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Ethnic minority representation in trial of cardiometabolic disease

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Disclosures

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Impact of underrepresentation of ethnic minority groups in research

Health difference across ethnicity may reflect **different disease pathologies** and **response to treatments (**Hussain-Gambles et al., 2004; Nazha et al., 2019).

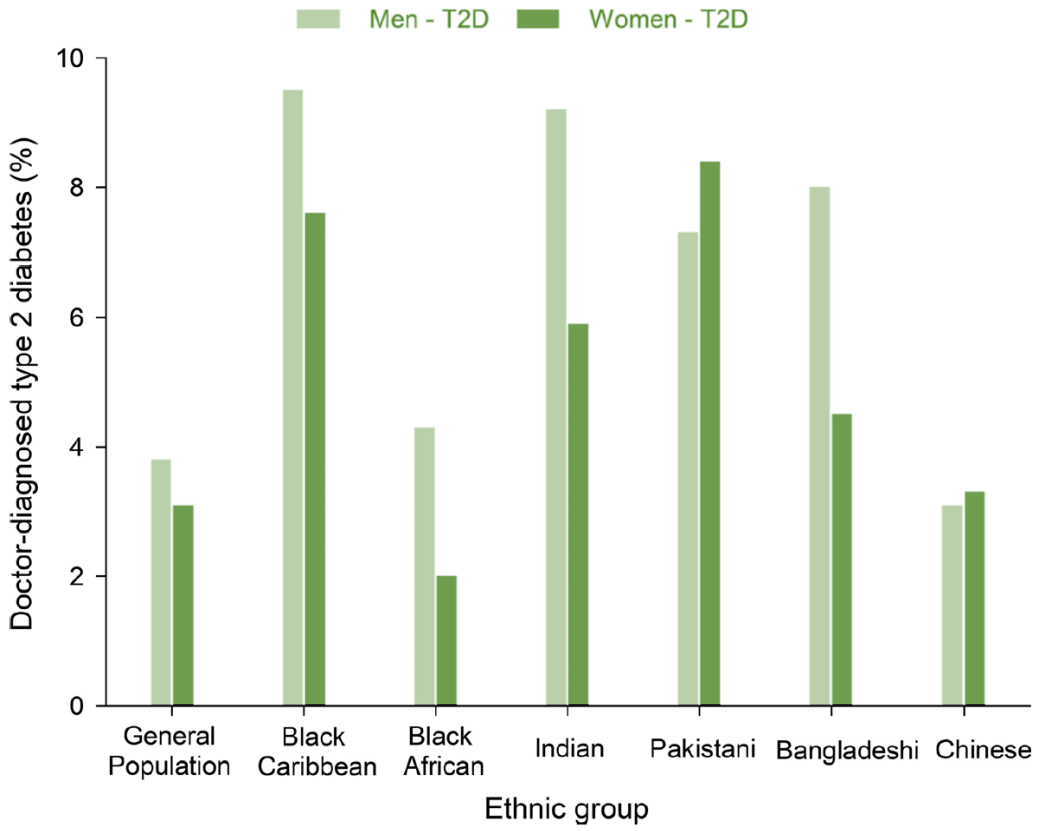
Culture and behavioral norms can shape Patients experience of navigating a complex healthcare system. Patients from an Asian background were among the least satisfied with aspect of care (Race Disparity Audit,2019)

Differences in effective doses of treatments: lower doses of *Warfarin* are required to be effective in Asian patients(3.4mg) compared to white (5.1mg) patients.

Implications: National evidence based guidelines may confer greater benefits to particular communities, particularly those who have helped shape the underpinning research

Prevalence of T2 diabetes higher in ethnic minority groups

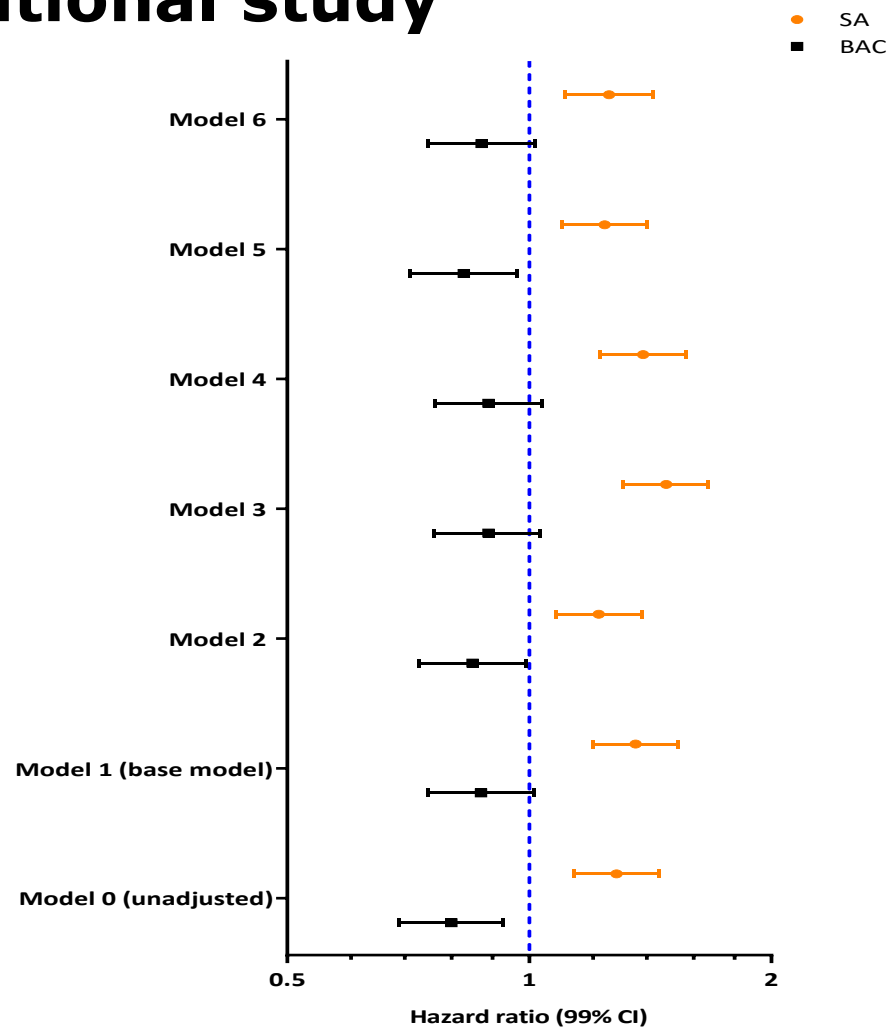
- Prevalence of type 2 diabetes is approximately three to five times higher among ethnic minority groups than the White British group
- Diabetes diagnosed 10-12 years earlier in ethnic minority groups



HSE 2004
Paul S et al. Diab Obes Metab 2017;19:1014-1023

Differences in the risk of cardiovascular disease across ethnic groups: UK Biobank observational study

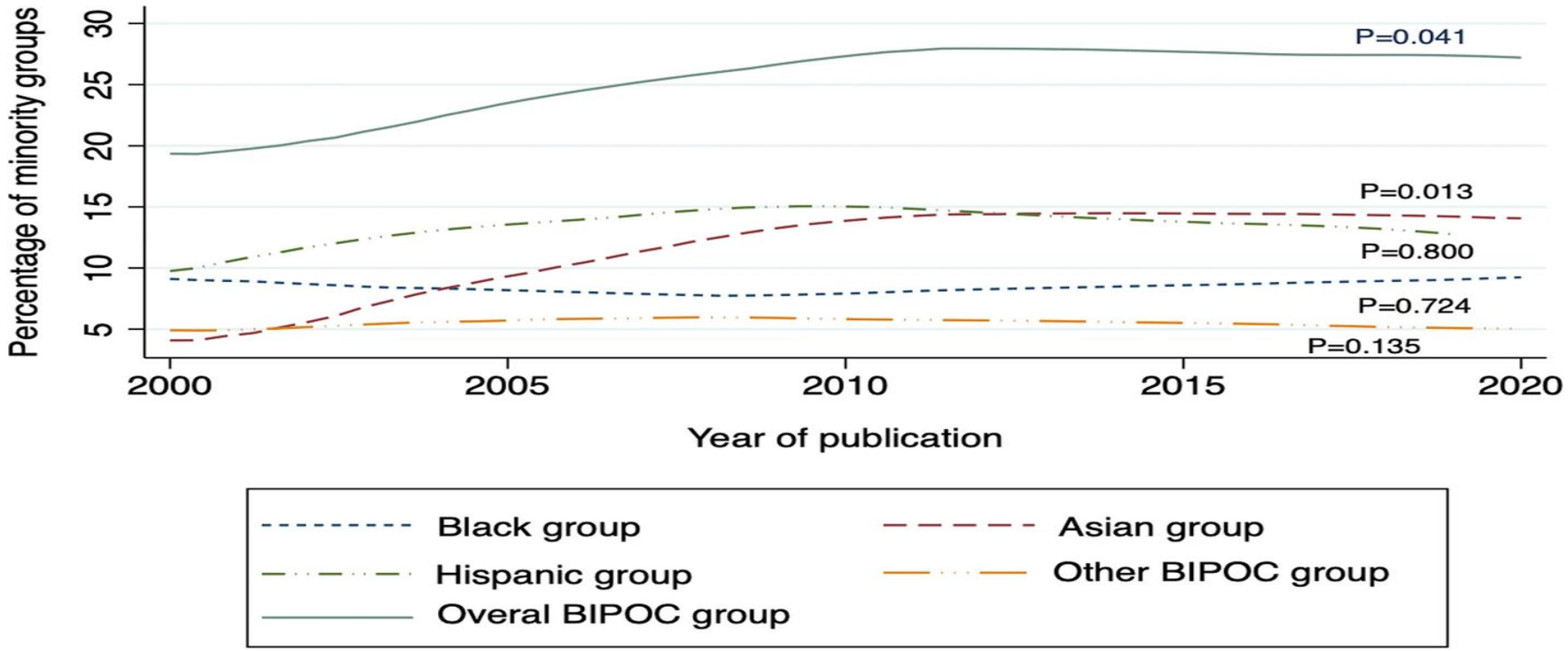
- 502,539 participants from UK Biobank.
- Three-point major adverse cardiovascular events (3P-MACE) as outcome.
- Higher CVD risk in South Asian individuals was independent of all sociodemographic, lifestyle, environmental and clinical factors.
- Black individuals generally had similar or lower CVD risk compared to white Europeans.



Razieh et al., (2022) Nutr Metab Cardiovasc Dis

Ethnic minority representation in diabetes trials

Twenty-year trends in racial and ethnic enrolment in large diabetes randomized controlled trials
405 RCTs included for analysis
Increase in trends ethnic minority enrolment for diabetes RCTs



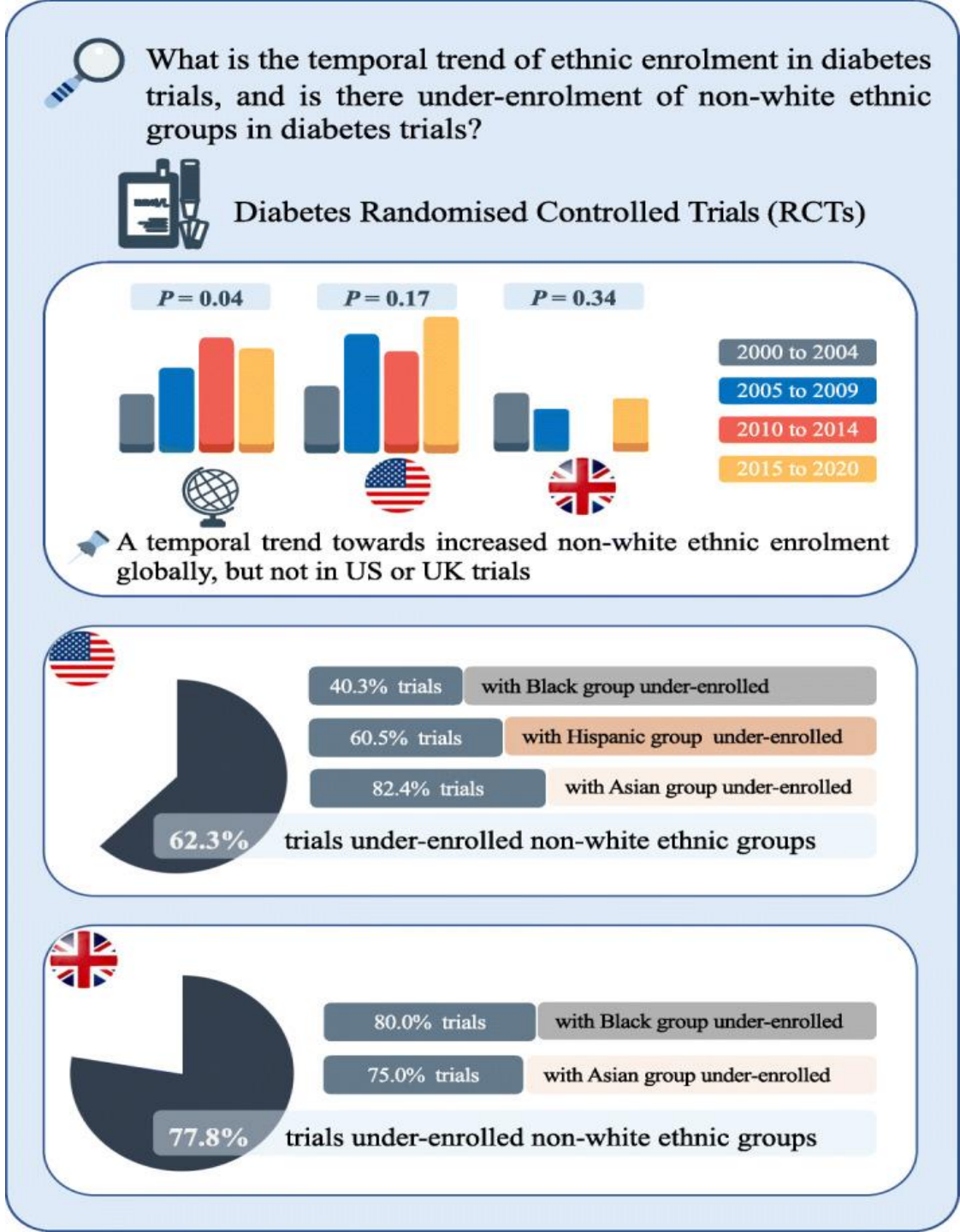
BIPOC = Black, Indigenous, and People of Colour

Zhang J, et al BMC Med. 2022 ;20:294.

Exploring ethnic representativeness in diabetes clinical trial enrolment from 2000 to 2020: a chronological survey

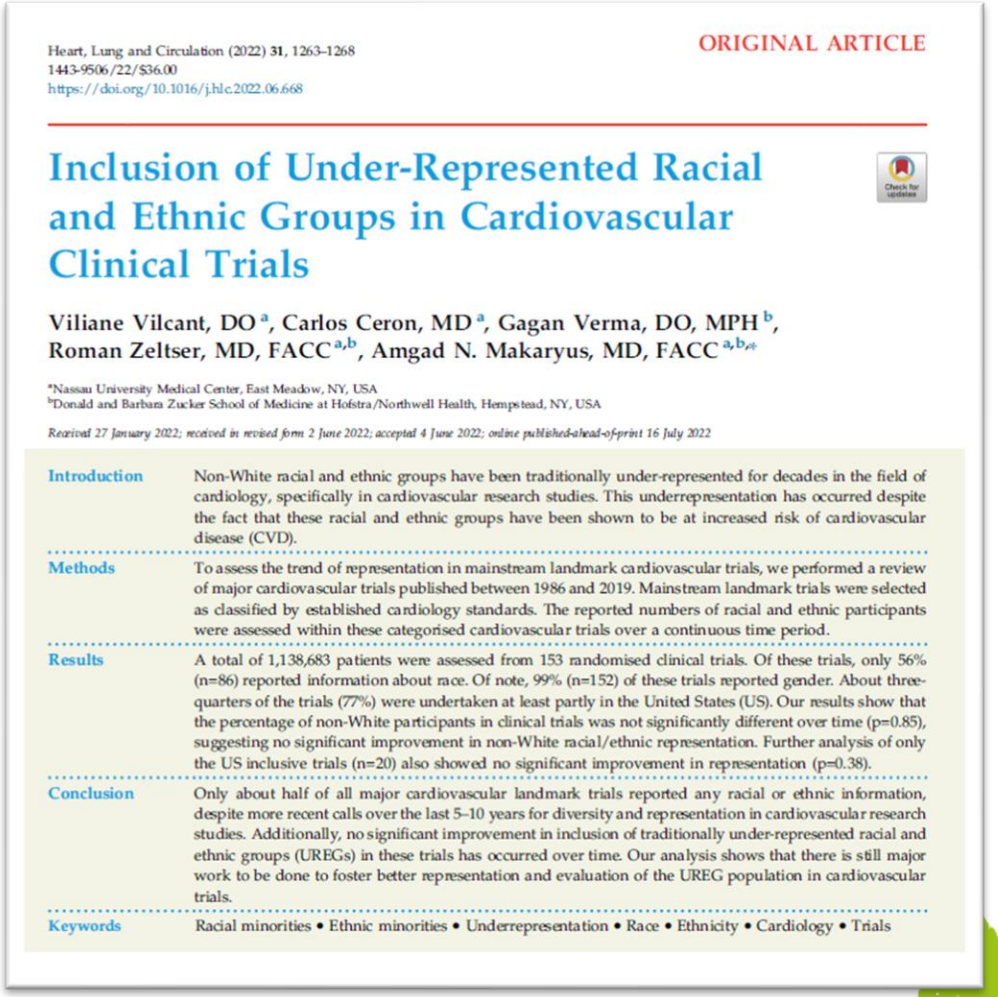
- 405 trials
- 78 single-country trials (69 in the USA and nine in the UK) and 327 multi-country trials.
- Non-white enrolment under-represented in majority of trials:
  - US Trials 29.0%
  - UK Trials 12%
- Temporal trends of increase in non-white participation-no significant trends in US or UK trials
- Non-white groups under-enrolled in US (62.3%%) and UK (77.8%) Trials
- 6.4% of all trials provided subgroup results or explored effect modification by ethnicity.

Li et al. Diabetologia 2022;65:1461-1472



Inclusion of Under-Represented Racial and Ethnic Groups in Cardiovascular Clinical Trials

- 153 RCTs with 1,138,683 patients were included (1986-2019)
- Only 56% reported race/ethnicity. (99% reported sex)
- Average % of Non-White ethnicity was 20% and did not change from 1986 to 2019.
- "These trials would 'under-represent' the Non-White population in many diverse countries such as the USA"



Heart, Lung and Circulation (2022) 31, 1263–1268
1443-9506/22/$36.00
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ORIGINAL ARTICLE

Inclusion of Under-Represented Racial and Ethnic Groups in Cardiovascular Clinical Trials

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Introduction Non-White racial and ethnic groups have been traditionally under-represented for decades in the field of cardiology, specifically in cardiovascular research studies. This underrepresentation has occurred despite the fact that these racial and ethnic groups have been shown to be at increased risk of cardiovascular disease (CVD).

Methods To assess the trend of representation in mainstream landmark cardiovascular trials, we performed a review of major cardiovascular trials published between 1986 and 2019. Mainstream landmark trials were selected as classified by established cardiology standards. The reported numbers of racial and ethnic participants were assessed within these categorised cardiovascular trials over a continuous time period.

Results A total of 1,138,683 patients were assessed from 153 randomised clinical trials. Of these trials, only 56% (n=86) reported information about race. Of note, 99% (n=152) of these trials reported gender. About three-quarters of the trials (77%) were undertaken at least partly in the United States (US). Our results show that the percentage of non-White participants in clinical trials was not significantly different over time (p=0.85), suggesting no significant improvement in non-White racial/ethnic representation. Further analysis of only the US inclusive trials (n=20) also showed no significant improvement in representation (p=0.38).

Conclusion Only about half of all major cardiovascular landmark trials reported any racial or ethnic information, despite more recent calls over the last 5–10 years for diversity and representation in cardiovascular research studies. Additionally, no significant improvement in inclusion of traditionally under-represented racial and ethnic groups (UREGs) in these trials has occurred over time. Our analysis shows that there is still major work to be done to foster better representation and evaluation of the UREG population in cardiovascular trials.

Keywords Racial minorities • Ethnic minorities • Underrepresentation • Race • Ethnicity • Cardiology • Trials

Vilcant et al. Heart, Lung & Circulation 2022;31:1263-1268

Hispanic representation in diabetes cardiovascular outcomes trials (CVOTs)

- 10 of 13 CVOTs with primary study results published January 2008 to October 2018.
- Compared Hispanic/Latino representation to Hispanic adults with diabetes in NHANES.
- Hispanics/Latinos comprised 18.5 % of trial subjects, which was similar to the proportion of US adults with diabetes who identify as Hispanic (18.2% in 2015).
- BUT Trial participants were younger, more likely to be female, and more obese than US Hispanics/Latinos.
- US Hispanics/Latinos differ from participants in diabetes CVOTs, limiting generalisability of trial findings.

Open access Research

BMJ Open Diabetes Research & Care

Hispanic representation in diabetes cardiovascular outcomes trials

A. Taylor Kelley,[1,2,3,4] Kara Mizokami-Stout,[1,2,3,4,5] Matthew J. O'Brien,[6] Michael E. Bowen,[7] Jeremy Sussman[1,2,3]

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ABSTRACT

Objective To examine Hispanic/Latino representation in diabetes cardiovascular outcomes trials for novel antidiabetic drugs.

Research design and methods We compared Hispanic/Latino representation, age, gender and body mass index in diabetes cardiovascular outcomes trials published from January 2008 to October 2018 to Hispanic adults with diabetes in the National Health Examination and Nutrition Survey over the same time period.

Results Hispanics/Latinos comprised 18.5 % of trial subjects, which was similar to the proportion of US adults with diabetes who identify as Hispanic. Trial subjects were significantly younger, more likely to be female, and more obese than US Hispanics/Latinos. At least 10 different Latin American countries and territories were represented across the 10 trials.

Conclusions US Hispanics/Latinos differ from subjects in diabetes cardiovascular outcomes trials, which may limit generalizability of trial results.

Significance of this study

What is already known about this subject?
- Incident type 2 diabetes is disproportionately high among US Hispanics/Latinos.

What are the new findings?
- Hispanics/Latinos included in diabetes cardiovascular outcomes trials differ from US Hispanics/Latinos in terms of age, gender, body mass index and country of origin, which may limit generalizability of trial results.

How might these results change the focus of research or clinical practice?
- The utility of diabetes cardiovascular outcomes trials may be enhanced by consistent reporting of Hispanic/Latino ethnicity and country of origin.
- Hispanic/Latino representation in diabetes cardiovascular outcomes trials may be improved to better reflect the US population. Clinicians should use caution in generalizing trial findings to their patients.

INTRODUCTION

The US Food and Drug Administration (FDA) is currently re-evaluating the role of diabetes cardiovascular outcomes trials (CVOTs) in determining the safety of new drugs for type 2 diabetes.[1] An important consideration will be the degree to which results from these trials can be generalized to patients with type 2 diabetes, both domestically and internationally.

Type 2 diabetes in the USA disproportionately affects adults from all racial and ethnic minority groups, including Hispanics/Latinos.[2] For example, the prevalence of diabetes in Hispanics/Latinos is twice that of non-Hispanic whites, Hispanics/Latinos with diabetes are three times as likely as non-Hispanic whites to develop end stage renal disease, and diabetes-related mortality is 50% higher.[3 4]

Additionally, disparities in treatment response to novel diabetes therapeutics, such as oral and injectable antidiabetic drugs, have been observed in clinical trials across racial and ethnic minority groups, including Hispanics/Latinos.[5] Recent studies have identified certain genetic markers disproportionately prevalent in some US Hispanic/Latino populations—especially those with origins from Mexico—that may partially explain observed disparities in diabetes prevalence and outcomes and may provide a basis for heterogeneity of treatment effects.[6] However, the number of clinical trials reporting outcomes for Hispanics/Latinos has historically been low.[7]

To address these disparities, the FDA has encouraged enrollment of racial/ethnic minorities in clinical trials and has provided guidance about how race and ethnicity should be reported in trial findings.[8] However, Hispanic/Latino representation for CVOTs has not been summarized across studies. Our objective was to examine the representation of Hispanic/Latino ethnicity in CVOTs compared with the entire population of US Hispanic/Latino adults with diabetes over the same time period to determine how international trial results may apply to Hispanics/Latinos in the USA.

Kelley et al. BMJ Open DR&C 2019;7:e000656

Representation of people of South Asian origin in cardiovascular outcome trials of glucose-lowering therapies in Type 2 diabetes

- 12 studies included.
- Among the 8 for which South Asian representation could be reliably estimated, 7 under-represented this group relative to the 11.2% of the UK diabetes population estimated to be South Asian.
- “Clinicians should exercise caution when generalizing the results of trials to their own practice”.

DIABETICMedicine

DOI: 10.1111/dme.13103

Short Report: Epidemiology

Representation of people of South Asian origin in cardiovascular outcome trials of glucose-lowering therapies in Type 2 diabetes

K. Khunti[1], S. Bellary[2], M. A. Karamat[3], K. Patel[3], V. Patel[4], A. Jones[5], J. Gray[5], P. Shepherd[5] and W. Hanif[6] on behalf of the South Asian Health Foundation

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Accepted 25 February 2016

Abstract

Aims Our aim was to investigate the proportional representation of people of South Asian origin in cardiovascular outcome trials of glucose-lowering drugs or strategies in Type 2 diabetes, noting that these are among the most significant pieces of evidence used to formulate the guidelines on which clinical practice is largely based.

Methods We searched for cardiovascular outcome trials in Type 2 diabetes published before January 2015, and extracted data on the ethnicity of participants. These were compared against expected values for proportional representation of South Asian individuals, based on population data from the USA, from the UK, and globally.

Results Twelve studies met our inclusion criteria and, of these, eight presented a sufficiently detailed breakdown of participant ethnicity to permit numerical analysis. In general, people of South Asian origin were found to be under-represented in trials compared with UK and global expectations and over-represented compared with US expectations. Among the eight trials for which South Asian representation could be reliably estimated, seven under-represented this group relative to the 11.2% of the UK diabetes population estimated to be South Asian, with the representation in these trials ranging from 0.0% to 10.0%.

Conclusions Clinicians should exercise caution when generalizing the results of trials to their own practice, with regard to the ethnicity of individuals. Efforts should be made to improve reporting of ethnicity and improve diversity in trial recruitment, although we acknowledge that there are challenges that must be overcome to make this a reality.

Diabet. Med. 34, 64–68 (2017)

Introduction

People of South Asian origin are an important target for the prevention and treatment of diabetes. In the UK, for instance, Type 2 diabetes is about two times more prevalent in this group than in white European people [1]. Furthermore, in the USA, ~ 17.4% of people of South Asian origin have diabetes [2]. The risks of diabetic retinopathy and end-stage renal disease are known to be higher in South Asian people than in the white European population, and individuals of South Asian origin are also known to have a higher mortality rate from coronary heart disease and stroke [1].

There is also some evidence suggesting that there are ethnic differences in response to diabetes therapies. For instance, glucagon-like peptide–1 receptor agonists have been found to lower HbA_{1c} levels to a greater extent in Asian-dominant studies than in non-Asian-dominant studies, perhaps reflecting a different pathophysiology of Type 2 diabetes in different ethnic groups [3].

As in other conditions, clinical practice in Type 2 diabetes is influenced heavily by various guidelines; these, in turn, are informed by clinical trials, with much weight being placed on cardiovascular outcome trials. The applicability of the results from trials to clinical practice is dependent on the representativeness of study participants' demographic characteristics. Studies in both acute and chronic conditions, however, have suggested that non-white ethnic groups are often under-represented in clinical trials [4–7]. Here, we report on the proportion of participants of South Asian origin recruited to cardiovascular outcome trials of glucose lowering in Type 2

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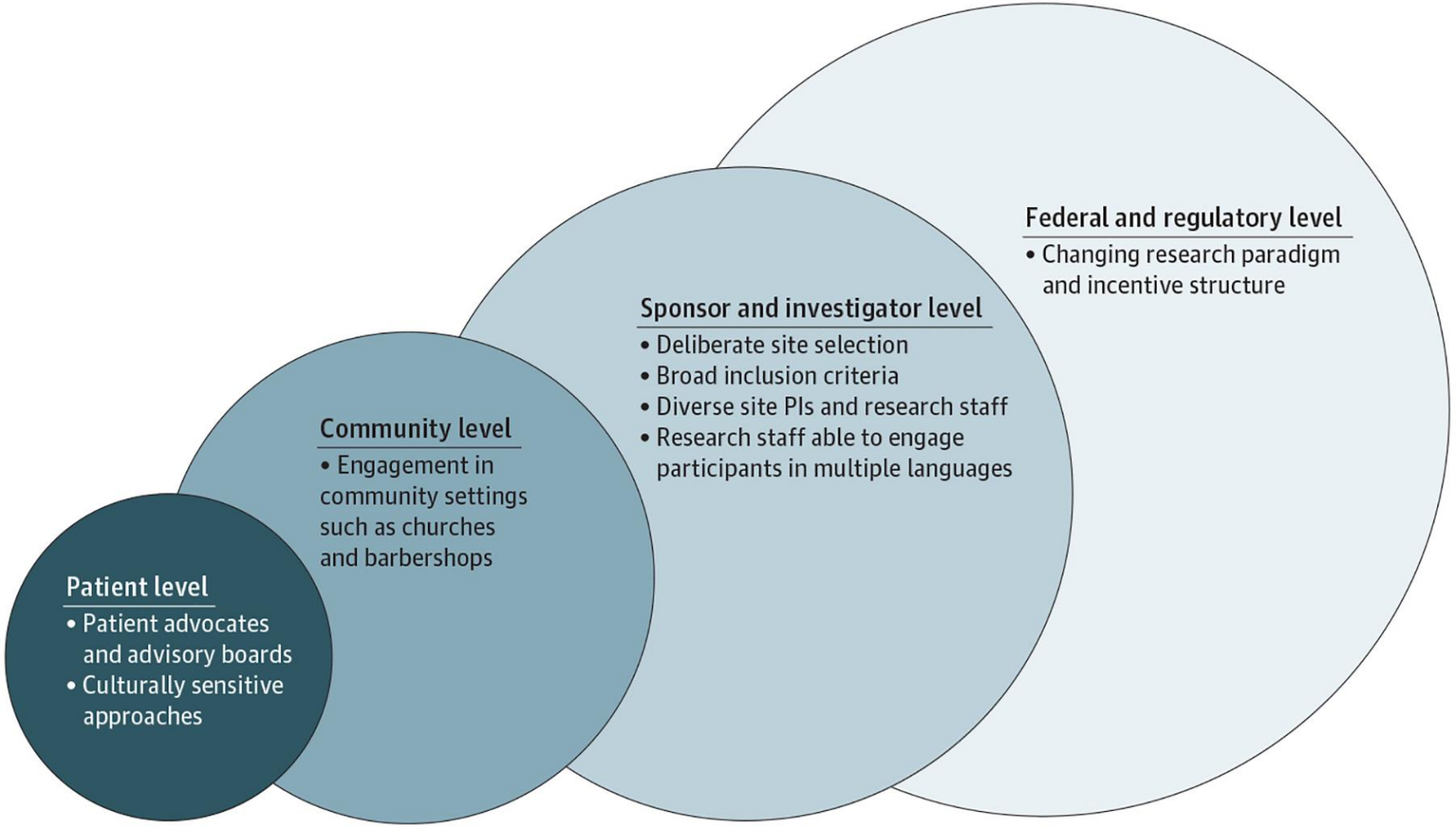
Khunti et al., (2016) Diabetic Medicine

A Roadmap for Increasing Enrollment of Underrepresented Populations in Heart Failure Clinical Trials



DeFillippis JAMA Cardiol 2022;7:540-548

Promoting inclusion in clinical trials

Bodicoat et al. Trials 2021;22:880

Capacity Building - Training programmes

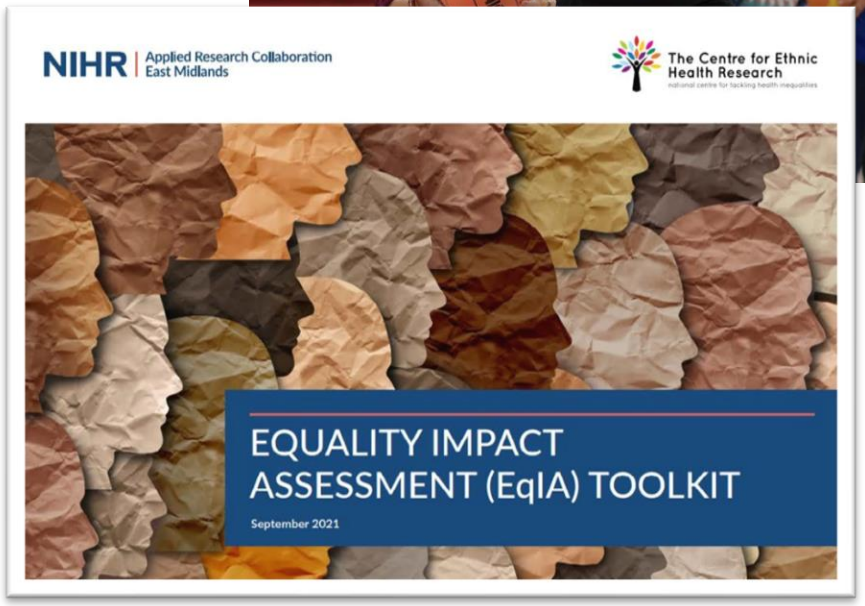
"I did learn new terminology and develop a greater understanding. I thought the self-awareness aspect was interesting"

"The course offered many eye-opening moments and clearly demonstrated the need for cultural competence being embedded in organisations, heath care and research"

https://ethnichealthresearch.org.uk/

Equality Impact Assessment Toolkit

- A process designed to improve equality analysis, practice and outcomes
- Toolkit has now been developed consisting of:
  - comprehensive training
  - a directory of useful resources
  - ongoing advice and guidance through webinars



https://ethnichealthresearch.org.uk/

Summary

- Much scope for improvement in ethnic minority recruitment
- Better monitoring of participation
  - Improve the recording and reporting of participation
  - Encourage proportionate representation across protected characteristics
- Further development and evaluation of strategies to increase participation
- Increased investment is needed
  - Highlighting the benefit of delivering more inclusive research
  - Capacity building for researchers/research teams

Thank you

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