Addressing Artificial Intelligence Bias in Retinal Disease Diagnostics

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ABSTRACT

Purpose: Few studies of deep learning systems (DLS) have addressed issues of artificial intelligence bias for retinal diagnostics. This study evaluated novel AI and deep learning generative methods to address bias for retinal diagnostic applications when specifically applied to diabetic retinopathy (DR). Bias often results from data imbalance. We specifically considered here a strong form of data imbalance corresponding to domain shift, where AI classifiers are faced at inference time with data and concepts they were not trained on initially (here the concept of diseased black individuals).

Methods:
A baseline DR diagnostics DLS designed to solve a two-class problem of referable vs not referable DR was used. We modified the public domain Kaggle-EyePACS dataset (88,692 fundi and 44,346 individuals), which was originally designed to be diverse with regard to ethnicity, as follows: 1) we expanded it to include clinician-annotated labels for race since those were not publicly available; 2) we excluded training exemplars for diseased black individuals in training, but not testing, to construct a new scenario of data imbalance with domain shift.

Results: For this domain shifted scenario, the accuracy (95% confidence intervals [CI]) of the baseline DR diagnostics DLS for whites was 73.0% (66.9%, 79.2%) vs. blacks of 60.5% (53.5%, 67.3%), demonstrating disparity (Welch t-test t=2.670, P=.008) of AI performance as measured by accuracy across races. By contrast, an AI approach leveraging generative models was used to train a new diagnostic DLS with additional synthetically generated data for the missing subpopulation (diseased blacks), which achieved accuracy for whites of 77.5% (71.7%, 83.3%) and for blacks of 70.0% (63.7%, 76.4%), demonstrating closer parity in accuracy across races (Welch t-test t=1.70, P=.09). The new debiased DLS also showed improvement in sensitivity of over 21% for blacks, with the same level of specificity, when compared with the baseline DLS.
**Conclusions:** These findings demonstrate how data imbalance and domain shift can lead to inequality of accuracy depending on race, and illustrate the potential benefits of using novel generative methods for debiasing AI.

**Translational Relevance:** These methods might decrease AI bias for other retinal and ophthalmic diagnostic DLS.
**Précis:**

Data imbalance and domain shift can lead to AI bias and inequality of accuracy depending on race; this study illustrates the potential benefits of using novel generative methods for debiasing AI. These methods might decrease AI bias for other retinal and ophthalmic diagnostic DLS.
INTRODUCTION

Current deep learning systems’ (DLS) applied to retinal diagnostics, for diseases such as diabetic retinopathy (DR) or age-related macular degeneration (AMD), have performance approaching that of clinicians [Gulshan2016, Ting2018, Burlina2017]. This success is motivating the deployment of AI-based prescreeners in clinical environments to address ophthalmologists’ workload, and is also being used for teleophthalmology. However, to promote further AI insertion in retinal clinical workflows, more efforts are needed to probe AI assurance, including the potential problem of bias in AI which may occur when training datasets are unbalanced (insufficient or no data for certain subpopulations), such as images of AMD in black populations, or DR for individuals over age 85 years [Parikh2009].

Specifically, DLSs may be affected by possible AI bias with regard to patients’ protected (e.g. race, gender, or age). AI should in principle behave “fairly and equally” -- irrespective of those. However, criteria for fairness can vary, and bias in AI can also have many different causes and manifestations. Two criteria for fairness have received increased attention, these are the so-called "equality of odds" and "equality of opportunity" [Mehrabi2019]. Translated into actual retinal use cases, these criteria can be illustrated as follows:

1) (In)equality of opportunity: consider individuals with different protected attributes (e.g. race, whites and blacks), but identical actual underlying risk factors for progressing to the advanced neovascular form of AMD; Then an AI system designed to prioritize ophthalmic treatment resources, and to assist in treatment planning, should estimate that both individual types have identical needs (i.e. they should both be administered anti-VEGF treatment and at identical frequencies, say every month). In other words, the
DLS should not discriminate based on race for preferential treatment if identical risks exist. An example of a healthcare recommendation system, already deployed clinically, and used for predicting individuals’ need for medical services, that manifested bias via inequality of opportunity, was reported in [Obermeyer2019].

2) **(In)equality of odds**: consider individuals that have different protected attributes (race), and identical actual stages of DR (say non-proliferative DR, or NPDR), then an AI diagnostic system should estimate and ascribe identical probabilities that these individuals have NPDR. With unequal odds, an AI diagnostic algorithm may result in varying and unfair performance characteristics (e.g. as measured via accuracy) for whites vs blacks, leading to what is referred to as an “unequal accuracy” type of bias. A common cause for unequal odds/accuracy is imbalance in the training data available for a specific population (say blacks). The case of unequal odds is the use case studied herein, where we also use the objective of equal accuracy as the desirable AI fairness criterion.

The aforementioned issue of data imbalance may be associated to a more generic problem in DL called “domain shift” or “distributional shift”. With some forms of domain shift, the DLS may be faced, at inference time, with out-of-distribution samples (hence the term “distributional shift”), when compared to training samples’ distribution. This problem may also be connected potential problems regarding lack of generalization. An interesting actual use case of domain shift this team has experienced in the past (in collaboration with the authors of [Ting2019]) arises when training an AMD diagnostics DLS on the AREDS dataset, mostly consisting of whites individuals, then testing on a Singaporean population that presented cases of polypoidal choroidal vasculopathy,
more prevalent in Asians, and that had been ungraded in AREDS cases, resulting in potentially lower performance for that DLS on Asian individuals.

In order to address these potential biases in automated retinal diagnostics, we evaluated this theoretic data imbalance and domain shift using a DR diagnostics use case.

**METHODS**

**Strategies for AI-debiasing and incorporating prior approaches:**

If the bias is due to unbalanced data (e.g., insufficient or missing training examples of black individuals with DR) then a possible solution suggested in [Prakish2019] may be to sample additional representative data for this group. When this solution is not practical, as is the case when AI is trained on retrospective data, or other constraints exist regarding time, costs, regulatory limitations, other logistics, or resources-related considerations, other remedial approaches to AI bias are needed. This study addresses this situation and uses an algorithmic debiasing solution.

Algorithmic solutions to imbalance may include simple approaches such as using reweighting of the training loss function or more complex such as using a DLS that requires less training data (so called ‘low-shot method’ [Wang2019, Burlina2020]): When addressing bias, the partitioning of data into factorized sets of specific protected attributes (age, gender, race) will irremediably result in ever smaller datasets that do not provide sufficient training images for a specific subgroup. Trying to get equal accuracy across specific subgroups is a difficult proposition, but one possible approach is “low-shot” DLS, wherein, while few training images are used, the DLS may still perform
satisfactorily. We have studied this situation and provided several such solutions in [Burlina2020].

Another approach could consist of using an anomaly detector [Chalapathy2019, Burlina2019a] that works by detecting distributional inlier vs outliers: consider the use case of having insufficient or no training data of DR-affected blacks, studied herein. One could rely on an inlier detection system that is trained exclusively on non-diseased blacks and whites and find DR by finding samples (anomalies) that do not conform to the inlier distribution.

Yet another algorithmic debiasing strategy that may address both issues of inequality of odds and inequality of opportunity, could consist of pairing a diagnostic DLS with an additional adversarial network that tries to guess the protected factors of the individual [Mehrabi2019], while the original DLS tries to disallow that, essentially rendering the original diagnostic DLS “blind” to this protected factors. A related approach may use a direct adversarial method to make the last representation layer of the diagnostic network blind to protected factors [Zhang2018].

Not all of the above strategies may be practical or suitable (e.g. adversarial networks with multiple objectives are hard to train) or beneficial (anomaly detectors performance is lower than traditional classifiers), hence the approach we choose here is to develop a DLS that generates more synthetic samples -- in a controlled way – to address the need for more data from populations with under-represented or missing factors.

To our knowledge, no retinal diagnostic AI study to date has specifically studied bias or offered a solution in the context of retinal diagnostics. The approach we propose here is
applied to use in automated DR diagnostics but is completely generic and potentially could be considered for other ophthalmic, medical, or image classification use cases.

**Problem studied:**
Our use case is automated binary diagnostics for DR, i.e., non-referable (stage 0,1) vs. referable (stages 2,3,4) DR to a health care provider -- for further follow-up or treatment (see [Cuadros2009] for definitions of these stages).

We further studied the case of racial bias in AI that results when training data are unbalanced, and domain shift exists.

To address the problem of data imbalance and domain shift -- where a concept present at inference/testing time was not known to the classifier at training time (specifically here the concept of ‘diseased blacks’) -- we created a new dataset by altering the original Kaggle-EyePACS dataset. In our altered dataset, training data is now available for only three subgroups of individuals consisting of specific combinations of two factors of variations which are “race” and “DR status”. These subgroups included: diseased-white (DW), healthy-white (HW), and healthy-black (HB) individuals. However, in this new domain shifted scenario, no training data was made available in our experiments for diseased-black (DB) individuals. This is a scenario of severe data imbalance that also translates into a domain-shift problem, as the DLS had seen examples -- and therefore learned to recognize features -- for factors of variations consisting of race as well as disease from those 3 groups; but then the DLS was faced with a distributional shift challenge at inference/test time, since it was also tested on the novel combination of
factors corresponding to diseased black individuals, in addition to the three other subgroups.

We investigated two questions: (QA) can the original data imbalance and domain-shift cause possible inequality of accuracy for the DR diagnostic DLS for blacks and whites? And (QB): if there is such a bias, does our proposed synthetic data augmentation using generative models help debias the DR diagnostic AI?

Dataset and labels:
To probe (QA) and (QB), we created a new dataset based on the original Kaggle-EyePACS that exhibited domain shift by excluding affected black individuals from training but not from testing. Note that the original Kaggle-EyePACS dataset, which has been widely used by many researchers -- does not inherently have any issues with diversity, bias, or domain shift (see more details in the discussion section). The original Kaggle-EyePACS dataset consisted of 88,692 public domain fundi of 44,346 participants [Cuadros2009]. We preprocessed each image as follows: we cropped it to its out-scribed square, padded it if needed, and resized to 256X256. To make the diagnostic task more challenging for the AI, we did not further process the data, and did not remove bad-quality or non-gradable images. All fundi in Kaggle-EyePACS already had annotations for DR (5 levels) which were then translated into a binary label (referable or not). Since labels for race or ethnicity were not made available publicly, we then added an additional gold standard label for “race” for each image – focusing on a binary case of white vs. blacks -- by asking a clinician (and co-author KP) to evaluate each image and classify it as one of three possible classes consisting of 1) blacks 2) whites 3) or “indeterminate/unknown”. Indeterminate images were not used, and only a binary race value was employed thereafter. Cues for rating images as 1) or 2) included the
appearance of the choroidal background influenced by the melanocytic concentration, although variations in flash, pupil size, axial length, and presence of staphylomatous abnormalities could affect this appearance as well. A subset of 1,555 images were manually annotated by the clinician. After annotation was completed, we trained a classification model, called the Race Extrapolation DLS, to extrapolate the race label to all other non-annotated images in the Kaggle-EyePACS dataset. This DLS architecture was identical to the Baseline DLS described next.

Baseline DLS:
For this problem we used a traditional DLS reproducing approaches commonly employed in most retinal AI diagnostic studies: Our system used fine-tuning of an existing network, here ResNet with implementation details reported in [Burlina2017]. This system was trained with the three subgroups consisting of (DW), (HW) and (HB) but no (DB), to classify referable vs not referable DR. We will henceforth refer to this as the Baseline DLS.

Data Partitioning for Baseline DLS Evaluation:
The Kaggle-EyePACS fundi were partitioned into training (17,056 images), validation (4,264), and testing (400) datasets to evaluate the Baseline DLS. The characteristic Table 1 details the partitions’ sizes. Since we aimed to keep class balance across diseased and healthy images, the combined number of training and validation fundi consisted of a total of 10,660 images for (DW), 5,330 for (HW) and 5,330 for (HB).
Testing included equal numbers (100 real Kaggle-EyePACS images each) for each subgroup (DW), (HW), (DB) and (HB), for a total of testing 400 images. Only real images that were directly annotated by the physician for race were included in this test set. The same test set was also used for performance evaluation of the Debiased DLS (detailed later) for fair comparison.

The train dataset of the Baseline DLS included some images directly annotated for race by our clinician, as well as images for which the race label was extrapolated (as was explained earlier).

We evaluated the baseline algorithm by using accuracy as a main performance metric but also computed sensitivity and specificity.

**Debiased DLS using Synthetic Data Augmentation via Generative Model and Factor Manipulation**

Our goal was to compare the Baseline DLS, trained on unbalanced data, and affected domain shift, to a DLS trained on data rebalanced via inclusion of synthetic images of the missing combination of factors (DB). We henceforth call this second diagnostic system the “Debiased DLS”.

Our high-level method was as follows: we used a generative model to generate new synthetic images of (DB) starting with a generative system as in [Burlina2019b]. But our new model was also redesigned to allow fine manipulation -- in latent space -- of specific factors of variations of the generated images. Specifically, this system used gradient descent to transform synthetic (but realistic) images of diseased individuals, into synthetic images of diseased black individuals, without changing other factors of
variations, in order to preserve realism. (see examples of such manipulations in Fig. 1) We then augmented the training dataset of the baseline DLS with these new synthetic training images of diseased black retinas (DB) to obtain an improved, debiased training set, which contained balanced amounts of data for race as well as disease status.

The details of the processing pipeline are described next and are also shown in the flow chart in Fig. 2.

Additional Details for Debiasing Pipeline

To generate more diseased black (DB) synthetic fundi we first used as foundation a generative model leveraging StyleGAN as in [Burlina2019b]. While that approach was able to generate realistic images most of the time, it was, however, not sufficient for this current study. Indeed, general-purpose generative methods are sometimes prone to creating images with artifacts, such as unrealistic vascular structures, when the generation process uses a latent space traversal process that is done arbitrarily (e.g. rectilinear traversal) or another process that does not precisely control the change in factors of variation in the image. Deep learning methods that discover, control, and disentangle factors of variations in images via generative models, are currently an active area of investigation, and no method to date as definitely “solved” this challenge [Paul2020].

To address this problem in DR diagnostics, we aimed to alter specific factors of variations in synthetic images, such as race, while keeping other factors unchanged
(specifically, leaving the vasculature as well as the retinal disease lesions of the generated images unchanged) (See Fig. 1).

Our method allowed us to start with synthetic images of diseased individuals (disease=D) and perform latent space manipulation on those images, via gradient descent, to generate new images that included the desired factor of variation (i.e. race=B).

To accomplish this, we first trained a StyleGAN model using the same training dataset used by the baseline DLS. We then generated pairs of (latent space vector \( \mathbf{w} \), image \( \mathbf{I} \)) tuples, by using the trained StyleGAN model, in inference mode (about 120,000 \([\mathbf{w}, \mathbf{I}]\) pairs).

Thereafter we trained a new model (Race DLS) working in image space, able to classify between whites and blacks, using the extrapolated race labels described earlier. The Race DLS differs from the Race Extrapolation DLS, in that the Race DLS is trained on more images, which are made up of equal amounts of white and black retinas.

Note that StyleGAN includes two latent spaces, one with an input vector \( \mathbf{Z} \) of size 512 which is mapped via a fully connected network to a new latent style tensor \( \mathbf{w} \) of size 16x512; the later latent space representation was used for manipulation of factor of variations.

Among all generated images, we then selected a subset of 10,660 generated images \( \mathbf{I} \) of diseased synthetic individuals. This was done by using the Baseline DLS diagnostic system described earlier.
We then created a classification of race model in latent space, called the Latent Race DLS, described as follows: we used the subset of the 120,000 synthetic images that were classified as healthy (using the Baseline DLS), we then inferred race labels for this subset (using the Race DLS), which we used as training labels for the Latent Race DLS. From the 120,000 synthetic images, we then took a subset of 10,660 images that were classified as diseased (using the Baseline DLS). We took the corresponding latent space representations of these sample synthetic images, \( w \), and applied a gradient descent method to accentuate the SoftMax value of the Latent Race DLS, thereby accentuating desired ‘race’ factor of variation and make these selected synthetic fundi present more as black individuals’ retinas. The gradient descent moved along a trajectory in latent space that was able to maximally transform images to the desired race (B), while still preserving the vasculature, as well as the disease lesions factors of variation, unchanged. This is in contrast with a rectilinear or arbitrary traversal that would have produced changes in all factors (race, disease, and vasculature). All image sizes synthesized were 256x256.

**Debiased DLS**

We subsequently trained a new DR Diagnostics DLS, but now also included the newly generated (DB) synthetic images in the training dataset. The number of training and validation images used now reflected parity for both race as well as DR disease status. These are also described in the characteristic Table 1.

**Debiased DLS evaluation**

The evaluation of the debiased DLS was done in an identical fashion and with the same test data described for the baseline DLS. In addition, we also evaluated the improvement
from baseline to debiased DLS for the specific subpopulation of (DB), reporting accuracy, over a set of 6291 real Kaggle-EyePACS images whose race label had been extrapolated.

RESULTS

Table 2 compares the accuracy, sensitivity and specificity with 95% CI for the baseline and debiased DLS broken down by race (white or black).

First, the results suggests a positive answer for question (QA): As shown in Table 2, the baseline DLS is biased with regard to the criterion of equal accuracy across races because it had accuracy of whites of 73.0% [66.85, 79.15] vs. blacks of 60.5% [53.52, 67.28], demonstrating statistically significant disparity (Welch t-test t=2.670, p=0.008) of AI performance as measured by accuracy across races (difference of 12.5%, 95% CI: 3.35% to 21.7%). For this case, we treat the accuracies as means and a debiased system as one that has equal means for the white and black populations. Thus, the Welch t-test states that, under the assumption that the system were to be unbiased, the probability of observing a statistic at least as significant as 2.670 is 0.8%, so this assumption does not match the data at hand based on a significance level of 5%.

The results also appear to suggest a positive answer with regard to our question (QB): The debiased diagnostic DLS appeared to achieve closer parity in accuracy for individuals of different races. Our debiased DLS resulted in accuracy for whites of 77.5% and for blacks of 70.0%, with Welch t-test t=1.707, p=0.089, difference = 7.5% (95% CI: -1.1% to 16.1%). For this system, the Welch t-test states that, under the assumption that this system is debiased, the probability of observing a statistic at least as significant...
as 1.707 is 8.9%, so this assumption does match the data at hand based on a significance level of 5%.

Table 2 also reports the sensitivity and specificity for black and white populations for the baseline and debiased algorithm. In particular, the table suggests that the debiased DLS achieved improvement for blacks, whereby the sensitivity of 35.0% (and 95% CI of [25.65, 44.35]) and specificity of 86.0% [79.2, 92.8] for the baseline algorithm were improved— for the debiased algorithm -- to a sensitivity of 56.0% [46.27, 65.73] and specificity of 84.0% [76.81, 91.19].

When evaluated on the leftover dataset of real data of black individuals, the accuracy was improved from 38.48% [37.28, 39.68] to 57.86% [56.64, 59.08], again suggesting the benefit of the debiased algorithm to improve the accuracy for the protected individuals.

**DISCUSSION**

This study considered a DLS used for DR diagnostics and demonstrated that data imbalanced and domain shift for specific race and disease factors could impart unfair outcomes whereby lack of parity existed in the performance (as measured via accuracy) of the baseline AI when applied to different race populations.

This suggests that the potential for bias exists due to data imbalance or domain shift, and needs to be carefully considered and tested in future studies and DLSs that are slated for clinical deployment.
Results also show that the proposed AI-based augmentation method may offer a path for debiasing diagnostic DLSs in some situations.

When looking at the situation from the perspective of other metrics including sensitivity and specificity: the debiased DLS was able to achieve parity for specificity as well. The debiased diagnostic DLS has specificity of 74.0% for white and 84.0% for blacks. The debiased DLS was able to significantly improve sensitivity for blacks (equal to 35% for the baseline DLS vs. 56% for the debiased DLS), but parity was not close (sensitivity was 81% for whites for the debiased DLS).

Several points should be considered here: There is first an obvious consideration here which makes it hard to reason on sensitivity and specificity since those correspond to different operating points in the ROC curve. There is also -- as reported by [Mehrabi2019] and others AI bias studies beyond healthcare -- the fact that AI bias has to be measured vis-a-vis one specific criterion (here accuracy), and parity cannot be achieved with regard to all or even a few criteria simultaneously.

It is important to note that we make no claims in this paper about the original Kaggle-EyePACS being biased, domain shifted or unbalanced. We want to emphasize it is not: The original EyePACS does represent racial diversity among those with retinal disease as efforts were made to include all races, not just black and white, into the dataset (including Asian, Indian subcontinent, and American indigenous descent retinas). Diversity of EyePACS has been one of its important attributes and this dataset has been used by numerous AI and retinal disease groups for experiments for this very reason. In discussions that occurred after our experiments were done, with a principal that helped lead the design of the Kaggle-EyePACS dataset, we were made aware of
statistics that clearly demonstrate that care was taken that this dataset be reflective of
diversity for races and ethnicities, including self-declared African American, Asian,
Caucasians, and other, including multiracial individuals. Based on those discussions: the
dataset contains approximately 5.4% of black individuals and about about 1.3% of
diseased black individuals. Therefore the proportion of subjects labeled as black have a
higher proportion of diseased individuals than the population as a whole (about 23% in
the dataset). Note that in this study we have used an experiment where we created a
novel scenario of domain shift by altering the original Kaggle-EyePACS dataset, which
we altered to fit this scenario, where data imbalance and domain shift arises by
disallowing the classifier from having access to diseased/black individuals in training --
but tested on data that did include this subpopulation.

The type of distributional imbalance we considered would seem to be different from
having assumed a few individuals present rather than none at all for a given
subpopulation (diseased black). That scenario should be more akin to a few-shot
scenario, which we may consider in the future, and have also considered in another
study but for a different situation [Burlina2020]. Another potential challenge arises in our
study, in that we did not have access to the original race or ethnicity labels. Using those
labels (which were not public) is another potential avenue for future endeavors if the
ground truth labels for race are made available. Also, even when the ground truth for
race labels become available, additional challenges still exist due to the nature of ‘self-
declaration’ by individuals for their ethnic and race ancestry. In sum, the problem of bias
has many different aspects that likely should be considered, and only one specific facet
was studied here.
Many DLSs that have shown the ability for retinal diagnostics tasks with human level performance. In some cases, some DLSs have also used a preponderance of non-diseased individuals, or preponderance of individuals of a given race. These data can match the demographic makeup of a specific region or country and can be shown to work well (i.e. with regard to metrics such as accuracy, AUC, etc..) when the trained and tested on identical data distributions. However, this success may still mask the fact that when broken down per protected factors, such as race or age, the DLSs still did not achieve equal accuracy objectives, or when faced with distributional shift, these methods’ performance degraded. In sum, and to our knowledge, the problem of bias, and more broadly of generalization and distributional shift should be given more attention in retinal AI studies. We hope that the method presented here and other methods in [Mehrabi2019, Zhang2018] can motivate future investigations to address those issues.

While we considered race, there are other forms of bias that exist such as age or gender. For example, when considering macular degeneration and an epidemiologic study like AREDS, then few participants were of age over 85, and it would be of interest to investigate if the AI exhibits similar disparity of accuracy for diagnoses in people over age 85, when only a few people over the age of 85 were included in the AI training set. This is left for a future study.

While our method was successful at debiasing and may help in other cases, it is easy to envision cases where it may hardly be applicable. There are bias situations that may not be well addressed by this approach, and may need other solutions, including sampling additional real training data. This is the case for example where additional real data may be needed to include the biological variability that may exist with each disease.
depending on the protected factor, and which may not be captured by traveling on the latent space of generative models. For example, there may be different presentations of diseases in Asian vs white vs black populations, or image acquisition conditions may have variations depending on the protected population, different refractive errors affecting optic nerve appearances in the setting of pathologic myopia, or different media opacity across various ages that may compromise our method.

Also, while the end point in our study was fairness via equal performance as measured via accuracy, a question remains as to how to address other specific criteria such as parity of metrics like F1 and AUC or other definitions of fairness. A future path of investigation we are currently pursuing to achieve fairness, is via the need for equal accuracy (or any other metric like F1 or Cohen’s Kappa), and that can be built directly into the loss function of the DLS or using disentangling generative methods. However balancing loss functions with various objectives and attribute disentangling models are often challenging to tackle, therefore the method presented herein confers some advantages for example because of its relative simplicity.

**CONCLUSION**

When considering retinal diagnostics of DR, we demonstrated that situations of data imbalance and domain shift can affect the performance of AI diagnostics algorithms applied to a task such as DR referable vs not referable images and result in AI bias.

Our results suggest the benefit of certain generative methods that allow specific control of certain factors of variation to allow the augmentation of the diagnostic DLS and obtain
parity with respect to accuracy.
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Figure 1: Workings of a proposed generative method to generate new images with only specific alteration of some attributes while keeping other attributes unchanged. Specifically, images in (a) demonstrate altering only the attribute ‘diseased’ which allows to create a diseased retina with DR lesions (right image) from a healthy retina (left image). The top retina is one of a white individual, and the bottom retina is one of a black individual. Note how the vasculature remains unchanged as well as the amount of melanin level. Conversely, images in (b) demonstrate altering the amount of melanin level but preserving the lesions as well as the vasculature factors of variations. This method is used specifically in this study to generate images that may be missing from the training set (i.e. of diseased black individuals).
### Table 1:

|        | HW  | DW  | HB  | DB  | Total | H   | D   | W   | B   |
|--------|-----|-----|-----|-----|-------|-----|-----|-----|-----|
| Train  | 5330| 10660| 5330| 0   | 21320 | 10660| 10660| 15990| 5330|
| Baseline |     |      |     |     |       |     |     |     |     |
| Train  | 10660*| 10660| 10660*| 10660**| 42640 | 21320| 21320| 21320| 21320|
| (Debiased) |     |      |      |     |       |     |     |     |     |
| Test   | 100 | 100 | 100 | 100 | 400  | 200 | 200 | 200 | 200 |

Table 1: characteristic table showing the number of samples used for each population including: HW (healthy whites), DW (diseased whites), HB (healthy blacks), DB (diseased blacks), and H (total healthy), D (total diseased), W (total whites) and B (total blacks), and broken down by rows corresponding to the trainning (including training and validation) for both baseline and debiased DLS, as well as test datasets. * denotes that these are oversampled by 2 to maintain the balance of healthy and diseased factors. ** denotes that these numbers are synthetic images.
### Testing dataset (400 images, see Table 2):

| Metric                  | Baseline DLS | Debiased DLS |
|-------------------------|--------------|--------------|
| Accuracy (Overall)      | 66.75 (4.62) [62.13, 71.37] | 73.75 (4.31) [69.44, 78.06] |
| Accuracy (W)            | 73.0 (6.15) [66.85, 79.15] | 77.5 (5.79) [71.71, 83.29] |
| Accuracy (B)            | 60.5 (6.78) [53.72, 67.28] | 70.0 (6.35) [63.65, 76.35] |
| Specificity (W)         | 61.0 (9.56) [51.44, 70.56] | 74.0 (8.6) [65.4, 82.6] |
| Sensitivity (W)         | 85.0 (7.0) [78.0, 92.0] | 81.0 (7.69) [73.31, 88.69] |
| Specificity (B)         | 86.0 (6.8) [79.2, 92.8] | 84.0 (7.19) [76.81, 91.19] |
| Sensitivity (B)         | 35.0 (9.35) [25.65, 44.35] | 56.0 (9.73) [46.27, 65.73] |

### Larger Leftover Set black individuals with DR (6291 images):

| Metric                  | Baseline DLS | Debiased DLS |
|-------------------------|--------------|--------------|
| Sensitivity (B) (= accuracy) | 38.48 (1.2) [37.28, 39.68] | 57.86 (1.22) [56.64, 59.08] |

**Table 2:** Comparing the performance of the baseline DLS (left column) and debiased DLS (right column) diagnostic DLS for metrics including accuracy, specificity, sensitivity and for black individuals (marked as ‘B’) and white individuals (marked as ‘W’), also showing 95% error margins in parenthesis and 95% confidence intervals in brackets.
Figure 2: This figure details the flow chart for the debiasing algorithm pipeline.