KNOWLEDGE AND INNOVATION BULLETIN

'Exploring the Issue of Diversity in Clinical Research, Special Edition, 3rd August 2020'

UNIVERSITY OF OXFORD

A Note from our Director…

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Clinical trials provide the critical evidence base for evaluating the safety and efficacy of new treatments. Such effects may differ between population subgroups depending on factors such as sex, age, race, ethnicity, lifestyle and genetic background, but racial and ethnic minorities continue to be underrepresented in clinical trials. Although barriers to diversity in trials are well recognized, solutions for overcoming them have proved elusive. There are striking examples where sex differences, when not taken into consideration during drug development, have led to unnecessary adverse consequences. An example is Zolpidem which was approved by the FDA for insomnia in 1992 at a dosage of 10mg. It was not until after around 700 reports of impaired driving and road accidents were reported that the label was revised to 5mg in women and 5 or 10mg in men. As researchers, it is vital our research reflects and represents the populations we are serving.

In addition, there continues to be an under representation of ethnic minorities in academic medicine. A recent paper from UCSF (https://doi.org/10.1080/10401334.2019.1670665) summarises differential experiences within the learning environment, lack of social support, and implicit bias in evaluations as barriers to the academic success of underrepresented groups and suggests the need for institutional approaches and responsibility to foster inclusion in academic medicine. Our own Medical Sciences Division is creating an Equality, Diversity and Inclusion Steering Group, to provide oversight of divisional strategy in all areas of equality and diversity, but we must all play a part in ensuring that research participants and staff truly represent our population and its needs. This month's bulletin highlights some of the issues and achievements so far, but also what still needs to be addressed.

Dr Vanessa Raymont
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IMPACT OF CLINICAL RESEARCH ON BAME POPULATIONS

Image from: ttp://www.infrastructure-intelligence.com/article/dec-2019/diversity-—-less-buzzword-more-buzz

BY GAYATHRI DELANEROLLE

Ethnicity is a highly specific and complex construct that goes beyond one's genetic makeup, culture and patterns of behaviour. Thus, ethnicity, in some respects could be an unrefined tool to examine various components within a general population. This isn't specific to the modern society, as ethnicity is associated with various constructs that's expansive across centuries and has raised various scholarly arguments which still remains as an unresolved matter at hand that shows disparities across domains such as education and healthcare. UK has had a well-established ethnic distinction associated with healthcare compared to most other countries within Europe. Hence, the classification of ethnic minorities has been stipulated even within intervention guidelines for some diseases such as those published within NICE (2011). Whilst, BAME concerns have become *the fundamental topic of the moment* in some ways, the issues surrounding disparities and inequalities has been in existence but was often an after-thought to many. If we examine, the modern-day multicultural chimaeras, these haven't changed as much but there are perceived thoughts to a greater extent, and that challenging times for BAME populations are a matter of the past. The challenges faced by all ethnic minorities across the UK and in other European countries are closely interconnected and are driven forth by complex factors. Therefore, unsurprisingly, ethnic disparities remain to influence clinical treatment outcomes. For example, community engagement within certain parts of a country could vary depending on the social class and ethnic as well as behavioural constructs. This leads to dismembered ways of accessing healthcare organisations that is meant to provide equal access to clinical care; whether this be within the research or general clinical context. One could also argue the inclusion of BAME populations within research is vital to avoid unjustified disproportioned data that could de-value the interventions translated into clinical practices. However, evidence published by Mason et al (2003), Ranganathan et al (2006), Godden and colleagues (2010) and Bhopal et al (2014) stipulate, BAME populations continue to be discriminated within UK research contexts. Mason et al (2013) suggests that the evidence based reports show reduced numbers from the South-Asian community amongst 6 Randomised Controlled Clinical Trials associated with a number of conditions that are vital for the BAME community. Jolly and colleagues (2005) reported that south Asian participants were likely to be excluded when recruiting in cardiac rehabilitation studies as compared to other populations of patients. Ranganathan (2006) and colleagues evaluated a cardiovascular cohort that showed the study design itself prevented BAME representation. Smart and colleagues (2008) reported that studies in medical genetics prevented recruitment or analysis based upon ethnic backgrounds. Godden and colleagues (2010) stipulated that cancer research primarily represented Caucasian patients. A key commonality across these evaluations is that, the controls introduced with the study design itself, would result in underrepresentation of BAME participants which in itself could be considered as 'deprivation'.

Similarly, there are challenges around understanding population level differences across primary and secondary care organisations, thus, the datasets may not always cover the range and breadth of details needed to understand the BAME population specific needs to be more involved within research. Whilst clinical research covers a range of diseases that all BAME populations may have in some way or the other, researchers may not always understand the mechanisms by which these groups could be identified unless, they were accessing primarily, secondary healthcare organisations. Larger NHS organisations, primarily in London have better BAME representation within clinical research, as most participants feel welcomed and they are also made aware of the importance of taking part in research through various communication methods. However, there is a counter-argument to this, in that, it could be said that London has always been a multicultural city that promotes globalisation, therefore, a better concentration of studies that are relevant to participants of all ethnicities is a reason to observe a high number of ethnic minority participants in comparison to other parts of the UK. In comparison, mental healthcare needs of BAME groups could pose added complexities to clinical research. Prevalence of mental disorders vary within the BAME community. Memon and colleagues (2016) reported that there is a high prevalence of depression and anxiety amongst South-Asian women compared with Caucasian women (63.5% compared to 28.5% respectively). Furthermore, there was a higher rate of psychotic disorders amongst Afro-Caribbean men compared to Caucasian men 3.1% compared to 0.2% respectively). Despite these figures, the patterns of access to mental healthcare services within the UK show that ethnic minorities are less likely to use this avenue compared to their counterparts. Thornton and colleagues (2020) discussed the report from the Race Equality Foundation which suggested lack of evidence of direct racial discrimination in assessments, although there was ethnic bias and inequalities linked to mental illness. This report also suggested that high quality data is required to develop better evidence-based policies and interventions in order to support BAME populations. However, amongst BAME populations, there is a considerable stigmatisation of mental healthcare literacy, thus, it is vital to address this issue through knowledge-based awareness. The transfer of information to these patients should allow them to feel that their cultural norms and personal belief systems will remain intact during their treatment process. Thus, tailored, inclusive and culturally sensitive care-based approaches would facilitate improved understanding of mental healthcare conditions and thereby, provide better outcomes from future BAME populations. Furthermore, if small groups of BAME populations start to take part in research, their experiences could be documented as strategies to improve engagement amongst future generations of patients. However, within the UK, an open question still remains to see if BAME groups are under-represented across all disease areas. Regardless of the outcome, it remains to be seen, if researchers and organisations that are research active within the UK, provide equal access and support to improve inclusion of BAME groups into research studies moving forward. This would be a positive step to influence a global movement to support equality and diversity, to move beyond white papers we so often see today.

'...the patterns of access to mental healthcare services within the UK show that ethnic minorities are less likely to use this avenue compared to their counterparts.'

ARE WE PERPETUATING OUR WORST BIASES WITHIN AI?

BY NATASHA SANDLE

New and rapid advancements in data analytics tools and technologies have significantly altered many areas of healthcare, from efforts to streamline clinical research to patient treatment. In patient care, such advancements have shown benefits in improving patient outcomes and cost reduction. Often patients discuss their '*lived experience*' and the impact of this with clinicians and researchers alike, although, the ability to influence healthcare practices often takes significant time. Lived experience is an important facet to continuously improving healthcare through evidence-based approaches generated via high quality research. Thus, currently, patients do not always feel their expectations have been met for a variety of reasons. This could potentially improve with the assistance of AI.

AI has offered the promise of addressing complex issues that are currently reported clinically. As a result, AI has influenced clinical research significantly. Due to the complex clinical needs of the current global population, clinical trial protocols have become increasingly complex hence, AI also has the potential to enhance outcome measures and deliver clinical trials in a shorter time period compared to the last few decades through advanced analytics, '*big data'* collection and subsequent analysis, advanced management proficiencies in trial management and quality by design methods embedded into trial designs at the onset of the trial life-cycle. Therefore, AI also has had a positive impact in refining clinical trial regulations and promoting better practices.

AI systems have the potential to become clinical aids and further enhance the clinical decision-making process that could have a positive and meaningful impact on patient care and experience although, the risks should also be equally considered. Many studies have shown that ethnicity and race can systematically influence health, independent of factors such as age, gender, and socio-economic status. Instances of racial bias within AI has been seen in many industries and healthcare is no different. Reports show of algorithms which were used to identify high-risk patients for complex health needs, have been unintentionally but systemically discriminating against black people (Obermeyer et al., 2019) or that images used to train algorithms to detect melanoma being predominately of white skin making it difficult for it to then detect cancerous moles on darker skin (Adamson and Smith, 2018). As such as AI is used to advance processes, reduce variation in care, and remove human biases from decision-making there is equal risk of eroding trust, by perpetuating ethnic disparities. Equally, AI does have the potential to overcome some current systematic biases within clinical research, the ability to analyse huge amounts of data on whole populations offers promise to make clinical research data more representative with possibly more balanced demographics. However, the growing concern is that algorithms may reproduce racial and gender disparities seen above via the people building them or through the data used to train them. For example, amongst other things if it is unknown how ethnically representative much of the data being used to feed AI are and there is no requirement for such data to be representative, the AI algorithm will not be trained to make relevant distinctions amongst target groups and therefore will not produce accurate outputs. Such biased data can lead to delayed or inappropriate care ultimately harming patients. Consequently, it is imperative that data used to train AI is diverse to help mitigate risk to BAME populations.

It is clear that if research involving AI fails to include people of all racial backgrounds, such systems may have the potential to worsen health inequalities between white and ethnic minority communities. As a result, AI could be favoured to be used as a vital tool within healthcare and clinical research to advancement of stakeholders knowledge base and innovations that are fit for purpose to ensure, more generalisability of novel interventions with minimal unintentional racial biases and improved health equalities using ethically sourced and clinically validated technologies.

UNDER-REPRESENTATION OF BAME POPULATIONS IN DEMENTIA RESEARCH

BY TONY THAYANANDAN

In a brief report, The British Psychological Society (2018) declared that individuals from BAME communities are frequently invisible because their ethnicity is discounted. In 2013, an editorial in the British Journal of General Practice, written by Gill and colleagues argued that the research community needs to make a conscious effort to target the imbalance. Gill and colleagues are quoted to stipulate, "*this often-inadvertent exclusion has serious implications for medical science by limiting validity and generalisability, and for social justice by affecting the allocation of resources for services and research*."

Another example of this is the Race Against Dementia Campaign (2016) which concluded that many strides had been taken in recognising the impact of dementia in BAME communities but there was still an enormous lack of urgency regarding the scale and scope of this issue. Researchers understand that in order to secure funding, proposals for dementia support must show an evidence-based approach. However, if the BAME community is largely invisible within this evidenced based practice, it will perpetuate the unjust situation whereby, despite a seemingly increased risk of dementia, they are less likely to receive a timely diagnoses and appropriate support than their Caucasian equivalents.

Is exclusion unintentional?

Alzheimer's Research UK (2018) found that 51% of people from a Caucasian background consider getting involved in medical research for dementia while only 44% individuals from BAME backgrounds would make the same consideration. Roche et al (2018) argued that recruiting BME participants in health research is difficult because the barriers are not understood and appear to be multifactorial and multilevel, with many researchers not considering this whilst designing a research study. Many researchers have highlighted the need for more tailored approaches to effectively engage in BAME communities. Researchers understand they must build trusting relationships, which is highlighted by the work of Roche and colleagues. The research team demonstrated that if you approached participants in a culturally competent way, black African and Caribbean participants were not only more likely to participate in research, they were also more likely to seek advice about dementia from their GP. Of course, these targeted and tailored approaches of BAME groups are more resource demanding and require additional funding, an approach not yet emphasised by most funding bodies.

The research community should understand that people of different ethnicities may have different experiences of illness, treatment and care, including prevalence and incidence of certain conditions, impact of co-morbidities, access to services and access to participation in research. Findings that are effective for the majority white population might not always apply similarly to people from BAME communities.

'...if the BAME community is largely invisible within this evidenced based practice, it will perpetuate the unjust situation whereby, despite a seemingly increased risk of dementia, they are less likely to receive a timely diagnoses and appropriate support than their white equivalents.'

Is legislation needed?

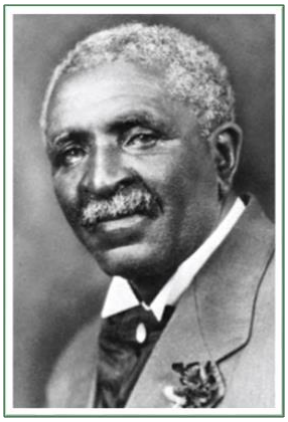
Since 1994, in America, in order to receive federal funding for clinical trials, researchers are required to analyse their findings for validity in terms of "sex/gender, race, and/or ethnicity" (National Institutes of Health 2017). The UK has no such mandate. Roche et al (2018), concluded the UK lags far behind American trials in terms of securing equal representation from the BAME community due to the lack of legislations and could explain the lack of ethnic diversity in research. It seems that despite long-standing evidence that individuals from BAME communities are under-represented in health research – and the inferences of this both for the validity of conclusions and for persistent disparities in health outcomes – some of the major research bodies have no sense of urgency about correcting this shortcoming. The NIHR does implore researchers to engage and involve communities who reflect the UK's diverse population, but this is not a requirement. Similarly, there is much discussion about inclusive cultures and bids to reduce inequalities, but the reality appears to be quite different based on the current evidence observed.

In order to fully incorporate all individuals into health research, and provide equality and diversity, the research community must understand that it will not be a simple tick box exercise. Researchers have to build trusting relationships with people from different communities, so they feel comfortable in agreeing to take part in research. Research teams, should preferably include people from diverse backgrounds, need to be culturally competent, respect their beliefs whilst remaining knowledgeable and open-minded, and, as with all work involving people with dementia and their families, adopt a person-centered tailored approach. Funding bodies should acknowledge that this will take time to cultivate, and project budgets need to reflect this although, equally, researchers should vocalize this within their grants.

A Race for Change in the NHS

By Natasha Sandle

Even in today's world, ethnic minority inequality amongst staff and patients is still prevalent in the NHS. There is a wide spectrum of research on racial inequalities in health and on the experience of healthcare staff and such differences reach every aspect of the NHS, causing disparities from ethnic minority maternal care to representation of BAME doctors in the institution's most prestigious and highly paid positions to name a few. Perhaps more alarmingly, there is also a distinct lack of suitable research on discrimination and health inequalities related to race. Additionally, a further emphasis on the absolute need for such action to both understand and eliminate these longstanding health inequalities, has been showcased as a result of the COVID-19 pandemic. The current pandemic has heightened the urgency for equality and diversity to go beyond a publication, especially with higher mortality and hospitalisation rates of BAME healthcare workers and patients reported (Pan et al., 2020).



George Washington Carver

First Black Researcher
(c. 1864-1943)

George Washington Carver was an African American agricultural scientist and inventor, who is best known for developing hundreds of products using peanuts, sweet potatoes and soybeans. Born enslaved, Carver went on to become a prominent scientific expert and one of the most famous African Americans of his time whilst also teaching at the Tuskegee Institute. He used his international fame to promote scientific causes in both professional and political circles for the remainder of his life. He wrote a newspaper column and toured the nation, speaking on the importance of agricultural innovation and the achievements at Tuskegee.

As such, NHS England and the NHS Confederation have called for decisive action by launching the NHS Race and Health Observatory as a new center to investigate the impact of race and ethnicity on people's health. The establishment of this observatory will hopefully lead the way for a deeper understanding of these existing issues, and encourage greater use of community participatory research, as well as find ways to identify and tackle the specific health challenges facing people from BAME backgrounds.

INCREASING DIVERSITY IN PATIENT AND PUBLIC INVOLVEMENT (PPI)? WE WOULDN'T START FROM HERE

BY SHONA FORSTER

Involving patients and the public in health research is generally accepted as a route to more equitable healthcare and better health outcomes. In the UK, we have an organisation within the NHS; INVOLVE which is dedicated to supporting PPI practice. INVOLVE is associated with a "*Patient and Public Participation Policy*" from NHS England where more than 200 people work to support the public involvement aspects in research within the National Institute for Health Research (NIHR) (Cooke,2018).

Yet there remains robust debate about the extent to which PPI contributors are sufficiently diverse to represent the beneficiaries of the research (Russell, Greenhalgh and Taylor, 2006). Data show that 13.4% of Caucasian British people have ever participated in medical research as opposed to 5.7% of those within the BAME populations (Smart and Harrison, 2016).This causes real problems in delivering healthcare interventions that are safe and effective for all at the point at which these are delivered within the routine clinical care domain. Lack of diversity in research only exacerbates the inequalities in the health system.

It could be argued that, to increase the involvement of BAME communities in PPI, we would not start from here. 'Here' is a society in which many ethnic minority populations do not engage with health services to the same extent, or in the same ways, as their White British neighbours. For example, Black African and Caribbean people are far less likely to use dementia services and receive drug treatments than the White British population despite developing dementia more often and at a younger age (Alzheimer's Society, 2019). This may be about the suitability of memory services for people from ethnic minorities for reasons such as language or familiarity. It may also be for cultural reasons such as attitudes to the condition. Whatever the reason, their under-representation in dementia healthcare is associated with being less likely to take part in dementia research and consequently, in PPI. Interestingly, there is evidence that BAME community participation in research is positively associated with poorer health, which may be an indicator of their greater engagement with health services (Crocker et al., 2018).

PPI contributors are, on the other hand, disproportionately more engaged in the health topics to which they contribute; they often have experience of the condition or

care pathway, either personally or via a family member. Indeed, researchers are often keen to identify contributors with a relevant '*lived experience'* to fulfil the role of equal partners in research, an approach which has shown better research outcomes. Consequently, it seems we need to put more effort into alternative ways of increasing the involvement of BAME communities in health research, rather than relying on the health system in which many communities are under-represented. We need to build on existing examples of successful outreach activity in BAME communities, such as the '*Women Celebrating Women*' event this year; it was co-created by the NIHR Oxford Health Biomedical Research Centre, Oxford Asian Cultural Centre and M&A Social Enterprise to share information and nurture debate about mental health and dementia amongst Asian women in a safe and supportive environment (NIHR Oxford Health BRC, n.d.). The event was a celebration of International Women's Day with music and food, as well as stalls and a workshop to explore mental health and dementia. Organisers were left with a deeper understanding of the cultural barriers to engage with healthcare messages; for example, 'how do you translate healthy dietary patterns like the Mediterranean diet into Asian cuisine?' (Cross-Bardell et al., 2015). It was also clear that collaborations like this need to continue to deliver benefits to the community over time to build the engagement and trust required for successful conversations about research and PPI. To increase the representation of BAME people in PPI we also need to change the culture within research organisations so that research design supports diversity in its recruitment. The NIHR issued new guidance in May this year requiring researchers working with them to document how they plan to recruit in order to achieve ethnic diversity, amongst other "Equality, Diversity and Inclusion" criteria (NIHR, 2020). Here at Oxford Health Biomedical Research Centre, Claire Murray, Patient and Public Involvement Manager, is already looking at our PPI response to that, including the development of an Equality Impact Assessment tool.

In conclusion, given we must start from '*here*', let us recognise that increasing BAME community involvement in PPI is a marathon, not a sprint. It demands investment in long-term programmes that engage people with health information and services that benefit the health of themselves, their families and their communities. In so doing, we gradually build trust and improved understanding between communities and health researchers that will lead to increased participation in PPI and research more widely.

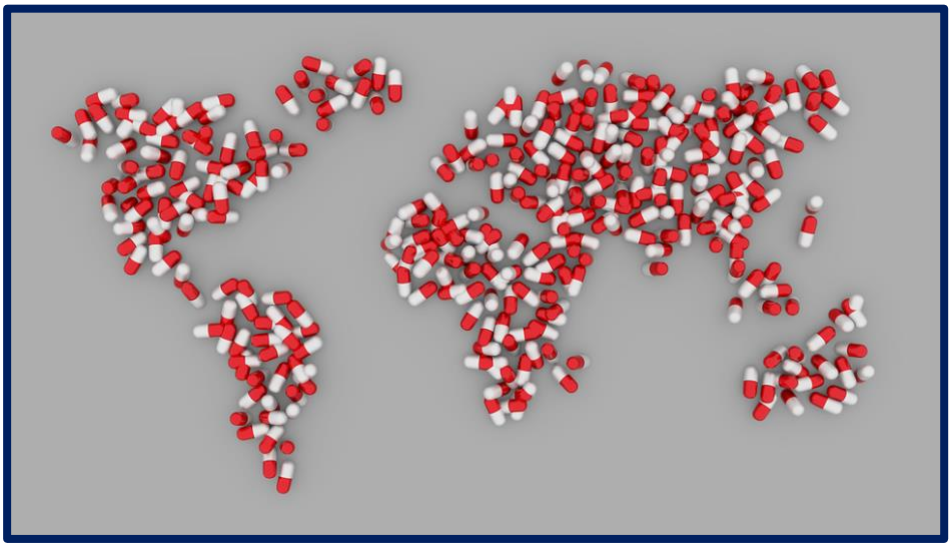
Tu Youyou

First mainland Chinese Nobel Prize winner in Scientific Category (1930-Present)

Tu Youyou is a Chinese scientist and phytochemist known for her isolation and study of the antimalarial substance qinghaosu, later known as artemisinin, one of the world's most-effective malaria-fighting drugs. She is the first mainland Chinese scientist to have received a Nobel Prize in a scientific category, and remarkably she achieved this without a doctorate, a medical degree, or training abroad. Tu has humbly described her team's findings, published in English in 1979, as "a gift from traditional Chinese medicine to the world."

DOES UNDERREPRESENTATION IN CLINICAL TRIALS COMPROMISE THE EFFECTIVENESS OF CANCER THERAPIES IN MINORITY GROUPS?

BY NYLA HAQUE



Clinical trials are an essential part of evaluating the safety, tolerability and efficacy of new cancer therapies. The licensing of cancer drugs are dependent on the outcome of phase I-III trials. Underrepresentation of BAME participants in each phase of a clinical trial could be a factor could introduce healthcare disparity associated with better clinical outcomes. If at each phase, the safety and efficacy data of a particular drug is gathered from a non-BAME population, there can be no certainty that the same drug will be as effective in the BAME population.

Thus, firstly, it is important to address the reasons for BAME under-representation in oncology clinical trials. Some may argue that in general, the reason for clinical trials predominately including participants from a Caucasian population would be that individuals from ethnic minorities are less likely to have a desire to take part. A survey of 156 participants who had been diagnosed with gynecologic malignancies found that there was no significant difference in the willingness to participate in a clinical trial prior to being approached based on the women's ethnicity (Patel et al., 2020). Interestingly, the survey uncovered that following women receiving further education material on clinical trials, although all women were more likely to participate in a clinical trial, there was still a significantly higher percentage of Caucasian women willing to participate in a clinical trial compared to their BAME counterparts. This study suggested that although participants initially had equal willingness to participate in a clinical trial, the approach used to inform patients about taking part in a clinical trial may need to be adapted based on the individual's ethnic background. This should be a key consideration in the recruitment strategy for clinical trials. Inclusion of individuals from BAME backgrounds into PPI groups would be a first

step in recognising the differences which exist between ethnic groups. In turn, these groups could help to formulate effective strategies to engage underrepresented ethnic groups into clinical trials.

Another factor could be due to the attitudes and behaviours of health care professionals that BAME populations may feel a level of discomfort to take part in research as cultural sensitivities and personal beliefs could be a strong factor associated within ethnic minority communities. Whilst there is limited data to support or deny that this is a contributing factor, a literature review exploring potential barriers to healthcare for ethnic minorities may be helpful to understand the disparity which exists. This study identified key themes which included biases and stereotyping, language and communication barriers, cultural misunderstandings and gatekeeping. These barriers to healthcare could in turn impact whether clinical trials are offered to patients from BAME groups.

It is widely accepted that subgroups of patients may respond differently to drug therapies due to multiple factors including gender and age. In a review of 357 ovarian, cervical and endometrial cancer studies including a total of 2483 participants, the breakdown of ethnic groups was only reported in 23% of the publications. This further highlights the need for clinical trials to not only diversify participant groups, but to also conduct sub-group analysis of the ethnic groups and report on differences that may exist. Often, epidemiological outcomes are not well considered within women's health based which in itself is problematic when designing healthcare services that are able to provide sustainable services that would benefit patients at large. Including epidemiological outcomes and sub-group analysis associated BAME groups would add value to the research being conducted as this step will ensure that the efficacy of the drug is generalisable and therefore, would be tolerated by patients that would reduce cost-pressure healthcare services often report.

Another key consideration is the stance taken by the regulatory bodies who govern the licensing of drugs. The Food and Drug Administration (FDA) recognises that differences exist in the response to drug therapies in ethnic subgroups and therefore promotes representatives of these groups within clinical trials. However, despite this recognition, often the diversity of a trial population does not reflect the real-world population the disease impacts. The FDA contributes to this issue by continuing to approve drugs which are not tested on a diverse population which purports the introduction of health inequalities not just for BAME groups in the USA but for other countries such as the UK who would purchase these interventions for their population. For example, despite the recommendations, 77% of gynecologic oncology phase 1 trials did not report on the ethnic and racial distribution of participants (Awad et al., 2020). For example, perhaps considerations should be made to include a mandated percentage of BAME participants to every clinical trial to ensure that as a minimum, interventions tested and deployed within healthcare could minimize the suitability and viability issues observed at the point at which research interventions become part of standard clinical care. This would encourage trialists to reconsider their study designs and recruitment strategies leading to equal representation within sample sizes that reflect population variability. This would further integrate any potential formal criteria

...considerations should be made to include a mandated percentage of BAME participants to every clinical trial...

set out by regulatory bodies that could emphasise the importance of ensuring drug therapies are effective amongst ethnic minority groups. Currently, the EMA and MHRA have not provided such policies.

In summary, with rapid increases in the cancer incidence and mortality rates more so in low-middle income countries (LMICs) and the WHO predicting that a 3rd of the global population may well have some form of cancer in the future, it is imperative to obtain cancer drugs that have been tested in a manner that is scientifically justified, ethically sourced and cost effective. With mass-migration being at its peak in recent years, it could be hypothesized, those in LMIC could be living within developed countries over the next few years which further changes the healthcare landscape as a result in change in diagnosis-treatment demands. This would undoubtedly change the clinical research requirements. As such, with any such predictions, and early 'diagnosis' to a problem being key to providing curative treatment, we, as trialists should consider making these changes in the near future to support the ever changing, complex needs of a diverse population. As not changing with the time would mean that we would continue to show a lack of inclusion of diverse populations in clinical trials leading to the licensing of drugs and/or medical devices that are effective to the Caucasian populations only. Furthermore, this is another factor that may explain differences in the response rates to cancer therapies that empirical evidence suggests and is reflective of the real-world population the disease impacts. In order to reduce health disparities in the response to cancer treatment, diversity in clinical trials must be prioritised.

REPRESENTATION OF BAME PARTICIPATION IN CLINICAL TRIALS

BY REMA RAMAKRISHNAN

Randomised controlled trial (RCT) is the gold standard in health research. Randomisation minimises differences between study groups leading to greater confidence in the robustness of the findings from RCTs due to high internal validity. However, most RCTs involve multiple inclusion and exclusion criteria thereby limiting the generalisability of the results. This may not be an issue if one is interested in studying exposure-disease relationships that are usually not restricted to certain subgroups or population. For example, Sir Richard Doll, the renowned epidemiologist conducted a study among British male doctors to find the link between cigarette smoking and lung cancer. One of the initial studies that was conducted to examine the relationship between physical activity and lower risk of coronary artery disease was the London Transport Workers study. These associations have been found in various populations worldwide. In fact, they have become such a part and parcel of our lives that no one would even question these findings anymore.

RCTs that are conducted to study the efficacy or effectiveness of drugs or interventions, may have differential responses to certain medications in subgroups such as BAME individuals. For example, patients from African ancestry have differential response to certain anti-hypertensive medications such as angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs);

consequently, these medications are not the first-line treatment for hypertension in this population. This problem is all the more important if one is a woman from the BAME population. Compared to men, women (especially pregnant women) are underrepresented in clinical trials even though the mechanism of action of drugs can differ between sexes.

One way to diversify representation of BAME individuals within the trial design is to oversample these participants and then use sampling weights in analyses to correct for biases that can result from oversampling. Well-known national surveys in the US such as the NHANES have successfully utilised oversampling as a method to have adequate statistical power to answer a multitude of research questions specific to the Black population. Another method to increase representativeness of BAME patients is by establishing collaborations that can lead the formation of a consortium of multiple RCTs globally so that there is adequate statistical power to detect an effect among certain ethnic/racial/cultural groups. This is a much better option compared to conducting subgroup analysis of a single trial that are usually underpowered to detect an effect. Take the example of the Blood Pressure Lowering Treatment Trialists Collaboration commonly known as the BPLLTC which was established in 1995 as a collaboration of major ongoing clinical trials of blood pressure-lowering medications that can answer questions relating to anti-hypertensive medications in certain subgroups with adequate statistical power.

An often forgotten and under-used method in RCTs is qualitative methodology. It has been found that inadequate representativeness of BAME participants can be attributed to stigma of participation in trials, mistrust in research, and lack awareness about the importance of participation in trials. Qualitative research techniques such as focus groups, in-depth and semi-structured interviews can be used in the pilot phase of a study to examine barriers and challenges to BAME participation in clinical trials. This information may be then used to modify recruitment process to increase participant representativeness in clinical trials.

We should not be complacent about underrepresentation of BAME participation in trials because lack of diversity in RCTs is a moral, scientific, and medical issue.

RESOURCES FOR FURTHER READING:

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