Mediterranean Diet, Related Antioxidants and Frailty (PESC Award)

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Specific Aims

- **Aim 1:** To determine the association of Mediterranean-Style Dietary Pattern Score (MSDPS) with the risk of frailty as well as progression of frailty over 16 years

  Hypothesis 1: Higher MSDPS at the baseline will be associated with reduced risk of frailty and slower progression of frailty over 16 years

- **Aim 2:** To determine the association of antioxidant intakes with risk of frailty and progression of frailty over 16 years and if these associations are mediated by biomarkers of oxidative stress

  Hypothesis 2a: Higher antioxidant intakes will be associated with reduced risk of frailty and slower progression of frailty over 16 years.

  Hypothesis 2b: Markers of oxidative stress will at least partly mediate these associations

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Background

- Frailty is a geriatric syndrome common in older persons
- Nutrition plays a key role in the complex pathogenesis but it is a vastly under-studied area
- Key areas of interest:
  - Dietary antioxidants and oxidative stress
  - Dietary quality in particular Mediterranean diet
  - Longitudinal studies
  - Clinical trials

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Rationale

- Mediterranean Diet (MD) emphasizes intake of fruits, vegetables, nuts, whole grains and olive oil - is rich in dietary antioxidants
- MD associated with a lower risk of developing frailty over 2-6 years in older adults from the Mediterranean region
  - Examined diet at single time point
  - Did not account for changes in diet over follow-up
  - Did not examine pre-frailty or progression of frailty over time
- Results from previous studies cannot be directly applied to an American population who do not normally consume MD and rely instead on the typical American diet (high in fat & low in fruit and vegetables). Overall, it is unclear if MD or it's components could prevent frailty or slow the progression of frailty in older Americans
- Link between MD and frailty is an essential first step before developing it as a nutrition intervention
- Study of underlying mechanisms related to dietary antioxidant and oxidative stress could provide new targets for intervention

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Innovation

- There have been no studies examining the benefit of the Mediterranean diet in Americans
- Dietary assessment at three time points in the Framingham Study provides cumulative exposure over 13 years and also provides information on change in diet over the follow-up
- Larger sample size allows for assessment of not just frailty but also pre-frailty and progression of frailty over 16 years
- Longitudinal study of antioxidants and frailty elucidate the pathways involved

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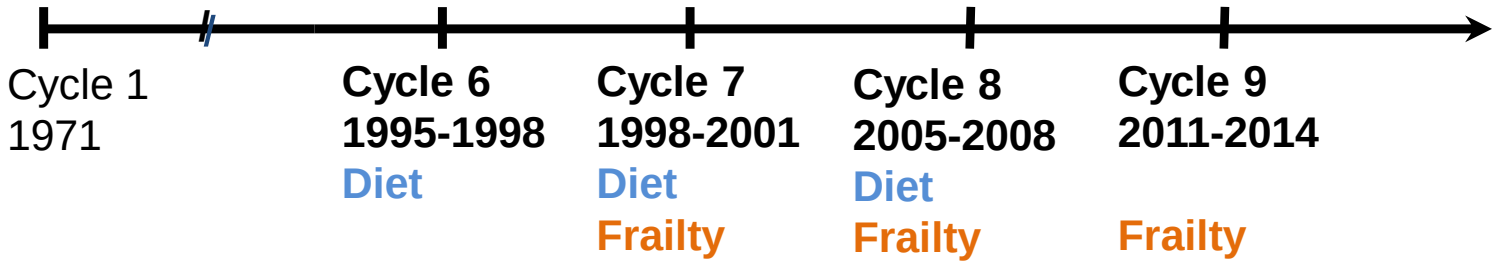
Approach

Framingham Offspring cohort (n=1,746)



- Dietary assessment
  - Harvard food frequency questionnaire
- Frailty
  - Fried criteria
  - Frailty Progression (from non-frail to pre-frail or from pre-frail to frail vs. no progression)
- Baseline oxidative stress
  - Interleukin-6
  - Isoprostanes
  - Lipoprotein phospholipase A2 (LpPLA2)

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Components of Mediterranean Style Dietary Pattern Score (MSDPS)

Food group components	Criteria for maximum score of 10[1]	Score[2]
	servings/d	*points/serving*
Whole grains	8	1.25
Fruits	3	3.33
Vegetables	6	1.67
Dairy	2	5.0
Wine		
Men	3	3.33
Women	1.5	6.67
	servings/wk	
Fish and other seafood	6	1.67
Poultry	4	2.5
Olives, legumes, and nuts	4	2.5
Potatoes and other starchy roots	3	3.33
Eggs	3	3.33
Sweets	3	3.33
Meat	1	10.0
Olive oil	Use only olive oil	0 (for no use of olive oil) 5 (for use of olive + other vegetable oils)

- Each component was calculated based on recommended intake in the Mediterranean diet pyramid
- Deduction in component score based on under-consumption or over-consumption
- MSDPS = [($\Sigma Si_{i=13 i=1}$/130) x 100] x P
  - *Si* is the individual item score
  - P is the proportion of total energy intake from Mediterranean diet pyramid foods
  - Range of the score 0-100

Rumawas M et al, Journal of Nutr 2009

Statistical Analysis

- OAIC Biostatistics and Analysis Core (Dr. Travison)
- For Aim 1 and 2a, continuation ratio models
  - Estimate the odds of being in a certain frailty category relative to the odds of being in that same category or a higher category
- For Aim 2b, mediation analysis
  - Covariates: age, time since baseline, sex, BMI, energy intake, status of frailty at previous examinations, current smoking, multivitamin supplement use, MMSE score and comorbidities

Participant Description in 1998-2001 Examination

Characteristics [median (IQR) or n (%)]	Frailty Status		
	Non-frail (N=1098)	Pre-frail (N=1273)	Frail (N=123)
Age, y	57.0 (52.0-62.0)	61.0 (55.0-68.0)	70.0 (64.0-73.0)
Women, n (%)	587 (54)	713 (56)	80 (65)
BMI, kg/m^2	27.0 (24.3-30.3)	28.1 (24.7-31.7)	27.8 (24.2-32.2)
Current smoker, n (%)	105 (10)	159 (13)	21 (17)
Energy intake, kcal	1794 (1434-2210)	1751.5 (1400-2161)	1702.7 (1345-2117)
MSDPS scores	25.3 (19.7-30.9)	24.9 (19.2-30.3)	24.9 (19.7-28.9)
Physical Activity Index	36.3 (34.1-39.6)	33.2 (31.6-35.8)	32.3 (30.6-33.1)
Gait speed, m/s	1.2 (1.1-1.4)	1.0 (0.9-1.2)	0.8 (0.7-0.9)
Grip strength, kg	33.0 (25.0-44.0)	28.0 (21.0-36.0)	17.5 (14.0-24.0)

Progress of Work

- Framingham Heart Study
  - Protocol approved
  - DMDA established
  - Data received
- Received IRB approval
- Data analysis underway

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Feasibility Studies to Complement Current OAIC Pilot Study

- Pilot funding: The Interventional Studies in Aging Center (ISAC) at the Marcus Institute, Hebrew SeniorLife
- Aim: To determine the effect of two meal plans over 2-week period on seated blood pressure and physical function among 45 independently living older adults in HSL's Jack Satter House
- Collaborators: Drs. Lew Lipsitz, Stephen Juraschek and Kenneth Mukamal from BIDMC
- PI will gain experience in:
  - Participant screening and recruitment
  - Meal cost and meal delivery logistics
  - Compliance and tolerability of meals
  - Measurement of physical function

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Next Steps/ Career Trajectory

- Develop preliminary data and publications in the area of nutrition and frailty
- Utilizing the preliminary data to develop an intervention study
- Design and implement Mediterranean diet as a nutritional intervention for prevention and treatment of frailty and consequent functional limitations in older Americans
- Submit R01 grant to the NIA

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Thank You