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Investigating highly pathogenic avian influenza variant associations with wild bird species in the New England region of the Atlantic Flyway to examine the role of host ecology in variant fitness

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OBJECTIVES/GOALS: Identify host ecology factors that lead to the emergence of highly pathogenic avian influenza (HPAI) variants shown to be more fit than others and that become variants of concern to agriculture, wildlife, and humans. Goals include targeted surveillance for these variants for enhanced biosecurity measures in agriculture and pandemic preparedness. METHODS/STUDY POPULATION: The study dataset of 721 HPAI-positive cases in wild birds in New England since 2022 was collected through a robust sampling effort by Tufts' Runstadler Laboratory together with a large network of wildlife rescue and rehabilitation partners. We will fit mixed-effects models to measure the association of variant fitness as a fixed effect with the odds of infection in species of either of the two bird orders most associated with HPAI – gulls and shorebirds or ducks and geese. Variant will be fit as a random effect, and covariates will include ecological factors. Fitness will be a leveled variable based on prevalence, geographic spread and host range. Using centroid spatial statistics, we will determine whether these variants traveled geographically distinct transmission routes, indicating distinct host ecologies. RESULTS/ANTICIPATED RESULTS: We anticipate that birds of the order Charadriiformes (seagulls and shorebirds) will be more associated than Anseriformes (ducks, geese) with HPAI variants that were not transmitted beyond the region and that the reverse will be true with variants that did achieve prevalence over a wide geographic range and range of host species, including agricultural species. We also anticipate that there are distinct transmission routes by variant that could better illuminate host ecology dynamics in this region that contribute to variant fitness. DISCUSSION/SIGNIFICANCE OF IMPACT: The current HPAI virus outbreak is perpetuated by evolution to new variants through co-infections in wild birds with low pathogenic avian influenza viruses they carry. This research could lead to study of the virulence to different wild bird host species of low pathogenic avian influenza subtypes that contributed genetic material to an HPAI variant.

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Milestone meta-analysis for survival data: A case study in first-line Mrcc

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OBJECTIVES/GOALS: To develop a novel meta-analysis model that estimates pooled risk ratios (RR) at prespecified milestones, accounts for unequal follow-up across trials, and leverages between-time correlation, thereby providing clinically interpretable estimates under potential non-proportional hazards (PH). METHODS/STUDY POPULATION: Our model combines study-specific RRs – the ratios of cumulative event probabilities – from Kaplan-Meier curves at prespecified times (12, 24, 36 months, etc.). Using the delta method, we derive within-trial variances for log-RRs and cross-time covariances to reflect correlation among milestones. These study-level estimates and variance-covariance matrices enter a multivariate random effects model to obtain pooled RRs. We illustrate this method with a meta-analysis of progression-free survival in 7 randomized clinical trials of first-line therapy immunotherapy combinations in metastatic renal cell carcinoma. RESULTS/ANTICIPATED RESULTS: Follow-up for PFS across the 7 trials was heterogeneous: all 7 trials contribute at 12 months, 6 at 24 months, 5 at 36 months, 4 at 48 months, and only 2 contributing at 54 and 60 months. This heterogeneity motivates a multivariate approach that borrows strength across times. PH diagnostics indicate deviations from PH for PFS in 3 trials, supporting the need for pooled effects at milestones rather than a single summary measure. We will report pooled RRs at 12, 24, 36, 48, 54, and 60 months. We expect the multivariate model to improve precision at shared milestones while honestly reflecting increasing uncertainty at sparse later times. DISCUSSION/SIGNIFICANCE OF IMPACT: When follow-up differs across trials and PH is questionable, a multivariate RR meta-analysis preserves interpretability and efficiently uses all available milestones without forcing a single-number summary. This approach clarifies when benefits accrue and provide clinically interpretable results.

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Environmental pollution, social disadvantage, and cardiovascular risk: Integrated analyses from the Emory Cardiovascular Biobank*

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OBJECTIVES/GOALS: To assess the association between pollution and CVD outcomes in a high-risk CAD population, and investigate how social drivers intersect with this association. METHODS/STUDY POPULATION: 1,602 participants enrolled in the Emory Cardiovascular Biobank were stratified into high vs. low pollutant exposure groups based on $PM_{2.5}$ (median 10.6 μg/m³), NO_x (median 39.4 ppb), and CO (median 635 ppb) levels. Demographics, cardiovascular (CV) risk factors, comorbidities, and SVI domains including socioeconomic status (RPL_THEME1), household characteristics (RPL_THEME2), racial/ethnic minority status (RPL_THEME3), housing and transportation (RPL_THEME4), and overall SVI ranking (RPL_THEMES) were compared between groups. Cox proportional hazards models were used to assess associations between pollutants and CVD outcomes (CV death, myocardial infarction [MI], stroke, heart failure, and the composite MACE. RESULTS/ANTICIPATED RESULTS:

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