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The use of race as a demographic variable in clinical research*

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SUMMARY

Background: *Researchers continue to categorise demograpic variables according to racial lines despite the fact that the definition of race has no scientific or anthropological validity.*

Purpose: *The aim of this article is to discuss the scientific rationale for using race as a demographic variable in clinical research and to explore other suitable alternatives such as ethnicity, genetics and the nasal index in rhinology research.*

Results: *There is consensus that research subjects should not be classified along racial lines. However, there is evidence that this practice remains prevalent. Ethnicity is not a good substitute for race. Whilst genomics is an objective measure of variation, it does not measure the impact of socioeconomic status, exposure to health risk factors and the availability of healthcare on populations.*

Conclusions: *It is important to define the population demographics in any study, but race appears to be a category without any scientific basis. Other parameters that may be important such as ethnicity and genetics are still not fully developed to be useful. At present there is no generally accepted way of describing and classifying the subjects. The nasal index may be a suitable discriminator of variation for studies in rhinology but more studies are required to define its clinical relevance.*

Key words: *race, ethnicity, research, rhinology, nasal index*

In any clinical or scientific study on humans, it is deemed important to describe the study population in a variety of terms such as age, gender, weight and height. In addition to these demographic data, it is also common to include the variable of race divided into Caucasian, African or Asian. Researchers continue to classify subjects in clinical trials according to racial lines despite the fact that race has no scientific or anthropological validity [(1)]. This practice has been occurring for many decades and has previously generated much literature in classifying races according to nasal dimensions [(2)]. It is difficult to explain this inertia in removing racial classification from demographics given that many medical journals have guidance on the use of ethnic, race and cultural descriptions in clinical research. For example, the British Medical Journal (BMJ) recommends that authors who use ethnicity or race as a variable in clinical trials should describe how the groups were distinguished [(3)]. For example, "black as a group description is less accurate than self assigned as black Caribbean, and Asian less accurate than UK born individuals of Indian ancestry or French born individuals of Vietnamese ancestry". According to Kaplan and Bennett, only a few journals have published explicit policy statements or guidelines, including the BMJ, Paediatric and Perinatal Epidemiology, Nature Genetics, and the Archives of Pediatrics and Adolescent Medicine [(4)]. Smart et al. reported five other journals have similarly advised authors against using race as a variable [(5)].

This article intends to discuss the scientific rationale for using race as a demographic variable in clinical research and to explore other suitable alternatives such as ethnicity, genetics and nasal index. The arguments for and against using race in biomedical research is also considered in this review.

THE ORIGINS OF "RACE"

The word "race", interpreted to mean "common descent", was introduced into the English language in the 16th century. The etymology of "race" can be traced to the French *rasse* and Spanish *raza*, which was derived from the Latin word *generatio* (a begetting).

Race is a multifaceted concept which has been studied and debated by many people over centuries. According to Smedley and Smedley, the 18th century was the period when race signified a new ideology about human differences and a new way of structuring society that had not existed before in human histo-

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ry. Individuals in ancient civilisations bearing widely varying physical appearances could become full members of a society by growing up within that society or by adopting the society's cultural norms [6]. The fabrication of a new type of categorisation for humanity and human identity was needed because the leaders of the American colonies had deliberately selected Africans to be slaves on the pretext that Africans were created separately from other, more human, beings [7]. These racial categories were based on externally visible traits, primarily skin color, features of the face, and the shape and size of the head and body, and the underlying skeleton [8]. These prejudices were justified by an assumption that dark-skinned people were considered inferior to fairer-skinned Europeans [9]. It imposed social meanings on physical variations among human groups that served as the basis for the structuring of society. This ideology has persisted despite the abolition of slavery and other great social changes (e.g. Nazism, apartheid), and it continues to permeate every aspect of modern civilization [10].

IS RACE STILL USED AS A DEMOGRAPHIC IN CLINICAL RESEARCH?

Race remains a predominant feature in medical research. In fact, the use of 'race' and 'ethnicity' as variables in medical literature has been increasing over the past 40 years [11]. A review of all original articles and case reports published in this journal over a two year period, from 2007 to 2008, revealed seven articles which have used race, ethnicity or nationality to describe the respective study populations. Two of these articles categorised the study population according to different races.

Sankar et al. surveyed a selection of high impact factor clinical research journals to examine how race or ethnicity was used to label the study population [12]. They reported that up to half (49.7%) of the articles reviewed used race as the label for the study population. Another 23% used race or ethnicity to label the study population, but did not report results using this term nor test any hypothesis related to it. None of the articles reviewed by Sankar et al. even defined the race or ethnicity of the study populations.

A longitudinal study covering 48 years of research articles published in a high impact factor journal focusing on research in nursing reported that race was mentioned in almost half (49.5%) of the 337 articles reviewed [13]. In this study, Drevdahl et al. also reported that the majority (77%) of these articles studied cohorts which were defined as either being white or Caucasian. They found an increasing trend of articles referring to race between 1952 and 2000. Despite this increased use of race, Ma et al. reported that the quality of race information collected in many clinical trials was generally poor [14]. After reviewing over 1,150 original research articles published between 1999 and 2003 in 4 high-impact general medical journals (Annals of Internal Medicine, JAMA, The Lancet, The New England Journal of Medicine), the investigators reported that the categorization of racial classes was ambiguous and variable, rendering comparability of data and application of clinical data across studies difficult. In addition, they found that few papers explicitly stated why race information was collected or used, even when authors examined for associations between race and outcome. They conclude with a caution to readers in the interpretation of racial data made in clinical trials. Similar ambiguity was also noted by Shanawani et al. who reported that 72% of 268 articles reviewed did not explain the methodology of assigning race or ethnicity of the study subjects [15].

IS THERE SCIENTIFIC RATIONALE FOR USING RACE?

Although self-reported race or ethnicity is widely used in clinical trial demographics, it is clear that race is neither a scientific nor physiological grouping. According to Hoover, skin colour is the indicator most frequently used for race [16]. Although skin colour is a continuous variable, it is used as a dichotomous variable despite the lack of specific guidelines for determining the point at which the boundary between colours is made. In order for race-based research to have any scientific basis, each individually defined or self-declared race would have to have 100% pure and homogenous gene pool. Humans share 99.9% genomic similarity and the small amount of real genetic difference (0.01%) highlights the difficulties of recognising the racial identity of individuals through their genes. As such, race is a crude marker of variability, and using self-identification as a member of a particular race is scientifically unsound, leading to a highly heterogenous group for study [17].

For example, BiDil® (isosorbide dinitrate/hydralazine hydrochloride) was approved by the Food and Drug Administration (FDA) in June 2005 for the treatment of heart failure in African-Americans [18]. This drug has been frequently cited as an example of race-based treatment. Critics have debated the fundamental flaws in the study which is based on several assumptions. According to Duster, the assumption that African-Americans have a significantly higher risk of developing and succumbing to heart failure compared to white Americans was wrong [19]. In fact, this risk was the same between the two groups. Duster also states that the BiDil study assumed that the drug had a higher effect on African-Americans than on white people when the study did not test this hypothesis.

Although comparatively rare worldwide, nasopharyngeal carcinoma (NPC) has substantial incidence and mortality in populations of southern Chinese ancestry in China and Southeast Asia. NPC is believed to result from a combination of genetic susceptibility, infection with Epstein-Barr virus, alcohol consumption, cigarette smoking and regular consumption of salted fish beginning in childhood [20]. However, the incidence of NPC has been noted to decrease in migrant Chinese populations. This indicates that environmental and lifestyle changes play an important role in the declining incidence of NPC over

time [21,22]. It can be appreciated that health screening programmes which target populations of a certain race may be ineffective when taken out of context.

Conversely, other authors have reasoned for the continued use of race and ethnicity in medical research. Doyle et al. wrote that race and ethnicity play an important part of a person's culture, diet and health behaviours [23]. For example, drug absorption and metabolism may differ depending on race-specific or ethnic-specific diets. Cultural differences in beliefs about medicine and medical practice which influences adverse event reporting, treatment response and disease progression are other reasons given by Doyle to try and differentiate groups for research. Cohn wrote that "the debate (therefore) should not be over the existence of population differences, but how to describe those differences with more precision" [24]. He argues that race may be used like age, blood pressure, cholesterol and sugar levels which have been used in medicine and clinical trials to identify patients at higher risk or greater likelihood of therapeutic response.

IS ETHNICITY A GOOD ALTERNATIVE?

As problems surrounding the use of race became increasingly apparent in the 20th century, the word "ethnicity" was promoted as a way of characterising differences between groups. Ethnicity typically emphasises the cultural, socioeconomic, religious, and political qualities of human groups. It may also encompass language, diet, dress, customs or historical identity. It would ostensibly appear that ethnicity is a better tool of taxonomy than race in research, and this has resulted in the significantly higher increase of "ethnicity" used in the literature compared to "race" as reported by Afshari and Bhopal [11]. However, the use of ethnicity as the alternative to race has not been the panacea as envisaged. In fact, its actual application has often been similar to race [25]. Both Ma et al. and Shanawi et al. found that the definition of ethnicity used in current research articles were just as ambiguous and vague as that of race [14,15].

It is evident that ethnicity is a term with multiple and frequently conflicting meanings and interpretations [26]. As a social construct like race, each ethnic group contains a history that alters over time. The researcher should be sensitive to the effects of changing economic status, social class, relations with other groups, discrimination, and relative political power when using ethnicity in research. Oppenheimer states that "its weakness is also a strength" [27]. If applied in its original sense to define a population socially or culturally, ethnicity can replace race in research when a researcher seeks a variable that corresponds to the behavioural aspects implied by the term, such as diet, occupation, social status, or health beliefs [26].

WHAT ABOUT GENETICS?

To the geneticist, a race is a population which differs from other populations in the frequency of its genes. In almost all parts of the world, intermarriage between neighbouring populations has resulted in gradual shifts in gene frequencies between one region and another, and genetic studies revealed a surprising degree of genetic similarity between the peoples of the world – far greater than is suggested by physical appearance. It is widely anticipated that recent advances in pharmacogenetics will pave the way for a new generation of more individualised therapies [28]. Geneticists believe that using genetic differences to separate groups will underscore the irrelevance of racial and ethnic labels for pursuing many research questions and health improvement objectives [6].

However, the use of genetics to stratify study cohorts in medical research is not without limitations. Genetics is a statistical concept that deals with populations, not individuals or groups of people. Yet in real life it is the individual differences that matter. Genetics will not substitute for the importance of race and ethnicity because these parameters are often un-related to any significant genetic differences, as they are more related to culture and society. Unlike genes, racial and ethnic categories are social constructs. Two persons with identical genetic make-up may well self-identify as being of a different race or ethnic origin. As race and ethnicity plays an important role not least in determining socioeconomic status, exposure to health risk factors and the availability of healthcare, it is thus conceivable that all three variables will have to be considered in healthcare research.

NASAL INDEX FOR STUDIES IN RHINOLOGY

In respect to studies on nasal physiology and airflow dynamics, the nasal index can be considered as a suitable adjunct to the common variables used in patient demographics. The nasal index compares the width of the base of the nose with the height of the nose. The index is calculated from the following formula:

Width of the nose x 100 / Height of the nose

A high index indicates a broad nose and a low index a narrow nose. A nasal index below 70 is described as lepthorrhine and when above 85 it is platyrrhine. An intermediate index of 70 to 85 is described as messorhine [29]. The leptorrhine, mesorrhine and platyrrhine nasal types were commonly associated with Caucasians, Asians and Africans respectively [30,31].

Previous studies have not demonstrated variations in nasal physiology with the nasal index [2]. As rhinology research is often confounded by classifying populations according to race, the nasal index may be a better discriminator of variation [2]. Apart from nasal aesthetics, the clinical relevance of the nasal index remains to be clarified. However, we hope that this review will stimulate future investigators to consider parameters such as the nasal index in rhinology research and to find better alternatives to the use of race in determining demographics.

CONCLUSION

As race is such an emotive concept, it is likely that its' relevance in biomedical research will be debated for years to come. There are those who refute the biological basis for race and those who accept that the concept of race has important scientific meaning. For supporters of the concept of race, race represents a proxy for social, cultural and economic variables, and the idea that a racialised way of life may affect predisposition to disease and health outcomes. Conversely, those who oppose the use of race believe that it is not an objective discriminator as compared to genetic typing. The authors' view is that race, ethnicity and genetics are all important in biomedical research, especially in public health studies. Racial and ethnic categories should not be eliminated from the demographics of studies but should be improved on by proper scientific description of how the classifications in the demographics have been obtained. In rhinology research where the main interest is on nasal variations, the use of the nasal index may provide more relevant information about the populations under study than any use of race in demographics.

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