# Ethnicity and pharmacokinetics: misconception or confusion?

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The questionnaire and methodology for this study was approved by the Faculty of Medicine and Health Sciences Research Ethics committee of the University of Nottingham (Ethics approval number: FMHS 362-1021).

**Consent**

Informed consent was obtained from all individual participants included in the study.

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**Authors’ contribution statement**

All authors contributed to the study conception and design. Olusola Olafuyi and Jennifer Koenig prepared and delivered the teaching sessions and questionnaires, and the focus groups were led by Rakesh Patel. Data collection and analysis were performed by Jennifer Koenig. The first draft of the manuscript was written by Jennifer Koenig and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

### What is already known about this subject

* There are a wide range of factors that can result in inter-individual variation in pharmacokinetics however genetic mechanisms such as single nucleotide polymorphisms have received the most attention in research and in teaching.
* Studies in the USA have suggested that misconceptions exist amongst students regarding ethnicity and genetic similarity with students tending to erroneously over-estimate the genetic differences between ethnic groups.

### What this study adds

* We outline the design of a teaching session to address inter-individual variation in pharmacokinetics and address the issue of potential misconceptions about ethnicity.
* We highlight the difference in use of the term ethnicity by students and in the pharmacological literature. Students typically use ethnicity to refer to culture, tradition and place whereas the pharmacological literature where ethnicity refers to large scale continental racial groups e.g. Black, white, Asian.
* We observed little evidence of genetic deterministic views but a considerable amount of confusion about ethnicity and genetic similarity.
* Teaching about inter-individual variation in pharmacokinetics reduced the tendency of students to propose a genetic mechanism for inter-ethnic differences in drug metabolism.

### Abstract (150-250 words)

Aims: To explore the impact of a teaching resource on student's understanding of variation in drug disposition between ethnic groups.

Methods: A questionnaire was administered to students from medical and medical sciences undergraduate courses immediately before and after a teaching session on inter-individual variation in pharmacokinetics. Their responses were analysed using a Wilcoxon signed rank test.

Results: Students were most likely to define ethnicity in relation to culture, traditions, and place in contrast to use of the term in the pharmacokinetics literature where it refers to large-scale continental racial groups, e.g., Black, white, Asian. There was a tendency for students to assume a genetic mechanism for ethnic differences and there was a change in this assumption after they participated in the teaching session.

Conclusions: Confusion around the use of the term ethnicity may contribute towards lack of clarity in teaching and in student understanding. Teaching about a range of mechanisms that can underly inter-individual variation in pharmacokinetic processes reduces the tendency of students to ascribe genetic mechanisms to differences in drug metabolism, clarifies some of the ways in which individuals can vary.

## Introduction

In clinical pharmacology there are several instances where race and/or ethnicity are noted, for example, the guidelines for the treatment of hypertension in the UK and heart failure in the USA recommend different drug classes as the first line treatment for those of Black African and Afro-Caribbean descent [1], [2]. It has been proposed that dose prediction algorithms could allow adjustment for ethnicity [3]. In our previous work, a scoping review investigating the relationship between ethnicity and pharmacokinetic processes [4], we found that the majority of papers showed similarities rather than differences in pharmacokinetics. In those that did show differences, genetic mechanisms were most commonly proposed, and the prevalence of certain single nucleotide polymorphisms (SNPs) was suggested to underly differences in drug metabolism and distribution. Furthermore, ethnic differences in pharmacokinetics were mostly attributed to genetic mechanisms that pharmacology teaching [4]. There are, however, many other factors that can account for inter-individual variation in pharmacokinetics as illustrated in figure 1.

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**Figure 1. Factors that can result in inter-individual variation in pharmacokinetics processes.**

Studies in genetics education research have shown that both high school and undergraduate students have significant misunderstandings regarding ethnicity and genetics: many think, erroneously, that there is more genetic variation between ethnic groups than within ethnic groups [5]–[7]. This is important because it has been suggested that those who learn about racial differences in the prevalence of disease are more likely to agree with a genetic argument for racial inequality [6]. Also, genetic determinism, the belief that genetic factors are more important determinants of phenotype than environmental or behavioural factors, has been demonstrated in studies of genetics understanding in the public [8]. There is therefore a need to ensure that, in teaching about pharmacokinetics, these misconceptions are not perpetuated.

Another cause of potential confusion could be the way in which students understand the terms ethnicity and race since these terms can have subtly different meanings in bioscience fields and in everyday use and which are changing over time [9]–[12]. How future doctors and scientists understand ethnicity matters because it has been proposed that the attribution of the prevalence of certain illnesses or conditions, e.g., cystic fibrosis, sickle cell anaemia and osteoporosis, more to a particular ethnic group can lead to the unintended consequence of underdiagnosis in other ethnic groups [13], [14].

In this paper we investigated how students understand ethnicity, whether they demonstrate gaps in understanding about genetics and/or hold genetic deterministic views or misconceptions about ethnicity and genetic similarity. We describe the design of a teaching session about inter-individual variation in pharmacokinetics and evaluate this to determine whether students understanding of ethnicity and any misconceptions were influenced by our teaching session.

## Methods

### Study design

The study design is summarised in Figure 2: a pre-questionnaire was prepared by adapting a questionnaire by Jamieson and Radick [14] see Supplementary Material S1 for the questionnaire. This was then administered to a range of university students and followed immediately by a teaching session about inter-individual variation in pharmacokinetics. A post-questionnaire was then administered immediately after the teaching session. Participation in questionnaires was voluntary whilst the teaching session was a normal timetabled part of the courses. The study was approved by the Faculty of Medicine and Health Sciences Research Ethics committee of the University of Nottingham (Ethics approval number: FMHS 362-1021). Respondents gave informed consent in accordance with the ethics approval.

**Figure 2. Study design.**

### Context and Population

Students were drawn from courses in Graduate Entry Medicine, MSc Drug Discovery and BSc courses in Medical Physiology and Therapeutics and Pharmacology in a large research-intensive University in central England.

### Questionnaire design

The pre-questionnaire (see Supplementary Material S1) included three sections:

1. **“Background information”** asked about prior study of biology and genetics.
2. **“Your knowledge”** contained a short true-false genetics knowledge quiz adapted from Jamieson and Radick [15],
3. **“Your opinions”** included questions asking students how they understand the term ethnicity, and statements about genes, disease, inheritance and ethnicity, adapted from Jamieson and Radick [15], with 5-point Likert-scale responses indicating level of agreement. Finally, there were two additional questions about the genetic and/or environmental aspects of drug action.

The post-questionnaire included section 3 only. Questionnaires were delivered through JISC Online Surveys ([www.onlinesurveys.ac.uk](http://www.onlinesurveys.ac.uk)) and responses were anonymous. Responses to the pre- and post-questionnaires were matched for subsequent analysis.

In the questionnaire results the summary response is given agree if the number of agree plus strongly agree responses was greater than the sum of strongly disagree, disagree and neutral. Similarly, the summary response for disagree was given if the sum of strongly disagree and disagree was greater than the sum of neutral, agree and strongly agree. Otherwise, the summary was given as inconclusive.

Free text responses to the question “What do you understand by the term “ethnic group”?” were sorted according to whether they mentioned the following terms: ancestry, genetics, culture, place of origin, appearance, race. Words such as skin tone, physical attributes or colour were categorised with appearance. Hereditary was categorised with genetics.

### Design of the Teaching Session

We designed a teaching presentation based on the work from our scoping review [4] that highlighted a range of factors, including diet, smoking, alcohol, age, sex, pregnancy, presence of drug-metabolising enzyme or transporter variants and isoforms, that can influence inter-individual variability. We were concerned about inadvertently giving race or ethnicity a biological basis and made sure to emphasise the following key points:

* individuals vary due to a variety of factors both genetic and non-genetic.
* we did not foreground one mechanism over any other.
* allele prevalence is not exclusive to a particular ethnic group e.g. the organic amine transporter OATP1B1 variants [16], [17] and therefore ethnicity should not be used as a proxy for genetics
* there is as much genetic diversity within ethnic groups as between them.

### Statistical Analysis

A priori estimate of sample size (performed using GPower 3.1) using effect size of 0.3 (medium), α = 0.05 gave a required sample size of 64 for a statistical power of 0.8 and 111 for a statistical power of 0.95.

The Likert scale data in the pre- and post-questionnaire responses were converted to numerical form, strongly disagree = 1, disagree = 2, neutral = 3, agree = 4 and strongly agree = 5 and the pre- and post-questionnaire responses were matched using the identification number. Similarly, in the questions about drug treatment, only environmental = 1, mostly environmental = 2, both genetic and environmental = 3, mostly genetic = 4 and only genetic = 5. Analysis was performed with GraphPad Prism 9 using a Wilcoxon Paired Signed Rank test to determine statistical significance (p < 0.05).

## Results

Our sample included 112 participants taken from four courses at a U.K. University: Graduate Entry Medicine, year 1, Medical Physiology and Therapeutics BSc year 2, Pharmacology BSc year 2, and Drug Discovery MSc.

### Prior study and general knowledge of genetics and biology

Most participants (81%) had studied biology to age 18 (final year of secondary (high) school) and 43% had previously studied biology and 37% had previously studied genetics in an undergraduate University degree. Overall students have a generally good knowledge about genetics with a median test score of 83%, (interquartile range 67%, 92%). Question level analysis is shown in Table 1 and revealed that students were least likely to correctly answer about the relationship between gene(s) and disease or gene(s) and traits as almost half of the students chose the incorrect answer for: “Human diseases caused by a single gene are more common than those caused by a combination of many genes”.

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| **Table 1. Student responses to a basic genetics quiz showing 12 statements, the correct answer and the percentage of students who entered the correct answer (n=112).** | |
| **Statement** | **% Correct** |
| Human diseases caused by a single gene are more common than those caused by a combination of many genes | 55 |
| Cells of different types (e.g. nerve cells, liver cells) in the same person contain different genetic information | 63 |
| There is a separate gene for each characteristic of a human being | 66 |
| Cells of the same type (e.g. brain cells) in different people contain the same genetic information | 68 |
| Two parents are carriers for the recessive disorder, cystic fibrosis, therefore there is a 1 in 4 chance that a child they have will have the disease. If the couple already have 3 unaffected children, a 4th child would be more at risk than the 1st child | 73 |
| If a woman is identified as having a BRCA1 mutation, she will develop breast cancer at some point in her life | 80 |
| The variety we see in humans can be completely explained by genetic differences | 83 |
| Overall, more human disease is caused by environmental factors (such as diet, lifestyle, exposure to bacteria, viruses or chemicals) than by genetic factors | 84 |
| The environment has no effect on the way in which our genes influence our characteristics | 89 |
| Many genes code for proteins which have important physiological functions in the body, such as haemoglobin in the blood, or insulin, which controls blood sugar levels | 93 |
| The genetic information is organized into separate units (genes) which influence different aspects of our development | 95 |
| Mutations in the DNA always lead to diseases/disorders | 95 |

### How do students understand ethnicity?

In response to a simple question asking for a free text response, students overwhelmingly defined ethnicity in relation to culture, place of origin and physical appearance (Figure 3a). Just over half of the students (57%) included only words indicating non-genetic mechanisms, i.e. those synonymous with culture, place and appearance and did not use words relating to genetics or ancestry (Figure 3b). A fifth (20%) used words relating to both genetic and non-genetic mechanisms. Ethnicity was defined in terms of race by 8% of students whilst 15% used words that reflected only genetics or ancestry. Overall students’ understanding of the meaning of the term ethnicity did not change after the teaching session.

### Do students display genetic deterministic beliefs?

Students did not respond in a manner that was consistent with showing genetic deterministic beliefs (Table 2). In 4 out of 6 statements, (Table 2 (b), (c), (d), (f)) most students chose a response that did not indicate genetic deterministic beliefs. In the remaining two statements, there was either a bimodal distribution (Table 2 (a)) or a large proportion of neutral responses (Table 2 (e)).

After the teaching session, for two statements where genes are related to traits and disease and the pre-questionnaire responses were inconclusive, there was a statistically significant shift after the teaching away from the genetic deterministic view (Table 2, these statements were (a) “Cloning can produce a copy of an animal identical in all respects with the original— so you could recreate a much-loved pet for example” and (e) “Genes have a greater role in most human disease than environmental factors do”).

**Do students tend to propose a genetic or environmental mechanism for proposed ethnic differences in pharmacology?**

In questions regarding pharmacological mechanisms, the largest proportion of students proposed both genetic and environmental mechanisms underlying ethnic differences in pharmacological treatment of hypertension (Table 3a) between Black and non-Black patients although there was a significant minority suggesting a genetic mechanism. The teaching session had no effect.

In contrast when asked to propose a mechanism for differences in drug metabolism prior to the teaching session, the majority of students proposed a genetic mechanism. After the teaching session there was a statistically significant shift away from a genetic mechanism towards environmental or both environmental and genetic (table 3b) reflecting the key messages contained in the teaching.

Chart

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**A**

Chart, pie chart

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**B**

**Figure 3. Students’ definition of ethnicity in a free text response.**

(a) Responses were categorised into six groups based on the free text responses. There were 87 individuals who answered this question in both the pre- and post-questionnaire. Some individuals used words from more than one category.

(b) In the pre-questionnaire, most students (57%) defined ethnicity as relating to culture and/or place of origin and/or physical appearance whilst 15% used words relating to genetics and/or ancestry. One fifth used words relating to both of the above groupings. Words used in free text responses were categorised as shown in (a) then grouped as shown. Responses are shown from 87 individuals who gave responses in both the pre-and post-questionnaires and there was no significant difference (p=0.3, Chi square test) between the pre-and post-questionnaire responses.

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| **Table 2. Summary of student responses to questionnaire statements about genes, traits and disease and change after the teaching session.** Difference between the pre- and post-questionnaires was assessed using a Wilcoxon Paired Signed Rank Test performed with GraphPad Prism 9. | | | |
| **Statement** | **Prediction if genetic deterministic beliefs** | **Pre-questionnaire** | **Post-questionnaire** |
| (a) Cloning can produce a copy of an animal identical in all respects with the original— so you could recreate a much-loved pet for example. | Agree | Inconclusive  disagree 42%  neutral 16%  agree 42% | Significant shift (p=0.0005) towards disagree |
| (b) Cloning could never produce a completely identical copy of a human being because our development is determined by much more than just our genes | Disagree | Agree 89%  neutral 7%  disagree 4% | No change |
| (c) The children of musicians are more likely to become musicians themselves not because they inherit musical talent but because they follow their parents’ example | Disagree | Agree 70%  neutral 18%  disagree 13% | Significant shift (p<0.0001) towards disagree |
| (d) Apart from changes that take place after birth and throughout their lifetime (such as accidental scars, hair style, clothing, tattoos, etc.) it is not possible to tell identical twins physically apart | Agree | Disagree 63%  neutral 10%  agree 27% | No change |
| (e) Genes have a greater role in most human disease than environmental factors do | Agree | Inconclusive  disagree 36%  neutral 37%  agree 28% | Significant shift (p<0.0001) towards disagree |
| (f) Changes in lifestyle (diet, exercise and so on) can never override a person’s genetic risk factors | Agree | Disagree 56%  neutral 19%  agree 25% | No change |

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| **Table 3. Summary of student responses to pre-questionnaire statements about pharmacological mechanisms and change after the teaching session.** Difference between the pre- and post-questionnaires was assessed using a Wilcoxon Paired Signed Rank Test performed with GraphPad Prism 9. | | | |
| **Statement** | **Prediction if genetic deterministic beliefs** | **Pre-questionnaire** | **Post-questionnaire** |
| (a) The guidelines for treating high blood pressure/heart failure recommend treating one ethnic group with a different class of drugs to that used for all other ethnic groups. Which of the following mechanisms do you think might underly this difference? | Genetic | Both genetic and environmental (57%)  Genetic 39%  Environmental 4% | No change |
| (b) Drug metabolism in the liver is the main mechanism for terminating its effect. A study has shown that some ethnic groups differ in the rate at which they break down the drug. Which of the following mechanisms do you think might underly this difference in treatment between these two groups? | Genetic | Mainly or only genetic (58%)  Both genetic and environmental 41%  Environmental 1% | Significant shift (p<0.0001) towards environmental |

## Discussion

Traditionally, inter-ethnic differences in pharmacokinetics teaching have focussed on genetic mechanisms, usually single nucleotide polymorphisms. In this study we redesigned our teaching to focus on inter-individual variation and addressed some issues identified in the genetics education literature that highlight misconceptions around ethnicity and genetics. We also investigated our students understanding of ethnicity and genetics misconceptions and explored the effect of our redesigned teaching.

### How do students understand ethnicity?

Students defined ethnicity mostly as a social construct with over half of the cohort using words relating to culture, place of origin and appearance and not words relating to genetics or ancestry (Figure 3). In everyday language the definition of ethnicity has changed over time and varies between countries [10]. Hamer et al [10] found that British participants most often related ethnicity to culture and traditions which was reflected in our participants’ view whereas US respondents related ethnicity to race. In the pharmacokinetics literature the terms used for ethnic groups are those of the continental racial categories i.e., Black, Asian, white which is clearly inconsistent with the students’ view of ethnicity as shared cultures and traditions. Human geneticists have called for use of ethnic group terms such as White British, Black African to stop since these terms, which were introduced centuries ago, are not relevant for understanding population genetics [9]. Likewise, Bhopal and Donaldson [18] argue that use of these racial terms encourages “division of society by skin color, reinforcing racial stereotyping, and hides a remarkable heterogeneity of cultures.” Following this line of argument, it is logical to suggest that use of these terms in the pharmacology classroom in the context of biological variation should be carefully considered.

During our teaching sessions we began to become aware of problems with terminology and that we and our students were not always completely clear about how certain words were best used. Many students used the term ancestry in their responses, and we included the term in a list of words students could choose from to indicate their understanding of ethnicity. As with many terms, it has an everyday meaning – a general connection to people or things in the past – and a more specific meaning in genetics i.e. the information about your ancestors and their genetic relationship to you [19]. On reflection, we decided to assume that students were using the term ancestry to describe genetic relationship to ancestors and therefore grouped responses that included the terms genetics and ancestry. It is possible that students ascribed subtly different meanings to the term ancestry.

### Did our students demonstrate genetic determinism or lack of understanding?

Genetic determinism is typically measured with the use of a questionnaire designed for use in genetics teaching and so contain considerable detail about genetic mechanisms or encompassed aspects of genetics and genomics technologies all of which were outside the scope of our subject teaching [20], [5], [8], [21], [22]. There does not appear to be a validated questionnaire that has been extensively used by several groups so we decided on a selection of questions derived from the questionnaires of Jamieson and Radick [15] and added our own questions about drug treatment as we were interested in how students responded in a pharmacological context.

Despite these caveats, we found no convincing evidence for genetic determinism as students did not, overall, respond in a manner predicted if they shared genetic determinist views (Table 2). Given the large proportion of neutral responses, it is quite possible that there was considerable uncertainty or confusion. A potential explanation is that students had gaps in their knowledge since only 55% were able to correctly identify as false the statement “Human diseases caused by a single gene are more common than those caused by a combination of many genes”. Castro‐Faix and Duncan [23] propose that there may be a disconnect between the teaching of molecular genetics and understanding of inheritance patterns. They show that students have difficulty linking what is happening at different levels of organisation, particularly from molecular to whole organism [23]. This is particularly complicated by the emphasis on Mendelian inheritance in the school and University curriculum and the lack of education about the importance of the interaction of many genes with environmental factors [24].

Nevertheless, several studies in the USA have detected genetic determinist views in biology students [5], [6], [7]. Our study is different to the above in a number of ways, not least that we are using a different questionnaire, students are in a Pharmacology classroom rather than genetics and we are situated in the UK rather than the USA. Since some of our participants have a previous degree in Biological Sciences, it is possible that our cohort, on the whole, have a relatively high genomics literacy and Donovan et al [7] have shown that students with greater knowledge of genomics are less likely to show genetic deterministic views.

**Was there evidence of misconceptions about ethnicity and genetic similarity?**

In the statements relating to pharmacological mechanisms there were differences in the way students responded. In the statement about drug choice in hypertension, the most common option (57%, Table 3a) was both genetic and environmental mechanisms. In comparison when predicting the mechanism underlying differences in drug metabolism, a genetic mechanism was the most commonly chosen (58% Table 3b). This likely reflects differences in background knowledge about these two topics. Lifestyle mechanisms for cardiovascular disease feature in the English school biology curriculum and are often mentioned in the media and general discourse. In contrast, it is unlikely that many of our students will have learned about mechanisms for ethnic differences in drug metabolism previously and, if they have, it is likely that a genetic mechanism was taught [4].

The observation that students were most likely to choose a genetic mechanism for ethnic differences in drug metabolism could indicate the presence of a misconception that there may be greater genetic similarity within an ethnic group than between one ethnic group and another. Stern et al [20] suggest that preconceptions are students’ conceptions prior to teaching and that genetic essentialism is a form of intuition, a spontaneous way of thinking about a subject. Applying this to our teaching of pharmacokinetics, we could conclude that our students are demonstrating a genetic essentialist intuition in their preconception as they have not previously studied ethnicity in relation to pharmacokinetics. It is also likely that students are influenced by the media and general discourse [22] and this may lead students to make assumptions about genetic mechanisms, even when they have little prior knowledge [25].

### What was the effect of our teaching session?

Where we had previously seen an overall inconclusive response regarding genetic deterministic views, we saw a statistically significant shift in thinking after the teaching session with students more likely to choose non-genetic mechanisms for inheritance mechanisms, the link between genes and disease (Table 2a, c, e) and in inter-ethnic differences in drug metabolism (Table 3b). Once we provided explicit teaching about the mechanisms that can underly inter-individual variation and a greater understanding of the term ethnicity in relation to science and medicine, then students are more likely to form a correct conception.

It has been proposed that there is an association with genetics teaching that followed Mendelian principles and genetic determinism [22] and with the majority of our students having received their secondary school education in the UK system, they will likely have been taught with a traditional Mendelian approach. Jamieson and Radick [15] took an historical approach and introduced a Weldonian curriculum to counter the influence of more simplistic Mendelian teaching and also observed a reduction in genetic determinism. In addition, Donovan et al [24] suggest that improved genetics education can reduce the likelihood of genetic determinism.

Whilst we have changed our teaching about ethnicity in pharmacokinetics, we have yet to explore the rest of our curriculum. In a study of preclinical faculty, Ibrahim et al [26] found a range of definitions for race, including an element of biological basis. In addition, race was often mentioned without any underlying mechanism explanation which could lead, as we have seen, to the implication of a biological basis. This raises the possibility that despite our students being unable to recall any teaching about ethnicity, it may have been mentioned in passing or may have been implied by previous teaching.

### Conclusions and next steps

Whilst we have some indications that our students may demonstrate genetic determinist views, there is a great deal of confusion over the meaning of the term ethnicity in the context of medical science. This is quite likely since the way students think of ethnicity relates to culture, traditions and place whereas the use of the term in the pharmacology literature relates more to continental-scale racial groups. Students may also have considerable gaps in their understanding of genetics and inheritance and in the use of language relating to ethnicity. We have successfully designed a new teaching session about inter-individual variation in pharmacokinetics which has helped to clarify our students’ thinking around ethnicity and highlighted the importance of being clear about any potential mechanisms that could underly apparent ethnic differences. However, it has become increasingly clear that we need to look at all our teaching around issues of race and ethnicity. Now that we have an example in the context of pharmacokinetics, we need to take the opportunity to consult with colleagues at a course-wide level. Specifically, we realise the importance of:

* sharing understanding about use of language and clarify terminology relating to ethnicity and ancestry.
* ensuring that the social basis for race and ethnicity are reinforced in a variety of contexts and any implication of a biological basis for race and ethnicity is identified and countered.

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