

ASSESSING CARDIOMETABOLIC HEALTH RISK AMONG U.S. CHILDREN WHO LIVE IN GRANDPARENT-HEADED HOUSEHOLDS

MinKyoung Song,¹ Karen Lyons,² Laura Hayman,³ Nathan Dieckmann,¹ and Carol Musil,⁴ 1. *Oregon Health & Science University, Portland, Oregon, United States*, 2. *Boston College, Chestnut Hill, Massachusetts, United States*, 3. *University of Massachusetts Boston, Boston, Massachusetts, United States*, 4. *Case Western Reserve University, Cleveland, Ohio, United States*

Many interventions have been designed to leverage parent-caregivers as change agents for improving children's cardiometabolic health (CMH), however very few have been designed to leverage grandparent-caregivers for that purpose. This is surprising since there has been a steady increase in children living in grandparent-headed households. As a first step in assessing the potential impact of interventions with grandparent-caregivers, we used data from the National Survey of Children's Health (2018) to compare CMH measures in children living in grandparent-headed households with CMH measures in children living in parent-headed households. Our hypothesis was that CMH risk might be higher in grandparent households – given that research shows that grandparents taking over caregiving from parents is associated with worse overall health outcomes for both grandparents and their grandchildren. Additionally, since research indicates that children who experience ≥ 4 adverse childhood experiences (ACEs) have significantly worse health outcomes, we assessed levels of ACEs. Our analytic sample included children aged 10-17 years ($n=14,941$). Adjusting for age, sex, race/ethnicity, and health insurance coverage status, children living in grandparent households were more likely to be obese (Adjusted Odds Ratio [95% confidence interval]= 2.04 [1.02, 4.09]), exposed to secondhand smoke (2.32 [1.49, 3.59]), and less likely to meet recommended age-appropriate standards for sleep (0.42 [0.27, 0.67]). The children living in grandparent households were more likely to experience ≥ 4 ACEs (8.59 [5.42, 13.62]). Our results provide indirect evidence that interventions with grandparent-caregivers may be particularly critical for improving CMH risk in families.

ASSESSMENT OF APPROPRIATENESS OF CARDIOVASCULAR PREVENTIVE MEDICATION IN ADULTS ≥ 75 YEARS

Milly van der Ploeg,¹ Rosalinde Poortvliet,² Jacobijn Gussekloo,² and Yvonne Drewes,² 1. *Leiden University, Leiden, The Hague, Netherlands*, 2. *Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands*

Physicians are confronted with dilemma's on cardiovascular preventive medication for older people with complex health problems. With accumulation of diseases, limitations and shortening life expectancy, questions arise for whom cardiovascular preventive treatment is still appropriate (the expected benefits of treatment exceeds the negative consequences by a sufficiently wide margin resulting that treatment is worth doing). There is a need for more guidance in clinical situations. With the RAND/UCLA appropriateness method (RUAM), we investigated the appropriateness of cardiovascular preventive medication in adults ≥ 75 years. The RUAM

is a systematic, formalized method, to combine available scientific evidence with the collective judgment of experts. Fourteen interdisciplinary panelists (9 physicians representing 6 medical disciplines, 1 medical ethics expert, 1 pharmacist and 3 older adults [lay man]), discussed and rated the appropriateness of starting and stopping of three medication groups (cholesterol lowering, blood pressure lowering and thrombocyte aggregation inhibitors) for different clinical scenarios (combinations of cardiovascular history, systolic blood pressure, complexity of health problems, age, life-expectancy, side-effects). Depending on the medication group, different patterns of appropriateness judgments across the clinical scenarios were found. In general, absence of cardiovascular disease, presence of complex health problems, a short life-expectancy or hindering side-effects were important factors to judge cardiovascular preventive medication as inappropriate. Results were summarized into colored reading maps. These findings can offer more guidance in clinical decision making about cardiovascular preventive treatment for adults ≥ 75 years.

REDUCTION OF ELEVATED PROTON LEAK REJUVENATES MITOCHONDRIA IN THE AGED CARDIOMYOCYTE

Huiliang Zhang,¹ Nathan Alder,² Wang Wang,¹ Hazel Szeto,³ David Marcinek,¹ and Peter Rabinovitch,¹ 1. *University of Washington, Seattle, Washington, United States*, 2. *University of Connecticut, Mansfield, Connecticut, United States*, 3. *Alexandria LaunchLabs, New York, New York, United States*

Rational: Aging-associated diseases, including cardiac dysfunction, are increasingly common in the population. However, the mechanisms of physiologic aging in general, and cardiac aging in particular, remain poorly understood. While effective medical interventions are available for some kinds of heart failure, one age-related impairment, diastolic dysfunction in Heart Failure with Preserved Ejection Fraction (HFpEF) is lacking a clinically effective treatment. Methods and Results: Using the pH indicator cpYFP in the model of naturally aging mice and rats, we show direct evidence of increased mitochondrial proton leak in aged heart mitochondria following a pH gradient stress. Furthermore, we identified Adenine Nucleotide Translocator 1 (ANT1) as mediating the increased proton permeability of old cardiomyocytes. Most importantly, acute (2 hours) in vitro treatment with the tetrapeptide drug SS-31 (elamipretide) reverses age-related excess proton entry, decreases the mitochondrial flash activity and mitochondrial permeability transition pore (mPTP) opening and rejuvenates mitochondrial function. Moreover, we show that SS-31 benefits the old mitochondria by direct association with ANT1 and stabilization of the mitochondrial ATP synthasome, leading to substantial reversal of diastolic dysfunction. Conclusion: Our results uncover excessive mitochondrial proton leak as a novel mechanism of age-related cardiac dysfunction and elucidate how SS-31 is able to reverse this clinically important complication of cardiac aging.

THE ASSOCIATION BETWEEN MYOCARDIAL STRAIN AND FRAILTY IN THE CARDIOVASCULAR HEALTH STUDY

Annabel Tan,¹ Sanjiv J. Shah,² Jason Sanders,³ Bruce Psaty,⁴ Anne Newman,⁵ Chenkai Wu,⁶