans are those lineages who have experienced 400 years of existence in America, including kidnapping and enslavement, institutional racism, discrimination, and segregation for as many as 16 generations of residency. Contemporary Legacy African North Americans reflect a broader degree of genetic variation than that express among current Nigerians. This is because these Diasporic Africans represent an amalgamation of African peoples from West, West Central and Southeast Africa with modest amounts of genetic admixture with North Atlantic and Iberian Europeans and specific local Amerindian groups. This unique gene pool has been created in the North American context with 212 years of separation from continental Africa. Due to this extensive separation and the ecological and subsistence differences of North America with much of West, West Central and Southeast Africa, Legacy African North Americans present distinctive profiles of gene-environment, gene-gene, and gene-protein interactions than do more recent voluntary immigrants from continental Africa. These differences reflect the specific ways in which Legacy African North Americans have adapted to the peculiarities of the North American environment. This leads us to predict major differences in the epigenomes of Legacy African North Americans compared to those of continental Africans [1].

The current Direct-To-Consumer (DTC) testing and the existing public databases are the main sources of genetic information on Legacy African North Americans. These databases consistently over represent Nigeria as the ancestral genetic homeland of Legacy African North Americans [2] yet these reference databases are significantly lacking in broad African genomic representation and are heavily skewed towards Yoruba Nigerians due to limitations in the original sampling strategies. Additionally, these reference databases do not include any of the relevant Amerindian groups that could have historically admixed with African North Americans [3]. In fact, the only fully accurate reference database currently for Legacy African Americans is that depicting North Atlantic Europeans ancestors [4].

The overrepresentation of Nigerian lineages in the ancestries of Legacy African North Americans reflects the confluence of many factors, beginning with the inadequacies of the existing African reference genomic database as well as weaknesses in comprehensively accounting for the geospatial history of modern Nigeria and that of contemporary Legacy African Americans. The weak integration of historical factors into the genomic studies has repercussions for the practice of internal medicine. This paper provides a mini-review of the relevant historical and epidemiological factors that have shaped aspects of Legacy African North American populations, particularly those events that have seemingly amplified the genetic signals of their Nigerian ancestry and then correlates these ancestral distortions with downstream ramifications for internists. We have identified seven main factors that have led to the current misrepresentation of the African North American reference genomic database with consequences for the practice of internal medicine.

The Artificiality of the Colonial Map in Africa

The borders of modern Nigeria are a post-colonial construction encompassing lands traditionally occupied by highly diverse ethnic groups with distinct languages, traditions, and cultures. Many of these groups formed highly organized empires and kingdoms that influenced areas beyond the current borders of modern Nigeria. The European colonial masters and their post-war agreements contrived Africa's current national borders,

creating fragile units in which ethnic, religious and linguistic groups were haphazardly thrown together or separated without any recourse to those groups‘ peculiarities, priorities, and aspirations [5-7]. This is part of the reason that these current political borders are not valid demarcation points for reconstructing historical patterns of ancestral genetics.

Regional Variation in the Proportions of Africans Brought From Different Regions into the Staging Areas of North America

Slavery was a legal institution in eastern North America in the 16th through 19th centuries. Immigration bias characterized the involuntary immigration of Africans to North America. For example, a large proportion 38% of the enslaved Africans brought into Chesapeake Bay was from the Bight of Bonny (Biafra) and was Ibo and Ibo-affiliated Africans [8]. This demographic distinction contrasts with the smaller proportions of Nigerian-derived Africans brought to either the Carolina Coast or the Mississippi Delta regions. The impact of this historic bias in forced immigration patterns from Africa has not yet been integrated into regional clinical practices in internal medicine.

Domestic slave trade introduces distortions into the African ancestries of african North Americans

In 1808, the US Congress barred the importation of enslaved Africans into the United States, significantly reducing the genomic influx of additional Africans from the continent into North America. However, the internal or domestic trade in enslaved Africans was left intact and took on a new importance in the slave-holding states. This domestic slave trade, and the interregional slave trade focused on enslaved Africans of the Chesapeake Bay region as the primary targets of this new strategy [9], disproportionately amplifying their genomes in subsequent generations of Legacy African North Americans. This is the basis of the artificial inflation of “Nigerian origins” in Legacy African North American

The role of slave rebellions in distorting african survivorship patterns

Rebellions among enslaved Africans and African Americans were a reoccurring source of European and European American fear and a basis for restrictive legislation in slave-holding states. As early as JA Rogers had identified 33 slave revolts, and this was undoubtedly just the tip of the iceberg. In the early decades of American slavery, participation in slave rebellions was often spiritually based, ethnically demarcated, and may have initiated African ethnicity-based selection against certain groups [10]. Unsuccessful rebellions, which were the majority, invariably ended in loss of life for the identified perpetrators, particularly those in the leadership, and loss of biological fitness if the rebel’s life was spared.

The emergence of african north american microethnic groups in the immediate post emancipation period

Remnants of state-sponsored chattel slavery and draconian segregation laws relegated a large proportion of Legacy African North Americans to populate the Southeastern part of the United States densely and disproportionately. It is within these settings that various Legacy African American micro ethnic groups emerged and proliferated [11]. Generations later, descendants of enslaved Africans are still clustered in the Southeastern states although few restrictions remained on the opportunities for within-country immigration.

Post enslavement migrations as significant initiators of displacement in african north americans

During the period of enslavement, the mobility of the average enslaved African North American was geospatially restricted. With emancipation, the migrations of previously enslaved individuals were pronounced, often to find lost family members, to seek employment opportunities, and to avoid the deadly backlash of white supremacist racial terrorism. The migrations of Legacy African Americans increased intra-group gene flow [12] despite the source populations being previously geospatially distinct.

Yoruba bias in public genetic databases

There is Yoruba domination in the early genetic databases such as 1000 Genomes and Hap Map [13,14]. That creates a deeply embedded Yoruba bias in our reconstructions of continental African diversity [15]. Evolutionary history [16,17] and Legacy African North American ancestry [18]. The use of continent-incomplete data sets to represent all of Africa introduces distortions in principle, including overrepresentation of high-allele frequencies, artifacts of small samples, over-extrapolations of Yoruba-specific patterns to other, unrelated Africans, and analysis of short genomic regions that underestimate long-range LD. Moreover, specific genomic regions examined may not be representative of genome wide patterns for LD [19] or CNV, potentially because of extreme natural selection at these regions. The Yoruba are not prototypical Africans [20] and assumptions that their demographic history is less complex than other groups [8] are simply not true and not consistent with Yoruba traditional history. It is important to note that the term Yoruba (or Yariba) did not come into use until the 19th century and was originally confined to subjects of the Oyo Empire. So most of the current ancestral genomic reconstructions are a historic and prejudiced by inadequacy.

Ramifications for the Practice of Internal Medicine

For internal medicine, this overrepresentation of Nigerians and specifically the Yoruba peoples in the ancestral lineages of Legacy African North Americans reinforces the use of long held cultural stereotypes in clinical and didactic presentations. This is irrespective of the subspecialty of internal medicine

practiced. The assumption that Legacy African North Americans are uneducated, poor, and fraudulent, for example, is amplified by the overrepresentation of Nigerian genetic ancestry, not because Nigerians exhibit these traits, but because the traits are part of the myth of African inferiority. Indeed, Nigerians today are among the most literate on the African continent and the GNP per capita of Nigeria is ranked as the 27th-largest economy in the world in terms of nominal GDP, and the 24th-largest in terms of purchasing power parity. The GDP in Nigeria is expected to reach 250.00 USD Billion by the end of 2020, according to Trading Economics global macro models and analysts' expectations. In the long-term, the Nigeria GDP is projected to trend around 360.00 USD Billion in 2021 and 450.00 USD Billion in 2022, according to many econometric models.

Internal medicine is generally divided into eleven subspecialities and in each; compassion is an expectation of patients, regulatory bodies, and physicians themselves. The Transactional Model of Physician Compassion (TMPC) [21] suggests that physician, patient, external environment, and clinical factors are all relevant components of the quality of care. A key assumption of TMPC is that the physician's perception of the patient's environment influences physician interaction and efficacy. However, for the practice of internal medicine, the uncritical appellation of Legacy African North Americans as "so many Nigerians" promotes "short cut" assumptions that may not be biologically or sociologically accurate, reduce physician compassion, and indeed may be harmful to patients. Assumptions lead to the wrong diagnosis, wrong treatment and can alienate clinicians and scientists from those we are trying to help. Everyone wants to fill in the blanks based on what we assume is true. However, when internists do that to diagnosis a patient, it can be dangerous. Internal medicine requires the constant calculation of probability; however, this probability must be based on comprehensive and accurate ancestral reconstructions [22,23].

Conclusion

The overrepresentation of Nigeria in the ancestral genetics of Legacy African North Americans can tend to support existing unconscious biases that harm holders and recipients of the biases and increase the magnitude of unintentional harm done to Legacy African North American patients. This further alienates this population, magnifying existing health disparities, increasing the potential for Adverse Drug Reactions (ADRs) and drug non-compliance, and further delaying patient access to accurate precision medicine. Since internal medicine physicians specialize in diagnosis, treatment, and prevention of disease in adult patients and are trained to offer care for a wide variety of health conditions and to counsel their patients on prevention and overall wellness, it is particularly essential that internists have accurate ancestral and individualized genomic knowledge of their patients. The medical "hesitancy" observed in many Legacy African North Americans can be best addressed with corrected ancestral genomic knowledge which can be beneficially integrated into clinical practice.

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