

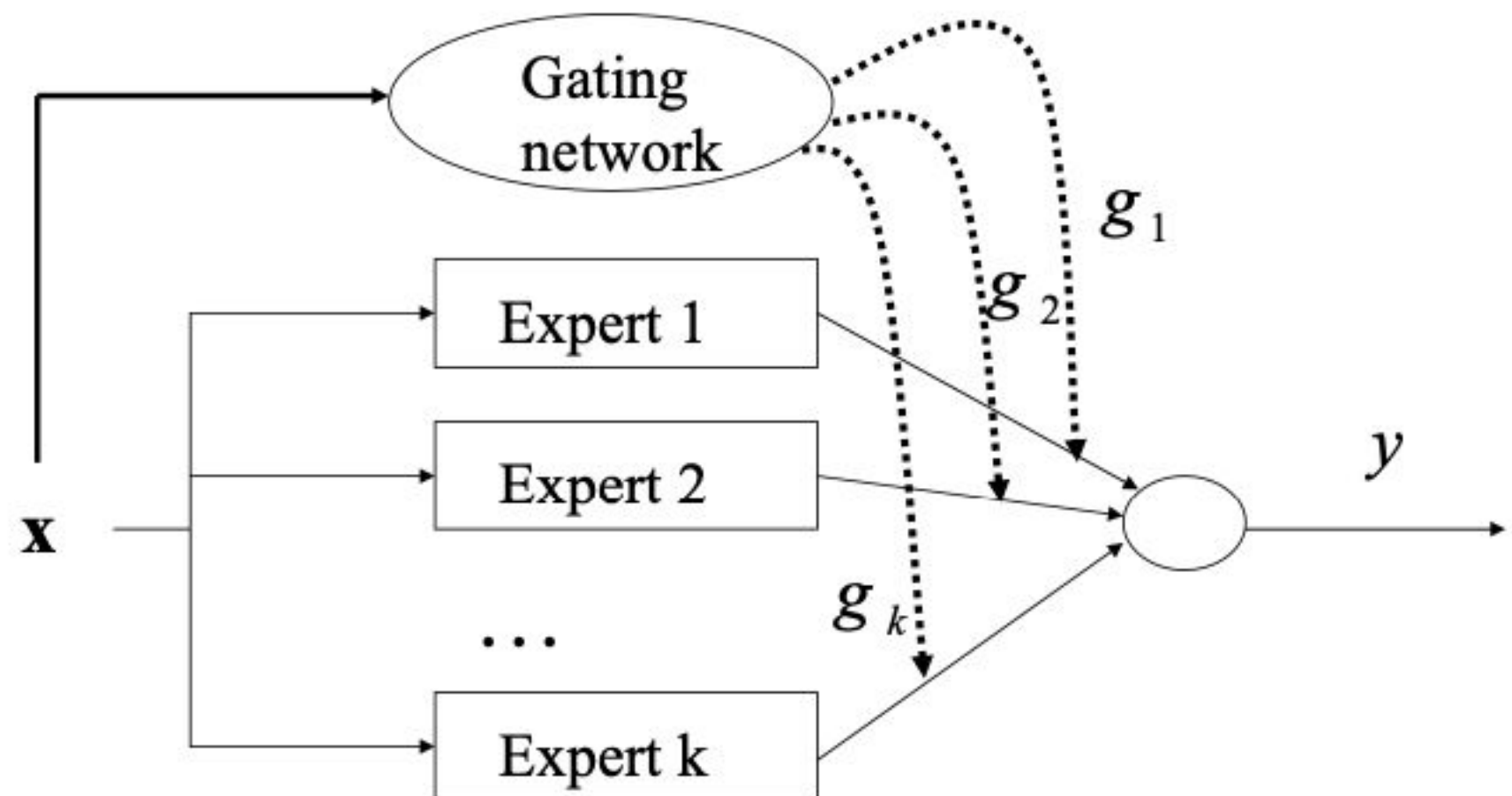
Learning to Defer & Uncertainty

(How to Combine Different Models)

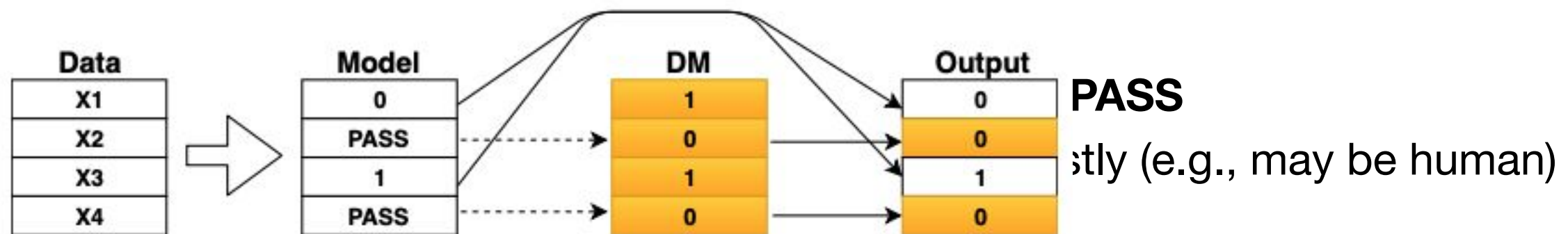


Mixture of Experts Models

- Define a variety of “experts” and a gating function
- Gating can be
 - “hard” if it chooses one expert (e.g., if different experts are good at different domains)
 - “soft” if it combines different experts’ outputs



Deferring



- Opaque
- Uses of first-stage model:
 - Flag difficult cases for review
 - Cull a large pool of cases
 - Audit DM for bias
 - ...

Model for Deferring

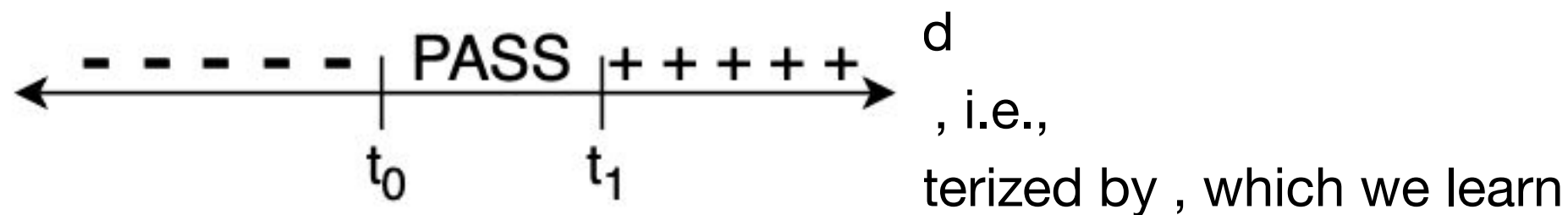
- Usual set-up:
 - inputs , output , additional inputs available only to DM
 - is another output of the model, 1 = PASS
- Model prediction:
- DM prediction: ; is “black box”
- System prediction:
- Defer decision:
- Learn max likelihood solution to , so **adapt** to

DECIDE

PASS

- Minimize negative log-likelihood
- where , the log probability of the label wrt prediction
- Like a mixture-of-experts learning problem, except that we cannot learn the parameters of DM

Learning a Deferral Model



- If we can assume that d alone (and M), then use two thresholds

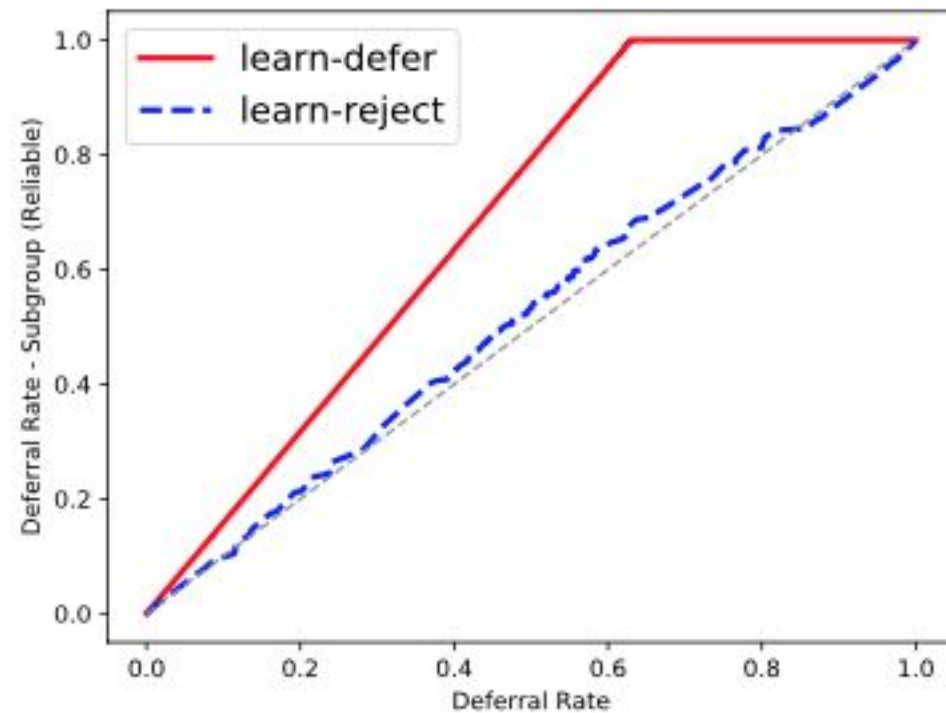
Train an ANN as a binary classifier with output in $[0, 1]$ and output according to its value compared to the thresholds.

- If d ; useful if DM depends heterogeneously on data, differently from M
 - Train by SGD, sampling d during training; + lots more hair!

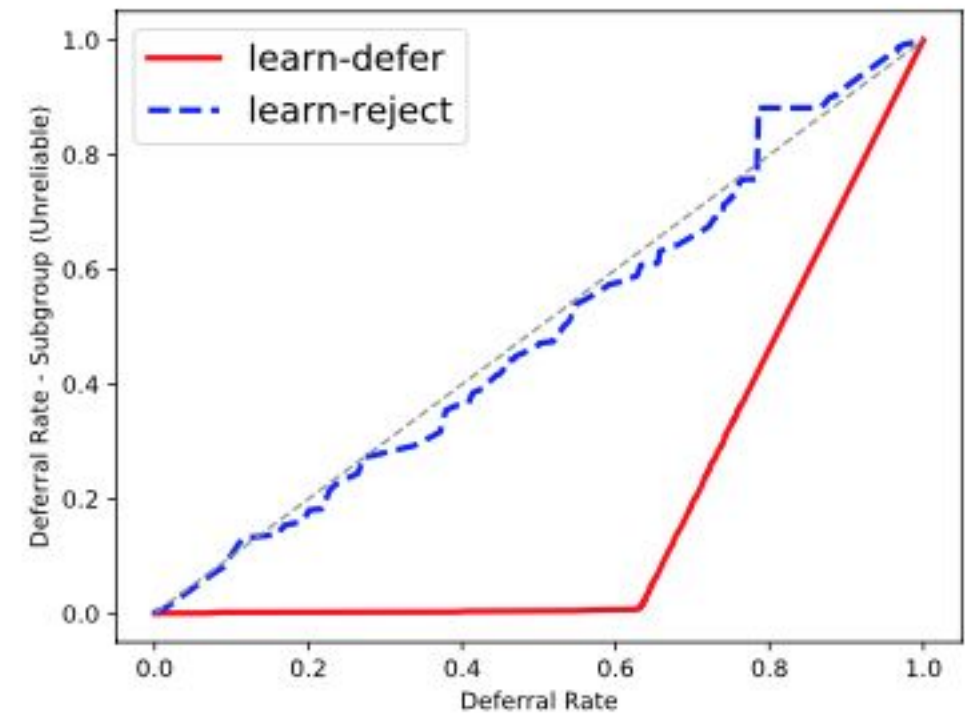
Fairness as Use Case vs. Inconsistency

- Many of their experiments study whether one can de-bias a black-box DM such as Compas
- Today, we focus on the case where the DM does well on some subset of cases but poorly on others
 - Example: Predict the patient's [Charlson Co-morbidity Index](https://www.mdcalc.com/charlson-comorbidity-index-cci) (*without discriminating by age*).
 - Probability of surviving for the next 10 years
 - De-biasing by age seems like an odd goal!
 - Extra information : patient's primary condition group
 - To exacerbate inconsistency, they post-hoc invert predictions on 30% of males
 - Must use model to learn to predict where DM is reliable or not

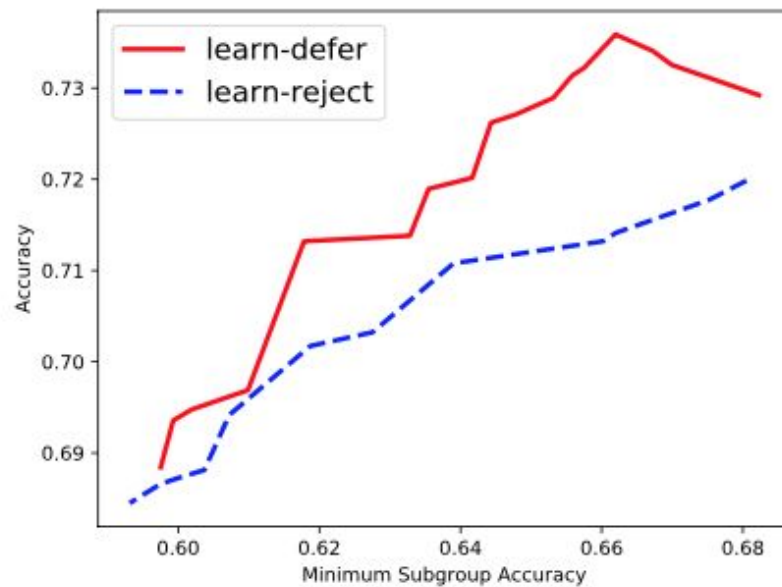
- On subset of cases where DM is reliable, system learns to defer frequently, but not on unreliable cases!



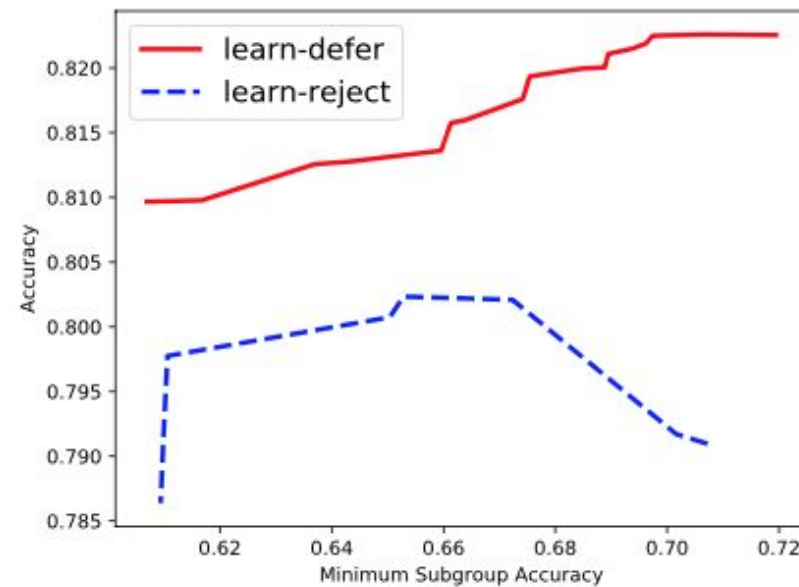
(c) Health, Reliable



(d) Health, Unreliable



(a) COMPAS dataset



(b) Health dataset

Figure 5: Each point is a single run in sweep over $\gamma_{reject}/\gamma_{defer}$. X-axis is the model’s lowest accuracy over 4 subgroups, defined by the cross product of binarized (sensitive attribute, unreliable attribute), which are (race, age) and (age, gender) for COMPAS and Health respectively. Y-axis is model accuracy. Only best Y-value for each X-value shown. Solid line is learning to defer; dashed line is rejection learning.

Second Opinion

- In medicine, patients facing a dangerous or expensive intervention often seek a second opinion
 - Not worthwhile for minor decisions, unless very easy/cheap
 - What are the relative expertise of the primary and secondary doctors?
 - How correlated are their opinions likely to be?
- Decision might be mapped to the “learning to defer” approach, except that we know very little about DM, since it might be almost anyone
 - Thus, difficult to train
- Recall that many studies find agreement by world-class experts only about 80% of the time.
- E.g., study of medical referrals; agreement on diagnosis

final = referral	0.12
refined	0.68
different	0.21

Examples of Referral vs. Final Diagnoses

TABLE 1 Examples of the comparison of referral and final diagnosis by category of agreement

Examples of referral and final diagnosis by categories		
	Referral Diagnosis	Final Diagnosis
Category 1 No change in diagnosis	Question fibromyalgia Low-back pain Feelings of anxiety Polymyalgia rheumatica Dizziness	Fibromyalgia Mechanical low-back pain-chronic Generalized anxiety Polymyalgia rheumatica Imbalance/vertigo
Category 2 Diagnosis better defined	Endocrine abnormalities Multiple constitutional symptoms over the last year Syncope Weakness Elevated PSA; spinal mass	Secondary adrenal insufficiency; suspect opioid endocrinopathy Acute CMV infection Syncope secondary to doxazosin Drug-induced rhabdomyolysis Metastatic prostate cancer to spine and lung
Category 3 Different diagnosis	Anemia Weight loss Body aches Weight loss and abdominal pain Fatigue	Autoimmune hepatitis Malignant lymphoma suggestive of Hodgkin lymphoma Acute myelogenous leukemia NSAID-induced gastropathy; irritable bowel syndrome Heart failure

Abbreviation: PSA, prostate-specific antigen; CMV, cytomegalovirus; NSAID, non-steroidal anti-inflammatory drug.

Disagreements Vary by Diagnostic Category

- “Findings from autopsies indicate that diagnostic errors contribute to approximately 10% of patient deaths and diagnostic errors account for 6% to 17% of adverse events in hospitals.”
- Mayo Clinic and its referring practices (!)

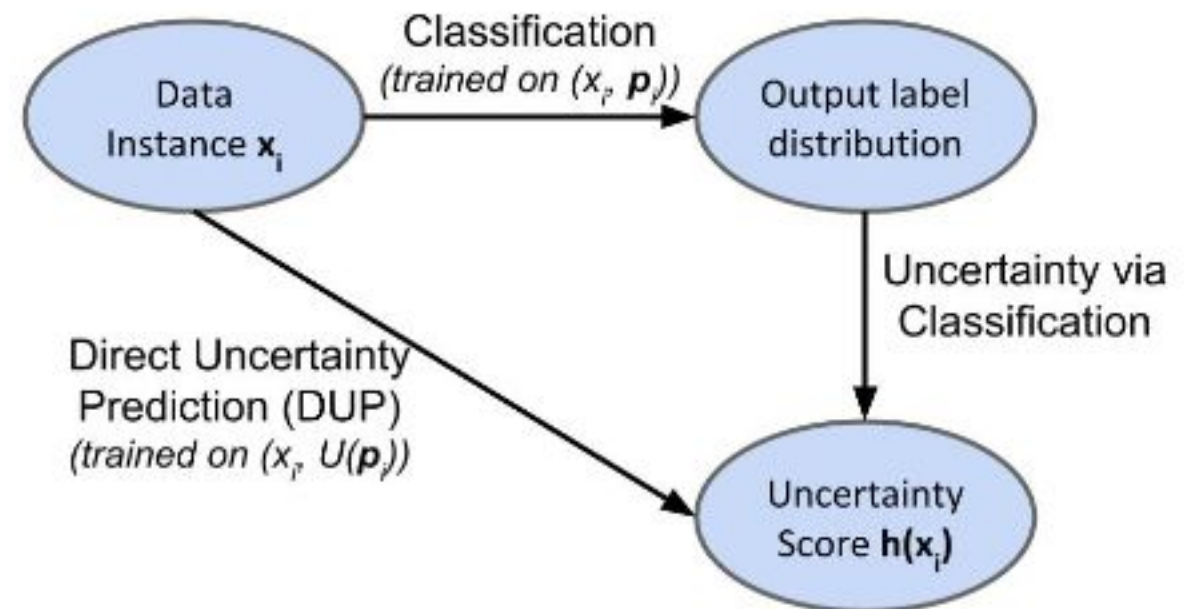
TABLE 2 Distribution of diagnostic comparisons within clinical classification system categories

Diagnostic comparisons by clinical classification system categories							
CCS Categories	Group 1 Same Dx	Group 2 Dx better defined	Group 3 Different Dx	Total	Percent Group 1	Percent Group 2	Percent Group 3
Musculoskeletal	7	42	12	61	11%	69%	20%
Signs and symptoms	8	24	7	39	21%	62%	18%
Nervous	8	19	4	31	26%	61%	13%
Circulatory	1	19	6	26	4%	73%	23%
Endocrine	1	20	3	24	4%	83%	13%
Respiratory	0	16	8	24	0%	67%	33%
Digestive	2	18	2	22	9%	82%	9%
Other(categories less than n = 20)	7	32	18	57	12%	56%	32%
Total	34	190	60	284	12%	67%	21%

Abbreviation: CCS, Clinical Classification Software.

Possible Approaches to 2nd Opinion Decision

- Uncertainty via Classification (UVC)
 - Train a classification model
 - Post-process its output distribution to estimate uncertainty
- Direct Uncertainty Prediction (DUP)
 - Train a different prediction model to estimate uncertainty directly from case inputs
- Which is better?
 - What is your intuition? Why?
 - What was mine?



How to Train

- Setup
 - Cases
 - multiple labels by experts,
 - represents uncertainty in the prediction of experts
- UVC
 - Classifier gives distribution over labels
 - In absence of expert judgment, distribution of (e.g., variance) can be used as estimate of uncertainty,
- DUP
 - Assume that the are all drawn from a set of possible *grades*, .
 - Empirical histogram is
 - Target uncertainty function from this empirical histogram

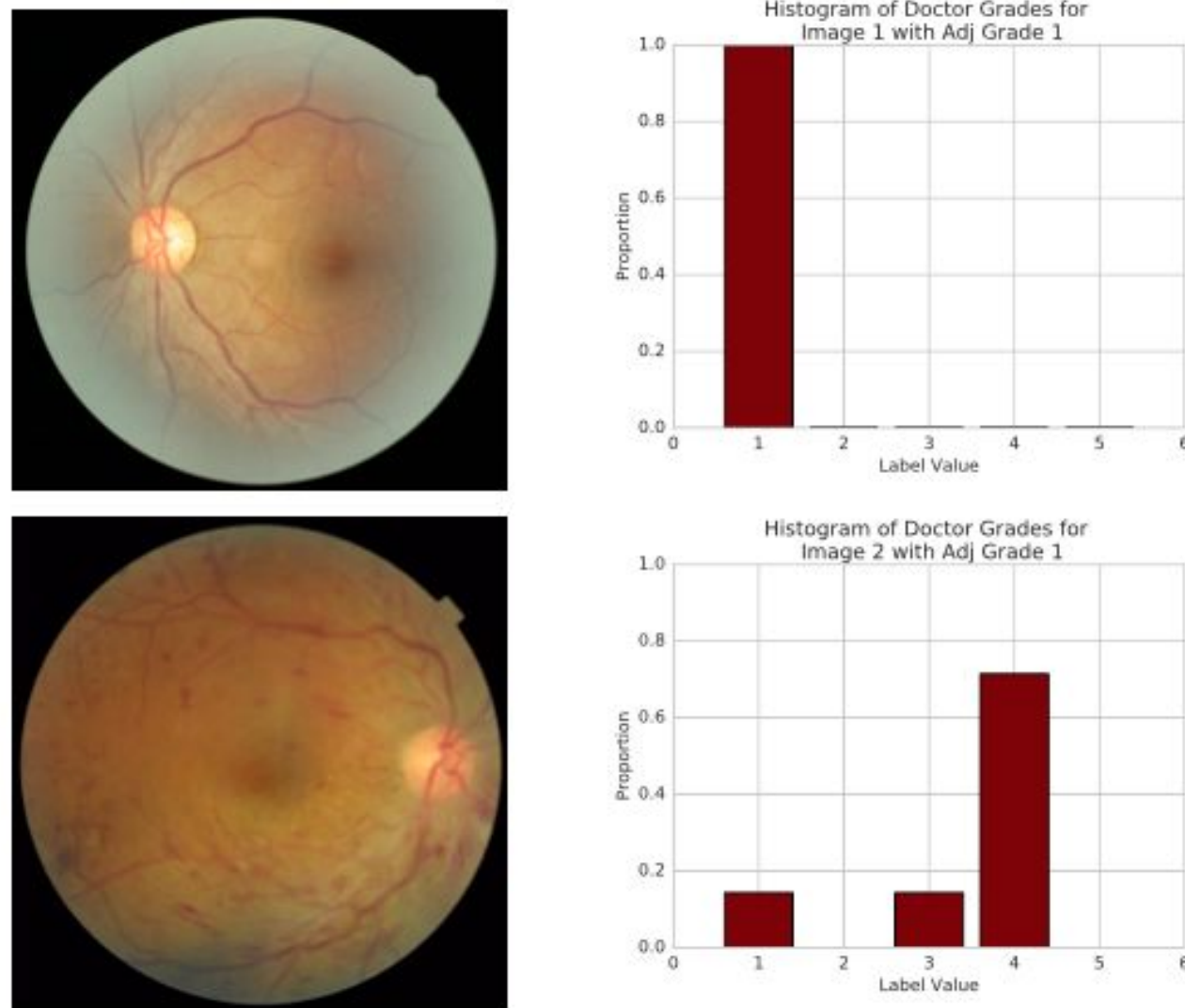


Figure 2. Patient cases have features resulting in higher doctor disagreement. The two rows give example datapoints in our dataset. The patient images x_i, x_j are in the left column, and on the right we have the empirical probability distribution (histogram) of the multiple individual doctor DR grades. For the top image, all doctors agreed that the grade should be 1, while there was a significant spread for the bottom image. When later performing an *adjudication* process (Section 5), where doctors discuss their initial diagnoses with each other and come to a consensus, both patient cases were given an *adjudicated* DR grade of 1.

Possible Versions of

- For many versions of [entropy, variance, ...], the paper proves that such estimators are unbiased, whereas UVC has a bias term.

-
- As in *learning to defer*, the doctors see more information than the model, which only sees
 - Doctors also see patient and family medical history, demographics, co-morbidities, etc.
 - Let \mathcal{D} be all data seen by doctors, and \mathcal{M} where “hides” some of the information from the model
 - Assume doctor-assigned grades,
 - Let \mathbf{x} be random variable for patient features, y be the doctor labels for
 - $p(\mathbf{x}, y)$ is a density function that assigns a probability to (patient features, doctor grade)
 - Let $p(\mathbf{x})$, and
 - Then $p(y)$ is a density over points
 - Marginal probability of patient features,

Predict Disagreement

- Doctors have seen
- Uncertainty of expected value of θ given \mathcal{D}
- For a specific patient, uncertainty is given by
 - but model sees only \mathcal{D}_i
 - Assume σ_i and σ is truly smaller than σ
- Computes expectation of uncertainties of all posteriors
- Computes uncertainty of the expected posterior
- See proof in the paper's appendix.

What is the bias of Uncertainty Via Classification?

- Bias of using
- Bias of using

Illustrative Simple Empirical Examples

Simple Mixture of Gaussians

, mixture probabilities
and marginal

Image classification

House numbers

Small images \Rightarrow {airplanes, cars, birds, cats, deer, dogs, frogs, horses, ships, trucks}

Model Type	(3d, 5G)	(5d, 4G)	(10d, 4G)
UVC	69.1%	62.0%	56.0%
DUP	74.6%	71.2%	63.4%

Table 1. DUP and UVC trained to predict disagreement on mixtures of Gaussians. We train DUP and UVC models on different mixtures of Gaussians, with (nd, mG) denoting a mixture of n Gaussians in m dimensions. Results are in percentage AUC over 3 repeats. The means of the Gaussians are drawn iid from a multivariate normal distribution (full setup in Appendix.) We see that the DUP model performs much better than the UVC model at identifying datapoints with high disagreement in the labels.

Model	SVHN (disagree)	CIFAR-10 (disagree)
UVC	75.8%	79.1%
DUP	88.0%	85.3%

Table 2. DUP and UVC trained to predict label disagreement corresponding to image blurring on SVHN and CIFAR-10. DUP outperforms UVC on predicting label disagreement on SVHN and CIFAR-10, where the labels are drawn from a noisy distribution that varies depending on how much blurring the source image has been subjected to. Full details in Appendix.

CIFAR-10: 60K 32x32 color images, 10 labels, balanced: {airplanes, cars, birds, cats, deer, dogs, frogs, horses, ships, trucks}

SVHN: Google Street View house number images, 600K, 32x32



Doctor Disagreement on Diabetic Retinopathy Images

- 587x587 retinal fundus images (back of the eye)
 - Can diagnose Diabetic Retinopathy (DR)
 - Leading cause of blindness
 - Treatable if caught early
 - DR graded on scale: {1=no, 2=mild, 3=moderate, 4=severe, 5=proliferative}
 - is *referable*
 - They used data from Gulshan *et al.* which has 2 datasets of
 - ~10K images from ~5K patients and
 - ~2K images from ~900 patients,
 - 7.8%, 14.6% referable in the two datasets



DR photo

<https://www.opsweb.org/page/fundusphotography>

DR Experiment

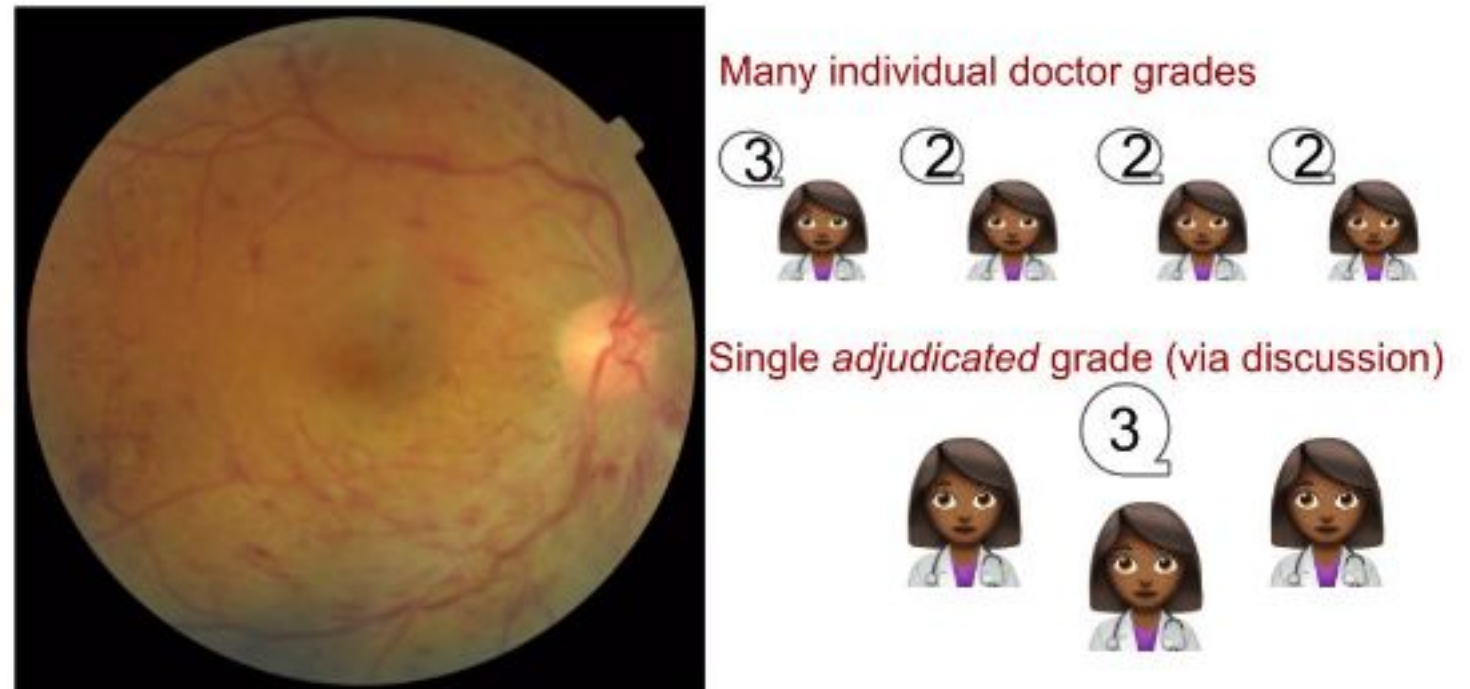
- Train: Test in 80:20 ratio, by patient id
 - (avoid correlations from multiple images of same patient)
 - focus on cases with more than one doctor-assigned label
- Interpreting DR grades:
 - Categorical: E.g., grade 2 always means micro aneurysms, grade 5 may refer to lesions or laser scars. is the appropriate measure
 - Continuous: Patients tend to progress sequentially through the grades. is the appropriate measure
- Train and on their Train data [using pre-trained ImageNet models]
- Consider Test and Train data sets specialized to and
- Binarize uncertainty measures, at 0.3 and 2/9, respectively
- Train a classifier, , on the Train data pairs
- UVC models trained on
- DUP models trained directly on pairs and , where is the binarized version of

Task		Model Type	Performance (AUC)
Variance Prediction	UVC	Histogram-E2E	70.6%
Variance Prediction	UVC	Histogram-PC	70.6%
Variance Prediction	DUP	Variance-E2E	72.9%
Variance Prediction	DUP	Variance-P	74.4%
Variance Prediction	DUP	Variance-PR	74.6%
Variance Prediction	DUP	Variance-PRC	74.8%
Disagreement Prediction	UVC	Histogram-E2E	73.4%
Disagreement Prediction	UVC	Histogram-PC	76.6%
Disagreement Prediction	DUP	Disagree-P	78.1%
Disagreement Prediction	DUP	Disagree-PC	78.1%
Variance Prediction	DUP	Disagree-PC	73.3%
Disagreement Prediction	DUP	Variance-PRC	77.3%

Table 3. Performance (percentage AUC) averaged over three runs for UVC and DUPs on Variance Prediction and Disagreement Prediction tasks. The UVC baselines, which first train a classifier on the empirical grade histogram, are denoted Histogram-. DUPs are trained on either $T_{train}^{(disagree)}$ or $T_{train}^{(var)}$, and denoted Disagree-, Variance- respectively. The top two sets of rows shows the performance of the baseline (and a strengthened baseline Histogram-PC using Prelogit embeddings and Calibration) compared to Variance and Disagree DUPs on the (1) Variance Prediction task (evaluation on $T_{test}^{(var)}$) and (2) Disagreement Prediction task (evaluation on $T_{test}^{(disagree)}$). We see that in both of these settings, the DUPs perform better than the baselines. Additionally, the third set of rows shows tests a Variance DUP on the disagreement task, and vice versa for the Disagreement DUP. We see that both of these also perform better than the baselines.

Adjudicated Evaluation

- Do high uncertainty scores correspond to cases where average doctor grade differs from adjudicated grade?



2

Figure 3. Labels for the adjudicated dataset *A*. The small, gold standard adjudicated dataset *A* has a very different label structure to the main dataset *T*. Each image has many individual doctor grades (typically more than 10 grades). These doctors also tend to be specialists, with higher rates of agreement. Additionally, each image has a single *adjudicated* grade, where three doctors first grade the image individually, and then come together to discuss the diagnosis and finally give a single, *consensus diagnosis*.

	Model Type	Majority	Median	Majority = 1	Median = 1	Referable
UVC	Histogram-E2E-Var	78.1%	78.2%	81.3%	78.1%	85.5%
UVC	Histogram-E2E-Disagree	78.5%	78.5%	80.5%	77.0%	84.2%
UVC	Histogram-PC-Var	77.9%	78.0%	80.2%	77.7%	85.0%
UVC	Histogram-PC-Disagree	79.0%	78.9%	80.8%	79.2%	84.8%
DUP	Variance-PR	80.0%	79.9%	83.1%	80.5%	85.9%
DUP	Variance-PRC	79.8%	79.7%	82.7%	80.2%	85.9%
DUP	Disagree-P	81.0%	80.8%	84.6%	81.9%	86.2%
DUP	Disagree-PC	80.9%	80.9%	84.5%	81.8%	86.2%

Table 4. Evaluating models (percentage AUC) on predicting disagreement between an average individual doctor grade and the adjudicated grade. We evaluate our models’s performance using multiple different aggregation metrics (majority, median, binarized non-referable/referable median) as well as special cases of interest (no DR according to majority, no DR according to median). We observe that all direct uncertainty models (Variance-, Disagree-) outperform all classifier-based models (Histogram-) on all tasks.

Larger Theme:

Decision Support between Machine and Human

- Explanation
- Trust
- Optimization over entire system

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Research and Applications



OXFORD

Research and Applications

Physician understanding, explainability, and trust in a hypothetical machine learning risk calculator

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Empirical Evaluation of Understanding and Trust

- GDPR requires patients to be able to receive “meaningful information about the logic involved” in an automated tool.
- Hypothetical ML risk calculator for pulmonary embolism
 - “You are a GP [general practitioner] who has reviewed a 50-year-old woman presenting with shortness of breath. After a history, examination, laboratory tests, ECG [electrocardiogram], and a chest x-ray, you are comfortable you have excluded the most concerning diagnoses. However, you are still considering pulmonary embolism. The practice has installed a piece of software that uses artificial intelligence to assist with ruling out pulmonary embolism. It can stratify patients as either; (1) low risk of pulmonary embolism: reassurance and discharge recommended; or (2) not low risk of pulmonary embolism: computed tomography pulmonary angiogram recommended. The software automatically analyses the electronic record, including your documented history, examination, and laboratory tests, and provides its recommendation.”
 - Control: “Your patient has a low risk ($<1\%$ chance) of pulmonary embolism. They should be reassured and followed up in the community as you deem appropriate. This recommendation is based on a cohort of 10 000 patients who were investigated for pulmonary embolism, of whom 1000 had a similar risk profile. The software has been externally validated.”

Four Possible Explanations (Control + one of these)

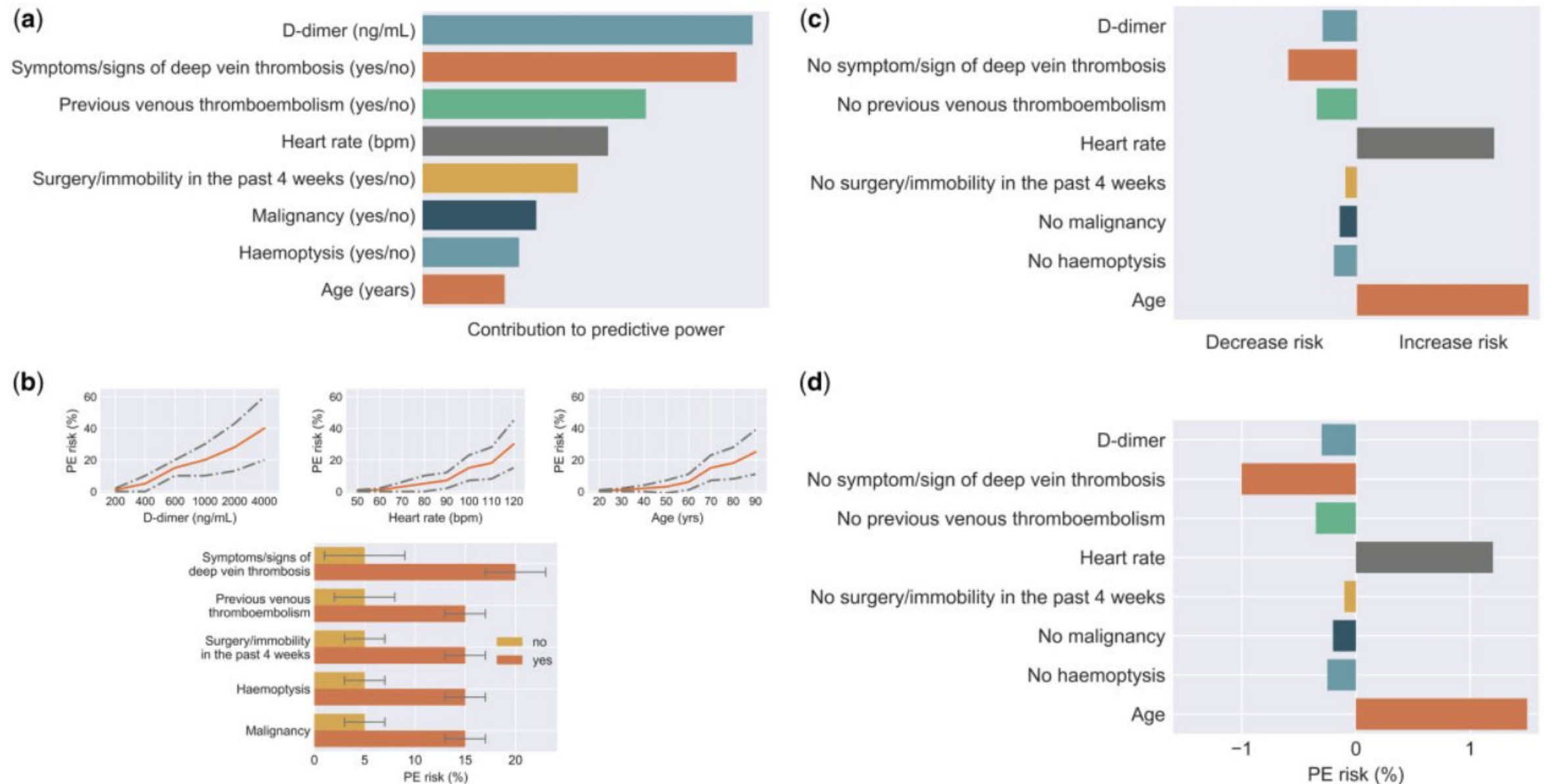
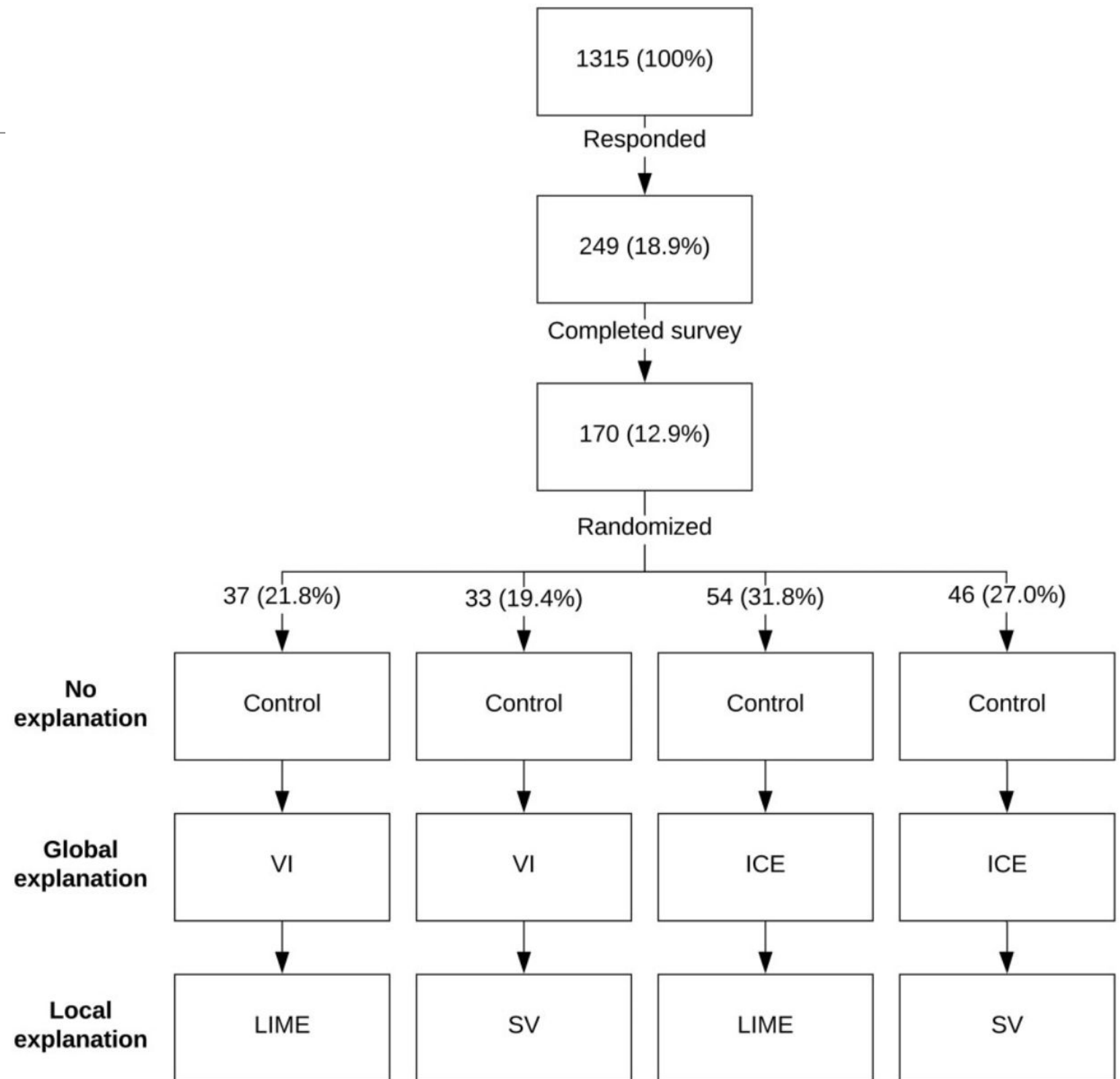


Figure 1. Graphical visualizations shown to participants with the following complementary explanation. (A) For variable importance (VI), the visualization shows the relative importance of each clinical factor used by the model. This is general information about the software's logic. (B) For individual conditional expectation plots (ICE), the visualizations show the average and standard deviation of the software's predictions for different values of the most influential clinical factors used by the model. This is general information about the software's logic. (C) For local interpretable model-agnostic explanations (LIME), the visualization shows the positive or negative relative impact of the most influential clinical factors used by the software to estimate your patient's risk of pulmonary embolism (PE). This profile is specific to your patient. (D) For Shapely values (SVs), the visualization shows the positive or negative contribution of each clinical factor to the risk estimated by the software. The sum of the bars is equal to your patient's PE risk. This profile is specific to your patient.

Survey

- Weak experiment. Only 249/1315 subjects responded, and only 170 completed survey.



Results

- Physicians who reported “Yes” to the question “Would you be able to explain the software’s decision to the patient” were more likely to respond “Yes” to the question “Would you follow the software recommendation?” ... No particular ML explainability method had a greater influence on intended physician behavior
- 87.8% of physicians preferred an ML output which contained a model-agnostic explanation, compared with 12.2% who preferred the control output (no model-agnostic explanation)
- Local explanations (LIME [32.1%] and SVs [29.9%]) were preferred over global explanations (VI [18.2%] and ICE [19.7%])

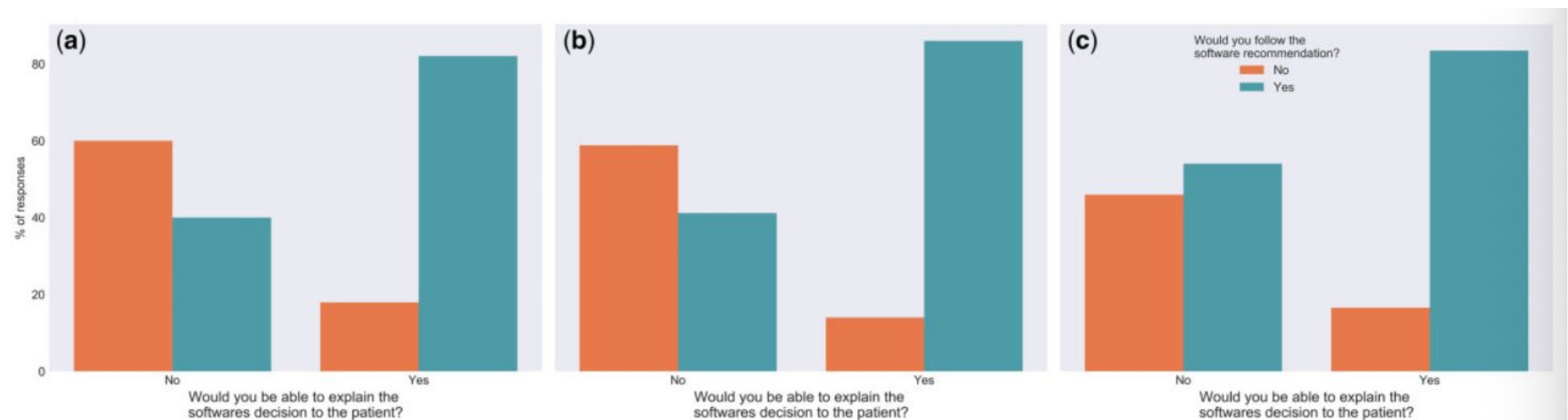


Figure 5. Relationship between explainability and trust. (A) Control condition. (B) Global explanation. (C) Local explanation.