A Clinical Pharmacology and Therapeutics Teacher's Guide to Race-Based Medicine, Inclusivity, and Diversity

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The relationship between race and biology is complex. In contemporary medical science, race is a social construct that is measured via self-identification of study participants. But even though race has no biological essence, it is often used as variable in medical guidelines (e.g., treatment recommendations specific for Black people with hypertension). Such recommendations are based on clinical trials in which there was a significant correlation between self-identified race and actual, but often unmeasured, health-related factors such as (pharmaco) genetics, diet, sun exposure, etc. Many teachers are insufficiently aware of this complexity. In their classes, they (unintentionally) portray self-reported race as having a biological essence. This may cause students to see people of shared race as biologically or genetically homogeneous, and believe that race-based recommendations are true for all individuals (rather than reflecting the average of a heterogeneous group). This medicalizes race and reinforces already existing healthcare disparities. Moreover, students may fail to learn that the relation between race and health is easily biased by factors such as socioeconomic status, racism, ancestry, and environment and that this limits the generalizability of race-based recommendations. We observed that the clinical case vignettes that we use in our teaching contain many stereotypes and biases, and do not generally reflect the diversity of actual patients. This guide, written by clinical pharmacology and therapeutics teachers, aims to help our colleagues and teachers in other health professions to reflect on and improve our teaching on race-based medical guidelines and to make our clinical case vignettes more inclusive and diverse.

Race is often considered an essential biological variable in diagnostic algorithms and treatment decisions. Examples of race-based medicine can be found in the clinical practice guidelines of virtually all medical specialties.[1,2] Many of these race-based recommendations directly or indirectly influence the choice of drug therapy, for instance the race-based corrections for estimating the glomerular filtration rate (GFR),[3–5] the specific treatment recommendations for hypertension in Black patients,[6–8] and the diverse medicines for which human leukocyte antigen (HLA)–typing is advised, often only for people with a certain ethnic background (e.g., HLA-B*5801 in patients of Southeast Asian or African American descent[9]). These and other race-based recommendations are increasingly criticized for being biased,[10,11] being unscientific,[12] and increasing rather than reducing healthcare disparities.[1,2]

As teachers in clinical pharmacology and therapeutics (CPT), we endeavor to equip medical and other healthcare students (such as nursing, pharmacy and dental students) with appropriate prescribing knowledge and skills in order for them to be able to prescribe medicines safely, effectively, and responsibly. Besides the

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required knowledge about pharmacology, side effects, and drug–drug interactions, this also entails teaching students to adopt an informed and critical attitude toward clinical practice guidelines and evidence-based medicine in general.[13,14] The controversies regarding race-based recommendations, however, are rarely explained by CPT and other "core medical science" lecturers. Medical students increasingly take issue with how their teachers explain the relationship between race and health, in particular because often, race is presented as a biological variable which may obfuscate issues of racism and historical oppression as root causes for ill-health.[15] One analysis found that 96% of preclinical lecture slides that mentioned race, presented it as risk factor for disease without explaining that race is not a biological but a social construct that is prone to bias.[16] Unfortunately, this situation reflects our own teaching experience at 11 academic institutions in seven EU countries and the United Kingdom where we, until recently, taught about race-based medical guidelines without discussing the controversies or considering the nuanced relationship between race and health. We suspect that the same is true for (CPT) teaching in the rest of Europe.

Teachers are insufficiently knowledgeable about the concept of race in relation to healthcare and insufficiently aware of their own bias and the potential harmful consequences of passing this bias on to the next generation of health professionals.[17] Yet, in talking with our (predominantly white) colleagues, we often experience reluctance to discuss these matters openly and believe that this is because fear for being called out as a racist is a barrier. Rather than critically considering that what we teach may be rooted in a racist history, we perceive it as offending our pure intentions and instinctively refute it. This response is known as white fragility[18] and underlies other often-heard responses such as "You can't say anything anymore these days" or the attention for inclusion and diversity ("wokeness") restricts academic freedom.[19]

This guide aims to help us as teachers of CPT and other health professions to examine our personal roles in propagating racial bias through race-based guidelines and clinical case vignettes. We first explore the concept of race, history of race-based medicine, and the fallacies and consequences thereof. We then provide practical ideas for teaching this knowledge to students. Lastly, we provide practical guidance toward creating more inclusive and diverse case vignettes. The guide is based on a review of the literature and consensus among an international consortium of CPT teachers established for the European Open Platform for Prescribing Education (EurOP^{2}E) project.

What is race, and how is it used in medical literature and guidelines?

Many systems have been used to classify humans into groups based on their physical appearance, the most controversial being that of Johann Friedrich Blumenbach (1752–1840). He divided the human species into five races, based mainly on the phenotypical appearance of the skull: Caucasian, Negroid, Mongoloid, American, and Malayan.[20] While reportedly holding markedly anti-racist views for his time, Blumenbach's classification formed the basis of ideologies claiming the superiority of the Caucasian race over other races.[21] Because of the historic burden of this nomenclature, it has been abandoned and should be discouraged.[22] Although it remains commonly used in both daily and scientific language, the word Caucasian is not exempt from these controversies.[23,24]

Since Blumenbach, race essentialism (i.e., the belief in a genetic or biological essence that defines all members of a racial category) has been widely discredited.[25] However, the concept of race remained in use and now reflects a social definition that is based on an individual's self-identification with a racial category. This contemporary use of "race" is intertwined with "ethnicity." According to the United Nations' recommendations on statistical data gathering regarding ethnicity: "Ethnicity can be measured using a variety of concepts, including ethnic ancestry or origin, ethnic identity, cultural origins, nationality, race, colour, minority status, tribe, language, religion or various combinations of these concepts. The subjective nature of the term requires that information on ethnicity be acquired through self-declaration of a respondent and also that respondents have the option of indicating multiple ethnic affiliations."[26] If, and how, countries gather data on race and ethnicity for census and/or scientific purposes varies.[27] In Europe these data are usually confined to the national identity or country of birth (of oneself and parents),[28] as recording race or more complex definitions of ethnicity is (historically) considered prone to abuse.[29] While the concept of race is intrinsically inclusive of color and physical characteristics, and ethnicity is not (per se),[30] both are measured by self-identification on the basis of subjective, personal, and overlapping criteria (such as ancestry and culture).[17,31] Therefore, we view these concepts as inseparable and use "race/ethnicity" for the remainder of the article.

For both race and ethnicity, any classification may be used and the United Nations (UN) recommends using precise and inclusive categories (e.g., regional, local, and self-perceived groups).[26] However, the most commonly used division in medical literature is based on the US Government Office of Management and Budget's (OMB's) Census Bureau definitions. They use a social definition, in which people self-identify with one or more of the following five racial categories: White; Black or African American; American Indian or Alaska Native; Asian; and Native Hawaiian or Other Pacific Islander. Additionally, and independent of race, people are asked to self-identify with one of two ethnicities: Hispanic or Latino and non-Hispanic or Latino. The OMB emphasizes the social nature of this classification and specifically states that it is not aimed at defining race anthropologically, biologically, or genetically.[32] Genomic research has confirmed that social definitions of race are not supported by genetic data.[25,33]

Because of concerns that ethnic differences affect the safety, efficacy, and/or dosing of medicines, some governing medical bodies require racial data for drug authorization. The US Food and Drug Administration (FDA) mandates reporting of effectiveness and safety data for racial subgroups according to the OMB's classification and additionally recommends reporting data separately for Hispanic or Latino and non-Hispanic or Latino populations.[34] The European Medicines Agency (EMA) accepts foreign clinical safety and efficacy data in their evaluation of new drugs if the pharmacokinetics of a drug are comparable across the most prevalent (self-declared) racial groups in the original country and Europe.[35] Because governing bodies require these data, it has become standard practice to report them in clinical trials. Many medical

journals now have reporting guidelines that encourage authors to report data by race and ethnicity.[36–38]

The way in which data on race/ethnicity are collected and evaluated is based on (fluid and socially determined) self-identification and therefore unlikely to have inherent biological consequences. Yet, there are numerous situations in which pharmacokinetics, drug efficacy, and/or drug safety differ across groups. For example, race/ethnicity has been found to be correlated with a number of health-related factors, such as (pharmaco)genetics (e.g., cytochrome P450 variations etc.), environmental factors (e.g., related to sun exposure), and diet (e.g., related to salt intake). Moreover, race/ethnicity is intertwined with socioeconomic status and both these factors are associated with health and known to influence access to health care. Because the relationship between race/ethnicity and the actual health-related factors is often multifactorial and the underlying reasons are almost never completely understood (or even properly investigated), race/ethnicity is used as a proxy for these health factors in race-based guidelines and algorithms.[11]

So, what is the problem?

In theory, using race/ethnicity as a marker of risk is not much different from using any other diagnostic marker. Race/ethnicity may help to predict outcomes, whether that is the likelihood of a diagnosis, treatment response, or estimation of a physical parameter (e.g., glomerular filtration rate), so what is wrong with this practice? Like other risk factors, correlations between race/ethnicity and outcome reflect different *average* results and it is difficult to translate these findings into *individual* patient decisions. Too often, the race-based distinction is considered to be an absolute, whereas in reality it fails to correctly identify all patients and incorrectly identifies others. This is explained in a Venn diagram (**Figure 1**). When the results of investigative tests are misinterpreted, this may cause potential harm and problems with race-based medicine come to light. **Table 1** shows examples of possible harm due to race-based guidelines. Harm may befall both those patients who are incorrectly identified by the race-based diagnostic and those who remain undetected. Both the probability and severity of harm differ in these populations, and therefore race-based recommendations tend to reinforce racial inequity.[1,2]

Additionally, using race/ethnicity as a diagnostic marker suggests that race/ethnicity is an inherent risk factor rather than a marker of underlying risk factors. This pathologizes race and thereby facilitates racial bias and stereotyping. Being exposed to racism negatively impacts health outcomes,[39–41] leading to a vicious cycle whereby the incorrect portrayal of race as a risk factor actually contributes to health disparities.[12,16,31]

Even when there evidently is a correlation between race and certain medical outcomes, we advise caution in applying race-based guidelines; however, this is rarely the case. It is beyond the scope of this guide to discuss the evidence behind the individual race-based recommendations, but three common fallacies limit the applicability of race/ethnicity as a diagnostic tool.

First, much of the research behind race-based recommendations in guidelines is biased. Groups that have historically been marginalized, such as Black people in the United States, are much more likely to have their race linked to pathology than other groups[10] and even under the best circumstances, research methodology cannot always correct for confounders such as socioeconomic status, racism, and discrimination.[11]

Second, race-based associations are often falsely generalized. Correlations found in one part of the world do not necessarily apply to patients of the same race/ethnicity living elsewhere as they are likely to have a widely dissimilar ancestry[42] and/or environment (impacting lifestyle, diet, etc.).[43] This is schematically shown in **Figure 2**. Moreover, the whole concept of race/ethnicity is viewed differently depending on geography, as do the used categories.[28] Therefore the reasons for self-identification (and groups that result from it) are largely incomparable.[1] For example, the

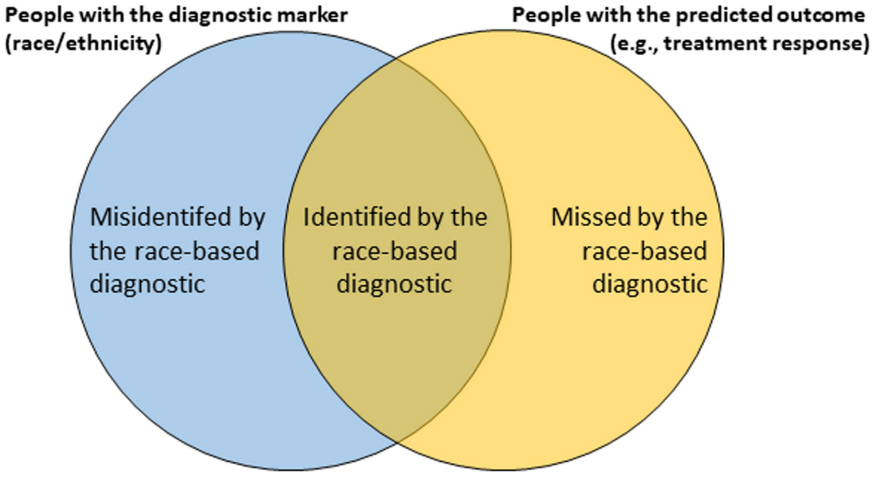

Figure 1 (In)accuracy of race-based diagnostic (schematic). The left circle represents people sharing the racial identification used as diagnostic marker (e.g., Black), the right circle represents people with the predicted outcome (e.g., people who respond better to calcium channel blockers or diuretics than ACE inhibitors or angiotensin receptor blockers. Only people in the overlapping part are correctly identified by the race-based diagnostic, those in blue are misidentified (the race-based recommendation is incorrectly applied), and those in yellow are missed (the race-based recommendation is incorrectly not applied). The sizes of the respective areas vary depending on the diagnostic used and are often difficult to estimate/investigate. ACE, angiotensin-converting enzyme.

Table 1 Examples of potential harm caused by race-based guidelines

Guideline/Algorithm	Rationale	How it is used in practice	Potential harm for identified patients	Potential harm for other patients
MDRD and (previous) CKD-EPI formulas for estimating GFR[3,5]	Applying the correction for patients identifying as Black was shown to improve agreement between measured and estimated GFR	The correction factor is applied to all Black patients	Kidney function of Black patients more likely to be overestimated (possibly leading to delayed diagnosis and referral for treatment)	Kidney function of patients of other race more likely to be underestimated (possibly leading to overdiagnosis and overtreatment)
Hypertension treatment guidelines[6–8]	In patients identifying as Black, greater blood pressure reductions were observed on diuretics and CCBs compared with ACEi and ARB	Only CCBs or diuretics are given to Black patients	Less likely to be treated with ACEi/ARB (even if this is the best treatment option)	More likely to be treated with ACEi/ARB (even if this is not the best treatment option)
CPIC Guidelines[57,58]	CYP2C19 poor metabolizer phenotypes are more frequent in Asian subpopulations compared with European	Reduced dosages or alternative medicines are advised for all Asian patients	Asian patients are more likely to receive subtherapeutic dosages or less effective medicines (insufficient effect)	Patients of other races are more likely to receive supratherapeutic dosages (adverse effects)

ACEi, angiotensin-converting enzyme (ACE) inhibitor; ARB, angiotensin receptor blocker; CCBs, calcium channel blockers; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CPIC, Clinical Pharmacogenetics Implementation Consortium; CYP2C19, cytochrome P450 2C19 isozyme; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

apparent greater effectiveness of calcium channel blockers and thiazide diuretics as opposed to renin-angiotensin-system inhibiting agents that was observed in Black American and African patients could not be reproduced in Black patients living in the United Kingdom.[44]

Lastly, in applying race-based recommendations, caregivers are faced with a false dichotomy. They must decide whether their patient fits the guideline category or not, even if the reality is more nuanced, for example because the patient identifies as multiracial.[2] A further mismatch occurs because caregivers usually "guesstimate" the race/ethnicity of their patient based on observations (of physical appearance, language, name, etc.), sometimes combined with limited questions of geographic ancestry.[45,46]

What should we do instead?

We must not forget that race-based recommendations were implemented in guidelines with a view to improve care. White (middle-aged, male) patients are overrepresented in clinical studies and most of what we consider evidence is not, or is insufficiently, studied in other groups. If we look again at the example of race-based corrections for estimating GFR, and if it is true that a correction factor is required for Black patients on average, then not using the correction factor may lead to underestimation of the GFR, putting many of them at risk of inadequate dosage of medication and subsequent adverse effects. Moreover, denying differences between people (or "racial color blindness") is just as problematic as oversimplifying or exaggerating the differences, because we avert our eyes to any health inequities that arise from racism.[47] This is also the reason why it is important that research into racial (health) inequities continues. While ideally we should not need to use proxies for pathology as rough and flawed as race/ethnicity, we must face the fact that they often remain the best markers of risk we have currently available. We therefore argue that we cannot simply stop using race/ethnicity-based guidance, but rather that we need to apply it with more care and respect for the aforementioned drawbacks.

There is no harm in trying calcium channel blockers or thiazides first in Black hypertensive patients, but there is potential harm in failing to understand that this may be a suboptimal treatment option for your individual patient. Likewise, there is no harm in applying the race-based correction for estimating GFR, but there is potential harm in not considering that this estimation may be wildly off. Cerdeña and colleagues advocated abandoning all race-based guidelines and replacing them with what they call race-conscious alternatives.[1] Sometimes, these are very suitable alternatives, such as the 2021 version of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, which provides a widely validated race-independent estimation of GFR.[48] Unfortunately, many of the other alternatives are not evidence-based solutions, but mere pragmatic approaches in which treatment is started independent of race/ethnicity and adjusted on the basis of effect and safety parameters. Of course, treatment should always be evaluated in this manner, and therefore we argue that this does not differ much from applying race-based guidelines while acknowledging their drawbacks.

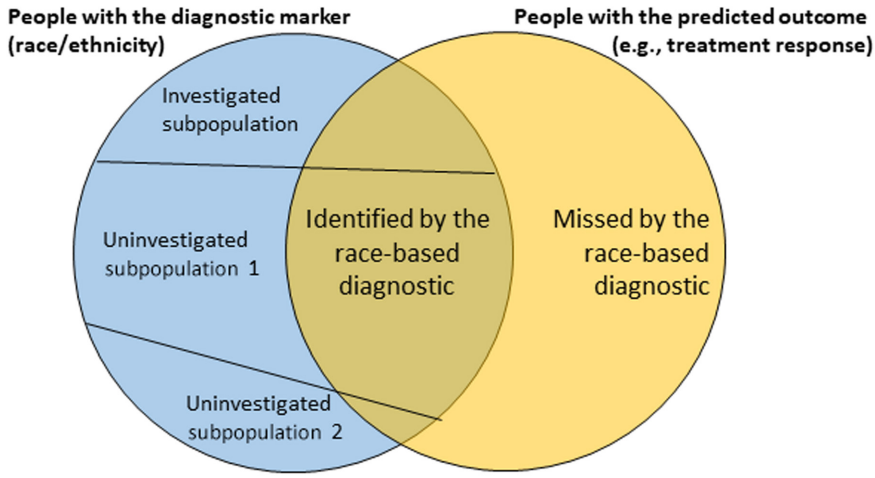

Figure 2 False generalization of race-based recommendations (schematic). As in **Figure 1**, the blue circle represents people sharing the racial identification used as diagnostic marker (e.g., Black). However, this schematic shows that the accuracy as observed in one subpopulation (e.g., Black people in the United States) cannot be generalized to other subpopulations (e.g., Black people in Europe). The sizes of the respective areas vary depending on the diagnostic used and are often difficult to estimate/investigate.

How should we change our teaching?

Diversity and inclusion are key concerns in higher education. In a recent survey among European higher education institutions (n = 159), nearly all respondents reported either having (85%) or developing (13%) strategies or policies to improve diversity, equity, and/or inclusion.[49] An increasing number of medical schools now offer lectures and/or elective courses on health equity, race, and bias.[16,50] However, these improvements have little effect when other ("core science") teaching continues to portray race as an important risk factor for disease with insufficient context.[17] We, as CPT teachers, cannot simply ignore the issue. When teaching about race-based guidelines, we should —at the very least—be nuanced about the value of race as marker of risk and explain the potential for harm and difficulties to translate study results into clinical practice. Additionally, we recommend consulting institutional diversity officer(s) (i.e., person(s) tasked with diversity and inclusion) to help examine your teaching and learn whether knowledge and attitudes toward the use of race in medicine is (or could become) part of the medical curriculum. We have good experience with interactive small-group discussions (both online and in class) in which we discuss the questions posed in the heading of this guide. We suggest a "bottom-up" approach to curriculum content development and delivery methods, which encourages transparency and coproduction with students.

Diversity and inclusion in clinical case vignettes

CPT is frequently taught using case vignettes debated among a small group of students.[13] Unfortunately, these vignettes are often stereotypical and full of (implicit) bias.[51,52] In this part of the guide, we look beyond race and ethnicity, because sex, gender, and religious or political beliefs may also relate to sickness and health, and just as with race or ethnicity, it may be difficult to decide what information, and how much, to provide about a patient's background when making clinical cases to use in medical education.[53]

Stereotyping is a big problem in case vignettes. Too often, the race (or sexual orientation, etc.) of a patient is stereotypically connected to their disease or a direct and oversimplified clue to the "correct" answer in case-based examinations or exercises.[54] By designing our assignments in this manner, we reward our students for their bias and teach them to see such characteristics as markers—markers that may ultimately prove harmful (lead to delayed diagnosis or suboptimal treatment, etc.) in real patient care. We should therefore be reflective of our own bias when making cases. More importantly, we must consider that our cases are about *individual* patients and that they do not always have to reflect the epidemiological *average* patient. In fact, we argue that it is better to make cases about patients that do not fit the norm, because this challenges preexisting ideas/opinions and because it is a more adequate reflection of clinical practice (as no individual is average in all respects).[51] Stereotyping may not only be problematic in relation to diagnosis and treatment, but also in relation to other aspects of a clinical case. For example, when a job description is provided in the case, care must be taken that this is not gender-biased (e.g., high positions more often allocated to male patients). Likewise, bias in terms of risk behavior, lifestyle, or employment should be avoided when treating immigrant patients (or patients with a "foreign-sounding" name).

Patients in simulated case scenarios should reflect the diversity of actual patients with respect to their gender, sexual orientation, race, ethnicity, disabilities, religion, political beliefs, and any other aspects that may shape their identity, as well as the intersection of these dimensions (intersectionality).[50,55] Therefore, when creating cases, it is advisable to add diversifying traits and characteristics to your patients. Care must be taken that this is done regardless of the teaching topic (e.g., not only in relation to sexual health problems or lifestyle diseases), avoiding stereotypical associations with other health-related aspects. Moreover, it is important to use inclusive and respectful language (e.g., when the patient is transgender or gender non-conforming, make sure to consistently address them by their preferred pronouns).[56]

An important aspect of being inclusive is to avoid using descriptors of gender, sexual orientation, religion, etc. in ways that are

irrelevant to the story. For example, mentioning a patient's religion (e.g., Christian, Buddhist, or Muslim) may be irrelevant for the treatment of a fractured leg and because there is no clear purpose for providing this information, it easily gets a discriminatory connotation. Creating inclusive cases while avoiding such unwanted connotations is difficult. However, rather than explicitly stating that the patient is, for example, Muslim, you can make the case more inclusive and avoid unwanted connotations with subtext, for instance by mentioning that he broke his leg in a fall down some steps at the mosque.

Lastly, it is important to be aware of implicit bias (at both your own and the reader's end) and avoid (inadvertently) communicating this bias. This is best achieved by being very specific with the information you provide.[51,56] For example, in a case about a possible sexually transmitted infection, the information that the patient is gay may imply that he is having unsafe sex with other men, whereas he may be sexually abstinent or having (monogamous) safe sex. It is therefore better to state whether he had unsafe sex or not, and whether his sexual partner(s) had an increased risk of sexually transmitted infections. Likewise, in a case about sickle cell disease, the information that the patient is Black is less informative than the information that his/her birthparents come from a malaria-endemic region in Kenya.

Final remarks

We have tried to provide a nuanced, scientific, and two-sided view of the issues that surround race-based medicine, diversity, and inclusion in medical teaching. We hope that this approach convinces CPT and other "core medical science" teachers that they have an important role in reducing the propagation of bias via medical guidelines and case vignettes, and that doing so is not at odds with academic freedom. However, some limitations to this article must be acknowledged. While we took effort to provide a thorough review of the literature through searching PubMed/Medline and Google Scholar and via "snowball referencing," the nature of this guide did not lend itself for a systematic review approach. As such, this article should not be viewed as a comprehensive overview of relevant literature, but rather as a selection of literature made by the authors. We took effort to improve the rigor of this article by discussing the contents in a relatively large international consortium until consensus. Nevertheless, we realize that it is impossible to write a guide that is not biased by our own opinions and the spirit of our times. Therefore, we see this guideline as a starting point for an evolving discussion aimed at improving education. On the European Open Platform for prescribing Education (EurOP^{2}E, www.prescribingeducation.eu), we aim to keep the discussion alive and provide more ready-to-use open (free to reuse, revise, and redistribute) teaching materials about race-based medicine and practical tools to improve diversity and inclusion.

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CONFLICT OF INTEREST

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