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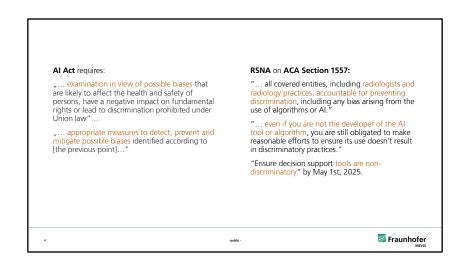
Bias has been observed in all areas of medical image analysis: Chest X-Ray analysis (most of the existing literature is on this), MRI, CT, dermatology, histopathology, classification/segmentation, etc.

Most bias analyses cover biases w.r.t. sex/gender, race/ethnicity, sometimes age. All other characteristics much less studied.

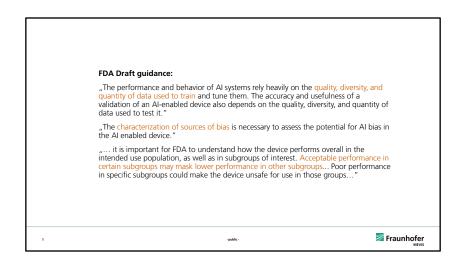
Many initiatives + guidelines to raise awareness and propose best practices.

STANDING Together: large consensus effort & detailed guideline, published in & endorsed by The Lancet in Jan 2025.

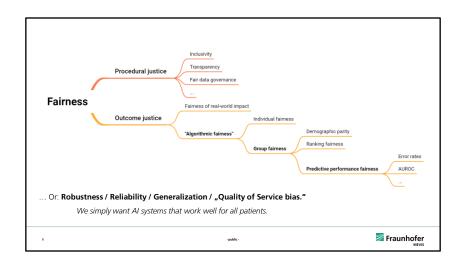
FAIMI: That's us! © Independent academic initiative, now also a MICCAI SIG. We organize events / workshops / special issues etc. Sign up for our newsletter (on faimi.org)!



Al Act: https://eur-lex.europa.eu/eli/reg/2024/1689/oj RSNA on ACA Section 1557: https://www.rsna.org/-/media/files/rsna/practice-tools/faq-for-section-1557-aca.pdf



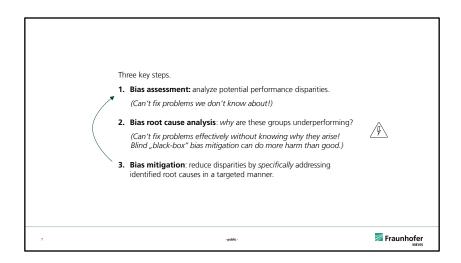
https://www.fda.gov/media/184856/download Document issued on January 7, 2025. (There was a public comment period; not entirely sure what happened to this.)



Fairness/ethics encompass many very different ethical considerations, many of which are relevant to the medical imaging context. See e.g. D'Antonoli (2020), Ethical considerations for artificial intelligence: an overview of the current radiology landscape, https://pmc.ncbi.nlm.nih.gov/articles/PMC7490024/.

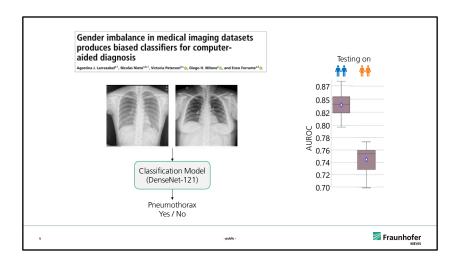
Here, we will focus on one very particular aspect: the "simple" question of whether models work equally well in different groups of patients, or whether there are groups for which models systematically underperform.

We will not care so much about differences between particular performance metrics (accuracy vs. sensitivity vs. specificity vs. AUROC vs. ...). This is, again, not to say that the choice of a clinically meaningful and appropriate target metric is not important – it is! – but rather that all our messages in the following will largely focus on simply **building better models**. This should translate into improvements across most, if not all, such metrics.



Our focus will mostly be on step 2 here (root causes), but we will also briefly talk about the other two steps.

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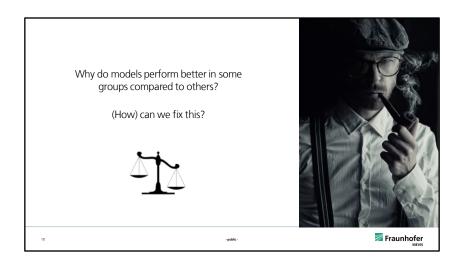
Pneumothorax: gas within the pleural space.

Tips to help to find pneumothoraces include:

- the lung edge: you should not be able to see the lung edge if you can, the region peripherally is likely a pneumothorax.
- absence of vessels: the lung should have vessels running through it, these are white branching structures on the x-ray. If there are no vessels, there may be a pneumothorax.
- I am to this day incapable of seeing a pneumothorax on an x-ray.

This is the gender-balanced case on the NIH dataset in the mentioned paper.

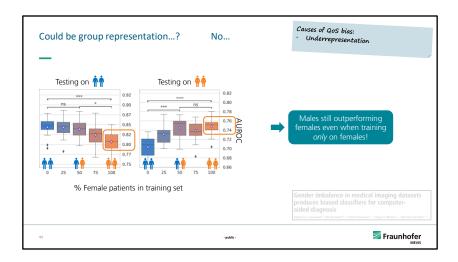
Larrazabal et al. (2020), Gender imbalance in medical imaging datasets produces biased classifiers for computer-aided diagnosis, https://www.pnas.org/doi/10.1073/pnas.1919012117.



Finding the root causes of bias can involve quite a lot of detective work! It's often highly nontrivial to uncover the source of observed performance disparities, as we will see in the following.

However, we need to find out what is *causing* a performance disparity in order to be able to say:

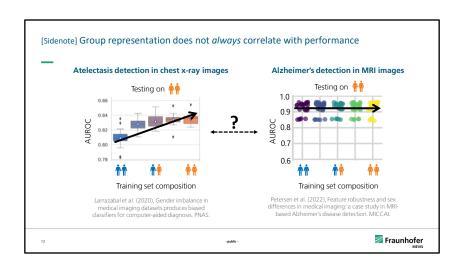
- 1. Whether or how the disparity can be fixed, and
- 2. Whether the observed disparity is indeed unfair. (There could be valid reasons for performance disparities, for instance if a task is just intrinsically much harder in one group for biological reasons.)



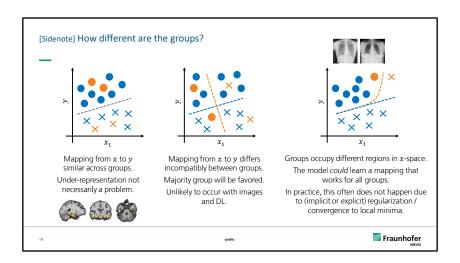
The first hypothesis for the previously shown performance disparity is often: were women under-represented in the training set?

This is not the case; that model was trained on a gender-balanced dataset. In fact, as we can see here, the model still performs better on men compared to women even when training *only* on female patients! (Note the different y axes in the two graphs.)

So: while under-representation is often a cause of under-performance (and the results in that paper very nicely show the effect of different group representations), this is clearly not the explanation for the observed performance gap.



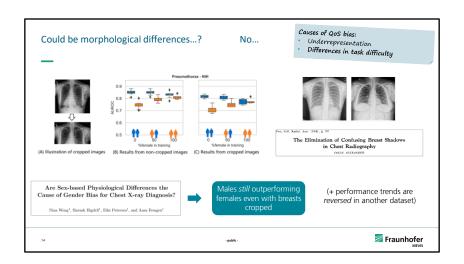
In a separate study on brain MRI-based AD classification (using the ADNI datasets), we found *no* effect of training dataset composition (in terms of gender representation) on model performance in both genders. Why is that? What is the difference between the two cases?



x: images, y: target labels, e.g. disease labels.

Simplified illustrative 2D illustration to understand the core issues; in reality the x-space (image space) is of course very high-dimensional.

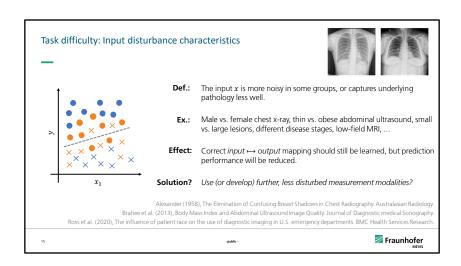
Note: these are *hypotheses* for what might be going on in the CXR / AD cases presented previously.



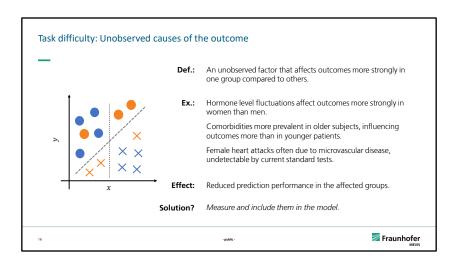
Breast shadows as an obstacle are known issue since at least 1958... => Maybe the observed performance differences are simply because breast shadows are obscuring regions of the lungs important for diagnosis, making the classification task intrinsically harder in women?

Apparently not, but it was another plausible hypothesis.

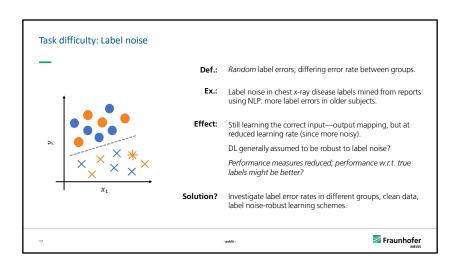
Morphological differences do not *have* to translate into differing task difficulty: here, for example, they did not.



Potential reason #1 for differences in task difficulty. In the plot, colors correspond to e.g. gender, dots/crosses to diagnosis.



Potential reason #2 for differences in task difficulty. Apart from the diagonal dividing line between disease or not, there is a second trend: the female are "high on disease" for larger x compared to men.



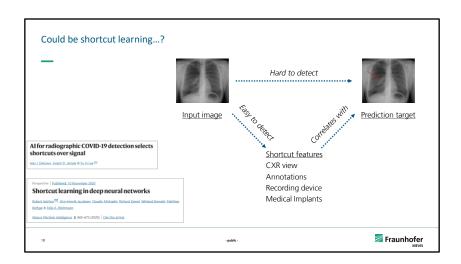
Potential reason #3 for differences in task difficulty.

See e.g.

Zhang et al. (2022), Improving the Fairness of Chest X-ray Classifiers. PMLR / CHIL.

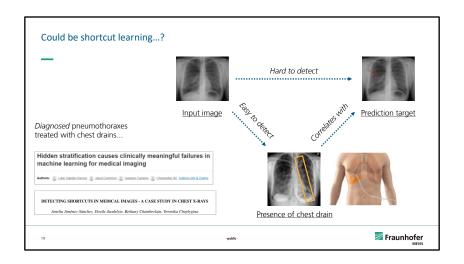
Frenay and Verleysen (2014), Classification in the Presence of Label Noise: A Survey. IEEE TNNLS.

Rolnick et al. (2017), Deep Learning is Robust to Massive Label Noise. Santomartino et al. (2024), Evaluating the Performance and Bias of Natural Language Processing Tools in Labeling Chest Radiograph Reports, https://pubs.rsna.org/doi/10.1148/radiol.232746



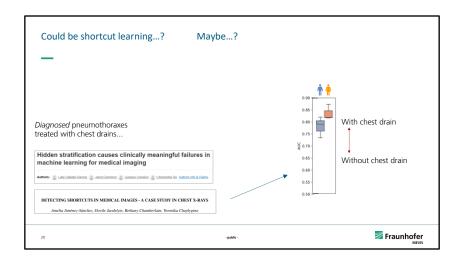
Back to our chest x-ray gender performance disparity example...

Shortcut learning is also an issue in segmentation, not only in classification: Lin et al. (2024), Shortcut Learning in Medical Image Segmentation, https://link.springer.com/chapter/10.1007/978-3-031-72111-3_59. The problem appears less severe there, however.



Chest drain visualization source Chest Tubes and Indwelling Pleural Catheters | Thoracic Key

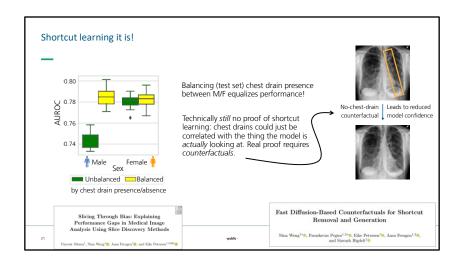
It had actually been reported earlier (in 2020, see the excellent Oakden-Rayner paper) that CXR pneumothorax diagnosis models are prone to picking up on the chest drain shortcut. (We did not know this when we started working on this, and the vast majority of the academic CXR diagnosis literature also seems to be blissfully unaware of this issue to this day.)



The figure is from the second paper (Jiménez-Sanchez et al.) and is on the NIH dataset (like everything until here).

When we split performance estimates by sex/gender and the presence/absence of a chest drain in the image, we see opposite disparities between the two genders/sexes!

Does this explain our observed gender performance disparity?



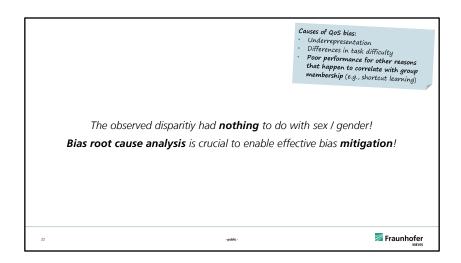
If we balance the test set such that chest drain prevalence is equal in the M/F groups, the previously observed performance disparities disappear!*

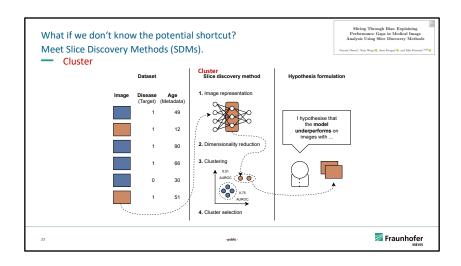
Thus, it appears that it is in fact the chest drain shortcut – which is "working differently well" in the two groups – that is causing these observed M/F performance disparities.

Additional evidence in the ECCV 2024 paper mentioned on the right (see https://fastdime.compute.dtu.dk/ or https://arxiv.org/abs/2312.14223): Artificially adding/removing chest drains from images significantly changes model confidence w.r.t. pneumothorax.

Olesen et al., Slicing Through Bias: Explaining Performance Gaps in Medical Image Analysis using Slice Discovery Methods, https://arxiv.org/abs/2406.12142

* These results are on the CheXpert dataset, where M/F performance disparities are reversed compared to the NIH dataset we were looking at, so far.





What if you don't know already what might be causing the issue? E.g., if we did not already know about the potential chest drain shortcut, how can we find our about such issues?

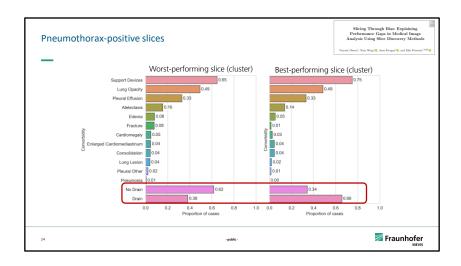
There is a branch of literature (under various different names such as "Automatic Slice Discovery", "Blind Spot Discovery", "Failure Mode Detection", …) that treats this problem.

(The nomenclature is a bit confusing especially in the medical imaging context, unfortunately – "slice" here does *not* refer to a 2D slice of a 3D image; it refers to a "slice" of data \approx a cluster.)

These methods can be summarized quite simply as:

- 1. Cluster images / volumes based on similarity.
- 2. Find clusters that are performing unexpectedly well/poorly. (-- statistical significance testing, multiple hypothesis corrections, ...)
- 3. Investigate these manually (visually = look at samples from them) or use multimodal models to automatically suggest captions for the different clusters. Try to find the defining feature of these clusters, thereby generating hypothesis regarding potential causes of good/poor performance.
- 4. Investigate these generated hypotheses further, such as what we did for the chest drain case on the previous slides. (Specific analyses will be hypothesis- and application-specific.)

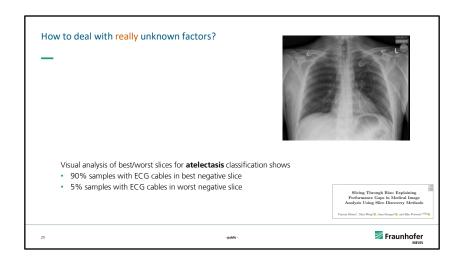
Cf. Olesen et al., Slicing Through Bias: Explaining Performance Gaps in Medical Image Analysis using Slice Discovery Methods, https://arxiv.org/abs/2406.12142



In our case, we already knew about the chest drain shortcut. But let's imagine we didn't – would our slice discovery method find this?

Indeed, we find that the major difference between the best and worst discovered (pneumothorax-positive) clusters/slices is the prevalence of chest drains.

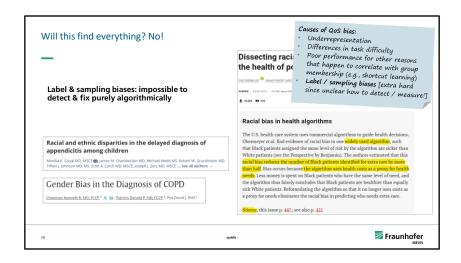
However, to generate the above plot, we already need chest drain labels / metadata! **What if we don't have labels for the potential shortcut factor?**



Here, we had such a case: we really did not know about this shortcut – and, to our knowledge, at least, this had also not been described before.

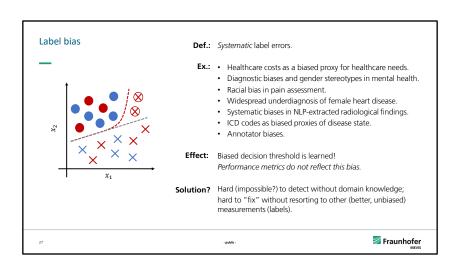
Based on our slice discovery method, we found several clusters that performed very differently w.r.t. atelectasis classification. Initial visual inspection of the resulting clusters indicated that a differentiating factor might be the presence/absence of ECG cables.

We then manually labeled only the images in the best/worst clusters in terms of presence/absence of ECG cables, and found the shown **very strong differences in ECG cable prevalence**, suggesting another instance of shortcut learning.



The Paper on the right is Obermeyer et al. (2019), Dissecting racial bias in an algorithm used to manage the health of population, Science.

- Algorithm predicts risk and suggests care
- Observation: At same disease state, black patients are assessed to have lower risk than white, receive less care
- Cause: Less money is spent on black patients, but care cost is used as a proxy (label) for need. (Bias comes from "trained practice" to under-spend on Black population)



See e.g.

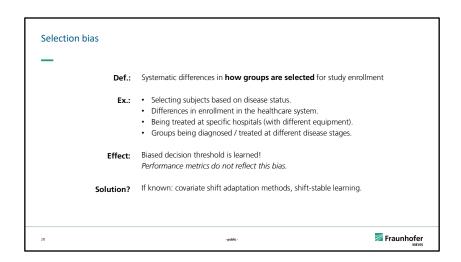
Obermeyer et al. (2019), Dissecting Racial Bias in an Algorithm Used to Manage the Health of Populations. Science.

Sigmon et al. (2005), Gender Differences in Self-Reports of Depression: The Response Bias Hypothesis Revisited. Sex Roles.

Hoffman et al. (2016), Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites. PNAS.

Wang et al. (2021), Fair Classification with Group-Dependent Label Noise. ACM FaccT.

Santomartino et al. (2024), Evaluating the Performance and Bias of Natural Language Processing Tools in Labeling Chest Radiograph Reports: https://doi.org/10.1148/radiol.232746

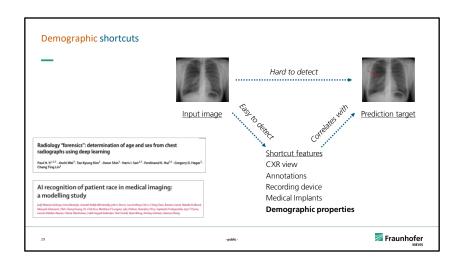


See e.g.

Ellenberg (1994), Selection bias in observational and experimental studies. Statistics in Medicine.

Natanson et al. (1998), The sirens' songs of confirmatory sepsis trials: selection bias and sampling error. Critical Care Medicine.

Zadrozny (2004), Learning and evaluating classifiers under sample selection bias. ICML. Subbaswamy and Saria (2019), From development to deployment: dataset shift, causality, and shift-stable models in health Al. Biostatistics.



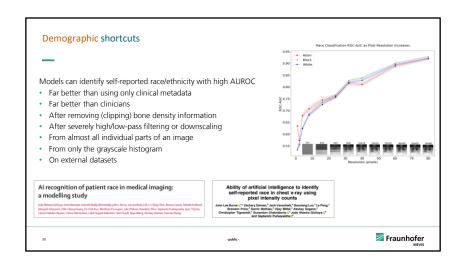
Most/all demographic patient properties can be reconstructed with very high accuracy and robustness from medical images. This raises the potential for models to exploit these potential shortcut features, i.e., learning that membership in a certain group increases or decreases the likelihood of a certain target (disease) label [0].

This is akin to a logistic regression risk prediction model that uses demographic properties as input variables [1,2]

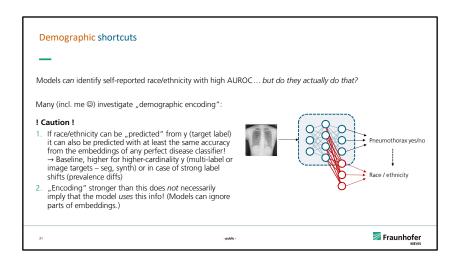
It is also arguably an instance of direct discrimination [3-5].

- [0] Banerjee et al. (2023), "Shortcuts" Causing Bias in Radiology Artificial Intelligence: Causes, Evaluation, and Mitigation, https://doi.org/10.1016/j.jacr.2023.06.025
- [1] Diao et al. (2024), Implications of Race Adjustment in Lung-Function Equations, NEJM
- [2] Zink et al. (2024), Race adjustments in clinical algorithms can help correct for racial disparities in data quality, PNAS
- [3] Deck et al. (2024), Implications of the AI Act for Non-Discrimination Law and Algorithmic Fairness, https://arxiv.org/abs/2403.20089
- [4] Gerards and Borgesius (2021), Protected Grounds and the System of Non-Discrimination Law in the Context of Algorithmic Decision-Making and Artificial Intelligence, Colorado Technology Law Journal
- [5] Wachter et al. (2021), Bias Preservation in Machine Learning: The Legality of Fairness

Metrics under EU Non-Discrimination Law, West Virginia Law Review [I am not a lawyer...]

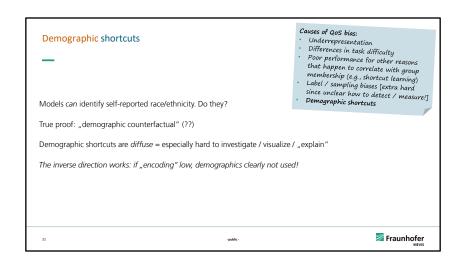


When looking at the plot, note that the inset images aren't at the right x axis positions. This makes you think the 1,2x2,4x4 already work, but they almost don't.



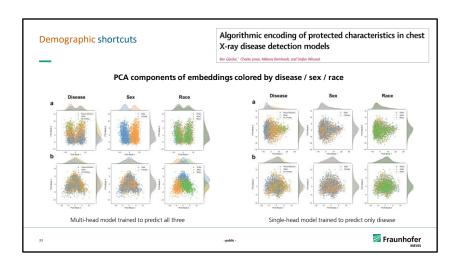
See e.g.

- Petersen et al., "Are demographically invariant models and representations in medical imaging fair?", https://arxiv.org/abs/2305.01397
- Brown et al., "Detecting shortcut learning for fair medical AI using shortcut testing", https://www.nature.com/articles/s41467-023-39902-7
- Glocker et al., "Algorithmic encoding of protected characteristics in chest X-ray disease detection models", https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(23)00032-4 ... among many others.



For a discussion on demographic counterfactuals + pointers to relevant literature, cf. Petersen et al., "Are demographically invariant models and representations in medical imaging fair?", https://arxiv.org/abs/2305.01397

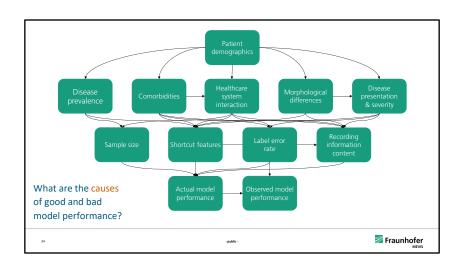
For the fact that shortcuts are diffuse, cf. Gichoya et al., Al Recognition of patient race ...



Empirically, there is actually not so much encoding (this is what the right figure shows) compared to how strongly models *could* encode demographics (this is what the left figure shows)!

I.e., for standard task-specific classifiers, we are clearly not in the ">90% protected attribute classification ability" space (which would be possible).

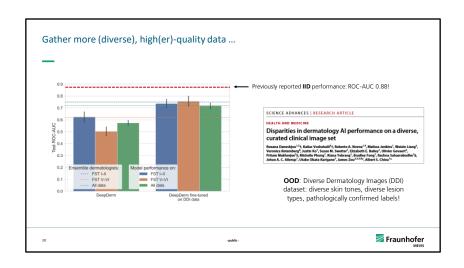
That means: the risk is lower than what we may have feared, but it is still non-zero. Do such models exploit demographic properties to *some* degree? We don't really know, and I have not seen an approach to investigate this that I personally find very convincing.



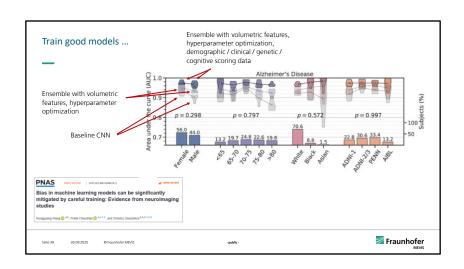
Many things can cause good or bad model performance in a demographic group. Figuring out the relevant cause for an observed disparity is often non-trivial, but it is necessary.

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- Diversity matters across *all* dimensions: demographic representation, technical acquisition parameters, disease presentations & subtypes, etc.
- "Higher-quality data" primarily means: (Diversity and) higher-quality target labels / outcomes!
- Clinicians often believe that high-quality image acqusition is of importance, but the opposite is true: models need to see representative real-world images with all the noise, potential confounders, acqusition errors etc. that will inevitably come up in real-world recordings.
- Remark for the plot: The "previous performance" is on IID data; we are here concerned with the within-OOD-performance comparison.



Plot: **Solid colors**: Ensemble using all data. **Translucent Color**: Only images. **Translucent Gray**: Baseline model. **Conclusion:** Preprocessing/HPT improves performance, but only diverse data achieves level performance in subgroups. [1]

Similar results in our MICCAI 2022 paper: https://link.springer.com/chapter/10.1007/978-3-031-16431-6_9

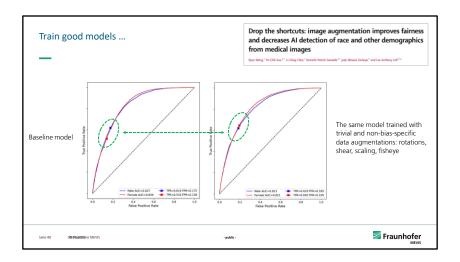
"Normalize away" any **unimportant** group differences wherever possible. (Harmonization, standardization, registration, removal of potential visual confounders, etc.) [2]

Personal, highly unscientific guesstimate: >50% of bias findings reported in the literature are simply a result of models being poorly trained, highly non-robust, and just generally not working very well.

[1] Excerpt from the figure caption: "For Alzheimer's disease, schizophrenia, and autism spectrum disorder, using data from different studies (e.g., ADNI-1, ADNI-2/3, PENN, and AIBL for Alzheimer's disease), we built an ensemble that uses **data from multiple sources** (MR imaging features, demographic, clinical variables, genetic factors, and cognitive scores); (SI Appendix). This ensemble was trained using preprocessing and hyperparameter optimization discussed in Materials and Methods. We also trained an ensemble using **only imaging features**. Bar plots denote the size of the subgroup/study (%); in many cases,

there is a strong imbalance in the data. Violin plots denote the test AUC on **five different held-out subsets of data**. Solid colors indicate that models used all features, while translucent colors indicate that models were trained only on imaging features. Translucent gray denotes the AUC of a baseline deep network (without appropriate preprocessing and hyperparameter tuning). White dots denote the average AUC of each subgroup/study. For the ensemble trained on multisource data, the P-values shown in the figure indicate that we cannot reject the null hypothesis that the AUC for different subgroups has the same mean (at significance level < 0.01). This is not the case for the baseline deep network.

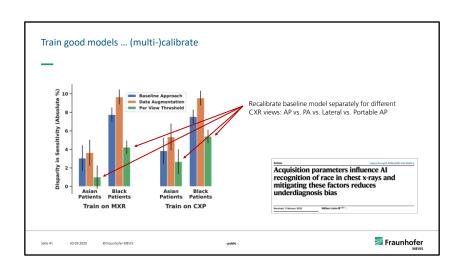
[2] Seoni et al. (2024), All you need is data preparation: A systematic review of image harmonization techniques in Multi-center/device studies for medical support systems, https://doi.org/10.1016/j.cmpb.2024.108200.



This is edema detection from CXR.

In the baseline model, men/women end up at very different TPR/FPR operating points in ROC space at the same decision threshold.

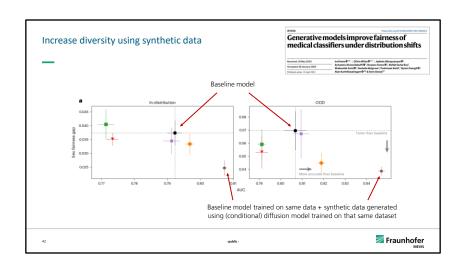
In the model trained with trivial data augmentations, the resulting operating points are very similar.



Ensure robustness to technical variations: scanner type, field strength, view position, lighting conditions, imaging protocol, potential confounders such as medical implants, ...

Note: Data augmentation worsens the performance, while here the thresholds help a lot. Neither use any balancing or "fairness" methods, don't even need to know sensitive attributes at train time.

Note that here, lower bars are better.



This is just another form of data augmentation, which appears crucial for achieving robustness, but can give very different results in general.

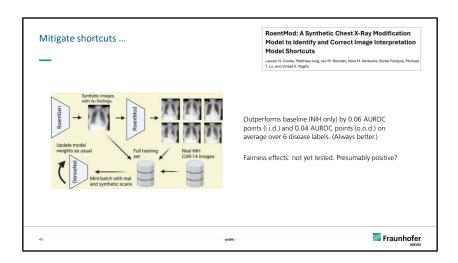
Plot: Average AUC values across several disease labels on CheXpert (In-distribution, left) and ChestX-ray14 (OOD, right). Excellent paper with convincing results in other domains (Histopathology, Dermatology).

This is again **not** a **specific bias intervention**! The generated synthetic images are only conditioned on the disease label, *not* on demographic group membership.

Also: various works on skin color augmentations in dermatology AI [1,2]

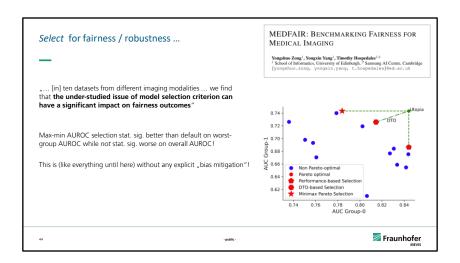
- [1] Rezk et al. (2022), Improving Skin Color Diversity in Cancer Detection: Deep Learning Approach, https://derma.jmir.org/2022/3/e39143/
- [2] Pakzad et al. (2023), CIRCLe: Color Invariant Representation Learning for Unbiased Classification of Skin Lesions, https://doi.org/10.1007/978-3-031-25069-9_14

Another very promising preprint mentioned in Prof. Langlotz' keynote: Improving Performance, Robustness, and Fairness of Radiographic Al Models with Finely-Controllable Synthetic Data | Abstract

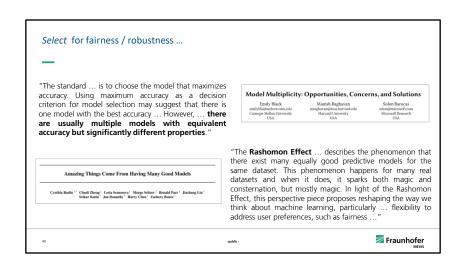


RoentMod: A Synthetic Chest X-Ray Modification Model to Identify and Correct Image Interpretation Model Shortcuts | PDF

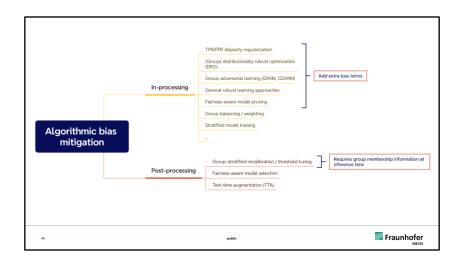
This is stable diffusion text-to-image (RoentGen) followed by image-to-image (RoentMod).



"Pareto optimal" = max min AUROC



Model multiplicity is an emerging and very active field with wide implications for robustness, fairness, interpretability, ...



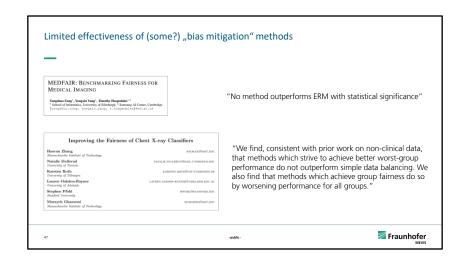
Many studies find that none of these consistently outperform standard (baseline) empirical risk minimization (ERM) in terms of resulting model fairness.

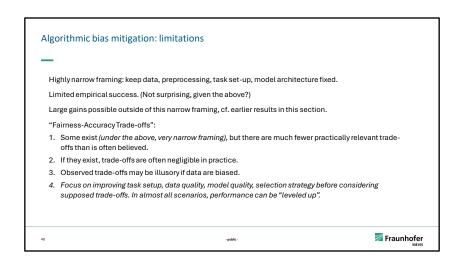
Personal opinion: I claim that this should *not* be what you spend most of your time on when dealing with potential bias issues. Focus on improving your data / preprocessing / augmentations / task set-up, "simply" training a good, robust model using standard ML best practices, and bias assessment first. *If* important issues remain, come back here.

The most impactful and practical strategy on this slide is probably fairness-aware *model* selection: simply select the model with the best worst-group performance [1,4]

For some overviews and implementations, see e.g.

- [1] Zong et al. (2023), MEDFAIR: BENCHMARKING FAIRNESS FOR MEDICAL IMAGING, https://arxiv.org/pdf/2210.01725
- [2] Yang et al. (2024), The limits of fair medical imaging Al in real-world generalization, https://www.nature.com/articles/s41591-024-03113-4
- [3] Hort et al. (2024), Bias Mitigation for Machine Learning Classifiers: A Comprehensive Survey, https://dl.acm.org/doi/full/10.1145/3631326 https://fairlearn.org/
- [4] Black et al. (2022), Model Multiplicity: Opportunities, Concerns, and Solutions, https://doi.org/10.1145/3531146.3533149.





On "limited empirical success", cf. e.g. Zong et al and Yang et al cited on the previous slide, + Zhang et al. (2022), Improving the Fairness of Chest X-ray Classifiers, https://proceedings.mlr.press/v174/zhang22a.html.

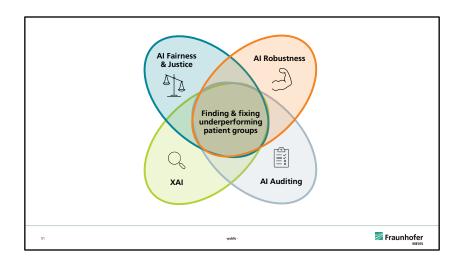
On "empirically negligible trade-offs", cf. Rodolfa et al. (2021), Empirical observation of negligible fairness—accuracy trade-offs in machine learning for public policy, https://www.nature.com/articles/s42256-021-00396-x.

On "fewer trade-offs than often believed", see e.g. Lazar Reich and Vijaykumar (2021), A Possibility in Algorithmic Fairness: Can Calibration and Equal Error Rates Be Reconciled? https://arxiv.org/abs/2002.07676 Wick et al. (2019), Unlocking Fairness: a Trade-off Revisited, https://proceedings.neurips.cc/paper/2019/hash/373e4c5d8edfa8b74fd4b6791d0cf6dc-Abstract.html

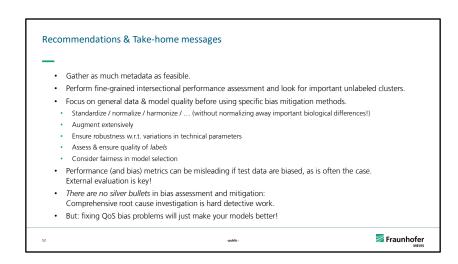
ii. iii. îv. v.	Introduction Causes of bias Case study 1 Coffee break (10:00 - 10:30) Case study 2 Bias mitigation	
	Conclusion & recommendations	
49	- public -	Fraunhofer MEVIS



There are no silver bullets in bias assessment and mitigation. Finding and fixing the causes of underperformance is a nontrivial endeavor but worthwhile.



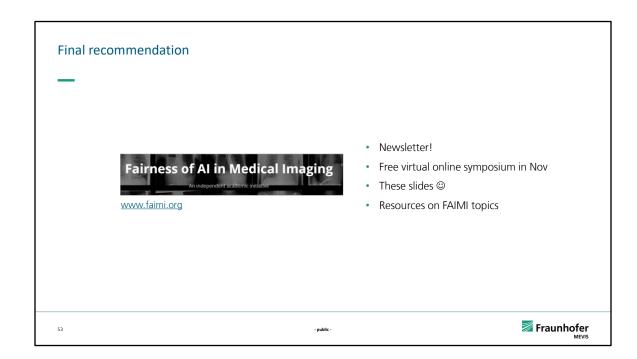
You *can* be interested in ethics, fairness, etc., but you don't have to be. This is still for you if you just want to build good models! Models that perform well on all patient groups are robust, trustworthy, and easier to get regulatory approval for.



Intersectional = considering sub-(sub-)groups, e.g., dark-skinned women aged 20-30y with comorbidity X.

In bias assessments, do not forget to:

- Quantify metric uncertainty: groups become small and performance measures thus more uncertain.
- Correct for multiple hypotheses testing: we are comparing many different groups.
- Correct for known confounding factors that might differ between demographic groups: this will help disentangle the *causes* of performance discrepancies.
- Also compare groups defined by non-demographic properties (e.g., technical acquisition parameters): this will help find other issues related to (a lack of) model robustness.





A reading list. Some that we referenced here, some that are good introductory reading material, some on more specific topics, some of our own prior work in this area.

Please reach out if looking for a reference on a particular topic!



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