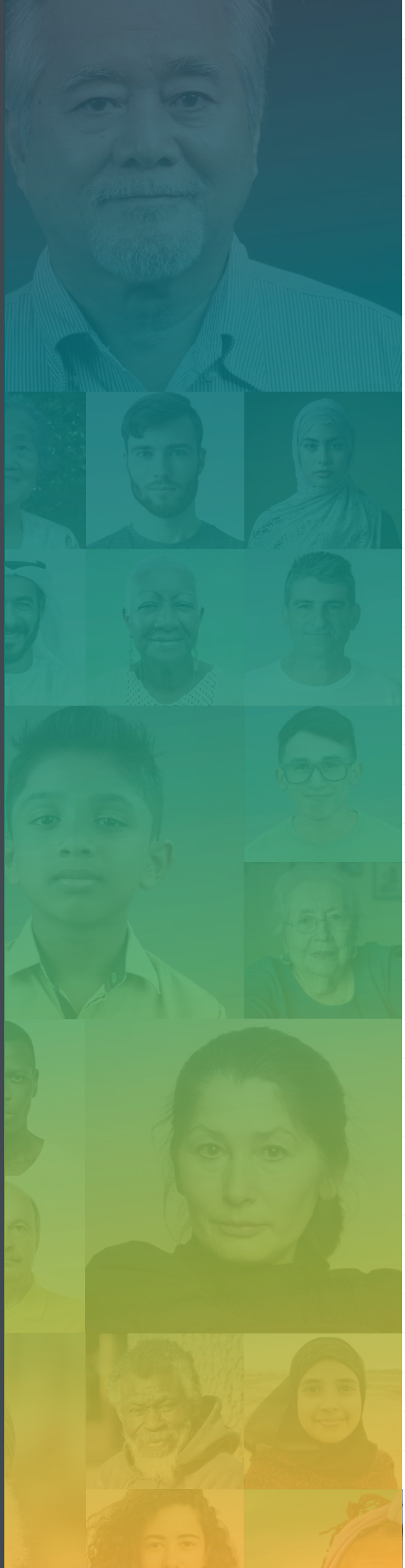
LITERATURE REVIEW – MAY 2020



DEMAND DIVERSITY

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INTRODUCTION

Firstly, let's consider what is meant by diversity: understanding that every individual is unique, and recognising individual differences and the positive value this brings. These differences include demographics such as gender, ethnicity, age, nationality, sexual orientation and socioeconomic background. It's important to note that increasingly, other characteristics are being considered beyond these traditional demographics; diversity now also encompasses personality types, educational background and knowledge bases.

Diversity is now being discussed more and more in all industries. It is a topic that has gained increased attention in the media through the film and TV industry, sparked debate and encouraged campaigns for change. However, although people have been talking about the issue for some time, it is not consistently being addressed, and many people are accused of simply paying lip service to the issue.

All organisations have a responsibility to actively encourage diversity and should have strategies and processes in place that allow for this. Diversity also directly links with inclusion and equality. These state that that people shouldn't be treated differently or discriminated against because of their characteristics, that everyone should be involved and empowered, and that the inherent worth and dignity of all people must be recognised. With this in mind, diversity ought not to simply be a box-ticking exercise and a way of a company portraying itself positively to the outside world. Diversity needs to ensure representation, and the workforce and leadership teams of a company should reflect the location in which it is based and the people it serves.

In the pharmaceutical industry, diversity needs to exist both inside and out. For pharmaceutical companies to be representative of the people they are providing for and targeting, their workforces and cultures need to be diverse. Once diversity is present inside the organisation, it should be easier to put strategies in place to ensure that clinical trials and healthcare reach diverse populations. This in turn can lead to enhanced commercial success and a healthier population. Because of the length of time that the pharmaceutical industry has been operating without diversity, proactivity is an absolute requirement to bring about change.

Here, we discuss current diversity issues within the pharmaceutical industry, and how overcoming these internally and externally can lead to maximised patient engagement, and ultimately, greater success.

THE CURRENT POSITION OF THE PHARMACEUTICAL INDUSTRY

Across all industries, people often recruit employees who resemble their own profile[1,2]. Where the people recruiting are not diverse, this can lead to a lack of diversity in the workforce. The consequences of this can be problematic both internally and externally. A lack of diversity can lead to company cultures that are toxic and non-inclusive, and result in development of products and services that do not meet the need of consumers.

Women are generally well represented at entry level in the pharmaceutical sector, but there is a growing gender gap as roles become more senior. There is also a significant gender pay gap[3-7]. Further to this, since women occupy fewer senior leadership positions, the difference between women's and men's bonuses can range from 20% to almost 50%[8]. Although gender pay gap reporting is mandatory and now commonly discussed in the United Kingdom (UK), this is not the case for other factors that represent diversity. A recent review of the UK Corporate Governance Code by the Financial Reporting Council showed there is still limited reporting on diversity and minimal discussion about assessing or monitoring diversity throughout large UK firms[9]. In most companies, action to tackle diversity was purely about gender. While reporting ethnic diversity and pay gaps has been under consultation by the UK government, it has not yet been made mandatory. Companies are beginning to report data voluntarily, and this could not only bring more issues to light, but also be a catalyst for proactivity and positive change. Even with those companies that rank well versus their competitors, there is likely still room for improvement.

Throughout healthcare, inequalities and a lack of diversity mean that people with certain characteristics are underrepresented, and their voices remain unheard. Further, there is a major need to increase diversity in clinical research, as studies fail to recruit sufficient numbers of people from certain ethnic groups, for example. This is an issue where certain diseases are more common in specific ethnic groups, or where differences in metabolism of drugs mean changes in effectiveness or side effects.

OVERALL VIEWS TOWARDS THE PHARMACEUTICAL INDUSTRY

There are many strong opinions – both positive and negative – voiced online towards the pharmaceutical industry[10]. Negativity is often associated with mistrust and a lack of awareness around what the pharmaceutical industry does. Conspiracy theories are also a common point of discussion. For example, while there is no evidence to support this theory, some people believe that a cure for cancer is deliberately not being found or revealed[11,12]. Some members of the public also believe that pharmaceutical companies are deliberately causing harm through medicines and vaccines[10]. Further supporting this apparent mistrust, a 2019 poll conducted in the United States (US) found that the pharmaceutical industry is the most poorly regarded industry, out of the 25 industries included in the survey[13].

The sense of mistrust against 'the system' can be very deep, but is only one of many barriers that can influence a patient's overall perception towards the pharmaceutical industry, including those relating to their general healthcare and clinical research. There are barriers to healthcare and clinical research that exist across all demographics[14-17]. These include fear about the side effects of treatments, costs (depending on their country and circumstances), location or lack of nearby services, low trust in healthcare providers, denial or fear of diagnosis, and previous negative experiences. In clinical trials specifically, common barriers to being involved are practical issues such as time and travel, work commitments, care commitments such as childcare, benefit/risk ratio, concerns about receiving the placebo and not the treatment, lack of awareness that trials exist, and limited understanding of how trials work.

BARRIERS TO HEALTHCARE AND CLINICAL RESEARCH

Barriers to diversity in healthcare and/or clinical research may stem from the individual's values and perspectives, or those of healthcare professionals and researchers. For the purpose of this review, a summary of barriers is presented, relating to ethnicity and culture, age, gender, socioeconomic status and health literacy.

ETHNICITY AND CULTURE

Patients' expectations, preferences, attitudes and behaviours towards healthcare and clinical research are shaped by their cultural and religious values, beliefs, practices and traditions[18,19]. Religious values can create specific barriers to healthcare and clinical trials, including not consuming certain ingredients (such as gelatine), the inability to receive blood transfusions or products, not being able to take oral medication during fasting, and the belief that God will determine health outcomes rather than medicine[20,21]. Gender-based caregiving also interferes with religious ideologies[20], for example some men may refuse to be treated by women, and some women may be barred from seeing male caregivers. Culture can also play a role in the healthcare people wish to receive. People from certain areas or cultures may be more likely to view modern medicine as secondary to traditional remedies, which reduces the relevance and value of medical advancement. According to studies, these include people of South Asian, Indian, Arabic, black Caribbean, black African and Chinese origin, and indigenous Australians[21-23].

Among people with religious and cultural beliefs, those with more traditional values are likely to be the hardest to engage with[21]. This may be because their perspectives are rooted more deeply in faith and tradition than in modern medicine. The failure of healthcare providers to recognise and understand the importance of these beliefs and values can lead to damaged relationships with patients and caregivers. Many patients do indeed feel that their religious and spiritual beliefs are dismissed as well as their beliefs concerning alternative medicine[24].

Mistrust of healthcare and research is more pronounced in certain ethnic groups than white people, particularly black African and Caribbean communities[21]. The way certain ethnic groups have been treated throughout history has left a lasting effect on people's perceptions of clinical research throughout the world, and these views have repeatedly been demonstrated in the UK and the US[25-27]. Exploitation, degradation and dehumanization have emerged as common themes in certain ethnic groups versus white people[21]; this is highlighted by people's suspicions about ingredients and fear of attempts to kill or stunt the development of a group[21]. Some research suggests that ethnic minority patients feel they are labelled according to their differences and treated according to stereotypes[24,28].

One study exploring views of African American and white adults regarding influenza vaccinations found that trust in institutions emerged as a significant theme; white people trusted federal institutions but questioned their competency, whereas African Americans were less trusting of the government and more likely to doubt its motives[29]. Interestingly, most respondents (white and African American, young and old, vaccinated and not), were aligned in distrusting pharmaceutical company motives, suspecting that the companies are motivated by profit rather than people's wellbeing[29]. Another study looked at interpersonal distrust in clinical research (distrust based on personal experiences of individuals in healthcare or clinical research) and societal distrust (global negative outlook based on society's perception of healthcare and clinical research). African American people were more likely to have high societal distrust than white people.

There were no differences of interpersonal distrust between the two groups. However, African Americans were significantly more likely than whites to think that they could potentially be used as guinea pigs without giving their permission, and to think that healthcare providers prescribe treatments as a way of experimenting on people without permission[30]. This was replicated in a study among African American and white parents surrounding their children participating in research. This study demonstrated that the extent of parental distrust toward medical research was significantly greater among African American versus white parents[31].

AGE

Evidence suggests that in clinical research, healthcare professionals may (inadvertently) put up barriers to enrolment of older people in clinical trials, such as perception about their treatment tolerance and drug metabolism, a lack of evidence for efficacy, and age bias[32,33]. Older people may also put up barriers of their own to joining clinical trials, such as lack of autonomy, concerns about quality of life and toxicities, accessibility to clinical trials, and logistical and financial difficulties[32]. Furthermore, older patients are more likely to have pre-existing comorbidities, which could conflict with inclusion and exclusion criteria[32]. Such comorbidities can also result in increased disease burden and symptoms that would make people less motivated to join a study. Factors such as mobility and/or ability to travel are more relevant in elderly populations, and could prevent or discourage access to healthcare or participation in clinical trials[34]. Elderly people are also more likely to be socially isolated, which could mean that they are less likely to find out about clinical trials that are relevant to them.

Younger age can also be a barrier to healthcare and clinical research. A study found that young people, including Generation Z (born between mid-1990s and early 2000s; aged between 16 and 23 at the time of the study) are less trusting of the pharmaceutical industry compared with baby boomers (born between mid-1940s and mid-1960s; aged between 54 and 72 at the time of the study)[35].

GENDER

Gender inequality in healthcare still exists today across the globe. In the UK, there have been dramatic increases in life expectancy, but these are stalling, and in some cases life expectancy is falling for women in some areas of England[36]. Although life expectancies in the US and the UK are greater for women than men, data suggest that women live more years of poor health compared with men[37,38].

While some studies have proportionately represented both males and females[39], most evidence suggests that since medical research began, women have been underrepresented[40]. Because of physiological differences between men and women, for example hormonal status, the prevalence, diagnosis, severity, and outcomes of conditions may also differ[41]. For example, women and men may present with distinct symptoms for the same condition. Additionally, pharmacokinetic and pharmacodynamic differences between men and women can affect treatment outcomes. Whether or not such differences are clinically relevant must be investigated to determine optimal dosing and ensure safety in women as well as men[42].

Transgender individuals should also not be overlooked within healthcare and clinical trials. Evidence shows that transgender individuals experience inequality that often stems from stigma and limited understanding, leading to significant barriers in terms of accessing healthcare services[43]. Other issues for transgender people seeking healthcare include financial barriers, discrimination, lack of cultural competence by providers, health systems barriers, and socioeconomic barriers[44].

SOCIOECONOMIC STATUS

In the UK, there are clear inequalities in both length of life and in length of healthy life, which closely relate to socioeconomic status and neighbourhood deprivation[36]. Research has found individuals with a lower socioeconomic status are more likely to have poorer health outcomes and lower life expectancy[45], and that those with lower wealth suffer from greater disease burden than those with greater wealth[46]. In 2014 to 2016, the gap in life expectancy between the most and least deprived areas of England was

9.3 years for males and 7.3 years for females[37]. The elevated mortality rates observed in more deprived areas are mostly due to heart disease, lung cancer, and chronic lower respiratory diseases. Smoking and obesity are the main risk factors for these diseases, and although smoking prevalence in England has declined, people who live in more deprived areas are more likely to smoke than people in areas that are wealthier[37]. Additionally, people living in the most deprived areas spend nearly a third of their lives in poor health, compared with only about a sixth for those in the least deprived areas[37].

Much research suggests that having a lower socioeconomic status can be a barrier to taking part in clinical trials, and that people from more deprived areas are underrepresented in clinical research[47-49]. One study also found that most subjects believed their socioeconomic status influenced the treatment they receive, access to care, and patient-provider interaction[50]. This could affect their trust in healthcare and healthcare professionals, erecting another barrier to participating in clinical trials.

GEOGRAPHICAL LOCATION

An individual's location in relation to a healthcare setting can be a barrier to healthcare and clinical trials, especially if participants are expected to travel to a test site on a regular basis. People living in rural areas, particularly, may find it difficult to access sites if they have to rely on public transport, and people who work or study full time could find that it's too far to travel with limited time available.

The UK has a 'north/south' divide, with areas in the south generally being wealthier. While many rural areas are more affluent, there are distinct variations between levels of wealth within the countryside. Even within the wealthiest areas, both rural and urban, there can be extreme poverty and associated ill health and inequalities[51]. Older age can increase the impact of living in rural or coastal areas on income and health inequalities[52].

Previous research has found that participation in clinical trials is low among rural communities, and investigators report difficulty in recruiting rural individuals. In one study that explored barriers among underrepresented people living in rural and urban locations, universal barriers included fear, side effects, limited understanding, limited time, and mistrust[54]. Notably, individuals living in rural areas were more conscious of the time commitment involved[53].In another study, both providers and patients said transportation was a barrier to participation in clinical trials, and this was particularly true for low-income urban patients and for those living in rural areas[54].

HEALTH LITERACY

We are now in a digital era where technology is continuously advancing. Despite this, the pharmaceutical industry mostly still engages using written word and printed materials, spanning information leaflets for vaccines or public health programmes, drug labels, medical device instructions, and clinical trial information. This poses an issue when those producing the materials do not consider or consult with the intended reader, given that health literacy (the skills, knowledge, understanding and confidence to understand and access healthcare) levels are universally low. For example, evidence demonstrates that up to 61% of the working age population in England finds it difficult to understand health and wellbeing information[55]. Because health literacy affects how people access healthcare, low levels of health literacy can have a huge impact on how likely people are to suffer from preventable conditions such as cardiovascular disease, what the outcomes are of conditions such as diabetes[56,57]. Further, literature consistently demonstrates the association between lower levels of health literacy and obesity, unhealthy dietary choices, and less exercise[58].

Limited health literacy is strongly associated with lower participation rates in clinical research[59]. The use of complex language in study materials (e.g. informed consent forms) can create a barrier to participation, particularly for people with lower reading levels, cognitive impairment or English as a second language. If people don't fully understand a study, including the benefits and risks, they will be unable to make an informed decision about whether to take part. Bias could also exist among healthcare professionals and study recruiters, who may falsely assume that people will not understand the study and not attempt to explain it to them.

THE RATIONALE FOR CHANGE, DIVERSITY AND INCLUSION

Inequalities in healthcare and limited diversity in clinical research both create potential barriers to clinical trial participation. This reduces the diversity in trial populations, making the results less relevant to the population who will eventually be taking the drugs. The first step in overcoming these issues is awareness. The next step is to factor in the perspectives and challenges of different stakeholders when considering how to improve diversity within healthcare and clinical research.

CORPORATE RESPONSIBILITY

All companies, particularly large, global organisations, have a corporate responsibility to ensure diversity. This spans the employees at all levels including leadership teams, who should ideally represent and reflect the people the organisation serves. This is particularly relevant for pharmaceutical companies, which affect the global population and ultimately have a huge impact on people's healthcare and lives. Diversity also comes under the umbrella of social justice, which organisations should also be committed to. It is important that leaders in the pharmaceutical industry proactively work to overcome barriers that people face because of factors such as gender, age and ethnicity.

Some companies are already moving away from the traditional approach of simply measuring demographics toward more sophisticated metrics, particularly those that determine the inclusiveness of the corporate culture. To truly be diverse and inclusive, all organisations will have to follow this in their own long-term strategies. Those creating diversity strategies need to be aware that while diversity itself is important, so is a culture that encourages diversity. Including 'diverse' people is the first step, but strategies must embrace inclusive leadership styles, perspectives and ways of sharing ideas.

MAXIMISED UNDERSTANDING OF CONSUMERS & PATIENTS

In the pharmaceutical industry, diversity plays an increasingly crucial role in preparing to meet the needs of a diverse consumer and patient population. Indeed, it seems obvious that a diverse workplace would lead to a better understanding of the positioning of a diverse consumer base. If pharmaceutical companies maximise how much they understand and connect with a diverse audience, the more likely they are to achieve success. But it is important to tackle this in the right way. A diversity and inclusion strategy should avoid a one-size-fits-all approach to cultural attitudes, and employees should be educated to understand and respect differences across all factors in diversity.

INCREASED TRUST AMONG THE GENERAL PUBLIC

Even if pharmaceutical companies have a greater understanding of consumers' and patients' wants and needs, without trust, the industry will achieve limited success. It is clear that there is a lack of

trust in the pharmaceutical industry among people with a wide range of characteristics, but this is more pronounced in certain groups of people and clearly relates to ethnicity and culture. Since the sense of mistrust can be extremely deep, with many people holding strong views, a huge amount of work needs to be done to win the trust of the general public. Damage needs to be repaired from previous scandals that have led to pharmaceutical companies having a negative reputation.
A well-considered, sensitive approach is needed to try and overcome mistrust that stems from the historical treatment of specific ethnic groups. Those working within the pharmaceutical industry need to be made aware of the reasons behind mistrust in order to try and rebuild relationships, which will require an education process. Building trust will likely make engaging with the public and patients a much easier and successful process.

IMPROVED REPRESENTATION IN CLINICAL RESEARCH

Clinical study populations are not currently representative of intended disease populations, as people of certain ethnicities, females and the elderly are typically underrepresented. At the same time, the prevalence and ways people respond to treatments can directly correspond to gender, age and ethnicity.

Currently, there is not a full understanding of what treatments work best for these individuals, and even after medical research is conducted, the optimal dosing and safety cannot be guaranteed. Improving the diversity of clinical trial populations will make the research more robust, safe and valid for those concerned.

Since the lack of diversity in clinical trial populations is clearly evident, there is increasing pressure from global regulatory bodies on drug manufacturers to provide evidence of drug safety and effectiveness in diverse populations. In July 2019, the FDA published draft guidance on enhancing the diversity of clinical trial populations[60]. The draft guidance includes considerations such as broadening eligibility criteria and adopting recruitment strategies that enhance diversity and inclusion.

Broaden eligibility criteria to include:
The elderly
Children
Over- and underweight people
Individuals with:
– organ dysfunction
– malignancies
– certain infections such as HIV

Create recruitment strategies that enhance diversity:
Reduce the burden of trial participation
– Fewer visits to site
– Study visits outside school and work time
– Virtual site visits
– Cover costs
Improve enrolment/retention practice
– Work with communities
– Recruit from more diversion regions
– Increase public outreach and education
– Make recruitment events accessible
– Facilitate the transfer of records between sites

Source: FDA[60]

In time, regulatory bodies may place greater emphasis on diversity, and it could become an essential requirement for product approval and market access.

A POSITIVE FINANCIAL IMPACT

Diversity can bring a competitive advantage to business. This is partly due to being able to gather a range of perspectives and backgrounds. For those offering solutions and services, a diverse workforce is more representative of the target population, and thus employees are more likely to have a balanced understanding of consumers' viewpoints, wants and needs. Supporting this theory, evidence shows that the companies with more diverse senior leadership groups are a third more likely to outperform their competitors[61]. Other research suggests that increasing the diversity of leadership teams leads to more and better innovation and improved financial performance[62], and that companies in the top quartile for ethnic and gender diversity are 35% and 15% more likely to have financial returns above their respective national industry medians, respectively[63]. Interestingly, there is a general distinction in how different generations view diversity and the impact it can have. Research shows that when defining diversity, millennials think beyond demographic differences and cite the blending of unique perspectives within a team. In addition, millennial definitions of diversity encompass differences in background, experiences and style, and believe that a team that is diverse in this sense is more likely to be innovative[64]. Diversity can be a key element of growth by providing access to a variety of different voices, experiences, opinions. Overall, it is evident that diversity has a positive effect on corporate success and mixed teams are more successful because they consider different experiences and perspectives.

In terms of clinical research, successful patient engagement encompasses engaging with a diverse group of people – this being the entire intended treatment population, not just those with certain characteristics. Several studies have demonstrated that effective patient engagement can reduce or remove the need for protocol amendments, and lead to increased enrolment, adherence and retention[65-68]. In turn, this can result in substantial cost savings, thus making patient engagement a method of improving the cost-effectiveness of research and development[65-68]. Alongside this, research suggests that patient engagement improves study sponsors' reputations and results in greater regulatory success[65,69]. In order to maximise these predicted benefits, diversity must be considered within a patient engagement strategy.

CONCLUSIONS AND FUTURE RECOMMENDATIONS

This review has just touched on some of the evidence surrounding diversity in the pharmaceutical industry, healthcare and clinical research, and still suggests that diversity needs to improve across the board. An inside out strategy, guided by the inner strengths, capabilities and diversity of the organisation, should be considered.

This strategy could firstly help improve and educate on diversity within pharmaceutical organisations, and secondly, increase diversity within healthcare and clinical trials. Patient engagement needs to consider diversity so that the pharmaceutical industry is truly engaging with everyone who is relevant. The benefits of this will be broad and deep across commercial aspects of the pharmaceutical industry and in terms of improving representation. Organisations may need support from external partners to drive diversity initiatives forward, and collaborations and sharing best practices will be vital. As we can expect to see a formal shift in the regulation of diversity within clinical research, it is imperative that pharmaceutical companies begin their quests to improve diversity as early as possible, to ensure they are prepared.

REFERENCES

1. Rivera LA. Hiring as Cultural Matching: The Case of Elite Professional Service Firms. *American Sociological Review*. 2012;77(6):999-1022.
2. Goldberg CB. Relational Demography and Similarity-Attraction in Interview Assessments and Subsequent Offer Decisions: Are we Missing Something? *Group & Organization Management*. 2005;30(6):597-624.
3. Burchell S. Tackling gender diversity in pharma leadership. 2019. https://pharmafield.co.uk/in_depth/tackling-gender-diversity-in-pharma-leadership/ Accessed February 2020.
4. Johnson & Johnson. UK Gender Pay Gap Report 2018.
5. Roche's Gender Pay Gap Statement 2018.
6. AstraZeneca Gender Pay Gap Report 2018.
7. Pfizer UK Gender Pay Gap Report 2018.
8. Lee A. Diversity and inclusion in the pharma industry. 2018. http://www.pmlive.com/pharma_intelligence/Diversity_and_inclusion_in_the_pharma_industry_1241040 Accessed February 2020.
9. Parker J. Ethnic Diversity Enriching Business Leadership. An update report from The Parker Review. 2020.
10. COUCH Health. Internal social listening research. 2020.
11. Gansler T, Henley SJ, Stein K, Nehl EJ, Smigal C, Slaughter E. Sociodemographic determinants of cancer treatment health literacy. *Cancer*. 2005;104(3):653-660.
12. Bruder M, Haffke P, Neave N, Nouripanah N, Imhoff R. Measuring individual differences in generic beliefs in conspiracy theories across cultures: conspiracy mentality questionnaire. *Frontiers in psychology*. 2013;4:225-225.
13. McCarthy J. Big Pharma Sinks to the Bottom of U.S. Industry Rankings. Gallup. 2019.
14. Anderson A, Borfitz D, Getz K. Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials. *JAMA Network Open*. 2018;1(6):e182969-e182969.
15. Moorcraft SY, Marriott C, Peckitt C, et al. Patients' willingness to participate in clinical trials and their views on aspects of cancer research: results of a prospective patient survey. *Trials*. 2016;17:17-17.
16. Taber JM, Leyva B, Persoskie A. Why do people avoid medical care? A qualitative study using national data. *Journal of general internal medicine*. 2015;30(3):290-297.
17. Pomey M-P, Ghadiri DP, Karazivan P, Fernandez N, Clavel N. Patients as partners: a qualitative study of patients' engagement in their health care. *PloS one*. 2015;10(4):e0122499-e0122499.
18. Degrie L, Gastmans C, Mahieu L, Dierckx de Casterlé B, Denier Y. How do ethnic minority patients experience the intercultural care encounter in hospitals? A systematic review of qualitative research. *BMC Medical Ethics*. 2017;18(1):2.
19. Hossain MZA-Ohoo, Khan HTAA-Ohoo. Barriers to access and ways to improve dementia services for a minority ethnic group in England. LID - 10.1111/jep.13361 [doi]. (1365-2753 (Electronic)).
20. Swihart DL, Martin RL. Cultural Religious Competence In Clinical Practice. [Updated 2019 May 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493216/.
21. Tipi Research and COUCH Health. Internal research. 2019.
22. Kumar K, Greenfield S, Raza K, Gill P, Stack R. Understanding adherence-related beliefs about medicine amongst patients of South Asian origin with diabetes and cardiovascular disease patients: a qualitative synthesis. *BMC endocrine disorders*. 2016;16(1):24-24.
23. Gall A, Anderson K, Adams J, Matthews V, Garvey G. An exploration of healthcare providers' experiences and perspectives of Traditional and complementary medicine usage and disclosure by Indigenous cancer patients. (1472-6882 (Electronic)).
24. Rocque R, Leanza Y. A Systematic Review of Patients' Experiences in Communicating with Primary Care Physicians: Intercultural Encounters and a Balance between Vulnerability and Integrity. *PloS one*. 2015;10(10):e0139577-e0139577.
25. Scharff DP, Mathews KJ, Jackson P, Hoffsuemmer J, Martin E, Edwards D. More than Tuskegee: understanding mistrust about research participation. *Journal of health care for the poor and underserved*. 2010;21(3):879-897.
26. Armstrong K, Ravenell KL, McMurphy S, Putt M. Racial/ethnic differences in physician distrust in the United States. *American journal of public health*. 2007;97(7):1283-1289.
27. Pacheco CM, Daley SM, Brown T, Filippi M, Greiner KA, Daley CM. Moving forward: breaking the cycle of mistrust between American Indians and researchers. *American journal of public health*. 2013;103(12):2152-2159.
28. Abdou CM, Fingerhut AW, Jackson JS, Wheaton F. Healthcare Stereotype Threat in Older Adults in the Health and Retirement Study. *American Journal of Preventive Medicine*. 2016;50(2):191-198.
29. Jamison AM, Quinn SC, Freimuth VS. "You don't trust a government vaccine": Narratives of institutional trust and influenza vaccination among African American and white adults. *Social Science & Medicine*. 2019;221:87-94.
30. Durant RW, Legedza AT, Marcantonio ER, Freeman MB, Landon BE. Different types of distrust in clinical research among whites and African Americans. *Journal of the National Medical Association*. 2011;103(2):123-130.
31. Rajakumar K, Thomas SB, Musa D, Almario D, Garza MA. Racial differences in parents' distrust of medicine and research. *Archives of pediatrics & adolescent medicine*. 2009;163(2):108-114.
32. Denson AC, Mahipal A. Participation of the elderly population in clinical trials: barriers and solutions. *Cancer control : journal of the Moffitt Cancer Center*. 2014;21(3):209-214.
33. Stahl SM, Vasquez L. Approaches to improving recruitment and retention of minority elders participating in research: examples from selected research groups including the National Institute on Aging's Resource Centers for Minority Aging Research. *Journal of aging and health*. 2004;16(5 Suppl):9S-17S.
34. Provencher V, Mortenson WB, Tanguay-Garneau L, Bélanger K, Dagenais M. Challenges and strategies pertaining to recruitment and retention of frail elderly in research studies: a systematic review. Archives of gerontology and geriatrics. 2014;59(1):18-24.
35. 3GEM Research and Insights and Pegasus. Generation Z: The Future of Health and Wellbeing. 2019.
36. Allen J, Sesti F. Health inequalities and women – addressing unmet needs. BMA. 2018.
37. Public Health England. Health profile for England: 2018.
38. Freedman VA, Wolf DA, Spillman BC. Disability-Free Life Expectancy Over 30 Years: A Growing Female Disadvantage in the US Population. *American Journal of Public Health*. 2016;106(6):1079-1085.
39. Labots G, Jones A, de Visser SJ, Rissmann R, Burggraaf J. Gender differences in clinical registration trials: is there a real problem? *British Journal of Clinical Pharmacology*. 2018;84(4):700-707.
40. Feldman S, Ammar W, Lo K, Trepman E, van Zuylen M, Etzioni O. Quantifying Sex Bias in Clinical Studies at Scale With Automated Data Extraction. *JAMA Network Open*. 2019;2(7):e196700-e196700.

REFERENCES

41. Pinn VW. Sex and gender factors in medical studies: implications for health and clinical practice. *JAMA*. 2003;289(4):397-400.

42. Miller MA. Gender-based differences in the toxicity of pharmaceuticals--the Food and Drug Administration's perspective. *International journal of toxicology*. 2001;20(3):149-152.

43. European Commission. Health4LGBTI: Reducing health inequalities experienced by LGBTI people. 2018.

44. Safer JD, Coleman E, Feldman J, et al. Barriers to healthcare for transgender individuals. *Current opinion in endocrinology, diabetes, and obesity*. 2016;23(2):168-171.

45. Signorello LB, Cohen SS, Williams DR, Munro HM, Hargreaves MK, Blot WJ. Socioeconomic status, race, and mortality: a prospective cohort study. *American journal of public health*. 2014;104(12):e98-e107.

46. Steel N, Hardcastle AC, Bachmann MO, et al. Economic inequalities in burden of illness, diagnosis and treatment of five long-term conditions in England: panel study. *BMJ Open*. 2014;4(10):e005530.

47. Sharrocks K, Spicer J, Camidge DR, Papa S. The impact of socioeconomic status on access to cancer clinical trials. *British journal of cancer*. 2014;111(9):1684-1687.

48. Mohd Noor A, Sarker D, Vizor S, et al. Effect of Patient Socioeconomic Status on Access to Early-Phase Cancer Trials. *Journal of Clinical Oncology*. 2012;31(2):224-230.

49. Mosenifar Z. Population Issues in Clinical Trials. *Proceedings of the American Thoracic Society*. 2007;4(2):185-188.

50. Arpey NC, Gaglioti AH, Rosenbaum ME. How Socioeconomic Status Affects Patient Perceptions of Health Care: A Qualitative Study. *Journal of Primary Care & Community Health*. 2017;8(3):169-175.

51. Public Health England and Local Government Association. Health and wellbeing in rural areas. 2017.

52. Public Health England. An evidence summary of health inequalities in older populations in coastal and rural areas. 2019.

53. Friedman DB, Foster C, Bergeron CD, Tanner A, Kim S-H. A qualitative study of recruitment barriers, motivators, and community-based strategies for increasing clinical trials participation among rural and urban populations. *American journal of health promotion : AJHP*. 2015;29(5):332-338.

54. Davis TC, Arnold CL, Mills G, Miele L. A Qualitative Study Exploring Barriers and Facilitators of Enrolling Underrepresented Populations in Clinical Trials and Biobanking. F*rontiers in Cell and Developmental Biology*. 2019;7(74).

55. Public Health England. Improving health literacy to reduce health inequalities. 2015.

56. Al Sayah F, Majumdar SR, Williams B, Robertson S, Johnson JA. Health Literacy and Health Outcomes in Diabetes: A Systematic Review. *Journal of General Internal Medicine*. 2013;28(3):444-452.

57. Schillinger D, Grumbach K, Piette J, et al. Association of Health Literacy With Diabetes Outcomes. *JAMA*. 2002;288(4):475-482.

58. Magnani Jared W, Mujahid Mahasin S, Aronow Herbert D, et al. Health Literacy and Cardiovascular Disease: Fundamental Relevance to Primary and Secondary Prevention: A Scientific Statement From the American Heart Association. *Circulation*. 2018;138(2):e48-e74.

59. Ownby RL, Acevedo A, Goodman K, Caballero J, Waldrop-Valverde D. Health literacy predicts participant understanding of orally-presented informed consent information. *Clinical research and trials*. 2015;1(1):15-19.

60. FDA. Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry. 2019.

61. McKinsey. Delivering through Diversity. 2018 https://www.mckinsey.com/~/media/McKinsey/Business%20Functions/Organization/Our%20Insights/Delivering%20through%20diversity/Delivering-through-diversity_full-report.ashx Accessed February 2020.

62. Lorenzo R, Voigt N, Tsusaka M, Krentz M, Abouzahr K. How Diverse Leadership Teams Boost Innovation. *BCG*. 2018.

63. McKinsey. Diversity Matters. 2015 https://www.mckinsey.com/~/media/mckinsey/business%20functions/organization/our%20insights/why%20diversity%20matters/diversity%20matters.ashx Accessed February 2020.

64. Smith C, Turner S. The Radical Transformation of Diversity and Inclusion The Millennial Influence. 2015.

65. Levitan B, Getz K, Eisenstein EL, et al. Assessing the Financial Value of Patient Engagement: A Quantitative Approach from CTTI's Patient Groups and Clinical Trials Project. *Therapeutic innovation & regulatory science*. 2018;52(2):220-229.

66. Oliver SR, Rees RW, Clarke-Jones L, et al. A multidimensional conceptual framework for analysing public involvement in health services research. *Health expectations : an international journal of public participation in health care and health policy*. 2008;11(1):72-84.

67. Drug Information Association (DIA). Capturing the value of patient engagement. 2017. https://www.diaglobal.org/en/resources/press-releases/2016/10-31-patient-engagement-study. Accessed February 2020.

68. Ashkenazy R, Schneider RF. A Patient Centricity Team Tool to Enable Patient-Focused Drug Development. *Therapeutic innovation & regulatory science*. 2016;50(5):577-580.

69. Price A, Albarqouni L, Kirkpatrick J, et al. Patient and public involvement in the design of clinical trials: *An overview of systematic reviews. Journal of evaluation in clinical practice*. 2018;24(1):240-253.

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