# DCMB - DEI Challenge Report

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# Overview

The objective of this work was to investigate if gene expression omnibus (GEO) datasets are biased related to the US population using DEI criteria (sex, ethnicity, ancestry). Towards this aim, the following salients stages were undertaken. In stage one, we collected and filtered datasets from GEO relevant to our objective, and in stage two, we analyzed and computed a rank for each dataset towards identifying and scoring the highest to the lowest of GEO datasets biased for DEI criteria. The following sections will discuss these stages in detail.

# Steps of the analysis

## 1. Data collection

### Extraction and filtering of GEO data

To extract datasets relevant to our task, we first filtered our search with three initial criteria (as mentioned in the instructions) these include (i) type of experiment, (ii) organism, and (iii) sample size. The filters were used directly in the GEO advanced search option. The result from this filtering step generated ~2563 series. To further make our search more stringent for the US population, we added the USA filter which further reduced our result to 1433 series. While looking at the generated results, we noticed that almost half of the datasets did not contain the DEI criteria under investigation (mainly gender/sex and ethnicity/race). To improve analysis time and efficiency we added a final filter for race and gender for our GEO search. The resultant search showed 582 series. A detail of the steps for data collection is outlined in **Figure 1A.** GEOquery package in R was used for extracting metadata for each data series.

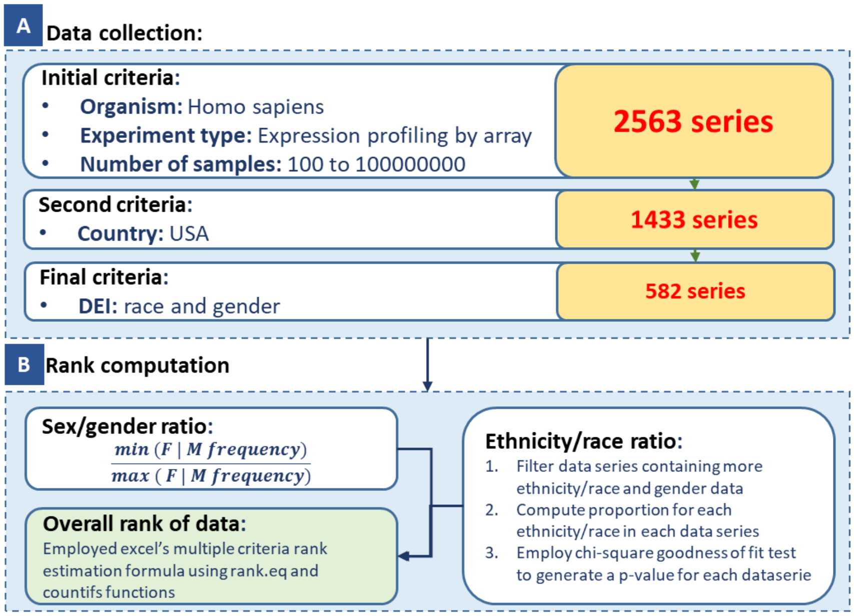

A
Data collection:
Initial criteria:
Organism: Homo sapiens
Experiment type: Expression profiling by array
Number of samples: 100 to 100000000
2563 series
Second criteria:
Country: USA
1433 series
Final criteria:
DEI: race and gender
582 series
B
Rank computation
Sex/gender ratio:
$\frac{min\ (F\ |\ M\ frequency)}{max\ (F\ |\ M\ frequency)}$
Overall rank of data:
Employed excel's multiple criteria rank estimation formula using rank.eq and countifs functions
Ethnicity/race ratio:
1. Filter data series containing more ethnicity/race and gender data
2. Compute proportion for each ethnicity/race in each data series
3. Employ chi-square goodness of fit test to generate a p-value for each dataserie

*Figure 1: Steps of the analysis*

### Challenges in data collection

Important to note here, the metadata in GEO, although well presented, is not uniformly structured. Meaning while collecting DEI information from the metadata, we noticed that for some data male and female were written as “male” and “female” while for others the authors used “M” and “F” conventions for naming. Similarly for ethnicity/race, both are used interchangeably and clearly distinguished, some data used the “ethnicity” label while others employed “race”. Additionally, some datasets also used short forms for labeling ethnicity/race such as “AA” for African Americans and “CAU” for caucasian. However, they do not mention the long term which we had to curate from original manuscripts for some. Moreover, some metadata also had poor formatting, while others were too large to download on local Rstudio. Due to the above-mentioned challenges, we had to manually check each metadata after downloading to be sure that the right column was being extracted and necessary data with no overlaps. Given this arduous process of data collection, out of the filtered 582 data series we were able to generate results for 211 of them. Further filtering for additional analysis requirements also filtered these numbers - details given below. The supplementary data for this challenge with all necessary data/information, initial information, formulas, etc can be found at the end of this document.

## 2. Scoring method/rank computation

### Sex/gender ratio

Towards computing a sex/gender ratio, we employed the following formula, in which out of the total male and female frequency calculated from each series, we used the smaller of the two numbers in the numerator and the larger of the two numbers in the denominator. This approach was undertaken for each data series. This showed that a ratio close to one would be a good ratio (suggesting balanced gender) whereas a ratio close to zero would be a bad ratio (indicating unbalanced gender) the total ratio cannot be more than one which came into use with overall rank estimation. An overview of the scoring method can be found in **Figure 1B.** In the results section, we have first calculated the rank of samples based on sex/gender ratio only and then we have incorporated additional criteria and added complexity for computing rank.

### Ethnicity/race ratio

For calculating the ethnicity/race ratio, we carried out the following steps:

(1) We first filtered those data series with both ethnicity and gender mentioned in their metadata so that we have more of these data for overall rank calculation.

(2) We then calculated the proportion of each ethnicity/race for each data series by dividing each ethnicity/race frequency from the total number. This result gave a good estimate of how much each ethnicity/race is contributing to the overall dataset. While carrying this out, we made sure we were not over-estimating by incorporating ethnicities not mentioned in the respective dataset. Only ethnicities mentioned in the metadata for that series were employed.

(3) We then employed the Chi-square goodness of fit test to estimate a p-value for each data series. This p-value indicates how much is the expected proportion different from

the observed proportion of races. A larger p-value indicated more balanced data for ethnicity/race whereas a smaller p-value indicates a more biased dataset. Since failure to reject the null hypothesis concludes that the data does follow a distribution with certain proportions and there is no evidence to suggest that there is a significant difference between observed and expected frequency.

### Overall rank computation

To estimate the overall rank for each data series we used our prior knowledge that:

- For sex/gender ratio, closer to 1 indicates unbiased
- For ethnicity/race ratio, a larger p-value indicates unbiased

Given the way we have structured our results, we know that the sex/gender ratio cannot be larger than 1, and the largest p-value would be the most unbiased for ethnicity/race. Therefore, we used excel's own rank computation formula we first rank the data series based on gender/sex ratio and builds on that with the ethnicity/race ratio. The exact computation and all necessary formulas used in these steps are present in the attached supplementary data.

# Results

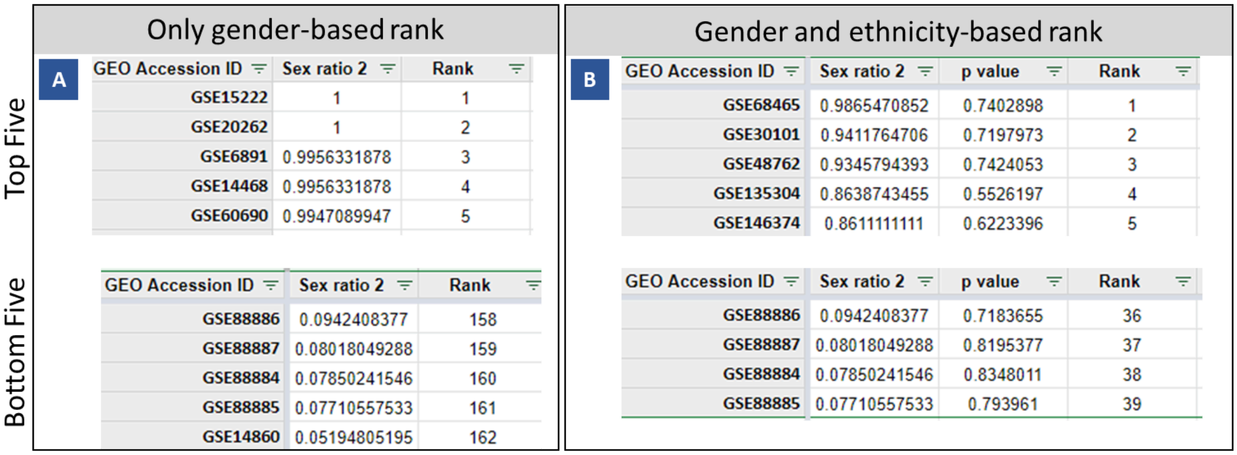
## 1. Investigating bias in Gene Expression Omnibus datasets using DEI criteria

### Data curated for DEI criteria investigation

To investigate whether Gene expression Omnibus (GEO) datasets are biased relative to the US population using DEI criteria we first added three different filters (i) expression profiling by array, (ii) homo sapiens, and (iii) at least 100 samples. This resulted in around 2563 series. Additional filters for USA and DEI criteria (sex/gender and ethnicity/race) were retrieved around 580 series. Due to poor structure of metadata, downloading issues, missing values, variability in labeling etc, out of 580 series we manually extracted relevant data for 211 of them - making sure we get the right frequencies. The raw data along with filters and necessary formulas can be found in supplementary data attached with this document at the end.

### Ranking GEO datasets based on sex/gender

To compute a rank for each dataset based on sex/gender-biased, we first calculated a ratio for estimating the proportion of gender/sex. A value close to one indicates a good or balanced dataset whereas a value near zero indicates a bad or unbalanced dataset. Twenty datasets had a ratio of 0 which indicated that they had only one of the gender mentioned. This might be because they focus on a gender-based study such as breast cancer is more prevalent in females whereas males subjects are more prone to prostate cancer. We removed these data series from our results. Some datasets were also removed because they did not contain gender/sex information (they contained race/ethnicity information). The top and bottom five datasets are highlighted in **Figure 2A**. The result shows that there are 116 datasets from 163 which are equal to and above 0.5 indicating a good balance of gender, whereas 43 were below 0.5 showing gender inequality.


Only gender-based rank
A
Top Five
Bottom Five
Gender and ethnicity-based rank
B

| GEO Accession ID | Sex ratio 2 | Rank |
|---|---|---|
| GSE15222 | 1 | 1 |
| GSE20262 | 1 | 2 |
| GSE6891 | 0.9956331878 | 3 |
| GSE14468 | 0.9956331878 | 4 |
| GSE60690 | 0.9947089947 | 5 |

| GEO Accession ID | Sex ratio 2 | Rank |
|---|---|---|
| GSE88886 | 0.0942408377 | 158 |
| GSE88887 | 0.08018049288 | 159 |
| GSE88884 | 0.07850241546 | 160 |
| GSE88885 | 0.07710557533 | 161 |
| GSE14860 | 0.05194805195 | 162 |

| GEO Accession ID | Sex ratio 2 | p value | Rank |
|---|---|---|---|
| GSE68465 | 0.9865470852 | 0.7402898 | 1 |
| GSE30101 | 0.9411764706 | 0.7197973 | 2 |
| GSE48762 | 0.9345794393 | 0.7424053 | 3 |
| GSE135304 | 0.8638743455 | 0.5526197 | 4 |
| GSE146374 | 0.8611111111 | 0.6223396 | 5 |

| GEO Accession ID | Sex ratio 2 | p value | Rank |
|---|---|---|---|
| GSE88886 | 0.0942408377 | 0.7183655 | 36 |
| GSE88887 | 0.08018049288 | 0.8195377 | 37 |
| GSE88884 | 0.07850241546 | 0.8348011 | 38 |
| GSE88885 | 0.07710557533 | 0.793961 | 39 |

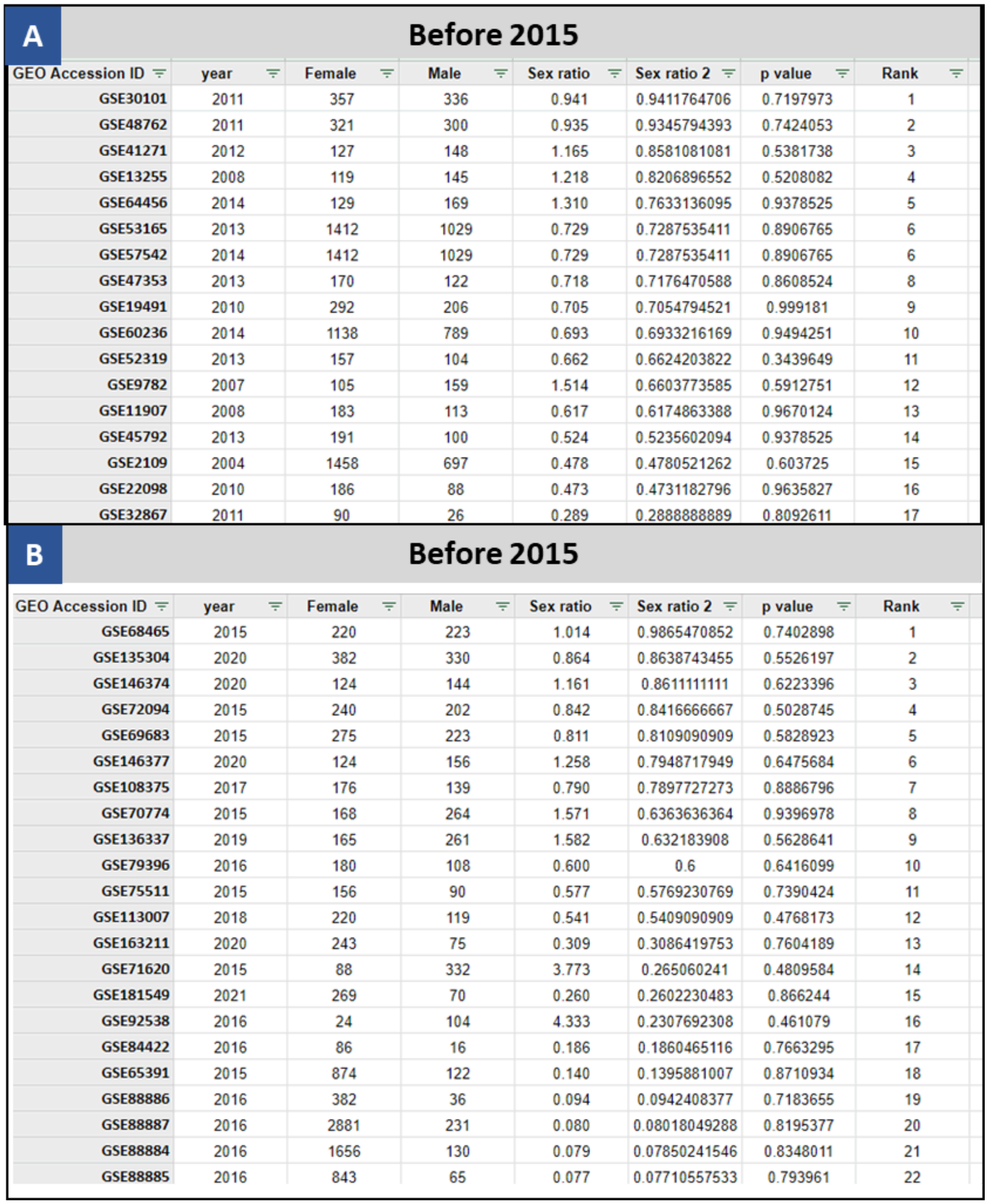
*Figure 2: GEO data ranking*

### Ranking GEO datasets based on sex/gender as well as ethnicity/race

To add additional criteria for ethnicity/race, we first extracted the number of individuals labeled for each ethnicity/race mentioned in the metadata. To note, for the purpose of this report, we are considering ethnicity and race the same. To compute an overall score, keeping in mind both gender and ethnicity, we only looked at datasets that contained both information. Then we computed the proportion of each ethnicity for that dataset. This gave us a probability of each ethnicity in the dataset. Next, we employed the Chi-square goodness of fit test to estimate a p-value for each data series. To note, since not every data had all ethnicities/races or the same ones therefore while calculating the chi-square test we made sure we were only looking at the ethnicities mentioned in the dataset under observation and ignored the rest. The expected null hypothesis is that there is no difference between observed and expected probabilities i.e, data does follow a distribution with certain proportions. Each ethnicity should exist in equal proportions in the dataset for unbiased evaluation. Therefore, under these assumptions, the Chi-square goodness of fit test gave us a p-value for each dataset. The larger the p-value, the higher chance of the null hypothesis being true, the more balanced, unbiased the data. Next, to compute the overall rank for each dataset, we used the gender/sex ratio (as mentioned above) and the p-value for ethnicity/race. The larger the gender/sex ratio and the higher the p-value the more balanced/unbiased the data. To calculate the rank based on two different criteria, we employed excel's rank equation and countif functions. The dataset for the top and bottom 5 datasets can be viewed in **Figure 2B.**

## 2. Evaluating GEO datasets before and after 2015 for DEI criteria

While collecting DEI-relevant information from GEO datasets, we also extracted the corresponding year of data submission from the metadata information. The year information can be employed to compare DEI bias scores for datasets before and after 2015. **Figure 3A-B** show the changes in sex/gender ratio and the p-value, however, a closer look at the distribution of the two show that for some patients after 2015, their sex ratio is more biased compared to their ethnicity ratio. This is indicated in **Figure 4A-B.** Due to the high variability in the scientific question that each study/dataset was addressing it is hard to say anything for sure. However, a closer inspection of a few of the datasets indicates that there are more women recruited for certain studies might be because women are generally higher in number in the world compared to men or because men mostly have financial priority and prefer not to take part in such studies or it can be due to gender disparity in science which is still very common or it can be because of the relatively small size of the datasets under inspection.



A

Before 2015

| GEO Accession ID | year | Female | Male | Sex ratio | Sex ratio 2 | p value | Rank |
|---|---|---|---|---|---|---|---|
| GSE30101 | 2011 | 357 | 336 | 0.941 | 0.9411764706 | 0.7197973 | 1 |
| GSE48762 | 2011 | 321 | 300 | 0.935 | 0.9345794393 | 0.7424053 | 2 |
| GSE41271 | 2012 | 127 | 148 | 1.165 | 0.8581081081 | 0.5381738 | 3 |
| GSE13255 | 2008 | 119 | 145 | 1.218 | 0.8206896552 | 0.5208082 | 4 |
| GSE64456 | 2014 | 129 | 169 | 1.310 | 0.7633136095 | 0.9378525 | 5 |
| GSE53165 | 2013 | 1412 | 1029 | 0.729 | 0.7287535411 | 0.8906765 | 6 |
| GSE57542 | 2014 | 1412 | 1029 | 0.729 | 0.7287535411 | 0.8906765 | 6 |
| GSE47353 | 2013 | 170 | 122 | 0.718 | 0.7176470588 | 0.8608524 | 8 |
| GSE19491 | 2010 | 292 | 206 | 0.705 | 0.7054794521 | 0.999181 | 9 |
| GSE60236 | 2014 | 1138 | 789 | 0.693 | 0.6933216169 | 0.9494251 | 10 |
| GSE52319 | 2013 | 157 | 104 | 0.662 | 0.6624203822 | 0.3439649 | 11 |
| GSE9782 | 2007 | 105 | 159 | 1.514 | 0.6603773585 | 0.5912751 | 12 |
| GSE11907 | 2008 | 183 | 113 | 0.617 | 0.6174863388 | 0.9670124 | 13 |
| GSE45792 | 2013 | 191 | 100 | 0.524 | 0.5235602094 | 0.9378525 | 14 |
| GSE2109 | 2004 | 1458 | 697 | 0.478 | 0.4780521262 | 0.603725 | 15 |
| GSE22098 | 2010 | 186 | 88 | 0.473 | 0.4731182796 | 0.9635827 | 16 |
| GSE32867 | 2011 | 90 | 26 | 0.289 | 0.2888888889 | 0.8092611 | 17 |

B

Before 2015

| GEO Accession ID | year | Female | Male | Sex ratio | Sex ratio 2 | p value | Rank |
|---|---|---|---|---|---|---|---|
| GSE68465 | 2015 | 220 | 223 | 1.014 | 0.9865470852 | 0.7402898 | 1 |
| GSE135304 | 2020 | 382 | 330 | 0.864 | 0.8638743455 | 0.5526197 | 2 |
| GSE146374 | 2020 | 124 | 144 | 1.161 | 0.8611111111 | 0.6223396 | 3 |
| GSE72094 | 2015 | 240 | 202 | 0.842 | 0.8416666667 | 0.5028745 | 4 |
| GSE69683 | 2015 | 275 | 223 | 0.811 | 0.8109090909 | 0.5828923 | 5 |
| GSE146377 | 2020 | 124 | 156 | 1.258 | 0.7948717949 | 0.6475684 | 6 |
| GSE108375 | 2017 | 176 | 139 | 0.790 | 0.7897727273 | 0.8886796 | 7 |
| GSE70774 | 2015 | 168 | 264 | 1.571 | 0.6363636364 | 0.9396978 | 8 |
| GSE136337 | 2019 | 165 | 261 | 1.582 | 0.632183908 | 0.5628641 | 9 |
| GSE79396 | 2016 | 180 | 108 | 0.600 | 0.6 | 0.6416099 | 10 |
| GSE75511 | 2015 | 156 | 90 | 0.577 | 0.5769230769 | 0.7390424 | 11 |
| GSE113007 | 2018 | 220 | 119 | 0.541 | 0.5409090909 | 0.4768173 | 12 |
| GSE163211 | 2020 | 243 | 75 | 0.309 | 0.3086419753 | 0.7604189 | 13 |
| GSE71620 | 2015 | 88 | 332 | 3.773 | 0.265060241 | 0.4809584 | 14 |
| GSE181549 | 2021 | 269 | 70 | 0.260 | 0.2602230483 | 0.866244 | 15 |
| GSE92538 | 2016 | 24 | 104 | 4.333 | 0.2307692308 | 0.461079 | 16 |
| GSE84422 | 2016 | 86 | 16 | 0.186 | 0.1860465116 | 0.7663295 | 17 |
| GSE65391 | 2015 | 874 | 122 | 0.140 | 0.1395881007 | 0.8710934 | 18 |
| GSE88886 | 2016 | 382 | 36 | 0.094 | 0.0942408377 | 0.7183655 | 19 |
| GSE88887 | 2016 | 2881 | 231 | 0.080 | 0.08018049288 | 0.8195377 | 20 |
| GSE88884 | 2016 | 1656 | 130 | 0.079 | 0.07850241546 | 0.8348011 | 21 |
| GSE88885 | 2016 | 843 | 65 | 0.077 | 0.07710557533 | 0.793961 | 22 |

*Figure 3: GEO Datasets before and after 2015*

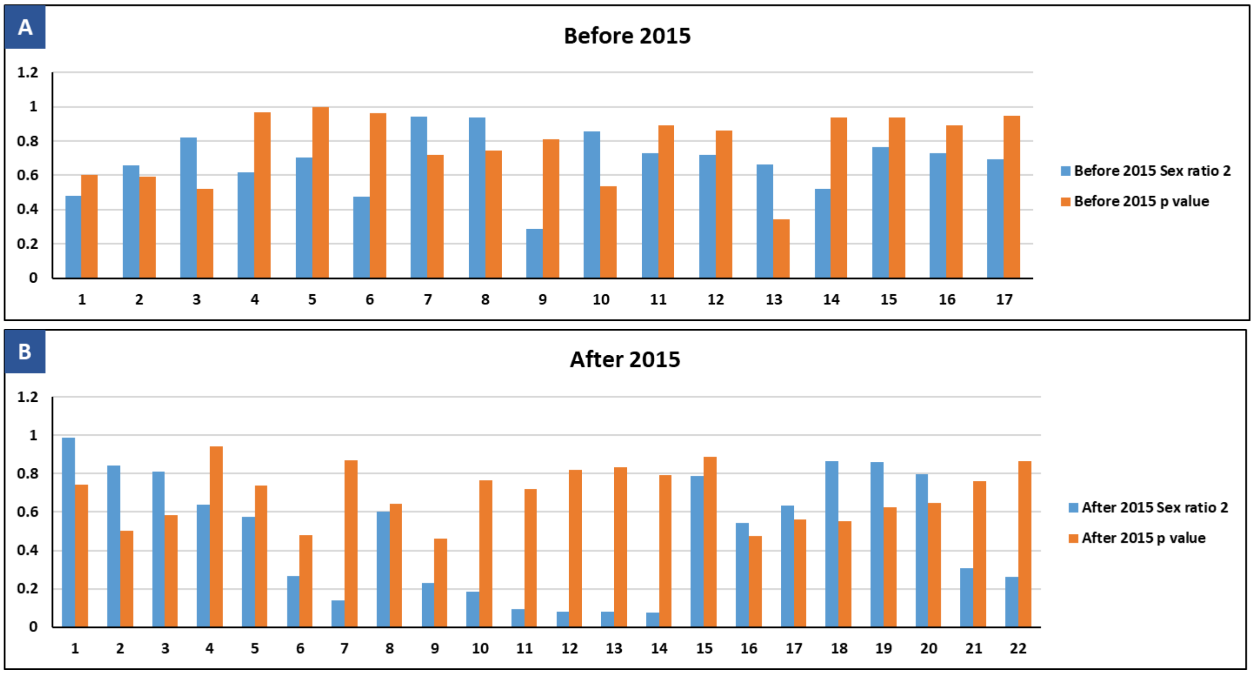


*Figure 4: Distribution of sex ratio and p-value for before and after 2015*

## 3. Performing exploratory analysis on curated data

A general overview of the curated datasets (**Figure 5**) shows that most of our data is biased with the following ethnicities white, caucasian, African American, and Hispanic.

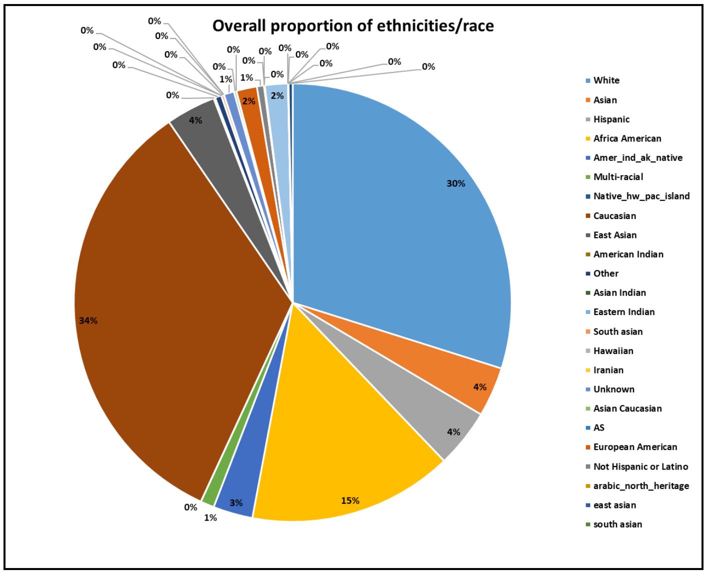


*Figure 5: Distribution of ethnicities/race in the curated data*

# Conclusion

In this challenge, we successfully extracted, filtered, and curated a dataset for investigating if Gene Expression Omnibus (GEO) datasets are biased relative to the US population using DEI criteria (sex, ethnicity, ancestry, race). We encountered issues pertaining to how different research groups classify different ethnicities and genders, to make sure we have good data entries, all 211 datasets result was manually examined and curated. Our results "*gender-only ratio"* show that there are 116 datasets from 163 which are equal to and above 0.5 indicating a good balance of gender, whereas 43 were below 0.5 showing gender inequality. From visual inspection, we can see that there are more female samples. This can be because we are only looking at a subset of the entire 583 datasets. Moreover, literature reports do indicate that there has been active recruitment of women in clinical settings [27011778], and the need for gender equality is now more seen than in previous times, although we still have a lot more road to cover. For our "*gender and ethnicity-based overall rank*" we observe that out of our 39 samples that have both gender and ethnicity data, we have a high p-value and sex ratio. This shows that we fail to reject null and our observed and expected ratio of ethnicities are similar and the high sex ratio indicates that our data is more neutral towards gender. However, this is an initial analysis on a limited dataset, a more broad and more inclusive approval needs to be taken especially while collecting datasets and computing the overall rank. Fisher test can perhaps give better results than the chi-square test, we can also try to include additional DEI criteria in our analysis, we can also try to investigate those studies which show a very high or very low score the study might itself be biased or they might have overlooked while recruiting their samples. This analysis, on the whole, indicates that there is a need to keep DEI in mind while designing, planning, and executing scientific endeavors, such biases cannot only lead to unjust result outcomes but can also be detrimental in policy and legislature when used in decision-making settings as ground truth. As researchers and scientists we need to develop universal criteria of acceptance, diversity, inclusion, and equality in health science, machine learning techniques, artificial learning so we do not overlook such important indicators/criteria in our datasets.

# Supplementary materials

1. **Supplementary data (raw, processed data, formulas, etc)**

GEO - DEI Challenge

2. **Dropbox link (data, R code, figure materials)**

https://www.dropbox.com/sh/4see41t2ovvo923/AADIm4pePJwMnaMLLuwa6vrWa?dl=0