sampling typically used for model development cannot give valid estimates of the Positive Predictive Value (precision) and may suffer from verification bias; in a pragmatic clinical trial, or under deployment, only the PPV can be measured, unless there is random confirmatory testing of predicted negatives. This is important for measuring sensitivity, specificity, and False Omission Rate as a fairness metric. DISCUSSION/SIGNIFICANCE OF IMPACT: By linking well-understood biostatistics principles (e.g., diagnostic testing) to machine learning classifier evaluation, we show what is required for rigorous evaluation of models in clinical practice. This will establish clear guidance and rigorous standards of practice for study design and analytic aspects of post-deployment monitoring.

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Statistically valid machine learning fairness evaluation

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OBJECTIVES/GOALS: Within the machine learning "fairness" literature, models audits are point estimates, and only effect size is considered. The well-developed frameworks in biostatistics for diagnostic testing apply directly to classifiers more generally; these principles can be extended to have statistically valid fairness audits. METHODS/STUDY POPULATION: We made original linkages between machine learning methodology and biostatistics, particularly to diagnostic testing, to get analytic biostatistical methods for model evaluation that are applicable to fairness testing. RESULTS/ANTICIPATED RESULTS: The use of odds ratios to compare ratios of binomial proportions is superior to taking ratios of binomial proportions directly, as is currently standard in machine learning. Odds ratios also have an analytic asymptotic approximation for standard errors, by which we can test if a point estimate (effect size) is greater than what we would expect from noise. In diagnostic testing, the odds ratios considered are generally across the cells of a confusion matrix, but we can form odds ratios for specific marginal quantities (positive predictive value, negative predictive value, true positive rate, true negative rate) for specific aspects of model performance or fairness. DISCUSSION/SIGNIFICANCE OF IMPACT: Biostatistics can make direct contributions to instantly improve the state of machine learning practice, giving ready-made methods that can take account generations of hard-won lessons about the importance of uncertainty quantification and sample size in making claims and conclusions.

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Exploring the biological embedding of adversity and cardiometabolic disease risk

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OBJECTIVES/GOALS: Conception to early childhood is reported to be one of the most critical developmental periods in human development. This study examines the role of adversity experienced by both mom and child during the pre-and post-natal periods on children's cardiometabolic disease risk (CMDR) outcomes. METHODS/STUDY POPULATION: Data include responses from 852 biological mother-child dyads from the Family Life Project. Adversity during pregnancy was measured using the Life Experiences Survey. The number of life experiences that mothers reported as "bad" was included in the analyses. Children's experiences with adversity were assessed using cumulative risk, a composite measure of adversity captured at four time points: 6, 15, 24, and 35 months. These variables were used to predict children's obesity and mean arterial pressure, markers of cardiometabolic disease risk. Children's obesity status was measured using standardized body mass index (BMIZ) values, assessed in children when they were 24, 35, 48, 58, 90, and 154 months. Mean arterial pressure was captured at 154 months. RESULTS/ANTICIPATED RESULTS: Less than half of mothers (42.4%) and children (44.6%) identified as Black. Roughly half of the children (49.1%) were female. Most (78.2%) mothers were categorized as being of low economic status. Preliminary analyses revealed that number of negative life experiences reported by mothers were not significantly correlated with MAP. Children's cumulative risk (CR) at 6 ($r=0.11$, $p<0.01$), 15 ($r=0.11$, $p<0.01$), 24 ($r=0.11$, $p<0.01$), and 35 ($r=0.10$, $p<0.01$) months were significantly correlated mean arterial pressure (MAP) at age 14. Associations between CR and MAP remained significant among girls at all time points and among boys only at months 6,15, and 24 months. There were no significant correlations between adversity experienced in utero on children's BMIZ values at any timepoint. DISCUSSION/SIGNIFICANCE OF IMPACT: The American Heart Association states that MAP is often used as an indicator of CMDR. Preliminary results from this study suggest a potential pathway from adversity experienced in infancy and adolescent MAP. Future studies should further explore these associations to better understand the pathways from early life adversity to high CMDR.

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Hepatocellular carcinoma etiology and incidence in a midwestern population-based cohort, 2010-2021

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OBJECTIVES/GOALS: Hepatocellular carcinoma (HCC) is the third leading cause of cancer deaths worldwide. The epidemiology of HCC has been changing over the past several decades. The aim of this study is to examine changes in etiology, incidence, and survival of HCC in a population-based cohort in the Upper Midwest. METHODS/STUDY POPULATION: The Rochester Epidemiology Project (REP) is a medical records linkage system between healthcare systems that centralizes patient records to a database for investigators to access for approved research projects. The REP now includes 27 counties in southeastern Minnesota and western Wisconsin, with

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