



Inaugural Annual Meeting

November 18, 2020

1:30-2:30 p.m. ET

How to Incorporate Important Geriatric Principles into Your Next Grant

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House Keeping

- All lines are muted
- Have a question? Enter in the Q&A box at the bottom of the screen
- Rolling – we will be recording...

Incorporating Aging Principles into Your Research and Specialty

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November 18, 2020





Disclosures



- I have no commercial financial relationships
- Funding that supports my research:
 - VA HSR&D CDA-2
 - PCORI
 - CTSA KL-2, NIA GEMSSTAR R03, ACR RRF, Cornell Roybal Center (TRIPLL) pilot
- Views expressed in this presentation do not reflect the position or policy of the US government



Rheumatology Research Foundation

Advancing Treatment | Finding Cures



National Institutes
of Health

Me and Aging

- Immunology, inflammation, targets, relationships, continuity, outcomes that matter most to my patients
- Rheumatologist focused on aging research
 - Not double boarded
- Sought formal clinical epidemiology/ aging related research training via T32 fellowship
- Life moved me to TX
- Nurtured mentor relationships outside of UTSW: Yale, Cornell, Spaulding
- Redefined and differentiated myself at new institution
- Opportunity to educate others
 - Culture shift

Lessons Learned

- Rheumatologists: we think we know how to take care of older adults with rheumatic disease
 - Arthritis occurs in older adults, BUT
 - One size fits all approach is not effective nor is it appropriate
- How to convince a field that it's time to expand knowledge about aging

Prominent in Aging

- Pain, arthritis, giant cell arteritis, polymyalgia rheumatica, osteoporosis
- Cataracts, hearing impairment
- Chronic kidney disease
- Isolated systolic hypertension, heart failure with preserved function, atrial fibrillation
- **Without considering general principles of aging, we fall short (diagnostically and therapeutically)...**

Pillars of Aging

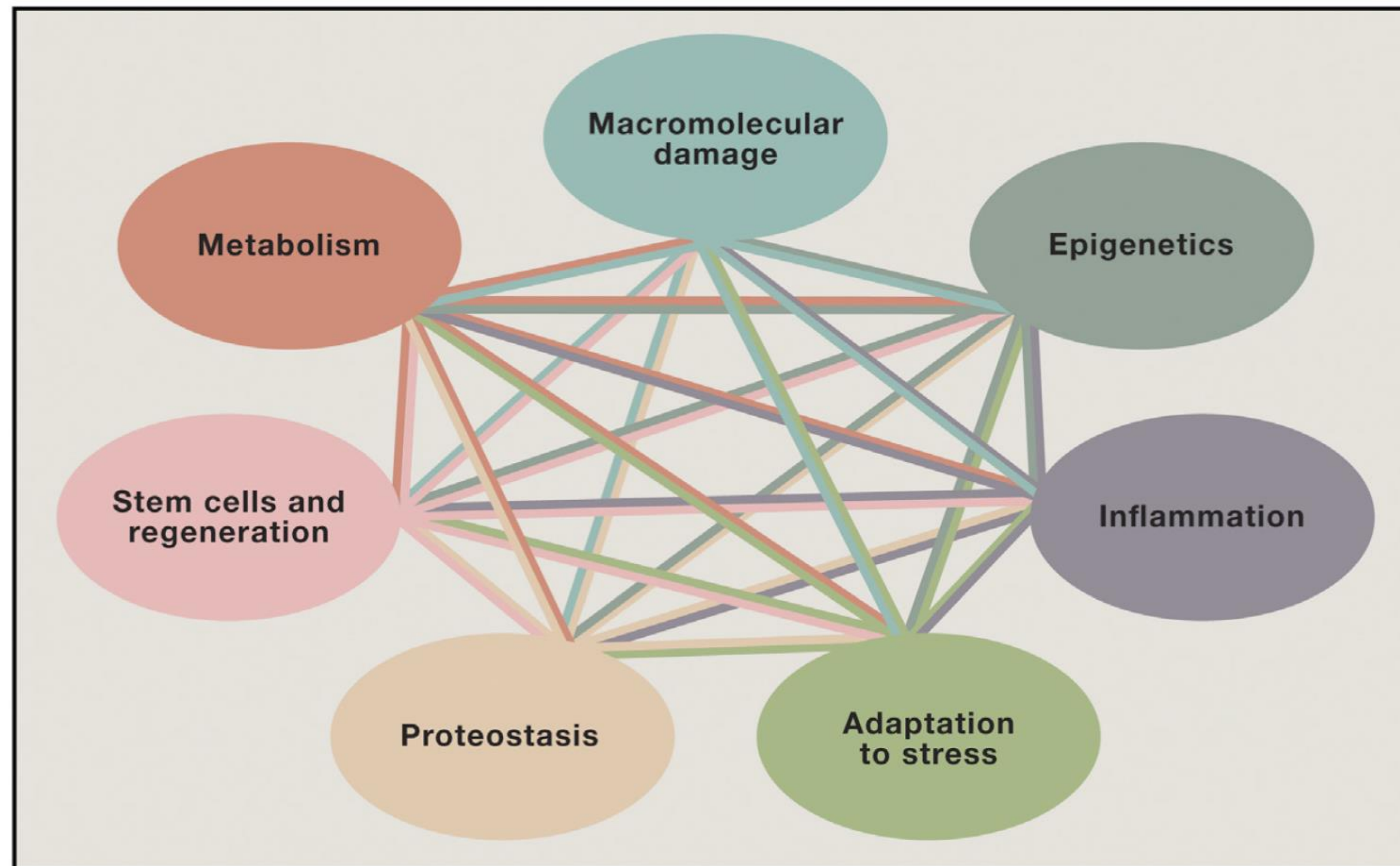
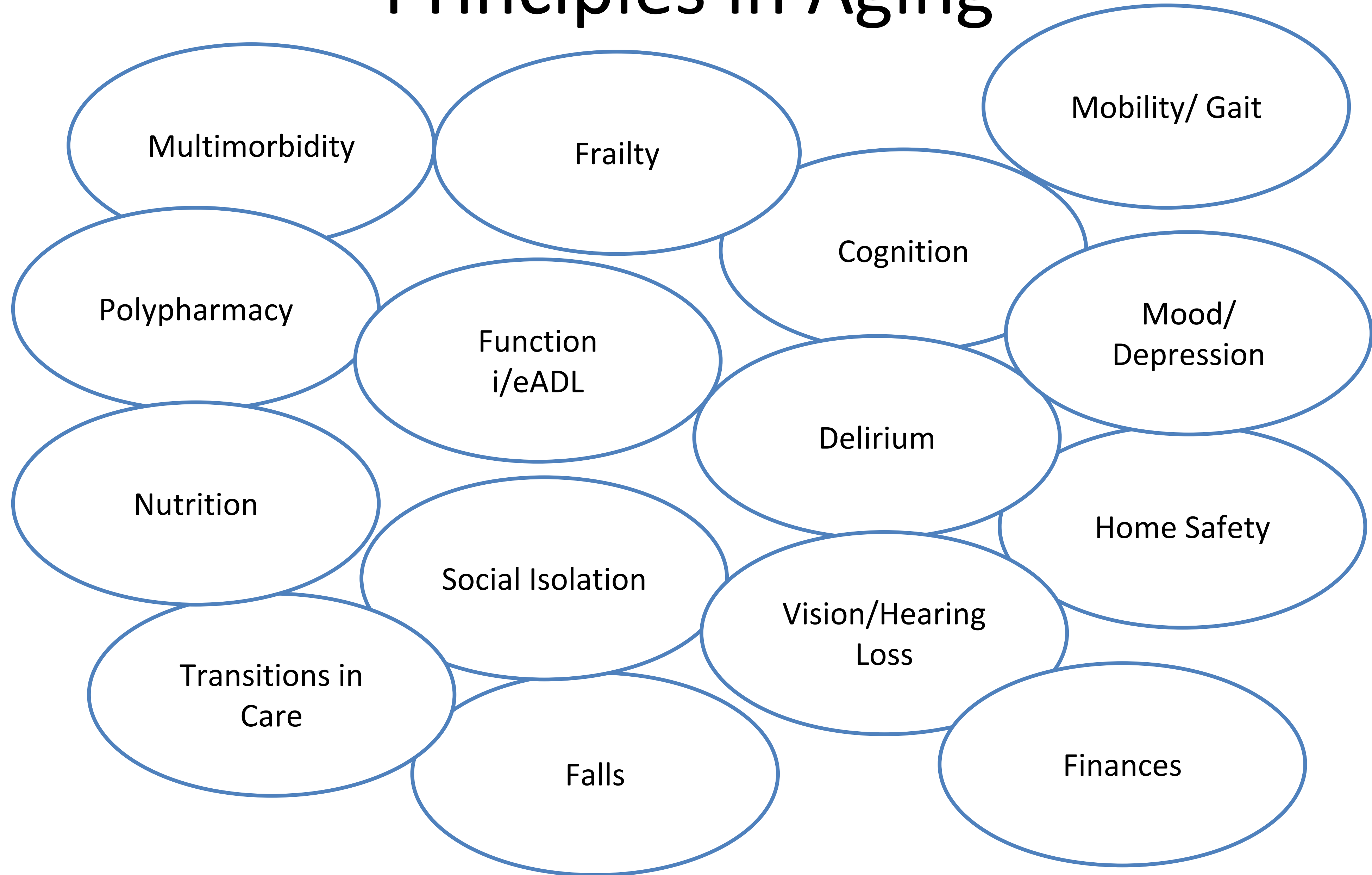


Figure 1. The Seven Pillars of Aging

Principles in Aging



The 5M of Aging

Multicomplexity	Geriatrics healthcare professionals¹ focus on these 4Ms...	When caring for older adults, all health professionals should consider...
<p>Multicomplexity describes the whole person, typically an older adult, living with multiple chronic conditions, advanced illness, and/or with complicated biopsychosocial needs.</p>	<p>Mind</p>	<ul style="list-style-type: none"> ■ Mentation ■ Dementia ■ Delirium ■ Depression
	<p>Mobility</p>	<ul style="list-style-type: none"> ■ Amount of mobility; function ■ Impaired gait and balance ■ Fall injury prevention
	<p>Medications</p>	<ul style="list-style-type: none"> ■ Polypharmacy; deprescribing ■ Optimal prescribing ■ Adverse medication effects and medication burden
	<p>What Matters Most</p>	<ul style="list-style-type: none"> ■ Each individual's own meaningful health outcome goals and care preferences

*Adapted by the American Geriatrics Society (AGS) with permission from "The public launch of the Geriatric 5Ms" [on-line] by F. Molnar and available from the Canadian Geriatrics Society (CGS) at <http://canadiangeriatrics.ca/2017/04/update-the-public-launch-of-the-geriatric-5ms/> Accessed July 14, 2020.

Opportunities to Seek Out, Locally

- Meet your colleagues and ask questions; go to their clinics
- Meet your leaders and tell them what you do
- Offer to serve as liaison for aging- [specialty]; model this for other specialties
- Go-to for aging related lectures and grand rounds*
- Invite/host local or national experts in geriatrics and/or geriatrics focused leaders in your specialty
 - Clin-STAR Visiting Professor program
- Attend didactic sessions/ lectures for geriatrics fellows, webinars (via OAIC and AGING, see Clin-STAR website)*
- Organize aging focused journal clubs for all levels of learners, across disciplines*
- Create a clinical rotation for aging-[specialty]: teach medical students, residents and fellows how you think about each patient encounter
- Develop culture of inter-disciplinary, team science
- Mentor!

Bridging the Chasm at Society Meetings

- Identify 2-3 national scientific meetings
- Organize aging study group/ special interest group, symposia, workshops:
 - **be present and persistent**
- Invite leaders in the field to your workshops (ACR: Dr. Studenski speaking on Mobility; Dr. Ferucci speaking on Inflamm-aging), Clin-STAR program
- Volunteer for positions/ committees: aging agenda
- Great opportunity to meet the funders or EIC of your journals: aging section or supplement?
- Develop specialty-aging curricula



Opportunities to Seek Out, Nationally

- Present your research at Grand Rounds, externally (national reputation important for promotion)
- Collaborate (multi-site projects), build your team with diversity in mind
- Study section reviewer (foundations, NIH, VA, PCORI); gently educate colleagues during a study section (if not focused on aging)
- Find ways to stay updated: journal TOC, twitter
- Seek out leadership training (AAMC, Tideswell ELIA)
- Join a community of aging- focused colleagues: Clin-STAR, Pepper Centers, NIA Research Centers Collaborative Network



Thank You

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Table 1. Critical Areas of Aging Research and Important Goals

Areas of Aging Research	Important Goals
Adaptation to stress	Bridge continuum from psychological to molecular stresses Differentiate hormesis from toxic stress Better align human and animal studies
Epigenetics	Biomarker development: chronologic vs. biologic aging Link age-related environmental inputs to epigenetic signatures Test small molecules that regulate enzymes controlling epigenetic events
Inflammation	Differentiate adaptive and maladaptive inflammatory responses Define age-related inflammatory sources and their systemic effects Determine how obesity and metabolic dysfunction alter inflammation with age
Macromolecular damage	Generate systems-level understanding of the types of macromolecular damage and their roles in chronic disease states Understand how stochastic damage influences the variability of aging
Metabolism	Define role of signal transduction pathways linked to metabolism in the aging process Understand contribution of circadian clocks to aging and metabolism Connect metabolic dysfunction with tissue-specific decline in aging
Proteostasis	Identify proteostatic pathways that are overwhelmed in specific chronic disease states Examine crosstalk between proteostasis machineries Understand non-cell-autonomous signaling and activation of proteostasis pathways
Stem cells and regeneration	Determine whether declining adult stem cell function drives aging and chronic disease Examine how aging and associated disease impair adult stem cell function Determine how macromolecular damage accumulates in aging adult stem cell pools



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Choosing Outcomes for Aging Research

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Geriatrician Perspective

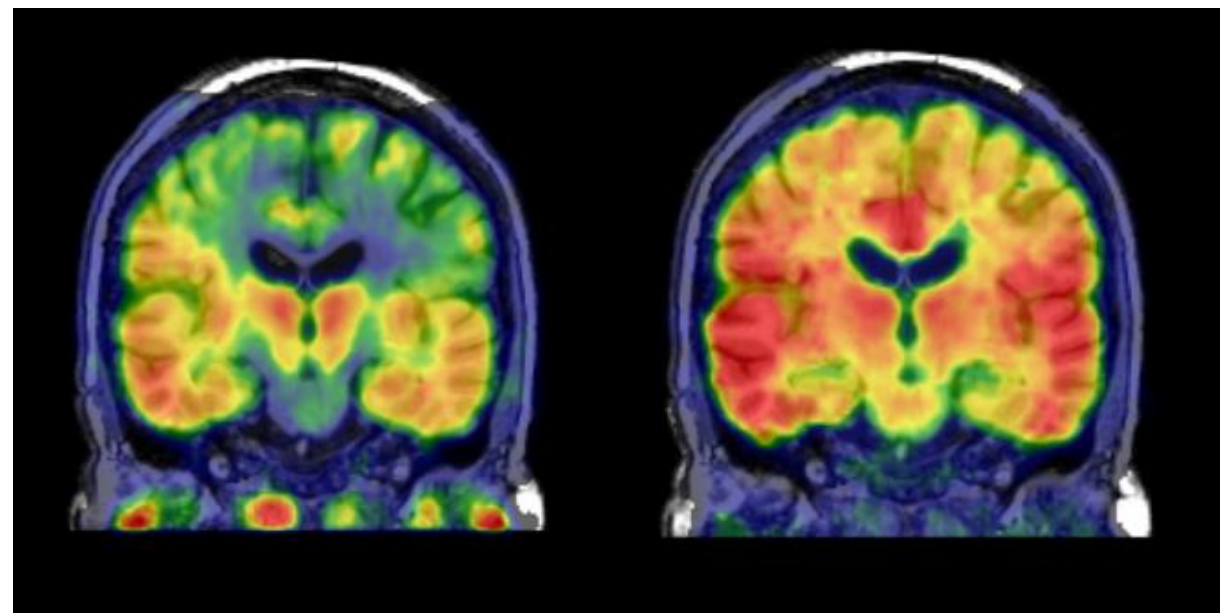
- **Preventive cardiology mentor during residency**
 - Poor representation of older adults in cardiovascular prevention trials at that time
 - Undertreatment of cardiovascular risk factors in older patients in clinical practice
 - When older adults were treated aggressively to “goal”, some couldn’t tolerate therapy
- **American Geriatrics Society meeting during fellowship**
 - Attended a talk by collaborative investigative team of urologist and geriatrician addressing cognitive impact of medications used for bladder spasms

How do I integrate patient-centered outcomes into my research?

Choosing Outcome Measures

Traditional Outcomes

- Mortality
- Disease outcome
- Biomarker or surrogate marker of disease outcome



Patient-centered Outcomes

- Symptoms
- Function
- Independence
- Mobility
- Cognition
- Quality of Life



Identifying Primary Outcome Measures and Key Covariates

- **What is my primary outcome? What are my key secondary outcomes?**
 - *Are they specific? Clinically relevant? Feasible? Validated?*
 - *Do they include biologic outcomes? Therapeutic targets? Patient-oriented outcomes?*
 - *How do they relate to my next planned research project?*
- **What additional factors could influence my ability to accurately characterize my key outcomes?**
 - *Comorbidities, medications, social determinants of health, sensory deprivation, cognitive deficits, etc.*

Identifying Primary Outcome Measures and Key Covariates

- *Review aging-related publications in your field*
- *NIA, Clin-STAR, and other aging specialty-related websites and webinars*
- *Discuss with geriatricians and older patients from diverse backgrounds*
- *Consider focus groups with diverse patients in your area of specialty*
- *Identify clinically-trained specialists in aging research and reach out to them for advice*
- *Make sure chosen instruments are validated in older adults in a research context; are they translated to different languages and/or culturally adapted*
- *Consider composite outcomes vs. focused outcomes*
- *Consider safety, feasibility, cost of measurements, participant burden*



Do Your Outcome Measures Bias Your Sample?

- **Do participants have to come to a hospital setting? Could some components be done remotely or in a community setting?**

Travel time, transportation, parking, mobility

- **Do participants have access to the necessary resources to participate?**

Access to computers, smart phones, internet services, transportation

- **Do participants understand the reason for the outcome measures?**

Health literacy, education, outreach events



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Tips in Grant Writing for Clinical Aging Research

- Do not assume that research in older adults is aging research!
- Align disease-relevant outcomes with patient-centered outcomes
- Ensure that specific outcome measures reflect the disease mechanisms you are investigating
- Demonstrate an understanding of the important aging-related covariates that will impact your key outcome measures
- Project how the proposed outcome measures will support the next step in your research trajectory



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Thank you!

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A Sampling of Statistical Considerations in Aging/Geriatrics Research

Michael E. Miller, PhD, FASA

Professor, WFSM Department of Biostatistics & Data Sciences

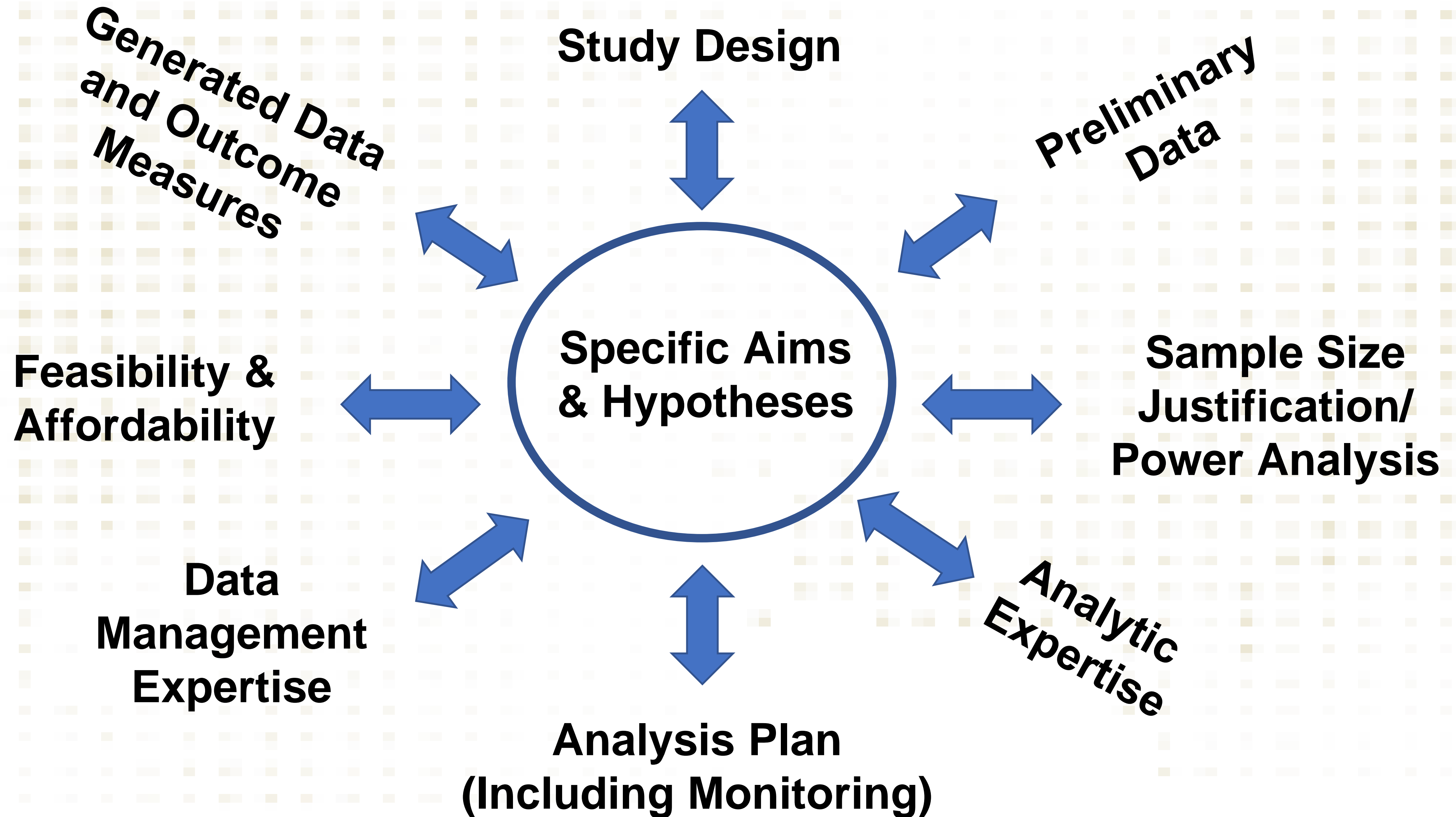
Core Leader, WFSM Older Americans Independence Center Biostatistics Core



Three Key Concepts

- Statistical concepts and considerations should be integrated and linked throughout the entire proposal
- Analytical approaches need to be tailored to the specific aims, design used to address those specific aims, interventions, and type of outcomes used in studies of older adults
- To achieve the previous two goals, writing a proposal is not a linear process and one often has to modify aims or design to account for multiple considerations, including feasibility (\$, access to populations/samples, ability to collect important variables)

Interconnectivity of Approach Descriptions



Analytical Considerations for Design and Interventions in Studies of Older Adults

- A multitude of designs are used in aging research, but there are some common considerations that must be aligned between design and analysis
 - The design may focus anywhere along a continuum (developmental/pilot, efficacy, effectiveness, implementation & dissemination), but depending on the end goal there are different analytical considerations ranging from feasibility of concepts to issues with more pragmatic implementation
 - Missing outcomes can frequently occur across all designs and should be dealt with in both design and analysis:
 - *Order of assessments*: Place most important assessments at the beginning of a visit as burden and fatigue are important considerations in studies of older adults
 - *Frequency and length of assessments*: Obtain some early assessments during the course of follow-up: “It is recommended that large-scale interventions of disability be powered on short-term outcomes but also examine long-term intervention effects” (Ferrucci et al., JAGS 2004, <https://doi.org/10.1111/j.1532-5415.2004.52174.x>)
 - *Proxy Reports*: Incorporate proxy reporting where possible, but consider the validity of instruments for proxies (Neumann et al., JAGS 2000, <https://pubmed.ncbi.nlm.nih.gov/11129756/>)

Analytical Considerations for Design and Interventions in Studies of Older Adults

- Interventions may be individual or group based, and may incorporate multiple components
 - In geriatrics research, many common and morbid health problems have multifactorial etiologies and multiple risk factors (e.g., falls, delirium, and functional disability).
 - *Multi-component interventions* seek to modify clusters of risk factors. (Allore et al., *Clinical Trials*, <https://pubmed.ncbi.nlm.nih.gov/16279575/>)
 - Selection of intervention components should take into account prevalence and correlation of risk factors
 - Too restrictive or too broad entry criteria have implications (e.g., generalizability and power)
 - *Group based interventions* are frequently used in behavioral studies of older adults and may focus on social groups or clinical settings. Ask the questions:
 - Should randomization of the whole group be considered to avoid contamination?
 - Are outcomes on one person independent of the randomized intervention that is given to another?
(Murray et al., *Ann Rev Pub Health*, 2020, <https://www.annualreviews.org/doi/10.1146/annurev-publhealth-040119-094027>)

Analytical Considerations for Outcome Selection in Studies of Older Adults

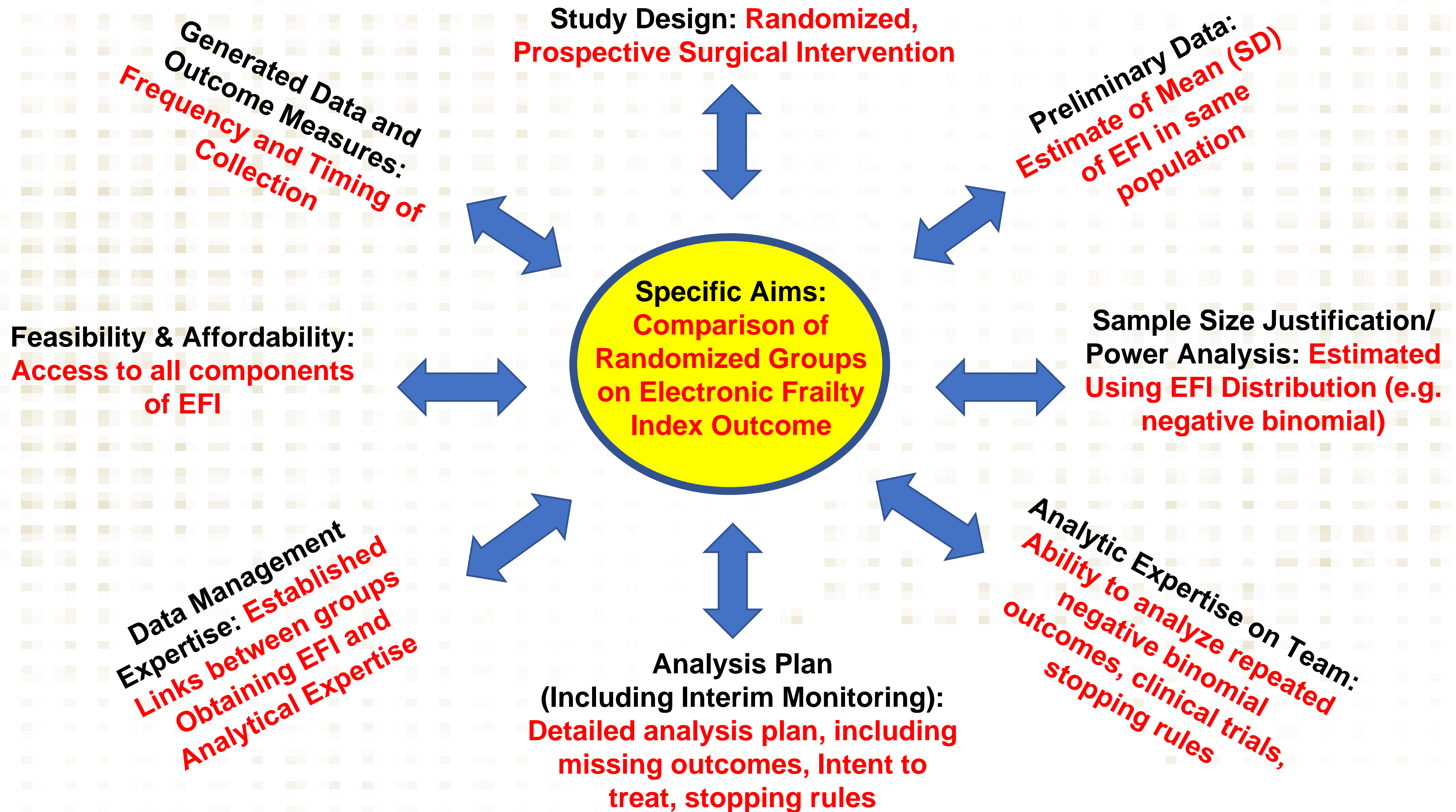
- *Composite Outcomes:* Outcomes in geriatric research often focus on function, independence, cognition, and an often used approach is to combine these into a composite outcome. Composite outcomes have special analytical considerations.
 - Will the intervention affect all components in the same direction?
 - Are all components available during follow-up on an equal schedule?
 - How will missing components be accounted for in analysis? (Is imputation used for each component?)
 - Is death a component of the composite or does the competing risk of death need to be accounted for in the analysis plan?

(See Freemantle, *BMJ*, 2010 for a commentary on the use of composite outcomes. <https://www.bmj.com/content/341/bmj.c3529>)

Analytical Considerations for Outcome Selection in Studies of Older Adults

- *Outcome Independence*: Is the selected outcome being obtained from patients seen by the same provider (e.g., multiple patients from the same surgeon with an outcome related to relapse time or health care utilization)?
 - Use analytical methods that account for this dependence and incorporate in power calculations
- *Potential for Bias*: Is the outcome one that may be impacted by bias due to who is included in the study (e.g., observational studies and selection of participants with complete data in an EHR)?
 - Consider generalizability and if associations are being investigated with the outcome, make certain the appropriate covariates have been collected to allow for adjustment for confounding
- *Tailor analytical method and collected data to question*:
 - Is this health equities research? Then, is a mixed methods analysis where you integrate qualitative and quantitative information applicable?
 - Have appropriate plans been made to incorporate sex as a biological variable? (e.g., collection of data, analysis, reporting)

An Example of Interconnectivity of Approach Descriptions



Extra Thoughts: 10 Things A Statistical Reviewer Might Focus On

- Is the study design appropriate for the study aims? How will randomization, control for confounding, etc., be implemented?
- What type of outcome data is being generated (continuous, event time, collected over equally spaced intervals) and are the analysis methods, sample size calculations and aims all consistent with data of this type?
- Have analysis methods that match each specific aim been specified?
- Can the planned sample size calculations be replicated from data provided?
- Does the analysis plan match the sample size calculations, e.g., alpha level, analysis method?
- Does the number of subjects to be recruited and followed match the sample size calculation and take into account LTFU?
- How are multiple outcomes handled relative to hypothesis testing and Type I error?
- Is an interim analysis needed for safety, efficacy or futility?
- Is the required statistical expertise present on the team?
- Have the validity, reliability, rigor and reproducibility of methods been justified?

Where to get statistical help....

- Locally is ideal as it can lead to long term collaborations –
 - Biostatistics Cores of 14 OAIC Pepper Centers (<https://www.peppercenter.org/>)
 - Shared Resources Cores through CTSI often have statisticians working in aging/geriatrics research
- National organizations may be able to help you find local help





Q&A

Have a question?

Enter in the Q&A box at the bottom of the screen