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Clinician Perspectives on Race and Genetic Ancestry Data when Treating Hypertension

A Thesis submitted in partial satisfaction of the requirements
for the degree Master of Arts

in

Anthropology

by

Chantal Rabay

Committee in charge:

Professor Amy L. Non, Chair
Professor Pascal Gagneux
Professor Ramya M. Rajagopalan
Professor Saiba Varma

2023

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University of California San Diego

2023

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ABSTRACT OF THE THESIS

Clinician Perspectives on Race and Genetic Ancestry Data When Treating Hypertension

by

Chantal Rabay

Master of Arts in Anthropology

University of California San Diego, 2023

Professor Amy L. Non, Chair

Despite the general consensus that there is no biological basis to race, racial categorization is still used by clinicians to guide diagnosis and treatment plans for certain diseases. In medicine, race is commonly used as a rough proxy for unmeasured social, environmental, and genetic factors. The American College of Cardiology's Eighth Joint National Committee's (JNC 8) guidelines for the treatment of hypertension provide race-specific medication recommendations for Black versus non-Black patients, without strong genetic evidence for racial differences in drug response. Clinicians practicing family or geriatric medicine (n=21) were shown a video of a mock hypertensive patient with genetic ancestry results that were discordant with their phenotype and self-identified race. After viewing the videos, we conducted in-depth interviews to examine how clinicians value and prioritize different cues

about race -- namely genetic ancestry data, phenotypic appearance, and self-identified racial classifications – when making treatment decisions in the context of race-specific guidelines, particularly in situations with patients of mixed-race. Results indicate that clinicians inconsistently follow the race-specific guidelines for patients with unexpected genetic ancestry relative to their skin color and facial features, and many emphasized clinical experience, side effects, and other factors in their decision making. Clinicians' definitions of race, categorization of the patient's race, and prioritization of racial cues greatly varied. The existence of the guidelines clearly influences treatment decisions even if clinicians were unsure of how to incorporate consideration of the patients' genetic ancestry. More research is needed to determine if there is a true racial difference in medication response and if guidelines exacerbate racial disparities in hypertension, and researchers should revisit the clinical justification for maintaining these race-specific guidelines.

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INTRODUCTION

Hypertension is the number one disease responsible for racial disparities in mortality in the United States and is found in 39% of Black individuals compared to 29% of White individuals (Fiscella and Holt, 2008). As a complex disease with biological, genetic, and sociocultural contributors underpinned by experiences of stress, racism, discrimination, and a contentious history of race-specific guidelines recommended for treatment, hypertension has been the source of heated debate around the use and value of race in medicine (Gravlee, 2009; Kaufman et al., 2015; Non et al., 2012). The treatment of hypertension is currently guided by the American College of Cardiology's JNC 8 race-specific guidelines, dating back to 2010, which recommend distinct treatment plans for Black versus non-Black patients. Specifically, the JNC 8 guidelines state that patients "in the general Black population" should be started on a thiazide diuretic and/or calcium channel blocker while patients "in the general non-Black population" are to be started on an Angiotensin-converting enzyme (ACE) inhibitor, a Angiotensin II receptor blocker (ARBs), a thiazide diuretic (TDs), and a calcium channel blocker (CCBs) (Armstrong, 2014). These guidelines are based on the 1994 *ALLHAT* study, which found that ACE inhibitors were not as effective in Black patients compared to White patients (ALLHAT, 2002). However, the validity of this study has been strongly debated for flaws in study design and analyses, too rapid peer review, and contradictory results from other studies (Davis et al., 2004; Meltzer, 2003). A major oversight in developing these guidelines is that race is not well-defined within the JNC 8 guidelines or the *ALLHAT* study, and neither account for individuals of mixed race who are poorly captured by the binary racial categories used.

While some studies have explored the efficacy of race-based guidelines (Cerdeña et al., 2022, 2020; Gopal and Francis, 2021; Reddick, 2023), few have investigated clinicians' use and general perspectives towards these guidelines, particularly in the challenging situations of patients who do not conform to expectations based on racial stereotypes. When deciding whether to follow a race-specific guideline, clinicians must consider the validity of the guideline, and whether they believe it is beneficial

in guiding a treatment plan. It is not clear how clinicians view these guidelines, whether they are implementing them in practice, and what factors influence their decision to do so.

Further, if clinicians choose to follow these guidelines, they are faced with the challenge of making determinations about a patients' race. Classifying race in a clinical setting can be a fraught task, particularly in patients with complex ancestry. Clinicians may choose between variable or contradictory factors such as physical appearance, patient self-identity or genetic ancestry, but their determinations are rarely discussed in clinical encounters. Little is known about how clinicians generally use racial cues in making medical decisions for hypertension, or in medicine in general, and whether they prioritize phenotypic appearance over self-identified race or genetic ancestry data. In fact, there is a lack of research on whether clinicians generally value or ever use genetic ancestry data when treating patients or classifying their race.

The purpose of this study is to explore clinicians' use, knowledge of, and general perspective around the race-specific guidelines for treating hypertension, a commonly racialized disease, and to determine which racial cues were prioritized in making these decisions. We analyzed interview data from 21 clinicians who were shown video cases of mock mixed-raced patients with early hypertension. The clinicians were asked to provide a description of the case along with a treatment plan and justification for their plan, and share their views on the role of race and genetic ancestry in the presented case and in medical practice in general. We analyzed which patient characteristics the clinicians prioritized when treating hypertension, and how they utilized race and genetic ancestry data in their treatment plans. The findings of this study have important implications for the value of JNC8 guidelines in clinical practice, particularly for patients with mixed or complex ancestries. Further, our findings speak to the need for clinician training around the role of race in medicine, and specifically the value and use of genetic ancestry data in clinical practice.

METHODS

Out of 104 clinicians practicing Adult Family Medicine at University of California San Diego Health Hospital contacted through email, 21 agreed to participate in the study. Participating clinicians completed a brief demographic survey to share their self-reported race, gender, age, time in practice, and location of medical training (Table 1). The sample included a roughly equal split by gender. Eight clinicians identified as White (one specified White Jewish and one specified White middle eastern), and three identified as Caucasian; for the purposes of this study we considered these 11 clinicians as "White." We considered eight clinicians as "Asian" (one identified as Asian, one as South Asian, one as Korean, three as Indian, two as Chinese). Two clinicians declined to state their race or ethnicity. The clinicians were interviewed by one of three White female researchers. The interviews took place between February 2019 and August 2019, ranged from 15 to 60 minutes in length, and were audio-recorded with participant permission. The study protocol was approved by the Institutional Review Board at University of California San Diego.

At the start of the interviews, participants were presented with one of two short 3–5-minute mock video cases designed intentionally to have genetic ancestry results that differ from the patient's self-identified race. Case 1 presented a patient who self-identified as mixed race. She noted that she was surprised to find she had only 15% African ancestry when she received her 23andme results. Case 2 presented a patient who self-identified as White. She reported that she was surprised to learn she had 53% African ancestry. No other ancestry components were shared with the clinicians. Patients did not state anything about their racial self-identity in the video, but it was included in a vital measures report shown to each clinician, which also indicated standard values for BMI, height, weight, respiratory rate, heart rate, temperature, oxygen saturation, and presented three elevated systolic blood pressure readings, indicating hypertension.

The clinicians were first asked to describe the patient's case, followed by more specific questions about their diagnosis and treatment plan, and their general views regarding race and genetic ancestry (See Appendix for the complete list of questions). Clinicians were specifically asked to provide a medication-

based treatment plan, assuming all other non-medication options were exhausted. The interviews were de-identified, transcribed, and corrected for mistakes. An initial codebook was created detailing themes of interest relevant to the questions in the interview guide, along with definitions for how to apply each code. Two coders independently coded six interviews, and met to review codes and revise the codebook and code definitions until consensus was reached. The codebook was then applied to the remaining interviews.

RESULTS

Table 1: Clinician Demographic Summary

Age	
Mean (SD)	40.17 (11.90)
Median	39.5
Range	28, 71
Gender, n (%)	
Female	10 (47.62%)
Male	11 (52.38%)
Race, n (%)	
White	11(52.38%)
Asian	8 (38.10%)
Not Reported	2 (4.76%)
Years in Practice	
Mean (SD)	8.42 (12.51)
Median	4
Range	1.0, 40.0

Initial Case Formulation

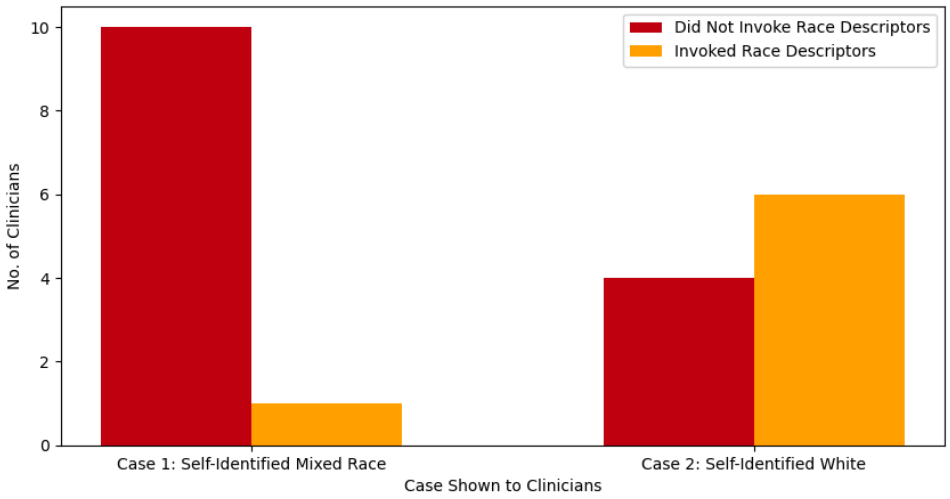

Figure 1: Initial Case Formulation – Bar chart summarizing whether clinicians invoked race descriptors when initially describing the case.

At the start of the interview, after viewing the video clip of the patient assigned to them, clinicians were asked how they would formulate or describe the case. Responses were categorized as race-related when clinicians used descriptors referring to the patient's supposed race or ethnicity, or non-race-related when clinicians summarized the case without reference to patient race. One third (7/21) of clinicians referred to patient race in their initial case summary, and the majority (6/7) of these race-related

descriptors were used in reference to the patient in Case 2. In contrast, 14 clinicians did not mention race in their initial case summary, the majority (10/14) of whom were asked to describe Case 1.

Typical of non-race-related responses, *Clinician* #15, a 28-year-old South Asian Indian female, described Case 1 as follows:

> Sounds like 35-year-old, previously healthy female, who is coming with concerns of elevated blood pressure over the last two months. And it doesn't sound like she has any significant, well, a known family history for it, but no other risk factors, anything in her diet or lifestyle or anything that would kinda point to the reason behind this type of pressure.

In comparison, the Case 2 summary of *Clinician* #1, a 34-year-old male who declined to state his race/ethnicity, represents a typical race-related response:

> Um, well, so it seems like… this is an otherwise healthy 35-year-old, partially African American female, uh, of mixed race, um, who was coming in with a new diagnosis of isolated systolic hypertension and has been advised by lifestyle attempts and is still having blood pressure, which is not, which would be considered appropriate for ambulatory populations.

There are several explanations for why race was more frequently invoked in initial formulations for Case 2. Clinicians may have been thrown off by the discordance between the patient's outward appearance and the genetic test results that suggested a large proportion of ancestry from Africa. In the context of Case 1, where only one clinician mentioned race, the rest may have felt discomfort, unwillingness, or uncertainty about drawing attention to the patient's race while actively engaged in a research study or felt a desire to appear "politically correct" in the context of a study interview. This may have motivated most clinicians to hold off on mentions of race until further prompted. It is important to note that while many clinicians did not mention race in their initial description of the case, race was later discussed throughout the interviews and a majority of clinicians would later mention race, if they had not already, when deciding medication choice. This suggests that clinicians may implicitly consider race as an

important variable when deciding between treatment or management plans for patients, whether stated or not.

Case-Specific Treatment Decisions

Medication Choice

After describing the case, clinicians were asked to provide a treatment plan for the specific patient case shown. Clinicians were prompted further to specifically recommend a medication choice if they did not provide one in the initial answer to the question. Responses consisted of the following: Angiotensin-converting enzyme (ACE) Inhibitor, Angiotensin II Receptor Blocker (ARB), Thiazide Diuretic (TD), Calcium Channel Blocker (CCB), or undecided. The JNC guidelines specifically state: "Initial antihypertensive treatment should include a TD, CCB, ACE inhibitor, or ARB in the general non-Black population or a TD or CCB in the general Black population." A clinician was categorized as undecided if they listed multiple medication choices without preferencing a singular choice. Of those that were undecided, some clinicians just had no preference over a handful of medications, or they wanted to know more information before deciding.

The JNC 8 guidelines list TDs and CCBs as the *only* first line options recommended for Black patients. TDs overall were selected by eight clinicians as first line treatment, and a total of 12 clinicians selected either a TD or CCB as first line treatment. Additionally, all four undecided clinicians included either a TD or CCB in their potential list of medications. Only five clinicians selected an ACE or an ARB for first-line treatment. CCBs and TDs were chosen more frequently in Case 1 and overall, which are among the first-line medications recommended for all individuals, regardless of race.

Table 2: Clinicians' Case-Specific Medication Preference

	No. of Clinicians (of 21 total), n (%)		
Medication Choice	Case 1: Self-identified Mixed-Race	Case 2: Self-identified White	Total
Angiotensin-converting enzyme (ACE) Inhibitor	2 (9.52%)	2 (9.52%)	4 (19.05%)
Angiotensin II Receptor Blocker (ARB)	0 (0.00%)	1 (4.76%)	1 (4.76%)
Thiazide Diuretic (TD)*	5 (23.81%)	3 (14.29%)	8 (38.09%)
Calcium Channel Blocker (CCB)*	3 (14.29%)	1 (4.76%)	4 (19.05%)
Undecided Totals (specific responses below):	1 (9.52%)	3 (9.52%)	4 (19.05%)
ACE, ARB, or CCB*	1 (4.76%)		
ACE, ARB, or TD*		1 (4.76%)	
ACE, CCB*, or Beta Blocker		1 (4.76%)	
ACE, CCB* or TD*		1 (4.76%)	

An asterisk (*) indicates the two medications recommended by JNC 8 Guidelines for initial treatment of hypertension in Black patients. For non-Black patients all listed medications are equally recommended.

Do clinicians use race in choosing medication for this case?

Clinicians were not only asked to provide a medication choice for the patient but were also further questioned on the reason for their choice and what factors were most influential in making their decision. All but one of the clinicians made mention of race to some degree when discussing medication choice, but only 12 of the 21 clinicians indicated that consideration of race impacted their decision of a treatment plan for the patient, while nine clinicians made it clear that race was not a factor in their medication choice. It is important to note that nearly every clinician mentioned and additionally prioritized factors beyond patient race.

There was considerable variation in the extent to which race was influential among those whose treatment plan was affected by race. While some clinicians were very straightforward in justifying their medication choice as directly from the guidelines, others used race in more nuanced ways. One clinician stated that they would consider following the race-specific guidelines only if their first-line medication choice failed, with one suggesting they would make the patient a part of the medication decision process and inform them of the literature that does exist. It should be noted that of the eight clinicians who

prescribed TDs to either patient, six were influenced to varying degrees by the race of the patient and only two made the decision regardless of race. In contrast, of the clinicians that chose CCBs, all four justified their medication choice using race.

Among clinicians choosing CCBs or TDs, it is difficult to determine whether this choice is motivated by the race-specific guidelines. The guidelines recommend these two medications for Black patients, but also for all patients, and for the cases presented, the clinicians had a difficult time specifying race. Thus, we cannot be certain clinicians used race in making their decision. For example, given the self-identified White patient also had an appreciable portion of genetic ancestry from Africa, some clinicians may have been swayed by the race-specific guideline to try TDs as a first-line treatment. In contrast, for the self-identified mixed-race patient, eight clinicians chose to prescribe TD or CCB. Some or all may have implicitly assigned Black race to the patient based on phenotype, or implicitly invoked the "one-drop" rule, in which individuals are assigned to a Black racial category based on any amount of African ancestry, leading to a medication choice that was consistent with the race-specific guideline.

In general, most of the clinicians indicated that they do not rely solely on the guidelines or racial cues when making a medication choice. Clinicians took numerous factors into consideration including side effect profile, patient lifestyle, personal experience with each medication, and personal knowledge of current medication literature. Of the clinicians who said their medication decision was not influenced by race, all prioritized other factors. Two of the clinicians for which race did not influence their medication decision expressed uncertainty in the guidelines, with one stating, "I'm probably not gonna change my approach based on [a race-specific guideline] cause it's not evidence based." Clinicians may also have default first-line preferences, based on their own clinical experiences. For example, when asked why they chose TDs for their treatment, one clinician with a non-race-related justification for medication choice responded, "It's easy. It works." This clinician preferred TDs as a first-line treatment regardless of patient race, but qualified this by adding that they would take race into account for second-line treatment if the patient did not respond well.

The JNC 8 race-specific guidelines may be shaping clinicians' decisions even among those clinicians who said they prioritize other factors. One clinician, a 35-year-old White female, justified treating the presented patient with an ACE inhibitor stating, "I usually opt for, just because of my own personal preference, ACE inhibitors, because they tend to have fewer side effects than some of the other ones." However, the clinician went on to state that had the patient been African American, she would have prescribed TDs or CCBs because "generally I still do kind of what's recommended by the JNC 8 guidelines." This clinician prioritized minimizing side effects when the patient was one whom they deemed to be non-Black, motivated by the race-specific guideline.

Awareness of the JNC 8 Race-Specific Guidelines and Supporting Literature

When asked whether they were aware of the JNC 8 guidelines for hypertension, all 21 clinicians indicated that they were either aware or somewhat familiar with them. Some clinicians did not know the specifics of the guidelines, with some indicating they would have to "look it up" when discussing the guidelines in the context of case-specific treatment. When asked if they were aware specifically of the literature supporting the guidelines, six clinicians responded that they were not, four clinicians responded that they were, and ten clinicians indicated vague familiarity, such as one clinician (28-year-old Indian female), who stated, "I don't know kinda the specific details of it."

Do clinicians perceive themselves as following the guidelines (in general)?

To assess their use of the race-specific guidelines outside of the challenging cases presented, clinicians were asked whether they generally follow them. Nearly half (10/21) of clinicians responded yes, five responded that they do sometimes, or that it depends on other factors, and four responded that they do not generally follow the guidelines. Surprisingly, some of the clinicians who responded that they generally follow the guidelines also indicated vague familiarity with them and/or with the literature supporting them.

For some clinicians, the utility of the guidelines is questionable when treating patients of mixed ancestry. One clinician, who was shown the phenotypically White patient with 53% African Ancestry, indicated that they would value the phenotype when applying the guidelines to a patient whose race they could more readily assess, but not in this ambiguous case:

> I'm aware of the guidelines. I guess I don't… If she had presented as being a typical African American, I would have started thiazide. Yes. Would I have started a combination? I would probably not have. I probably would have looked at her kidney function before I decided on that ACE. (*Clinician* 9)

It is interesting to note that at least half of the clinicians claimed to generally follow the race-specific guidelines, but when presented with a challenging case of mixed ancestry, there was no consensus around what treatment to suggest.

Is genetic ancestry data relevant for treating hypertension in this case?

When clinicians were asked if they viewed genetic ancestry data as relevant or useful for treating hypertension in the presented case, the majority (15/21) responded no. Two clinicians were very uncertain about the relevance, and only four stated confidently that it was relevant. Among those who said the data were not relevant, the most common explanation was the general lack of clinical evidence that genetic ancestry is associated with hypertension. A few clinicians explained that evidence is lacking, since past studies about hypertension treatments were all based on self-reported race, not genetic ancestry. One of these clinicians (40-year-old White male) specified he did not know the relative risk of any of the ancestry alleles, so he wouldn't know how to interpret the ancestry data. A 37-year-old Indian female clinician similarly speculated that genetic ancestry data may be "more meaningful than race," but still qualified this statement to say that most of the studies on hypertension were done without genetic ancestry data, so "how do we extrapolate?" Two other clinicians (a 49-year-old Iranian male and 54-year-old Afghani male) rejected the data's relevance by questioning the accuracy of the ancestry tests themselves.

In this particular mixed-race case they also said they didn't believe the patient qualified as African American. One clarified that it wasn't relevant in this particular case because the patient was mixed, "but if somebody is just African American [then] yes."

Among the four clinicians who initially responded that the ancestry data were relevant, all also expressed uncertainty about using it. One clinician (35-year-old Indian female) stated the data were only relevant because African Americans are at higher risk for hypertension, but she didn't say it would change her treatment plan. Two of the four clinicians (71-year-old male clinician of unknown race and a 33-year-old White male) stated ancestry data were relevant because of the existence of the race-specific guidelines, but they contradicted these statements by also questioning the validity of the guidelines.

The majority of clinicians rejected the relevance of the genetic ancestry data entirely. However, a couple of responses illustrate how some clinicians may prioritize genetic ancestry in medical practice. A few clinicians stated they would have followed different treatment if the patient had a higher proportion of African ancestry because, in their view, they would then have qualified as Black. While these were a minority of responses, such reasoning demonstrates that these clinicians would prioritize genetic data over phenotypic data to assess race, if there were a compelling enough proportion of African ancestry, reflecting a "geneticization" of racial identity (Bliss, 2011; Hunt and Merolla, 2022), whereby genomic data takes precedence over social or cultural contributors to identity. But interestingly, these few clinicians were also countering the historic "one-drop" rule by arguing that these patients may not have enough African ancestry to qualify for the race-specific treatment, despite the fact that no studies have quantified how much African ancestry is needed to justify differential treatment or alter disease outcomes.

Interestingly, the majority of clinicians (16/21) reported that no patient had ever actually brought genetic ancestry reports to their clinic. However, when asked hypothetically if they would include a patient's ancestry results in their clinical file, about half (9/21) responded positively. Most said, while ancestry results wouldn't change their treatment plans, they would include them anyway, either to satisfy patient requests and/or in case of future utility. At the same time, a 40-year-old female White clinician dismissed the value of the ancestry results this way: "I mean it'd be kind of like putting their birthday card

in the file or something. Like I don't know what to do with that." Thus, despite uncertainty about its utility for the presented case, many of the clinicians viewed these data as not completely irrelevant, willing to admit the possibility of future relevance down the line.

Is genetic ancestry data relevant for hypertension and other diseases in general?

In response to questions about the relevance of genetic ancestry data in treating hypertension in general, 12 of the 21 responded it was not relevant, five responded with much uncertainty, and four responded "yes." Those who responded negatively reasoned similarly about the specific cases and hypertension in general, claiming lack of evidence, and that genetic ancestry data would not change their treatment plan. Among the four who responded yes, two stated it was relevant simply because hypertension is more common among African Americans, but one of these said side effect considerations would take priority over ancestry in their treatment recommendation. Only one clinician (33-year-old White male) said it was relevant due to the existence of the race-specific guidelines, implying it would affect his treatment plan. The fourth clinician (female, South Asian, 49 years) who said yes quickly clarified that genetic data are less useful than we thought in the past. Among the uncertain responses, a few clinicians said the ancestry data wouldn't be relevant in determining first line treatment but could be relevant down the line in treating the disease, particularly as they know hypertension can be more aggressive in African Americans, but they didn't specify how or in what instances they would use it. One clinician (33-year-old Chinese male) specified he may consider genetic ancestry more in more challenging to treat cases. Others who responded with uncertainty said they lacked data to determine relevance. In aggregate, these responses reveal low confidence in the utility of genetic ancestry data for treating hypertension, while also expressing much confusion around the value of race-specific guidelines.

When clinicians were asked about the relevance of genetic ancestry to any other diseases, the majority (16/21) were confident that ancestry data are useful for screening for other diseases, while five rejected it outright as useless. Notably, clinicians used the terms race and genetic ancestry interchangeably in these discussions. The only area clinicians confidently discussed race or ancestry to be

relevant was for screening purposes. Even among those clinicians who thought genetic ancestry was useful for disease screening, they were generally uncertain about how it should be used in treating diseases. Only one clinician specified a treatment that would be affected by race or ancestry (i.e., warfarin dosing). A subset of clinicians responded that the data were only relevant for Mendelian diseases, or rare diseases, but not for complex diseases, for which "every race is high risk," as expressed by a 37-year-old female Indian clinician. For complex diseases, they stated the ancestry information is not useful, but may be in the future. Still, clinicians gave examples of both Mendelian and complex diseases they viewed as having higher prevalence among specific racial and ethnic groups (e.g., African Americans were described as being at higher risk for sarcoidosis, sickle cell anemia, and prostate cancer), regionally isolated groups (e.g., familial Mediterranean fever), and religious groups (e.g., Ashkenazi Jews at risk of Tay Sachs, breast cancer, fanconi anemia). Some clinicians said they were taught - and/or observed - certain diseases to be more common among certain racial/ethnic/religious groups, justifying screening some diseases more frequently in these groups.

Assigning Race to Patient Cases

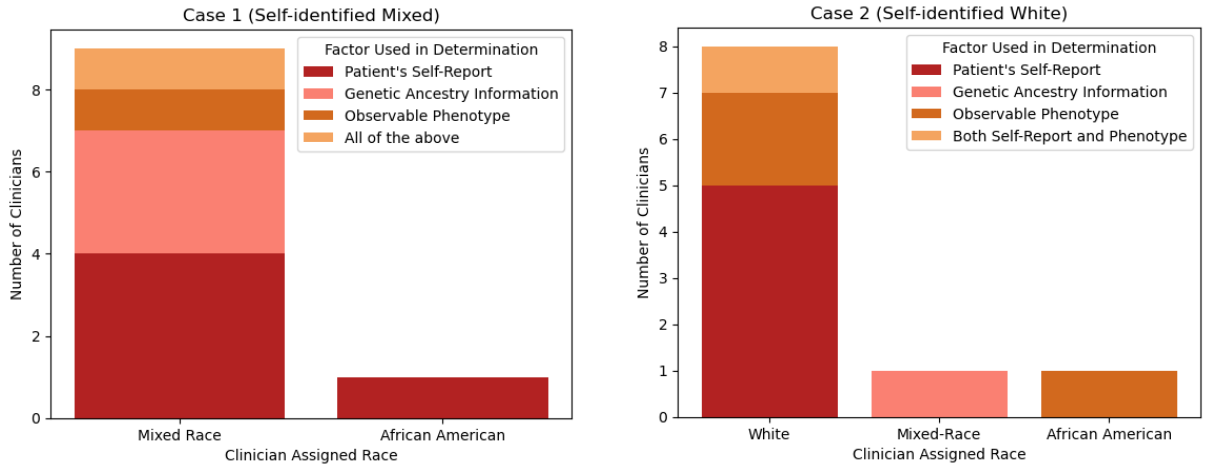

Figure 2a. Clinicians' classification of race for patient Case 1 (self-identified Mixed). For one clinician who viewed Case 1, this question was not asked. 2b. Clinicians' classification of race for patient Case 2 (self-identified white).

One of the reasons that the guidelines are so challenging to follow is because assigning race can be very difficult in patients of mixed ancestries. In order to assess how clinicians were classifying a patient's race in clinical encounters, we asked both how they assessed race for this specific case, and in general. In response to the question about classifying race in Case 1 (self-identified mixed), two-thirds of respondents (9/11) said they would describe the patient as mixed race (Figure 3a). Four respondents described making these determinations primarily based on patient's self-report, three respondents mentioned genetic ancestry information, one respondent used observable phenotype, and one mentioned all of these factors. One respondent said they would classify the patient as Black or African American, based on the patient's self-report. For clinicians presented with Case 1, most did not invoke race in the initial description, though they did in other parts of the interview, typically describing the case as "mixed." It may be that respondents who determined that the patient was mixed did not vocalize it when describing the case because they did not know what to do with that information, since most race-based guidance for medical decision-making is based on mutually exclusive continental racial identities.

Among those viewing Case 2, 8/10 said they would describe the patient as White (two mentioned using observable phenotype, five mentioned self-report and one used both to make this determination) (Figure 3b). The remaining two viewing Case 2 were split between identifying the patient as mixed race based on genetic ancestry test results (1) and African American based on phenotype (1). The fact that Case 2 elicited more race-related responses in initial case formulations suggests that clinicians presented with this case had a more difficult time reconciling this individual's phenotypic and genetic readouts. For example, a 58-year-old White female clinician said, "So she says she's 53% ... is she African American, is she of African descent or is she White?" Interestingly, for both cases clinicians were not unanimous in their assessment of race, or in the factors they used to determine it.

The above data reveal four noteworthy aspects of how clinicians conceptualize race when deciding if and how to assign descriptors to patients. First, self-report, phenotype, genotype (to a lesser extent), and sociocultural aspects of race all appear to play roles of varying degrees in clinicians' perceptions of patients' race, depending on the information available about a particular case, clinicians'

own working definitions of race, and their perception of its salience in the medical management of a particular case. Notably, more senior clinicians (those with >10 years in practice) tended to rely more on phenotype and genotype, while early-career clinicians (those with <10 years of experience) favored self-report as the means to identify a patient's race, irrespective of the case they were presented.

Second, none of the clinicians invoked discussion of sociocultural or environmental factors as possible mediators of these patients' racial self-identity. This may be because no such information was explicitly offered to them in the patient case descriptions. At the same time, none of the clinicians questioned that omission or explored the relevance of environment or culture to the way that these patients, with potentially incongruous phenotypic and genetic ancestry markers, chose to identify. Several clinicians were satisfied with proceeding according to the patient's self-report, but some may have overlooked the patient's self-identified race on the vital measures report.

Third, responses to both cases suggest that implicit ideas about non-Whiteness, stemming from the "one-drop" rule in the early 20th century, persist within the healthcare system. In their responses, some clinicians, even if unintentionally, demonstrated that their perceptions and expectations around an individual's racial background continue to be shaped by this rule. For example, two clinicians did not classify Case 2 as White, based on the patient's genetic ancestry readout that suggested a majority of ancestry from Africa, despite phenotypically presenting and even self-identifying as White.

Finally, for both cases, only African ancestry percentages were provided as part of the genotypic information presented to clinicians (Case 2: 53%, Case 1: 15%). Almost no clinicians noted the omission of ancestry proportions from other world regions. Clinicians may have made private inferences about where the balance of ancestry could be traced to for each case. The majority of clinicians who saw Case 2 assessed her race as White because of her self-report and/or phenotypic presentation. Furthermore, although the genetic data suggested that a significant component of this patient's ancestry derived from Africa, only three of ten clinicians considered this genetic information salient to mention and to use in classifying the patient's race. For these three respondents, the genetic data were seen as complicating an easy categorization of this individual as White. Clinicians clearly grappled with whether and how to use

the ancestry data. This suggests that genetic ancestry data, when available and even if imperfect or incomplete, may inform how some clinicians view patients' race.

Defining Race

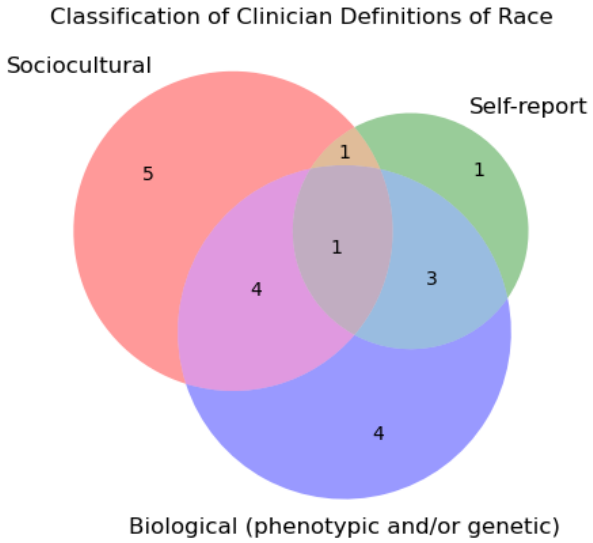

Figure 3: Clinicians' definitions of race, classified as sociocultural, biological, or individual self-report.

In order to understand how clinicians make decisions about assigning race, we also asked how they defined race in the abstract. All interpreted it as a question about the criteria by which race descriptors should be assigned to individuals. Responses incorporated various combinations of biological, cultural, and self-descriptive criteria or factors that contribute to an individual's race (Figure 3). Clinicians responded to this question in two ways. The first is encapsulated by responses that attempt to pin down the criteria by which an individual's race might be determined, whether through objective or subjective measures. As Figure 4 illustrates, clinicians specified a range of criteria which were coded as "biological" (having to do with measured genotypic or phenotypic differences), "sociocultural" (having to do with environment, culture, or upbringing), or "self-report" (the descriptors an individual identifies for themselves). Nine clinicians invoked overlapping categories of criteria in their definitions of race. Eleven said they view race as partially or entirely influenced by environment or culture, explaining that the way an individual identifies is informed by family upbringing, traditions or customs, and/or cultural

background. Of those who viewed race as primarily sociocultural, many elaborated that race is a lived experience, deeply connected to living conditions and resource access, as exemplified by a 33-year-old Chinese male clinician: “It’s one thing to be one race and to be living one way. And it’s one thing to be the same race and to be living in a different environment.” Eleven clinicians said race is at least partially defined by one’s biology or genetics. Only one held the position that in general an individual’s self-report was the ultimate authority on their own racial identity, regardless of their phenotype or genotype. Nevertheless, five clinicians mentioned self-report as one criterion within a larger definition that included sociocultural and/or biological components. Some clinicians also responded to this question by reflecting on the utility of race in the practice of medicine, or to its salience in the specific context of an individual’s health. As a 43-year-old Asian male clinician stated, “It’s not just what they look like or where they’re from. It’s what [cultural] things predispose them to having positive health outcomes.”

Interestingly, the criteria that clinicians mobilized to assign race to specific patients, and in particular Case 2, were different than those invoked in their definitions of race in the abstract. There were five instances of non-concordance between how clinicians defined race in the abstract, and the factors they used to assign race to the particular patient cases they were presented. Of these, four occurred among clinicians presented with Case 2, and only one occurred with Case 1. In four instances, clinicians defined race in nuanced or complex ways, as being socioculturally determined or based on how an individual chose to self-identify, but in the specific patient case they resorted to using biological (phenotypic or genetic) criteria to determine the patient’s race. One clinician viewing Case 2 defined race as genetic but used observable phenotype to assign the race of the patient. In summary, no clear consensus emerged among this sample on how to define race either for the specific patient cases presented, or in the abstract, suggesting that clinicians may operate using a variety of non-standardized, overlapping, and often conflicting definitions of race.

DISCUSSION

Our study empirically evaluates how clinicians value and prioritize racial cues and race-specific guidelines when treating patients with hypertension. Our findings suggest that existing guidelines for race-specific hypertension management are differentially interpreted and unevenly applied by clinicians, especially for patients who present multiple contradictory racial cues. Importantly, this ambiguity leads to considerable clinician-to-clinician variation in their interpretation and application. Clinicians struggle with the guidelines, particularly when confronted with patients who identify as mixed-race or individuals with complex ancestries, for whom there is no clear guidance. This confusion is exacerbated by the idiosyncratic use of race within the guidelines, which only offer guidance for Black/African American individuals but do not offer a standardized definition or criteria for determining to whom these racialized guidelines should apply. Black individuals bear a disproportionate burden of risk factors resulting in higher rates of hypertension, yet experience poorer hypertension control (Aggarwal et al., 2021). The lack of clear guidelines from which to derive robust standards of care limits treatment options for underserved individuals and is likely to exacerbate racial/ethnic health disparities.

Defining Race of Patients

The JNC-8 race-based guidelines for treating hypertension exist under the assumption that two discrete racial categorizations, Black and non-Black, accurately approximate factors that significantly affect patient medication response. Race is a concept widely acknowledged as socio-politically constructed and ill-defined, including by the American Academy of Family Physicians (AAFP) and the American Academy of Pediatrics (AAP) (Reddick, 2023; Wright et al., 2022). In order to follow the guidelines as intended, it would be necessary for clinicians to understand how to categorize their patients in practice. However, the JNC guidelines fail to provide explicit definitions or guidance on categorizing patients, leaving the decision at the discretion of the clinician. Additionally, our findings demonstrate that clinicians define race using myriad criteria and apply these criteria in sometimes non-convergent ways to

assess race for the same patient. The variability in clinician assessments of race is likely increased when they are presented with patients with racial and ethnic identities that challenge or defy typological expectations, a common phenomenon in an increasingly diversifying US context. It is not clear that the guidelines have clinical utility for any individual given the inconsistent processes through which race is determined in clinical settings and the difficulty of classifying individuals into discrete racial groups.

Of note, clinicians in our study never classified Case 1 (self-identified mixed-race patient) as White, potentially invoking the "one-drop" rule. Dating back to colonial America, the "one-drop" rule, or rule of hypodescent, classified individuals with any amount of Black ancestry as Black. Interestingly, clinicians classified the Case 2 patient as White despite a genetic ancestry report specifying 53% ancestry from Africa, suggesting that clinicians' consideration of genetic ancestry data may complicate implicit applications of the "one-drop" rule, warranting further study. Regardless, medical science continues to implicitly rely on this rule when assigning patient race in clinical settings. The application of the "one-drop" rule has been highly criticized in race-corrected algorithms (Lujan and DiCarlo, 2021; Sehgal, 2020), yet binary race-based guidelines, such as the JNC-8, create situations in which clinicians are compelled to classify patients into Black or non-Black categories, often making decisions based on hypodescent.

In addition to insights gained regarding how clinicians classify race of their patients, our study also provided insight into how much race plays a role in initial clinical encounters. It is of interest to note that 14 of the 21 clinicians in our study did not mention race in the initial case formulation, and those that did were presented more often with Case 2 (self-identified White). This aligns with other findings, such as one study that US medical students are taught to mention race in the initial case formulation at only 11% of schools, but at 63% of medical schools surveyed, faculty teach students to mention race in select circumstances (Nawaz and Brett, 2009). Educators implementing medical school curricula may want to consider adding critical discussions of race to help medical trainees evaluate its utility in different circumstances.

A notable feature of virtually all the interviews was the ways in which clinicians struggled with describing race, and tended to contradict themselves when talking about race, race definitions, and racial classification. Depending on the question asked, different factors moved individual clinicians to prioritize race, or invoke race concepts. This suggests that clinicians continue to grapple with ambiguities and inconsistencies inherent in prevailing race concepts and categories, as well as with assessing their importance for medical treatment or management. If clinicians believe they are following published practice guidelines, but at the same time classify patients inconsistently, there is likely to be considerable variation in how clinicians actually apply guidelines in clinical settings. This underscores the need for further work to clarify how clinicians conceptualize and prioritize race in actual clinical settings and for differently presenting patients.

Insufficient Justification for Race-Based Medicine

Virtually all interventions in the evidence-based practice of modern medicine are predicated on high standards and requirements for rigorous and robust supporting data. Yet justifying the use of race, whether in risk assessment, diagnosis, or treatment, is typically not held to the same evidentiary standards. The race-based guidelines for hypertension treatment are a case in point. They were derived from the ALLHAT study, which, in addition to the methodological shortcomings discussed above, did not adequately specify how racial categorizations were determined, or demonstrate strong, replicable race-specific differences in medication effects, or identify any underlying biological differences supporting race-based treatment(Reddick, 2021; Westby et al., 2020). Clinicians, as many voiced in our study, both expect and rely on robust evidence to ensure that adopted interventions improve standards of care, ideally for all. Because of the potential for harm, such evidentiary requirements should apply just as equally, if not more so, to the use of race to guide diagnosis and treatment. The default should not be to simply assume that a race-specific difference exists. Instead, race should not be considered a contributing factor unless and until a burden of proof is met by researchers for its continued use.

This, and other examples of race-based medicine, are built on the presumption that there exist clinically relevant, race-based biological differences that affect efficacy across racial identities. However, physiological or metabolic explanations for supposed differences are glaringly missing. Instead, race is often used implicitly, as a proxy for supposed differences in genetics, biology, environment, culture, or socioeconomics, without elucidating exactly which of these it is standing in for. Hepatitis antiviral treatment, and combination vasodilators such as BiDil, are examples of race-based treatments that epitomize this approach (Morton, 2009). While BiDil was not considered by clinicians in our study because it is not a first-line treatment for hypertension, it is an important drug for symptomatic heart failure, and represents a similar dilemma for clinicians about whether to follow race-specific drug recommendations. A study conducted in 2014, exploring cardiologists' perspectives on BiDil's race-based drug label, found that while such labels were perceived as empowering doctors to prescribe effective medications sooner, more than half expressed concerns about race-specific drug prescribing as overly simplistic and harmful, reflecting insufficient understandings of gene/drug/environment interactions, and potentially denying some patients a beneficial drug simply because of their race (Callier et al., 2019).

Similar concerns have been raised around the use of race in algorithms for risk assessment, diagnosis, and treatment, such as those for impaired lung function and risk of atherosclerotic cardiovascular disease, prompting calls by professional societies and organizations for further research to justify the continued use of race in these algorithms or an end to the use of race in the algorithms altogether (Bhakta et al., 2023; Vasan et al., 2023). Our findings support these calls, demonstrating that such concerns extend to race-based clinical guidelines, and furthermore, calling into question the utility and applicability of race-specific guidelines amidst the rapid demographic diversification of the US population. In light of the general confusion we have identified surrounding the clinical practice of race-based guidelines for first-line hypertension treatment, and coupled with the lack of strong evidence of relevant physiological differences by race, a re-consideration of these guidelines is warranted.

Limitations and Strengths

Limitations of this study should be acknowledged. The sample of clinicians was relatively small and restricted to one university hospital system, with a limited range of demographic diversity among clinicians, patient demographics, and workplace practices. We identified almost no meaningful differences in clinician responses by race/ethnicity, age, gender, or seniority, but trends could emerge with further research in larger samples and in more diverse settings. The clinicians in this study practiced primarily in La Jolla, a relatively affluent neighborhood of San Diego, California, with Black residents making up only 1% of the population. Many clinicians noted seeing few African American patients in practice as a result of their location. Also, we note that none of the interviewed clinicians in this study identified as African American, and it would be of interest to explore in future studies how clinicians who are racialized themselves may conceptualize race in their own lives and clinically. Additionally, our focus was on mixed-race cases that were challenging to assess; future studies could explore how individual clinicians respond to multiple and more ancestrally diverse mock patients.

Despite these limitations, our study is among the first to explore clinical perspectives on racial guidelines for hypertension in an empirical manner. This study pilots a timely approach that can be used to assess clinician responses to other race-specific guidelines across medicine, which have come under increasing scrutiny (Cerdeña et al., 2022; Vyas et al., 2020). Amidst rapid demographic shifts in the proportion of individuals who identify as mixed race, this type of approach can help assess the utility (or lack thereof) of binary guidelines in clinical practice, especially among diverse patient communities who likely did not initially inform their design.

Conclusions and Future Directions

Moving beyond a racialized guideline would mean taking an individualized approach for each patient, and there is strong evidence that factors beyond race should be considered by clinicians. In fact,

our study showed that many do consider other factors based on their clinical experience prescribing different medications. For example, hypertensive medication nonadherence disproportionately impacts Black individuals, a major factor in failed management of hypertension (Ferdinand et al., 2017). Several studies have shown that side-effects, poor taste, and high costs all correlate with lower levels of hypertensive medication adherence (Al-Noumani et al., 2019). It is important that clinicians educate their patients on treatment options and corresponding side effects and encourage open communication around side effect experiences throughout treatment. It is possible that the way in which the guidelines limit treatment options for Black patients restricts the ways in which clinicians can work around factors that promote adherence. Frameworks for treating hypertension in a personalized manner already exist (Melville and Byrd, 2019) but have thus far been recommended mainly as a means for dealing with more complex cases rather than the standard of care for all.

Some organizations have made efforts to move beyond a race focused approach. Most recently, the American Heart Association issued a statement in support of removing race from the risk calculator for cardiovascular disease, along with other edits (Khan et al 2023). In regards to the most current (2022) blood pressure target guidelines, the American Academy of Family Physicians (AAFP) recommends reducing targets for adults with hypertension, advising that medication for treatment should be chosen based upon “cost, ease of use, adverse effect profile, and comorbid conditions,” with no mention of race as a risk factor (Coles et al., 2022). More generally, the AAFP strongly advocates against using race as a proxy in clinical decision making. While the AAFP has endorsed the JNC-8 guidelines in general, they have separately written against the race-based component of the JNC-8 guidelines. Given ongoing debate and disagreement even among professional organizations about the utility of race in hypertension treatment guidelines, it is critical to reconsider the inclusion of race in these guidelines. In light of the continued existence of race-based guidelines despite lack of guidance on how to define race, medical school training for future physicians should also encourage critical reflection on the use and relevance of race in medicine.

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