A Public Health Blueprint for Healthy Aging

Red Ribbons, Silver Threads:
Healthy Aging in the Era of HIV/AIDS

Linda P. Fried, M.D., M.P.H.
Longevity with HIV/AIDS: Adding successful aging to clinical and public health planning
Persons 50 and older living with HIV in New York State 2007

<table>
<thead>
<tr>
<th>Male (50+)</th>
<th>30,716</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (50+)</td>
<td>11,462</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42,178</strong></td>
</tr>
</tbody>
</table>
We are an aging society

• U.S. by 2030: 23% >65;
  – As many older adults as children
• Best educated, healthiest group of older adults in history
• Health status in last third of life critically important: to individual, to families, to cities, to society
Public Health Goals for an Aging Society

Life expectancy: 79 years

*Will people be living longer years healthy or ill?*
Chronic Diseases Become the Norm

Adults 65 and older:
80% 1 or more diseases
50% 2 or more diseases
40% with disability in walking
“Compression of Morbidity”

• Improving healthy later years through delaying onset of morbidity and disability to latest points in the lives of older adults.

• *Public health and clinical goal for improving the health of an aging society.*
THE COMPRESSION OF MORBIDITY

AGE (years)

PROTOTYPIC LINGERING CHRONIC ILLNESS

EFFECTS OF THE POSTPONEMENT OF CHRONIC DISEASE
Scenarios for Change in Population
Burden of Disability from 1990 to 2040

1990
Disability-Free Life Expectancy
Life Expectancy
78.8 years

Scenario 1: Stable Population Morbidity
2040
Disability-Free Life Expectancy
82.8 years
Life Expectancy
82.8 years

Scenario 2: Compression of Morbidity
2040
Disability-Free Life Expectancy
82.8 years
Life Expectancy
82.8 years

Scenario 3: Expansion of Morbidity
2040
Disability-Free Life Expectancy
82.8 years
Life Expectancy
82.8 years

Yellow: Years of life free of disability (Active life expectancy)
Red: Years disabled (Disabled life expectancy)
Changing realities
Age- and Disease-Associated Outcomes Emerge, 65+

- Chronic diseases (>80%)
- Multimorbidity (>50%)
- Frailty (7-10%)
- Falls (31%)
- Disability (40%)
Specific Diseases Cause Disability

- Heart disease
- Knee OA
- Hip fracture
- Diabetes
- Stroke
- Claudication
- COPD
- Visual Impairment
- Depression
- Cognitive Impairment
Onset of physical disability in high energy mobility tasks, men and women 65-101 in Cardiovascular Health Study

Event
- CHD
- CHF
- stroke
- random

proportion without difficulty

Months before or after incident event

-36 -30 -24 -18 -12 -6 +6 +12 +18 +24 +30 +36
Health Disparities Persist

• Disability in Inner City African Americans 49-65 years:
  – Occurs 10 years earlier than in suburban AAs and whites
  – Prevalence: 60% with >1 disability (women > men)
  – Mediated by race and SES

Miller D et al, 2005
WHAT we DO Matters with aging: Improving Health Outcomes

• Physical Activity
• Cognitive Activity
• Social engagement:
  – Social networks and support; loneliness
  – Structured activities
  – Meaningful, productive roles
  – Leaving a legacy
Historic opportunity: Shifting life stages

- In developed countries, people will be living >1/3 of their lives after retirement
- Greater longevity has created a “third age” and a “fourth age” of aging, with new opportunities and needs
Psychological Development Continues over the Life Course

(Erickson; Cohen G; others)
"generativity" is key to successful aging

- Leaving a legacy; Leaving the world better for future generations (Erikson)
  - Productive, meaningful engagement
Successful Aging is Multidimensional

- Avoidance of disease and disability
- Maintenance of high physical function
- Sustained engagement in social and productive activities

*Rowe and Kahn, 1998, from MacArthur Network on Successful Aging*
Definitions and Predictors of Successful Aging
A Comprehensive Review of Larger Quantitative Studies

Predictors of Successful Aging

• Higher Income/ educations
• Male sex (controversial)
• White ethnicity
• Current marriage/ large social network
• Better cognitive performance and memory
• Better physical performance/ Muscle strength
• No smoking/ moderate alcohol consumption
• High physical activity
• Better self-rated health
• Biomedical markers
  • High HDL cholesterol
  • No overt obesity
  • No hypertension/diabetes/CHD/cancer/OA/stroke
• No hearing problems
• No depression/ Positive attitude toward aging
• High life satisfaction/ self-efficacy/ mastery
• Positive attitude toward Aging
Potential for Prevention and Compression of Morbidity
We now know how to accomplish healthy and successful aging – enough to get started....

Translation, and new knowledge, will be key
Chronic Diseases

• Prevention and treatment make BIG differences into the oldest ages:
  – **Primary prevention:** disease *onset*
  – **Secondary prevention:** disease *remission* or prevention of progression
  – **Tertiary prevention:** *minimize* symptoms, outcomes; *maximize* quality of life
## Approaches Demonstrated: Prevention or Treatment of Chronic Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Med Tx/Prev</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>+</td>
<td>+</td>
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<tr>
<td>High Blood Pressure</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Heart Attack</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Angina</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cancer</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Lung Disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Stroke</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>
### Impact of Effective Prevention: Change in U.S. death rates, 1950-1997

<table>
<thead>
<tr>
<th></th>
<th>Age Group</th>
<th>% change</th>
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</thead>
<tbody>
<tr>
<td><strong>Heart Disease</strong></td>
<td>65-74</td>
<td>-58%</td>
</tr>
<tr>
<td></td>
<td>75-84</td>
<td>-54%</td>
</tr>
<tr>
<td></td>
<td>85+</td>
<td>-31%</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>65-74</td>
<td>-76%</td>
</tr>
<tr>
<td></td>
<td>75-84</td>
<td>-65%</td>
</tr>
<tr>
<td></td>
<td>85+</td>
<td>-46%</td>
</tr>
</tbody>
</table>

* Bureau of the Census*
Decline in CVD Mortality, U.S.

- Decline in CVD mortality, 1980-1990: 34% overall

- Contributing factors:
  - 25%: primary prevention of CVD
  - 29%: secondary prevention
  - 43%: improved medical care for patients with CVD

Hunink M, ..., Goldman L JAMA, 1997
Disability Rates are Declining


Source: Authors' tabulations using the National Health Interview Survey.

What will healthy aging require?
1. Life course approach to Prevention of Chronic Conditions
Chronic diseases develop over many years; prevention is key.

Prediction of Lifetime Risk for CVD by Risk Factor Burden at 50 Years of Age

Donald M. Lloyd-Jones, MD, ScM; Eric P. Leip, PhD; Martin G. Larson, ScD; Ralph B. D’Agostino, PhD; Alexa Beiser, PhD; Peter W.F. Wilson, MD; Philip A. Wolf, MD; Daniel Levy, MD

Optimal risk factors: TC 180 mg/dl; BP 120/80 mm Hg, nonsmoker, and nondiabetic.
Not optimal risk factors: TC 180 to 199 mg/dl, DBP 120-139 mm Hg, DBP 80-89 mm Hg.
Elevated risk factors: TC 200-239 mg/dl, SBP 140-159 mm Hg, DBP 90-99 mm Hg.
Major risk factors: TC>240 mg/dl, SBP >160 mm Hg, DBP>100 mm Hg, smoker, and diabetic

(Circulation. 2006;113:791-798.)
Predictors of cognitive decline and/or dementia in older ages

• **Childhood exposures:**
  – Education
  – Environmental risks and stressors

• **Mid life:**
  – Stroke risk factors and subclinical CVD in mid life predict cognitive decline
  – Mid life cognitive activity, joined with social activity, protective against onset of dementia in male twins; 25-44% decreased risk (Carlson et al 2008)

• **Late life:**
  – Cognitive activity (Carlson) and physical activity (Kramer) associated with increased brain activation and cognitive function
  – Stroke predicts cognitive losses
Cumulative risk manifests at older ages

- Health disparities in older adults
  - African American older adults manifest
    - More chronic diseases
    - Disability 10 years earlier than whites

(Miller, Wolinsky, et al)
Excess disability in inner city African-Americans 49-65, compared with suburban sample

- Excess Disability:
  - 30% excess disability: walking one-half mile
  - 215% excess disability: managing medications

Miller D et al, J Ger: Med Sci, 2005
2. Knowledge of how health, prevention and care needs change with age
With longer age comes serious health issues not found at younger ages:

- Geriatric conditions
- Multimorbidity
- Frailty
- Disability
Diseases/conditions can contribute to other outcomes

Prevention of distal outcomes is key
Onset of physical disability in high energy mobility tasks, men and women 65-101 in Cardiovascular Health Study

Event
- CHD
- CHF
- Stroke
- Random

Months before or after incident event
Hearing Loss and Incidence of Dementia
A longitudinal analysis in the *Baltimore Longitudinal Study of Aging*

Submitted (not for citation)
The Effect of Obesity Combined with Low Muscle Strength on Decline in Mobility in Older Persons: Results from the InCHIANTI Study

S Stenholm, D Alley, S Bandinelli, ME Griswold, S Koskinen, T Rantanen, JM Guralnik, and L Ferrucci.

Intrinsic physical and cognitive reserves evolve with aging

*Baltes Hypothesis: loss of reserves with aging*
Decreased reserves necessitate:
- new approaches to understanding vulnerabilities in aging,
- new approaches to prevention, care
Frailty Phenotype – Definition [1]

An individual is “frail” if ≥ 3 components - of 5 - are present

- Physical shrinking (unintentional weight loss)
- Weakness (grip strength)
- Slowness (time to walk 15 feet)
- Low physical activity level (weighted score of kcal/week)
- Exhaustion (self-reported)

Validated phenotype and medical syndrome [2]

Theorized and validated components of phenotype of frailty with aging, related in an adverse feedforward cycle

Frailty status predicts poor outcomes
Unadjusted 3 Year Survival Estimates by Frailty Category
CHS: Baseline Frailty Status Predicts Adverse Outcomes Clinically Associated with Frailty

<table>
<thead>
<tr>
<th>Event</th>
<th>Hazard Ratios* Estimated Over 3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident Fall</td>
<td>1.29</td>
</tr>
<tr>
<td>Worsening Mobility</td>
<td>1.50</td>
</tr>
<tr>
<td>Worsening ADL Disability</td>
<td>1.98</td>
</tr>
<tr>
<td>First Hospitalizations</td>
<td>1.29</td>
</tr>
<tr>
<td>Death</td>
<td>2.24</td>
</tr>
</tbody>
</table>

* Covariate Adjusted, p ≤ .05

Fried et al, 2001
Theoretical Pathogenesis of Frailty [1,2]

- Aging-associated energy dysregulation syndrome
  - Phenotype is a vicious cycle
  - Triggered at multiple points in cycle
  - Triggered by many diseases as a final common pathway
    - E.g., CHF, COPD, diabetes, cancers, renal impairment, HIV, possibly others
  - Greater number of abnormal physiologic systems associated non linearly with increased risk of frailty
    (emergent property)

Older adults: Health status changes over time, varies greatly

- Robust: 10-20%
- 1 Chronic Disease: 30%
- Multiple Chronic Diseases: 50%
- Frail: 7%
- Disabled: 30%
- Dependent: 10-20%
- End of Life

Time
Age
Older age has many faces
3. Health promotion for those living with HIV

Aging-related needs
• HIV as a “chronic disease”
  – Chronic disease care and prevention principles
  – Co-morbidities / toxicities (malignancies, metabolic pertubations, cardiovascular, kidney, liver, neurologic) - which have an age component
  – Geriatric conditions:
    • Polypharmacy
    • Falls
    • Frailty
    • Disability
  – Mortality
Duration of HIV Infection is Associated with Presence of Frailty-related phenotype (FRP) - Pre-HAART

Odds ratio [95% CI] to manifest the FRP*

- 3.4 [1.2-9.1]
- 13.0 [6.6-25.4]
- 14.7 [7.6-28.4]

Same FRP prevalence between a 55-year old man infected < 4 years and a >65-year old uninfected man

*Logistic regression models (GEE)
Prognostic Effect of FRP on HAART Response – Results

% alive without clinical AIDS

Logrank p-value < 0.01

No FRP before HAART

FRP before HAART

N  Events  Adjusted HR

No FRP before HAART 436  69 (16%)  1

FRP before HAART 36  13 (36%)  1.6 [0.9-3.1]
Age-specific and health needs-specific public health and health care approaches matter

Integration of public health and medicine – in both prevention and care
4. An older population will require new approaches to both public health and health care delivery

- Transformed Systems: care and prevention
- Contents: Geriatrically knowledgable
- Distributed locations – for health promotion & care
- Integration of public health and medical care
- Workforce: geriatrically knowledgable
- Environment: built and physical
- Opportunity: for giving back, productive and social engagement
Challenge: The Health Care System Not Ready for Chronic Care Needs of Older Adults

• Acute event-based care in a chronic disease world

• Effective geriatric care not implemented or reimbursed
  – Community-based coordinated continuum of care needed

• Prevention needs to be inserted into medical care and linked to community-based approaches
  – Institute of Medicine. Retooling for an Aging America: Building the Health Care Workforce, 2008
Continuum of Geriatric Care Models (Fried & Hall, 2008)

- Robust
- Chronic Disease
- Multiple Chronic Diseases
- Frail
- Disabled
- Dependent
- End of Life

Outpatient:
- Ambulatory
- Ambulatory Clinic/outpatient specialties

Inpatient:
- Acute Hospital
- ACE Unit
- Geriatric Assessment
- Chronic Care
- Nursing Home
- Palliative Care
- House Call, Home hospital
- PACE
There are now evidence-based interventions for geriatric syndromes that *improve* outcomes

- Medications management
- Delirium
- Falls
- Incontinence
- Weakness, frailty, mobility
- Function, disability
- Transitions in care

*These interventions are linked to positive outcomes*
Sarcopenia modifiable

• In “frail”, disabled nursing home patients, resistance exercise increased:
  – muscle mass by 180%
  – strength by 100%

Fiatarone et al, 1993
Building Blocks for Effective Health Promotion for an Aging Population beyond Disease Focus

<table>
<thead>
<tr>
<th>Access to Care</th>
<th>Meaningfully engaged</th>
<th>Financial Resources</th>
<th>Environmental Stressors</th>
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<tbody>
<tr>
<td>Polypharmacy</td>
<td>Disability</td>
<td>Health Disparities</td>
<td></td>
</tr>
<tr>
<td>Frailty</td>
<td>Multimorbidity</td>
<td>Falls</td>
<td>Depression/Loneliness</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Primary, Secondary Prevention; Disease Management</td>
</tr>
</tbody>
</table>
Key Policy Challenge: Who is on first?

• Public health and aging services networks are siloed
Designing New York to support successful and healthy aging
Age-Friendly City: Key Domains (WHO)

• Housing
• Transportation
• Outdoor spaces and buildings
• Social participation
• Civic engagement and employment
• Respect, social inclusion v. ageism, fear
• Communication re: services
• Community support and health services
Accomplishing positive health behaviors for an aging population will require novel, multilevel, community-based approaches.
Walkability Index

- Community Districts
- Green Space
- Airports, Landfill

Best

Worst

Walkability of Communities

Increasing Physical Activity in Older Adults: public health and health care working together

- Physician prescription
- Communities that permit/support being active
- Exercise programs
- Community-based approaches to enhance usual physical activity
Community-based approaches to health promotion: Generativity as a vehicle

Meaningful roles to make a difference:

*Experience Corps* as an example
Causal Pathway: Experience Corps

Intervention

Experience Corps Participation - Generative Role Performance

Primary Pathways

Physical Activity

Cognitive Activity

Social Activity, Engagement

Mechanisms

Strength, balance

Cortical plasticity; Memory Executive function

Social Integration & Support Generativity

Performance-based measures 
Secondary outcomes and intermediate mechanisms

Primary/ [Self Report] Outcomes

Falls

Walking Speed

Frailty

Complex task performance

IADLs

Mobility Function

↑ or preserved function or delayed decline in:

Social Integration & Support Generativity

Psycho-Social Well-being

Walking Speed

Mobility Function

↑ or preserved function or delayed decline in:

Social Integration & Support Generativity

Psycho-Social Well-being

Performance-based measures

Secondary outcomes and intermediate mechanisms

Primary/ [Self Report] Outcomes

↑ or preserved function or delayed decline in:

Social Integration & Support Generativity

Psycho-Social Well-being

Performance-based measures

Secondary outcomes and intermediate mechanisms

Primary/ [Self Report] Outcomes

↑ or preserved function or delayed decline in:
Preliminary evidence: EC Baltimore Pilot RCT, Physical Activity

• For those previously with low activity:
  – Increased physical activity within range obtained by exercise trials ($\leq 700$ kcal/wk)
  – sustained dose; high retention
  – Increase sustained over 3 years, relative to comparison group

• Participation by high risk subsets, including African American older adults

(Tan et al, 2006, 2009)
“IT SEEMED A GOOD OPPORTUNITY TO HELP OUT.”

DICK FRYER, 73, HAS A PRIVATE CHAT WITH A SECOND-GRADE OUTSIDE THE CLASSROOM. A RETIRED CIVIL ENGINEER FROM PERRY HALL, FRYER LEARNED ABOUT THE EXPERIENCE CORPS THROUGH AN AARP MAILING.
Change in Executive Function in EC volunteers v. controls

-Low normal executive function at baseline
- 6 month follow-up

(Carlson et al 2009)
Evidence for neurocognitive plasticity in at risk older adults: EC pilot study

- EC (8) v. matched Controls (9) at risk for cognitive impairment:
  - African-American women, mean age 68, HS education, low income, mean MMSE 25-26

- Baseline and 6-month follow up

- Intervention-specific short-term gains:
  - Executive Function
  - Activity of prefrontal cortical regions (fMRI)

Carlson et al JGMS, 2009
EC participants > Controls on test of executive function following 6 month exposure

PFC= prefrontal cortex; ACC= anterior cingulate cortex

Carlson, Erickson, Kramer, …Fried, JGMS 2009
“YOU ARE A FRIEND IN THE CLASSROOM.”
AUDREY WEEMS, 70, READING A STORY TO STUDENTS IN A THIRD-GRADE CLASS AT WAVERLY. A MOTHER OF EIGHT, SHE WORKED AT THE SOCIAL SECURITY ADMINISTRATION FOR 35 YEARS, RETIRING IN 2002. WEEMS LEARNED ABOUT THE BALTIMORE EXPERIENCE CORPS PROGRAM THROUGH HER CHURCH.
Role of Public Health in Goals for an Aging World

• Population goals: “compression of morbidity”
  – Individuals: Health behaviors; life course perspective for health promotion
  – Health system redesign: hospital, clinic, home & community; integration

• Design for an aging society which all ages will benefit from
  – Families, communities and cities
Healthy, successful aging: a critical societal goal
<table>
<thead>
<tr>
<th>TOPICS/ISSUES</th>
<th>Community</th>
<th>Home-Based or Institutionalized Care</th>
<th>End-of-Life/Hospice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A MOBILITY / PHYSICAL ACTIVITY</td>
<td>High Functioning/Robust</td>
<td>Usual Functioning - at risk</td>
<td>Low Functioning</td>
</tr>
<tr>
<td>B CIVIC ENGAGEMENT</td>
<td></td>
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<tr>
<td>C MENTAL HEALTH</td>
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<tr>
<td>D ISSUES OF ISOLATED OLDER ADULTS</td>
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<tr>
<td>E *EMERGENCY PREPAREDNESS/SAFETY/MONITORING</td>
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<tr>
<td>F ENSURING RECEIPT OF NEEDED CLINICAL CARE</td>
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<tr>
<td>G CHRONIC DISEASES PREVENTION &amp; MANAGEMENT</td>
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</table>
**FRP in the 3 years before HAART initiation independently predicts subsequent clinical AIDS or death** (N= 596 men in MACS) - adjusting for other predictors (multivariate Cox models)

<table>
<thead>
<tr>
<th>Exposures at HAART initiation</th>
<th>AIDS-free at HAART (N=472)</th>
<th>AIDS at HAART (N=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aHR, P-value</td>
<td>aHR, P-value</td>
</tr>
<tr>
<td>Education ≥ college</td>
<td>1.01, 0.96</td>
<td>0.87, 0.70</td>
</tr>
<tr>
<td>Ethnicity = White non Hispanic (vs others)</td>
<td>1.32, 0.45</td>
<td>0.64, 0.38</td>
</tr>
<tr>
<td>Age (per 10 years increase)</td>
<td>1.43, 0.03</td>
<td>1.31, 0.32</td>
</tr>
<tr>
<td>Nadir CD4+ T-cell count (per 100 cell/mm3 increase)</td>
<td>0.85, 0.05</td>
<td>0.94, 0.61</td>
</tr>
<tr>
<td>Maximum plasma viral load (per 1 log_{10} copies/ml increase)</td>
<td>2.08, &lt;0.01</td>
<td>1.31, 0.38</td>
</tr>
<tr>
<td>Proportion of FRP + visits before HAART (for a 25% increase)</td>
<td>1.35, 0.04</td>
<td>1.63, &lt;0.01</td>
</tr>
</tbody>
</table>

FRP, frailty-related phenotype; aHR, hazard ratios adjusted for variables listed in the table; 1 adjusted hazard ratios for AIDS/death; 2 adjusted hazard ratios for death only; 3 within the 3 years before HAART
Definitions and Predictors of Successful Aging
A Comprehensive Review of Larger Quantitative Studies

Components for the Definition of Healthy Aging

- Disability Physical Functioning
- Cognitive Functioning
- Life satisfaction/Well-Being
- Social/Productive Engagement
- Illness/Disease
- Longevity
- Self-Rated Health
- Personality
- Environment/Finances
- Self-rated successful aging

Physical disability in community-dwelling persons 70 and older, U.S.: due to chronic diseases

• 10% incidence/year

• Difficulty: Men Women

  - Walking 30% 33%
  - IADLs 13% 7%
  - ADLs 22% 17%

NCHS, 1999
Preliminary Evidence of Intermediate Effects: EC vs. Controls

• Behavioral Risk Factors:
  – Physical activity
  – Cognitive activity
  – Social supports

• Intermediate effects:
  – Cognition (executive); brain activation
  – Strength, performance, energy, falls
  – Depressive symptoms
Why is Executive Function Important?

• Ability to plan, initiate, and carry out a course of action, shift flexibly and modify goals

• Integral to performing many independent activities of daily living (e.g., Grigsby et al., 1998; Carlson et al., 1999)

• Age-related changes in executive function may precede changes in memory (Carlson et al.)
Large-scale RCT of Experience Corps being conducted in Baltimore, MD

- Funded by NIA BSR, plus AmeriCorps, Weinberg Foundation, MacArthur Foundation
- Initiated Fall 2006
- Randomizing 600 people 60 years and older to EC or low-activity volunteering control;
- 20+ public elementary schools to EC; matched controls
- Outcomes for older adults: physical disability, mobility, frailty, fall risk, memory and intermediate neurocognitive changes
- Outcomes for children: standardized scores;
Implications of Experience Corps Design

- Generative potential attracts and fulfilled generativity retains older adults
- Lifestyle activity, in a 15-hour/week dose, shows increased physical, cognitive and social activity and is neurocognitively protective
- High longterm retention: sustained dose of prevention
- Designed for a win-win
  - Social model for health promotion
  - Harnessing social capital of aging society
New York: growing older

- 2005, New York City
  - 65 and older: 12% of New York City; 17% of some neighborhoods
    - 43% with some disability
    - 18.1% poor (U.S. 9%)
    - 12.1% poor and disabled (U.S. 5.5%)
Life course approach to healthy aging is essential
Chronic Disease & Susceptibility Over the Life Course

- Cumulative disease processes develop chronically and progressively over the life course
- Initiators, Promoters, Modifiers and Mediators are active
- In many trajectories, exposure and intervention at any point can make a difference; however, there may be points of particular opportunity for prevention
- At different ages, additional age-specific issues emerge and may require unique interventions

“... the ills that flesh is heir to... it must be that many a taint grows deeply, mysteriously grained in their being ...”
-Virgil, The Aeneid, 1st Century BCE
Smoking, Physical Activity, and Active Life Expectancy

Luigi Ferrucci, Grant Izmirlian, Suzanne Leveille, Caroline L. Phillips, Maria-Chiara Corti, Dwight B. Brock, and Jack M. Guralnik

1. Higher physical activity positively impact ALE more than DLE
2. Smoking has the highest impact on longevity
3. However, people who never smoked and were sedentary have the same longevity but shorter ALE than those who smoked and were physically active
4. These findings are consistent in men and women and according to age group
5. Women live longer but have only slightly longer ALE than men.
Trends in the overall CHS cohort

Difficulty in physical function: high energy tasks
In full CHS cohort

Year since baseline

- dead
- severe
- moderate
- mild
- none

percent

0 1 2 3 4 5 6 7 8 9

0 100 80 60 40 20 0
Reduced Disability and Mortality Among Aging Runners: A 21-Year Longitudinal Study

Eliza F. Chakravarty, MD, MS; Helen B. Hubert, PhD; Vijaya B. Lingala, PhD; James F. Fries, MD

Arch Intern Med. 2008;168(15):1638-1646
Self-reported physical function: medium energy tasks

Months before or after incident event

proportion without difficulty

Event
- CHD
- CHF
- stroke
- random

-36 -30 -24 -18 -12 -6 +6 +12 +18 +24 +30 +36
Compression of Morbidity: Major public health goal for an aging society

- Push back development of disease and disability to latest points in human life span
- Add “life to years”
Life Course Across the Lecture

- Frederica Perera
  - *in utero* environmental exposures and effects in childhood and beyond
- Ezra Susser
  - latent and transgenerational effects
- Bruce Link
  - disparities and disease risk
- Linda Fried
Chronic Diseases Emerge Over the Life Course
Health Biography of Older Age
Burden of Illness/Disability from 1990 to 2040

Scenario 1: Stable Population Morbidity
- 1990: Active Life Expectancy - 78.8 years
- 2040: Active Life Expectancy - 82.8 years
- Years of life free of disability: 78.8 years
- Years disabled: 4 years

Scenario 2: Compression of Morbidity
- 1990: Active Life Expectancy - 78.8 years
- 2040: Active Life Expectancy - 82.8 years
- Years of life free of disability: 82.8 years
- Years disabled: 0 years

Scenario 3: Expansion of Morbidity
- 1990: Active Life Expectancy - 78.8 years
- 2040: Active Life Expectancy - 82.8 years
- Years of life free of disability: 82.8 years
- Years disabled: 4 years
Compression of Morbidity:
Major public health goal for an aging society

- Push back development of disease and disability to latest points in human life span
- Add “life to years”
Potential for Prevention and Compression of Morbidity
Impact of Effective Prevention: Change in U.S. death rates, 1950-1997

<table>
<thead>
<tr>
<th>Age Group</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Disease</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>-58%</td>
</tr>
<tr>
<td>75-84</td>
<td>-54%</td>
</tr>
<tr>
<td>85+</td>
<td>-31%</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>-76%</td>
</tr>
<tr>
<td>75-84</td>
<td>-65%</td>
</tr>
<tr>
<td>85+</td>
<td>-46%</td>
</tr>
</tbody>
</table>

Source: Bureau of the Census
# Approaches Demonstrated: Prevention or Treatment of Chronic Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Med Tx/Prev</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Angina</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cancer</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Lung Disease</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
(moderate/vigorous) and 5-year mortality, Men and Women 65-101 years of age, CHS

<table>
<thead>
<tr>
<th>Kcals/week:</th>
<th>Death rate/1000 person-years</th>
<th>RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 67.5</td>
<td>52.1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>67.5-472.5</td>
<td>32.8</td>
<td>0.78</td>
<td>(*)</td>
</tr>
<tr>
<td>472.5-980</td>
<td>28.7</td>
<td>0.81</td>
<td>(*)</td>
</tr>
<tr>
<td>980-1890</td>
<td>22.9</td>
<td>0.72</td>
<td>*</td>
</tr>
<tr>
<td>&gt;1890</td>
<td>15.5</td>
<td>0.56</td>
<td>*</td>
</tr>
</tbody>
</table>

Fried. JAMA, 1998
## Erikson’s 8 Stages of Psycho-Social Development

<table>
<thead>
<tr>
<th>Stage</th>
<th>Language Phase</th>
<th>Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Infancy</td>
<td>0 to 18 months</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Toddlerhood</td>
<td>18 months to 3 years</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Early Childhood</td>
<td>3 to 5 years</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Middle Childhood</td>
<td>5 to 12 Years</td>
</tr>
<tr>
<td>Stage 5</td>
<td>Adolescence</td>
<td>12 to 18 years</td>
</tr>
<tr>
<td>Stage 6</td>
<td>Young Adult</td>
<td>20s +</td>
</tr>
<tr>
<td>Stage 7</td>
<td>Middle Adulthood</td>
<td>25 to 65 years</td>
</tr>
<tr>
<td>Stage 8</td>
<td>Older Adulthood</td>
<td>60 years+</td>
</tr>
</tbody>
</table>

- **Trust vs Mistrust**
- **Autonomy vs Shame & Doubt**
- **Initiative vs Guilt**
- **Industry vs Inferiority**
- **Identity vs Role Confusion**
- **Intimacy vs Isolation**
- **Generativity vs Stagnation**
- **Ego Integrity vs Despair**
• Goal: Healthy aging
• Opportunities for optimizing health and wellbeing?
• When to intervene?
Times of particular risk, of development and of malleability

- Perinatal
- Infancy
- Childhood
- Adolescence
- Young adulthood
- Middle age
- Young-old
- Old-old
Falls prevention through multirisk factor intervention leads to 30% decline in falls, 1 Year of Follow-up.

Frailty: A Brief Overview

Definition

“A central definition of frailty in geriatric medicine is that it is a clinical state of vulnerability to stressors, […] resulting from aging-associated declines in resiliency and physiologic reserves and a progressive decline in the ability to maintain a stable homeostasis.” [1]

Frailty is a predictor of poor outcomes

- Falls
- Hospitalization
- Institutionalization
- Disability
- Mortality [2]

WHO/IOM Pathway to Disability

Pathology/Disease → Impairments → Functional Limitations → Disability

Frailty
WHAT older adults DO affects their health...

• Activity and engagement
  – Physical
  – Social
    • Networks, support
    • Engagement;
    • Regular structured activities
  – Cognitive
A Social Model of Health Promotion for an Aging Society: Experience Corps

- High intensity volunteering for older adults
- High impact roles in public elementary schools improving outcomes for children
- Critical mass of older adults:
  - Shift outcomes for schools
  - Force for social benefit
  - Social networks and friendships
- Health promotion program embedded
  » Fried et al, 2004
Aging issues in HIV/AIDS

- Frailty
- Multimorbidity
- Polypharmacy
- Disability
HIV and Aging

• Similarities between HIV and aging at the biological level
  – T-lymphopenia, decreased cellular immunity
  – Replicative senescence of T-lymphocytes
  – ↑ pro-inflammatory markers (IL-6, TNF-α, IFN-γ)

• Similarities between HIV and aging at the clinical level
  – Sarcopenia, weight loss, wasting
  – Cognitive disorders, dementia
  – Rheumatologic disorders, decrease in bone mineral density
  – Frailty-like clinical presentation presaging death
Definition of a frailty-related phenotype (FRP)

- The FRP definition was based on the frailty phenotype of Fried et al.
- Components of the frailty phenotype:
  - Physical shrinking (unintentional weight loss) - available
  - Weakness (grip strength) - not available *
  - Exhaustion (self-reported) - available
  - Slowness (time to walk 15 feet) - approximated (SF-36) *
  - Low physical activity level (a weighted score of kilocalories/week) - approximated (SF-36)

Exhaustion: During the past 4 weeks, as a result of your physical health, have you had difficulty performing your work or other activities (for example, it took extra effort)?
Slowness: Does your health now limit you in walking several blocks?
Low physical activity: Does your health now limit you in vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?

* Grip strength and time to walk have recently been incorporated in the MACS
Figure 2. Adjusted prevalence of having a frailty-related phenotype according to age and presence and duration of HIV infection, for fixed values of ethnicity (white non-Hispanic) and educational level (college), among HIV-seronegative and seroconverted men in the Multicenter AIDS Cohort Study (MACS) between April 1994 and January 1, 1996 when (a) all person-visits were included and (b) excluding person-visits occurring later than 6 months before the first AIDS-defining illness. The ratio of the areas (and middle vertical length) of any two shaded polygons equals the ratio of the two corresponding prevalences written in their centers. For example, the area corresponding to a prevalence of 1.7% is equal in a and b, and is the equivalent of half the area corresponding to a prevalence of 3.4%.

Summary

- HIV-1 infection was associated with a >10-year earlier occurrence of a phenotype related to frailty (FRP) [1]

- Non-linear association between CD4 cell count and FRP
  - Risk of FRP increased with decreasing CD4 cell count, especially when CD4 cell count < ~400/mm³ [2]

- After adjusting for ages and CD4 cell count, FRP prevalence decreased after the introduction of HAART, but has not further diminished with the establishment of HAART [2]

- Older age, lower educational level, and clinical AIDS were independently associated with FRP among HIV+ men [1]

- Proportion of visits with FRP prior to HAART initiation independently predicted the subsequent risk of AIDS or death, even after HIV suppression

- True Frailty Phenotype is under investigation.

Completing the epidemiologic transition: preventing chronic disease - associated with aging

*Transitioning to a chronic disease world*

- Chronic, progressive
- Multifactorial etiology
- Multilevel solutions

*Both public health and medical care*
Challenge: The Public Health System Not Ready for Aging

- Evidence on primary, secondary and tertiary prevention for older adults not implemented through public health

- 20% of older adults in community isolated, without access to care; ineffective links to clinical care provision

- Responsibility for public and community health for an aging population not allocated
Challenge: Public Health could lead by designing an integrated health system – that invests in prevention.

Public health and medical care in one coordinated system.
Building Blocks for Effective Health Promotion for an Aging Population beyond Disease Focus

<table>
<thead>
<tr>
<th>Access to Care</th>
<th>Widowhood</th>
<th>Financial Resources</th>
<th>Environmental Stressors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypharmacy</td>
<td>Disability</td>
<td></td>
<td>Health Disparities</td>
</tr>
<tr>
<td>Frailty</td>
<td>Multimorbidity</td>
<td>Falls</td>
<td>Depression/ Loneliness</td>
</tr>
<tr>
<td>Primary, Secondary Prevention; Disease Management</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Community-based Continuum of Living Situations and Services: Matching Needs

- Robust 10-20%
- 1 Chronic Disease: 30%
- Multiple Chronic Diseases: 50%
- Frail: 7%
- Disabled: 30%
- Dependent 10-20%
- End of Life

Time

Age
Age-Friendly City: Key Domains

- Housing
- Transportation
- Outdoor spaces and buildings
- Social participation
- Civic engagement and employment
- Respect and social inclusion; address ageism, fear
- Communication and information re: services
- Community support and health services
WHAT we DO Matters with aging: Improving Health Outcomes

- Physical Activity
- Cognitive Activity
- Social engagement:
  - Social networks and support; loneliness
  - Meaningful, productive roles
  - Leaving a legacy
Population-based studies show that lack of activity and engagement adversely affect health outcomes for older adults.

- Social isolation
- Loneliness
- Non-stimulating environments
- Sedentariness
- Little sense of purpose
Few meaningful roles for older adults

- At the same time, society needs the contributions of older adults:
  - Only increasing natural resource
  - Best educated cohort of older adults in history of world
  - Time, experience, wisdom
  - Wanting to leave the world a better place
Ho: “generativity” is key to successful aging

- Leaving a legacy; Leaving the world better for future generations (Erikson)
  - Productive, meaningful engagement
What if we could create new, meaningful, generative ways for people to stay engaged after retirement - and design them to promote health?

A win-win: target roles to societal unmet needs
Public health for an aging society will benefit all of us

- Systems for health designed to prevent and ameliorate chronic conditions
- Healthy older adults; successful aging
- Healthy communities
- Healthy cities
- Institutions that support continued engagement and productivity with aging
- Strengthening win-wins across generations
- Who we are as a society
Challenge: The Health Care System Not Ready for Chronic Care Needs of Older Adults

• Acute event-based care in a chronic disease world

• Effective geriatric care not implemented or reimbursed
  – Community-based coordinated continuum of care needed

• Prevention needs to be inserted into medical care and linked to community-based approaches
  – *Institute of Medicine. Retooling for an Aging America: Building the Health Care Workforce, 2008*
Continuum of Geriatric Care Models

Robust
|
| Chronic Disease
|
| Multiple Chronic Diseases
|
| Frail
|
| Disabled
|
| Dependent
|
| End of Life

Outpatient: Ambulatory
|
Inpatient: Ambulatory Clinic/outpatient specialties
|
Acute Hospital
|
ACE Unit
|
Geriatric Assessment
|
Chronic Care
|
Nursing Home
|
Palliative Care
|
PACE
Challenge: The Public Health System Not Ready for Aging

• Evidence on primary, secondary and tertiary prevention for older adults not implemented through public health

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<td>Falls</td>
<td>Depression/Loneliness</td>
</tr>
</tbody>
</table>

Primary, Secondary Prevention; Disease Management
FIGURE 1. Estimated prevalences of a FRP as a function of CD4 T-cell count in the MACS for fixed values of age (45 years), fixed percentage for ethnicity (80% white non-Hispanic), education (52% >=college), and prevalence of AIDS (20%), in the pre-HAART era (1994-1995; dotted line), introduction of HAART era (1996-1999; dashed line), and established HAART era (2000-2005; plain line). The curves for the 2 HAART eras do not differ significantly from each other, but both are significantly different from that of the pre-HAART era (see text for odds ratios and P values comparing the 3 different eras).

Figure 1. Estimated prevalence of a frailty-related phenotype (FRP) as a function of age among 1977 HIV-seronegative individuals from the Multicenter AIDS Cohort Study (MACS) cohort (April 1994–November 2004) (95% confidence interval [CI]).

Area Profile
New York State

2007

New York State Department of Health
Bureau of HIV/AIDS Epidemiology
Persons* Ages 13 and Older, Living with HIV/AIDS by Gender, Risk and Current Age
New York State

Male
N = 82,219

Female
N = 36,892

13-24
N=2,746
N=1,852

25-49
N=48,757
N=23,578

50+
N=30,716
N=11,462

Percent

MSM
IDU
MSM/IDU
Hetero
Blood
Pediatric
Unk/Under Investigation

* Includes prisoners.
### Persons Living with HIV/AIDS and Cumulative AIDS Cases*

#### New York State

<table>
<thead>
<tr>
<th>Region of Residence at Time of Diagnosis</th>
<th>Living with HIV (non AIDS)</th>
<th>Living with AIDS</th>
<th>Cumulative AIDS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York City</td>
<td>35,640</td>
<td>57,029</td>
<td>144,887</td>
</tr>
<tr>
<td>Rest of State</td>
<td>10,400</td>
<td>16,860</td>
<td>35,787</td>
</tr>
<tr>
<td>New York State</td>
<td>46,040</td>
<td>73,889</td>
<td>180,674</td>
</tr>
</tbody>
</table>

*Includes prisoners.
Estimated numbers of persons living with HIV/AIDS, by year and selected characteristics, 2004–2007—34 states and 5 U.S. dependent areas with confidential name-based HIV infection reporting (Numbers derived from Table 9)

<table>
<thead>
<tr>
<th>Age</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–54</td>
<td>53,903</td>
<td>60,030</td>
<td>67,082</td>
<td>74,582</td>
</tr>
<tr>
<td>55–59</td>
<td>28,077</td>
<td>33,023</td>
<td>38,186</td>
<td>43,985</td>
</tr>
<tr>
<td>60–64</td>
<td>13,363</td>
<td>15,309</td>
<td>17,705</td>
<td>20,962</td>
</tr>
<tr>
<td>≥65</td>
<td>10,512</td>
<td>12,361</td>
<td>14,363</td>
<td>16,982</td>
</tr>
</tbody>
</table>

Note. These numbers do not represent reported case counts. Rather, these numbers are point estimates, which result from adjustments of reported case counts. The reported case counts have been adjusted for reporting delays and missing risk-factor information, but not for incomplete reporting.

Estimated numbers of persons living with AIDS, by year and selected characteristics, 2003-2007 - United States (50) and the District of Columbia (numbers derived from Table 12)

<table>
<thead>
<tr>
<th>Age</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–54</td>
<td>46,661</td>
<td>53,125</td>
<td>59,045</td>
<td>66,003</td>
<td>72,991</td>
</tr>
<tr>
<td>55-59</td>
<td>23,976</td>
<td>28,149</td>
<td>33,279</td>
<td>38,626</td>
<td>44,298</td>
</tr>
<tr>
<td>60-64</td>
<td>11,224</td>
<td>13,232</td>
<td>15,265</td>
<td>17,878</td>
<td>21,196</td>
</tr>
<tr>
<td>≥65</td>
<td>8,842</td>
<td>10,450</td>
<td>12,232</td>
<td>14,386</td>
<td>17,005</td>
</tr>
</tbody>
</table>

90,703 104,956 119,821 136,893 155,490

Note. These numbers do not represent reported case counts. Rather, these numbers are point estimates, which result from adjustments of reported case counts. The reported case counts have been adjusted for reporting delays and missing risk-factor information, but not for incomplete reporting.

Frailty and HIV in the Multicenter AIDS Cohort Study (MACS)

Joseph B. Margolick, L. Desquilbet, L. P. Fried, L. P. Jacobson
Studies of a Frailty-Related Phenotype in the MACS

- 4954 MSM followed semiannually since 1984
- The FRP was present if $\geq 3$ of the above 4 components were answered “yes” (#1 and #2) or “yes, limited a lot” (#3 and #4)
- Covariates: Age, Education, Ethnicity, CD4 cell count, HIV RNA
- Study population
  - MACS individuals enrolled before 1996
  - Seroconverter and seroprevalent men
  - $\geq 1$ measurement of CD4 cell count between visit 21 and visit 41
- Visits:
  - All HIV+ visits between visit 21 and visit 41
- Final study population: N = 1045 (N person-visits = 12,916)
  - 98 men had no measurement of CD4 count
## Number of person-visits (1994-2004)

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=2,660)</td>
<td>(N=5,104)</td>
<td>(N=5,152)</td>
</tr>
<tr>
<td>Visits with FRP % (N)</td>
<td>7.6% (184)</td>
<td>5.3% (247)</td>
<td>4.4 (198)</td>
</tr>
<tr>
<td>Current age*</td>
<td>41 (37-46)</td>
<td>44 (39-48)</td>
<td>48 (44-52)</td>
</tr>
<tr>
<td>Current CD4 cell count*</td>
<td>320 (133-500)</td>
<td>415 (262-609)</td>
<td>489 (324-696)</td>
</tr>
<tr>
<td>Current CD4:CD8 ratio*</td>
<td>0.31 (0.15-0.51)</td>
<td>0.42 (0.26-0.63)</td>
<td>0.51 (0.33-0.75)</td>
</tr>
</tbody>
</table>

* Median (IQR)
Relationship between CD4 T-cell count and Prevalence of Frailty-Related Phenotype, by Calendar Period

Effect of Age Decreases for Low CD4 T-Cell Counts

- **Prevalence (%) of FRP [95% CI]**
  - 14
  - 10
  - 6
  - 2

- **Established HAART era**
  - **Estimated %**
  - **95% CI**

- **CD4 T-cell count (cells/mm³)**

- **Prevalence (%) of FRP [95% CI]**
  - 100
  - 200
  - 300
  - 400
  - 500
  - 600
  - 700
  - 800
  - 900
  - 1000

- **55 years old**
- **40 years old**
Time to AIDS or Death After Starting HAART, by Presence or Absence of a Frailty-Related Phenotype

- No FRP before HAART
- FRP before HAART

P-value < 0.01

N_{event} = 32

N_{event} = 8
Acknowledgements

- Multicenter AIDS Cohort Study (MACS)
  - J. Phair (Chicago)
  - R. Detels, B. Jamieson (Los Angeles)
  - L. Jacobson (Baltimore)
  - C. Rinaldo, M. Holloway (Pittsburgh)

- Columbia Mailman School of Public Health
  - L. Fried

- Parisian National Veterinary School
  - L. Desquilbet
Association of number of physiological systems at abnormal levels with being frail, women aged 70-79 years (p < .01 for qualitative trend)

### Observed FRP prevalence according to CD4 count (1994-2004)

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>FRP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>322</td>
<td>169</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>155</td>
<td>204</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>131</td>
<td>246</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>152</td>
<td>294</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>179</td>
<td>351</td>
<td>180</td>
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<tr>
<td></td>
<td>165</td>
<td>398</td>
<td>222</td>
</tr>
<tr>
<td></td>
<td>165</td>
<td>350</td>
<td>266</td>
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<tr>
<td></td>
<td>163</td>
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<td>330</td>
<td>310</td>
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<tr>
<td></td>
<td>116</td>
<td>297</td>
<td>336</td>
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<tr>
<td></td>
<td>104</td>
<td>227</td>
<td>325</td>
</tr>
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<td>71</td>
<td>219</td>
<td>280</td>
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<td>69</td>
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<td>76</td>
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<td>131</td>
</tr>
<tr>
<td></td>
<td>174</td>
<td>4541</td>
<td>103</td>
</tr>
</tbody>
</table>

*Table 1: Observed FRP prevalence by CD4 count and year of diagnosis (1994-2004).*

*Note: FRP = Fungal Respiratory Pathology.*
### Effect of FRP status at HAART Initiation on Outcomes

#### Among AIDS-free men

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>FRP prior to HAART¹</th>
<th>No (n=475)</th>
<th>Yes (n=36)</th>
<th>Total (n=511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No outcome</td>
<td></td>
<td>394 (83)</td>
<td>22 (61)</td>
<td>416 (81)</td>
</tr>
<tr>
<td>AIDS/death</td>
<td></td>
<td>81 (17)</td>
<td>14 (39)</td>
<td>95 (19)</td>
</tr>
<tr>
<td>Among AIDS/death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td></td>
<td>54 (67)</td>
<td>8 (57)</td>
<td>62 (65)</td>
</tr>
<tr>
<td>Death with no previous AIDS</td>
<td></td>
<td>27 (33)</td>
<td>6 (43)</td>
<td>33 (35)</td>
</tr>
</tbody>
</table>

**FRP, frailty related phenotype**

¹ within a 3-year period prior to HAART

#### Among AIDS-diagnosed men

<table>
<thead>
<tr>
<th>Outcome</th>
<th>FRP prior to HAART¹</th>
<th>No (n=91)</th>
<th>Yes (n=50)</th>
<th>Total (n=141)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No outcome</td>
<td></td>
<td>71 (78)</td>
<td>29 (58)</td>
<td>100 (71)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td>20 (22)</td>
<td>21 (42)</td>
<td>41 (29)</td>
</tr>
</tbody>
</table>

**FRP, frailty related phenotype**

¹ within a 3-year period prior to HAART
Disability Status at Four Years According to Baseline Summary Performance Score Among Those Non-Disabled at Baseline (Iowa – EPESE)

ADL = activity of daily living
Current HAART Era: Age Issues

- Immunologic mechanisms leading to worse HIV disease
  - Decreased T-cell replacement
  - Decreased cellular response to HAART
  - Decreased function on a per lymphocyte basis
  - Dysregulation leading to impaired responses
  - Exacerbation of normal age-related immune deterioration
    - Immune activation (remains present on HAART)

- Non-immunologic mechanisms leading to worse prognosis
  - Frailty - may have immunologic basis even without HIV
  - Age-related morbidities
    - Interactions with HAART

- Possibility of immune-modulatory therapy for HIV

- Vaccine responses
  - HIV
  - Others

(Margolick, JB, unpublished)