were significantly associated with hypokalemia. In multivariate analysis, age (OR 0.961, 95% CI [0.936, 0.985], p = 0.00167) remained significant, and creatinine clearance (OR 0.986, 95% CI [0.974, 0.999], p = 0.0386) became significant. BMI, weight, systolic and diastolic blood pressure, sex, and urine protein concentration were not significant. DISCUSSION/SIGNIFICANCE OF IMPACT: In the multivariate analysis, age and creatinine clearance was statistically significant; however, their effect sizes were small and unlikely to be clinically meaningful. The underlying reasons for the high prevalence of hypokalemia in this population remain unclear, warranting further investigation to identify contributing factors.

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Unraveling the genetic architecture of aging through comparative genomics

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OBJECTIVES/GOALS: To identify the genomic mechanisms underlying cross-species regulation of longevity among mammals and birds and to characterize the impact of those conserved pathways on human aging. More broadly, this study aims to develop a novel evolutionary approach to understand the genetics of complex traits. METHODS/STUDY POPULATION: High-quality genome sequences for 194 bird species and 295 mammal species with reliable longevity and body size data were obtained from publicly available resources. The data include coding sequence alignments of 16,863 mammalian and 14,565 avian one-to-one orthologous genes. Gene-wise relative evolutionary rates (RERConverge) and maximum likelihood phylogenetics (PAML) were computed to assess for evidence of purifying selection and positive selection for longevity. As part of ongoing analysis, human orthologs of selected results will be examined in the UK Biobank for validation. RESULTS/ANTICIPATED RESULTS: Preliminarily, we have found a signal of concordant positive selection between two classes of vertebrates separated by hundreds of millions of years. Several genes show signals of positive selection in long-lived species of both birds and mammals. Ongoing work focuses on elucidating the relationship between relative evolutionary rates and positive selection, the overlap in selection signature between long-lived animals with large body sizes and those who are exceptionally long lived for their body size, and further elaborating on convergence between mammals and birds. DISCUSSION/SIGNIFICANCE OF IMPACT: Currently, most scientific knowledge about aging is from experiments on short-lived model organisms. By systematically studying the genomes of long-lived mammals and birds, we aim to develop a new method for studying complex traits and uncover novel insights into the mechanisms of longevity.

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The Resist! Project: Use of a mixed-methods approach to identify substance use resistance factors

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OBJECTIVES/GOALS: The aim of the study is to identify resistance factors for substance use (i.e., factors that explicitly help to avoid or reduce drug use). Identification of resistance factors could inform strategies that seek to reduce the prevalence of substance use and related disorders. METHODS/STUDY POPULATION: Adult twins aged 30–70 years were recruited from the Mid-Atlantic Twin Registry. A mixed-method approach, group concept mapping, was used to identify factors influencing participants to resist using substances. Approximately 155 participants produced 97 statements reflecting substance use resistance factors. Hierarchical cluster analysis and multidimensional scaling assessed how participants sorted and rated statements for their lifetime and current importance. Factor analysis was used to reduce data dimensionality. Reliability analyses were conducted to identify a subset of statements anticipated to consistently represent each cluster. Results were shared with participants to assess accuracy with their experiences. RESULTS/ANTICIPATED RESULTS: Participants sorted 97 statements into 9 thematic clusters: (1) Controlling Personal, Negative Consequences; (2) Concern About Health and Well-being; (3) Lack of Desire; (4) Outside Influences; (5) Social Norms and My Reputation; (6) Career and Legal Impacts, (7) Avoiding Harm to Family and Relationships; (8) Preserving Family Relationships; and (9) Family and Friends Impact on Me. Participants consistently identified health concerns as an important substance use resistance factor. The statements will be further reduced to represent a smaller subset for future use as a scale to measure exposure to resistance factors. DISCUSSION/SIGNIFICANCE OF IMPACT: Health concerns related to substance use were identified as an important resistance factor. This has been supported by research on smoking cessation and implemented in smoking prevention campaigns. Therefore, prioritizing health-related outcomes in prevention may be important to reduce substance use prevalence.

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Retrospective analysis of sociodemographic and geographic risk factors for presenting keratitis severity in a South Indian population

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OBJECTIVES/GOALS: Infectious keratitis is the leading cause of corneal blindness worldwide, causing two million cases of monocular blindness per year. Of these cases, developing countries are disproportionately affected, in part due to sociodemographic disparities. Our study examined risk factors for severe keratitis presentation in a South Indian population. METHODS/STUDY POPULATION: 156 patients aged ≥ 16 years with clinically diagnosed infectious keratitis presenting to Aravind Eye Hospital in Pondicherry, India, from January 1, 2023 to July 31, 2024, were retrospectively reviewed. Univariate logistic regression was used to evaluate associations between specific potential risk factors (including age, sex, awareness of keratitis, travel distance to hospital, education level,

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