**Appendix A**

**Summary of Results**

**First Author Date Country**

**Design Setting**

**Sample Outcomes Measured Key Findings Factors Associated**

**with Frailty**

**Onen 2010 USA**

**Ness 2013 USA**

**Althoff 2014 USA**

**Chode 2016 USA**

descriptive correlational

HIV clinic

St Louis, MO Jan 2008 to

Dec 2008

descriptive correlational, prospective subset

subset of St Jude Lifetime cohort

date not reported

descriptive correlational,

prospective interval

subset from a larger cohort study

four US cities Oct 2007 to

Sep 2011

descriptive correlational, longitudinal

St Louis, MO Sep 2000 to

Jul 2001, &

2010

N=445 patients seeking HIV+ related care

33-49 years

71% male

30% Caucasian

63% African American

N=2263 CCS (n=1922),

CCS subset (n=162)

control group (n=341)

18-60 years CCS subset at

baseline and 3.5 years

N=1946 MWHSWM

HIV positive (n=989)

control group (n=1048)

50-64 years

Maximum 8 visits

N=998

African Americans

DM (n=222)

control group (n=775) and

49-65 years

Baseline and 9 years

sociodemographic, frailty, risk behavior assessment, disclosure of HIV status, STI testing

chronic conditions, sex, race, cancer- related variables, BMI, social history, prior radiation, chemotherapy, surgery, frailty

demographics, depression screen, AIDS history, drug therapy, co- morbidities, inflammatory markers, HIV serostatus, CD4 T- cell count, viral load, frailty phenotype conversion

disability, function, physical performance, inflammatory markers, frailty

nine years later: new ADLs ≥ 1,

mortality

Frail individuals were older than non-frail.

Frail individuals were more likely to disclose HIV status to family than non- frail individuals.

Baseline frailty was associated with increased mortality risk and chronic condition onset.

Positive phenotype conversion among all men at all visits was 25%.

HIV positive: 12% positive phenotype conversion.

Control group: 9% positive phenotype conversion.

Frailty scores were ↑ for African Americans with DM vs control group.

Middle-aged African American with DM with ↑ frailty scores are at increased risk of 9-year mortality, falls in the previous year, and ADLs ≥1.

*Physical:*

age

*Social:*

HIV status disclosure to family

*Physical:*

age, abdominal/pelvic radiation, cranial radiation in females, BMI<18.5 or >39.9

kg/m2,

*Psychological:*

smoking

*Physical:* age, HIV positive, diabetes, kidney disease, hepatitis C

*Social:*

black race,

lower educational attainment

*Psychological:*

depressive symptoms, smoking

*Physical:*

diabetes, increased disability and functional limitations, higher cytokines (TNFR1 & TNFR2)

**Hadenfeldt 2017**

**USA**

descriptive, cross- sectional

Two free clinics in the Midwest

Jun 2014 to

Aug 2015

N=38

seeking medical care at free clinic

40-65 years

68% female

63% single

68% high school education or less

50% $0 to $500 monthly income

demographics, frailty Psychological, social

and environmental factors that may adversely affect health were identified.

Descriptive statistics only.

**Palmer 2017**

**United Kingdom**

**Demircioglu 2018**

**Turkey**

**Griffin 2018 USA**

**Haider 2019**

**Austria**

descriptive correlational, cross- sectional

Subset from a larger cohort study, adults registered with English general practices

2013 to 2014

descriptive correlational

outpatient HD clinic

Oct 2016 to

Nov 2016

descriptive correlational, longitudinal

secondary analysis of larger study (HANDLS)

in Baltimore, MD

Aug 2004 to

Nov 2008

descriptive, correlational

N=8095

community- dwelling adults

50-65 years

46% males

63.7%

unemployed

N=74

CKD patients receiving hemodialysis for at least 12 months

18-65 years

44.6% male

86% married

18% employed N=2541 urban-

dwelling adults

* 1. years

56% female

58% black

40% below 125% of the federal poverty limit Baseline and 6.6

years

N=100

seropositive RA patients

* 1. years

age, social class, employment status, employment related outcomes and perceptions, physical frailty symptoms, frailty

demographics, serum vitamin D, hemoglobin, albumin, parathyroid hormone, comorbidities, frailty

age, sex, race, poverty status, education, BMI, physical function, IADL, grip strength, self-rated health, polypharmacy, frailty

6.6 years later: mortality

sociodemographic, RA disease activity and duration, pain intensity, physical performance, meds,

Frailty symptoms were associated with unemployment, HRJL, sick leave, and not coping at work.

62% unemployed participants left their last job for health- related reasons.

Frailty score positively correlated with age.

Frailty was associated with low albumin, hemoglobin, and vitamin D levels.

Frailty was associated with the lowest average survival

>6.6 years, then prefrail, then non- frail.

Higher proportion of frailty in whites than blacks among aged 45-54 years.

Higher RA disease activity and longer duration, unemployment, higher pain intensity,

*Social:*

unemployment, sick leave, HRJL, adverse employment outcomes, not coping at work

*Physical:*

age,

lower vitamin D, lower hemoglobin,

lower albumin

*Physical:*

age, female gender, taking more than six medications, higher BMI

*Psychological:*

lower self-rated health

*Social:*

below poverty status, lower educational attainment

*Physical:*

higher pain intensity, higher RA disease activity and duration

*Social:* unemployment

**Paolillo 2019 USA**

**Rubtsova 2019 USA**

**Salem 2019 USA**

outpatient clinic in Vienna

Nov 2015 to

Aug 2016

descriptive correlational

subset from a larger cohort study, San Diego

enrollment date not reported

descriptive correlational

subset from a larger cohort study, San Diego

enrollment date not reported

descriptive correlational

four homeless shelters in CA

Feb 2015 to

May 2016

66% female

59% employed

71% married/in a relationship

N=210

HIV+/MA+ (n=43) HIV+/MA- (n=75)

control group (n=92)

35-65 years

N=127

People living with HIV (PLWH)

(n=65)

Control group (n=62)

35-65 years

80% male

53% Caucasian

N=130

homeless, formerly incarcerated, women

18-65 years

40% African American 46.9% high

school education

13.4% married

inflammatory markers, frailty

sociodemographic, HIV serostatus, psychiatric, frailty assessment, neurocognitive assessment, functional assessment

Sociodemographic, frailty assessment, psychosocial factors, biomedical variables, comorbidities

sociodemographic, psychologic factors, social factors, physical factors, frailty assessment

were associated with a higher frailty score.

Comorbid HIV+/MA+ group had higher mean FI scores than the HIV+/MA- group and the control group.

HIV+ groups displayed worse global and executive functioning than the HIV-/MA- groups.

Positive psychosocial factors reduced odds of frailty in all subjects.

Positive Resources/ Outlook were more strongly associated with decreased odds of frailty for PLWH than for HIV negative adults.

Frailty subscales (mean):

physical=2.0 (0-8), psychological=

1.7 (0-4),

social=1.1 (0-3)

Daily alcohol use was associated with less social frailty.

*Physical:*

HIV infection, comorbidities

*Psychological:*

methamphetamine use disorder

*Physical:*

HIV infection

*Psychological:* depression, higher perceived stress, lower grit, lower optimism, lower personal mastery

*Social:* higher number of negative interactions, lower social support

*Physical:*

older age, bodily pain

*Psychological:* drug use/dependency, depressive symptoms, increased emotional regulation difficulty, witnessed violence, PTSD symptoms

*Social:*

homelessness, jail/prison time, prior violence

*Abbreviations:* ADL, activities of daily living; BMI, body mass index; CCS, childhood cancer survivors; CKD, chronic kidney disease, DM, diabetes mellitus; HANDLS, Healthy Aging in Neighborhoods of Diversity across the Life Span; FI, Frailty Index; HIV, human immunodeficiency virus; HRJL, health related job loss; IADL, independent activities of daily living; MWHSWM, men who have sex with men; RA, rheumatoid arthritis; PLWH, people living with acquire immune deficiency syndrome; PTSD, post-traumatic stress disorder; STI, sexually transmitted disease; TNFR, tumor necrosis factor receptors.

**Appendix B**

**Quality Appraisal Results**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No | First Author | Year | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Percent Yes |
| 1 | Althoff | 2014 | N | Y | Y | Y | N | NA | Unclear | Y | 57% (4 of 7) |
| 2 | Chode | 2016 | N | Y | N | Y | N | NA | Unclear | Y | 42% (3 of 7) |
| 3 | Demircioglu | 2018 | Y | N | Y | Y | NA | NA | Unclear | Y | 67% (4 of 6) |
| 4 | Hadenfeldt | 2017 | Y | Y | Y | Y | N | NA | Unclear | Y | 71% (5 of 7) |
| 5 | Haider | 2019 | Y | Y | Y | Y | NA | NA | Unclear | Y | 83% (5 of 6) |
| 6 | Griffin | 2018 | N | Y | Y | Y | Y | Y | Y | Y | 88% (7 of 8) |
| 7 | Ness | 2013 | N | Y | Y | Y | N | NA | Unclear | Y | 57% (4 of 7) |
| 8 | Onen | 2010 | N | Y | Y | Y | N | NA | Unclear | Y | 57% (4 of 7) |
| 9 | Palmer | 2017 | N | Y | Y | Unclear | NA | NA | N | Y | 50% (3 of 6) |
| 10 | Paolillo | 2019 | N | Y | Y | Y | N | NA | Unclear | Y | 57% (4 of 7) |
| 11 | Rubtsova | 2019 | N | N | Y | Y | N | NA | N | Y | 42% (3 of 7) |
| 12 | Salem | 2019 | Y | Y | Y | Y | NA | NA | Y | Y | 100% (6 of 6) |

Quality appraisal results using the Joanna Briggs Institute checklist for analytical cross-sectional studies [25].

**Appendix C**



**Appendix D**

**Study Purpose, Frailty Measure(s), and Frailty Prevalence**

First Author Year

Study Purpose Frailty

Measure(s)

Prevalence of Frailty and Prefrailty

Onen 2010

Ness 2013

Althoff 2014

Chode 2016

Hadenfedlt 2017

Evaluate differences in sexual behaviors and prevalence of sexually transmitted infections between frail and non-frail HIV-infected individuals in a clinic population.

Estimate prevalence of frailty among adult childhood cancer survivors and examine associations with current and future morbidity and subsequent mortality.

Examine the relationship of frailty and aging with HIV.

Examine the associations of diabetes with frailty on health outcomes in a middle-aged African American population.

Determine if factors suggestive of frailty were present in adults ages 40 to 64 years who received care in a free clinic.

\*Fried’s

criteria

\*Fried’s

criteria

\*Fried’s

criteria

†FRAIL

‡SOF

Fried’s criteria Frailty Index

§CFAI

Fried’s criteria

7 researcher - generated questions

9% (39 of 445) Frail

... Prefrail

11% (125 of 1122)

Frail

28% (314 of 1122)

Prefrail

...

...

§CFAI:

63% (24 of 38) Frail

11% (8 of 38) Prefrail Fried’s Criteria:

13% (5 of 38) Frail

55% (21 of 38) Prefrail

Griffin 2018

Examine association of race and poverty with

†FRAIL scale scores and how sex, race and poverty may modify the relationship of frailty and survival.

\*†FRAIL 11% (278 of 2541)

Frail

36% (924 of 2541)

Prefrail

Palmer 2017

Assess the prevalence and relationship of symptoms of physical frailty and explore their

\*Fried’s

criteria

3.9%

Frail

(313 of 8095)

Demircioglu 2018

associations with various adverse employment outcomes.

Investigate the frequency of frailty and the association between vitamin D levels and the frailty phenotype among non-geriatric dialysis patients.

Fried’s criteria

31.6% (2560 of 8095)

Prefrail

53% (39 of 74) Frail

18% (6 of 74) Prefrail

Haider 2019

Paolillo 2019

Assess the prevalence of prefrailty and frailty and the associated demographic and clinical factors in seropositive rheumatoid arthritis patients of working age.

Study lasting effects of past methamphetamine use disorder on frailty among middle‐aged to older people living with HIV.

¶SHARE-FI 15% (15 of 100) Frail

30% (30 of 100)

Prefrail

\*Frailty Index ...

Rubtsova 2019

Assess association between multiple psychosocial factors and frailty phenotype as

\*Fried’s

criteria

50% (64 of 127) Frail

... Prefrail

Frailty in Young and Middle-Aged Adults

Salem 2019

measured by the Fried Frailty Index among people living with HIV.

Explore physical, psychological and social frailty among formerly incarcerated, currently homeless women.

Tilburg Frailty Indicator

...

\*Tool or tool criteria was adapted to meet the needs of the study or sample.

†The International Academy of Nutrition and Aging frailty scale measuring fatigue, resistance, ambulation, number of illnesses, and loss of weight.

‡Study of Osteoporotic Fractures frailty scale

§Comprehensive Frailty Assessment Instrument

¶Frailty Instrument for Primary Care of the Survey of Health, Ageing and Retirement in Europe

*Abbreviations:* HIV, human immunodeficiency virus

# Frailty in Young and Middle-Aged Adults