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Non-AIDS Related Comorbidities In People Living With HIV in West Africa

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OBJECTIVES/GOALS: METHODS/STUDY POPULATION: This study utilizes the IeDEA W. Africa cohort to evaluate the prevalence and burden of hypertension and diabetes type II among people living with HIV (PLWH) in sub-Saharan Africa (SSA), and to assess how sex and aging impact the development of these NACM. The cohort is a large, international collaboration across eight countries and 19 treatment centers. Established by the National Institute of Allergy and Infectious Diseases in 2006, the W. Africa cohort is now in its fourth renewal (2021-2026). Participating countries include Senegal, Mali, Cote d'Ivoire, Burkina Faso, Ghana, Togo, Benin, and Nigeria. Data are collected from affiliated cohorts in the regional data center every 24 months. The cohort currently includes >65,000 adult PLWH on anti-retroviral therapy. RESULTS/ANTICIPATED RESULTS: The prevalence of several NACM, such as hypertension and cardiovascular disease, have significantly increased among PWH over time, surpassing prevalence observed in the general population. We therefore expect similar patterns in the W. Africa IeDEA cohort and a high prevalence and burden of both hypertension and diabetes type II in this sample. Additionally, evidence suggests that increasing age and female sex serve as independent risk factors for the development of NACM in PLWH. We anticipate that both increased age and female sex, separately and synergistically, are associated with increased prevalence and burden of hypertension and diabetes type II in this cohort. DISCUSSION/SIGNIFICANCE: With more than 37 million people currently living with HIV, the HIV/AIDS epidemic continues to pose a serious threat to global public health. SSA bears a disproportionate burden of the epidemic with greater than two-thirds of global cases. NACM are now driving morbidity and mortality among PLWH, and increased age and female sex may modify this effect.

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Normative beliefs about tobacco products differ by age: Implications for smoking cessation and harm reduction*

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OBJECTIVES/GOALS: The prevalence of combusted cigarette (CC) smoking among older adults is stagnant, with zero declines attributable to e-cigarette (EC) use. Normative beliefs predict quitting and switching to ECs (a behavior likely to yield health benefits for those unable to quit), so this study seeks to characterize the role of age in norms about CC and EC use. METHODS/STUDY POPULATION: Data come from Wave 5 (2018-2019) of the adult Population Assessment of Tobacco Use and Health (PATH) study, a nationally-representative, U.S. longitudinal cohort. Analyses were restricted to people with established CC use (smoked CCs in the past year, currently smoke regularly, and smoked ≥100 lifetime CCs; n=8,590). Cross-sectional weighted estimates of the prevalence of normative beliefs about CCs and ECs were calculated by age using the Balanced Repeated Replication (BRR) method with Fay=0.3. We used chi-square tests to examine the association of age group (18-24, 25-34, 35-44, 45-54, 55-64, or ≥65) with the prevalence of 2 descriptive and 4 personal social norms. RESULTS/ANTICIPATED RESULTS: The prevalence of the normative belief that most people disapprove of CCs (p DISCUSSION/SIGNIFICANCE: Older adults are more likely than younger adults to endorse anti-tobacco norms, which prior work shows is associated with quitting smoking. These beliefs could be leveraged to create targeted communications towards older adults encouraging smoking cessation. More research is needed to assess age-related tobacco beliefs and switching from CC to EC.

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Novel statistical methods to unlock the clinical potential of liquid biopsy sampling*

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OBJECTIVES/GOALS: Decoding the origins of cell-free DNA (cfDNA) released from dying cells in a liquid biopsy sample (e.g. blood) can provide insight into the dynamic, organism-wide changes reflective of health and disease state. Making cfDNA an ideal target for genomic monitoring of disease-related changes. METHODS/STUDY POPULATION: Methylome-wide sequencing (WGBS) data present unique statistical challenges. To this end, we developed a novel statistical method using an Expectation-Maximization algorithm to decode the cellular origins of cfDNA fragments in liquid biopsies. Our flexible, probabilistic method leverages the co-regulation of neighboring CpG sites on the individual sequencing read to facilitate tissue of origin analysis, as opposed to prior methods that focus on the methylation rate of a single CpG site. We assess the performance of our model in various simulated settings and apply our model to an important clinical example in which we are able to detect early off-target tissue damage from radiation therapy via minimally invasive blood draws. RESULTS/ANTICIPATED RESULTS: We found our model more effective at capturing the range of biologically plausible methylation patterns on cfDNA read fragments compared to prior models that use single CpG sites. We also show our model is robust to high levels of noise inherent with WGBS data. We demonstrate the accuracy of cell-type proportion estimation on in-silico mixed cfDNA samples from real WGBS data. Finally, we use our model in a clinical application. We detect significant ($p < 0.05$) increases in cellular contributions from lung and cardiac tissue in breast cancer patients (n=15) undergoing radiation therapy compared to baseline. We also detect novel signals of radiation induced toxicity to the liver in right-sided breast cancer patients (n=8) receiving radiation treatment compared to matched left-sided breast cancer patients (n=7). DISCUSSION/SIGNIFICANCE: Here we address an unmet need in developing novel statistical methodologies that can handle the unique complexities of methylated cfDNA obtained from liquid biopsy samples. We also demonstrate the far-ranging clinical utility of serial liquid biopsy sampling to complement and advance standards of clinical care in oncology and other pathologies.

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