The Association Between Geriatric Syndromes and Survival

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OBJECTIVES: To ascertain the effect on survival of eight common geriatric syndromes (multiple comorbidities, cognitive impairment, frailty, disability, sarcopenia, malnutrition, homeostenosis, and chronic inflammation), identified by an expert panel of academic geriatricians.

DESIGN: A systematic literature review sought studies from a variety of sources to compare survival and life expectancy of individuals with geriatric syndromes with those of the general population.

SETTING: Studies used reflected the general population.

PARTICIPANTS: Community-dwelling persons aged 65 and older.

MEASUREMENTS: Eight geriatric syndromes (multiple definitions) and survival.

RESULTS: Two thousand three hundred seventy-four publications were retrieved, and 509 publications of 123 studies were included. Seven geriatric syndromes (multiple comorbidities, cognitive impairment, frailty, disability, malnutrition, impaired homeostasis, and chronic inflammation) were associated with poor survival. In each case, the prevalence of a syndrome was negatively associated with mortality. Malnutrition and impaired homeostasis exerted twice the influence of factors such as multiple comorbidities and frailty. From age 65 to 74, only those who are very ill or frail (e.g., impaired homeostasis, low body mass index, or advanced dementia) have a higher risk of mortality than average older adults. In the old-old, particularly aged 90 and older, the added value of predicting survival beyond 1 year is minimal.

CONCLUSION: Geriatric syndrome information is helpful to understanding survival for younger old persons but provides little information about survival for the very old. Complex survival models add comparatively little benefit to more simply measured and calculated models. **J Am Geriatr Soc 60:896–904, 2012.**

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A basic tenet of geriatrics holds that age is not as good a predictor of outcomes as specific information. Clinicians assessing older persons must consider the extent to which the presence of specific syndromes might inform the expected clinical course. A number of geriatric syndromes have been shown to predict death, but their relative influence is less well appreciated. A recent study suggests that predicting death is difficult.[1] Preventive care decisions about older persons must consider the underlying risk of mortality. This systematic literature review examines how information about the presence of a syndrome affects mortality predictions otherwise based on demographic information and how the operational definition of each syndrome affects its effect.

METHODS

A technical expert panel of academic geriatric physicians, epidemiologists, and nurses (see list of committee members in Acknowledgments) used consensus judgment to identify eight geriatric syndromes that would inform recommendations for preventive health services in older adults. A syndrome is not a specific disease but rather conditions common to older adults that were believed to affect mortality. The syndromes selected were multiple comorbidities, cognitive impairment, frailty, disability, sarcopenia, malnutrition, impaired homeostasis, and chronic inflammation. The panel recognized that, in some instances, the various syndromes could occur simultaneously. The authors of the articles reviewed effectively determined the definitions of the syndromes. These definitions are shown in Table 1.

A variety of databases were searched, including MEDLINE through Ovid and PubMed, Cochrane databases, WorldCat, and Web of Science, and the search was supplemented with manual searches of reference lists and the Centers for Disease Control and Prevention Web site,

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Table 1. Definitions and Prevalence of Geriatric Syndromes and Component Parts

Syndrome	Definitions	Prevalence, %
Multiple comorbidities	3–4 chronic conditions	31
	Polypharmacy	21.8
	Poor self-perceived health	3
Cognitive impairment[60]	Mild cognitive impairment (amnestic). Subjective complaint of memory impairment with objective memory impairment adjusted for age. Normal general cognitive function. Intact ADLs and IADLs	17
	Mild cognitive impairment (multiple) deterioration in at least one nonmemory cognitive domain in addition to memory impairment without sufficiently severe functional impairment or loss of IADLs to constitute dementia. Normal general cognitive function	4.7–11
Frailty	Phenotype—>3 criteria present: Weight Loss Unintentional or Sarcopenia	24
	Weakness	
	Poor endurance	
	Slowness	
	Low activity	
	Accumulation deficit—up to 75 criteria including chronic diseases and disability; from 0 = absence of a deficit to 1 = full expression of the deficit. The individual deficit scores are combined in an index, where 0 = no deficit present to the maximum score as a sum of all presented deficits	14
Disability		
Any ADL disability	At least 1 ADL items present	5.0–18.3
Moderate ADL disability	2 ADL items	16.1–20.5
Severe ADL disability	$\geq$3 ADL items	6.0–7.8
Individual ADL disability items	Measure only contains 1 ADL item (bathing, dressing or hygiene, eating, toileting, transferring, walking)	0.8–20.6
Any IADL disability	At least1 IADL items present	12–47
Moderate IADL disability	2 IADL items	15–31
Severe IADL disability	$\geq$3 IADL items	4.5–21
Individual IADL disability items	Measure contains only 1 IADL item (finances, housekeeping, meal preparation, shopping, medication management, telephone, transportation)	2.2–15
Impaired homeostasis		
Impaired homeostasis	Diminished capacity to respond to varied homeostatic challenges, such as changes in ambient temperature, orthostasis, fluid load, or dehydration	NA
	High plasma tonicity, >300 mOsm/L	
	Greater intraindividual variability in fasting glucose, pulse pressure, and BMI	
Abnormal allostatic load[19,46,61]	High biological burden reflected in declines in cognitive and physical function	1
	CRP (>5.0 mg/L) (high sensitivity)	
	Albumin (<3.6 g/dL)	NA
	IL-6 (>2.76 pg/mL)	
	Aldosterone (<4.5 ng/dL)	NA
	Urinary cortisol	NA
	Men (<25.0 or > 72.0 mg/24 hours)	
	Women (<8.0 or > 37.0 mg/24 hours)	
	Dehydroepiandrosterone sulfate	NA
	Men (<79.5 mg/dL)	
	Women (<15.5 mg/dL)	NA
	Epinephrine (>24.0 pg/mL)	
	Norepinephrine (>433.0 pg/mL)	NA
Excessive response to stressors	Sympathetic responses to common challenges are excessively large and prolonged	NA
	High urinary epinephrine	
	High urinary free cortisol	
	High urinary norepinephrine	
	Stress hormone index	
Malnutrition		
Poor nutritional status	Significant weight change	
	a) 10% of body weight in 6 months	21
	b) Involuntary loss of >10 pounds in 6 months	NA
	Anthropometric data	NA
	BMI < 20.0 kg/m^2	2
	Laboratory data	
	Serum prealbumin <15 mg/dL	NA
	Serum transferrin <200 mg/dL	NA

(Continued)

Table 1. (Contd.)

Syndrome	Definitions	Prevalence, %
	Serum albumin <3.5 g/dL	3.1
	Anemia with nutritional deficiencies	NA
	Transthyretin, mg/L	NA
	Micronutrient deficit	1–10
Composite nutritional score	Nutritional risk using the "Determine Your Nutritional Health Checklist"	
	Low nutritional risk (0–2), moderate risk (3–5) and high risk ($\geq$6)	2.8
Sarcopenia	Presence of low muscle mass and low muscle function (strength or performance)	
	Lean mass/height^2 in the lowest 20% of the sex-specific distribution of the index using cut points of 7.2 kg/m^2 in men and 5.7 kg/m^2 in women	50.4–51.9
Chronic inflammation		
High levels of individual biomarkers	High high-sensitivity CRP	24
	High levels of IL-6	5
	CD4/CD8 ratio	18.4
	Increased levels of tumor necrosis factor alpha	5
Inflammatory indices	Balance between pro-inflammatory and anti-inflammatory markers	
	High levels of several biomarkers	24.4
	High CRP	24.4
	High IL-6	5
	High tumor necrosis factor alpha	5
Prognostic inflammatory and nutritional indices	The prognostic inflammatory and nutritional index was defined as (CRP $\times$ alpha 1-acid glycoprotein)/(albumin $\times$ transthyretin)	NA

ADL = activity of daily living; IADL = instrumental activity of daily living; BMI = body mass index; IL = interleukin; CRP = C-reactive protein; NA = not availalable.

which listed all publications from the Longitudinal Study of Aging.

Because the search was looking for evidence of prevalence as well as prediction of mortality and because the basic study design used for prediction relies on epidemiological analyses, epidemiological population-based surveys and cohort studies, systematic reviews, and meta-analyses published in English from 1990 through April 2010 were included. The studies had to report the prevalence of syndromes or the association that syndromes had with survival in community-dwelling adults aged 65 and older. To maximize generalizability, only nationally representative population-based surveys and prospective cohort studies were included. Studies of hospitalized individuals, nursing home residents, and disease-specific populations were excluded because they did not reflect the general elderly population.

Systematic review guidelines were used to direct data extraction and to evaluate study quality.[2] Primary outcomes abstracted were syndrome definitions, syndrome prevalences, adjusted relative measures of the association between syndromes and survival, and all variables included in multivariate-adjusted models. Study traits, including sample size, descriptive information about populations, and time to measure outcomes, were also abstracted. The results of individual studies were summarized in evidence tables (Appendix S1). The U.S. Preventive Services Task Force (USPSTF) criteria were used to evaluate study quality and the level of evidence.[3]

Several analyses were performed. Pooled prevalence was estimated from studies with the same operational definition of the geriatric syndrome.[2] Meta-analysis was used to assess the consistency of the association between syndromes and outcomes with random effects models.[4] Chi-square tests were used to assess consistency in study results.[5] STATA software (STATA Corp., College Station, TX) was used to calculate pooled prevalence and association estimates with random effects models. All calculations were conducted at a 95% confidence level.

U.S. Period Life Tables[6] were used to estimate life expectancy for participants with each syndrome and compared with the general population. Previously validated composite comorbidity weighted indexes that take into account the number and the seriousness of comorbid diseases were analyzed.[7]

The number of deaths among 1,000 older persons with each syndrome was estimated using calculations based on a simulation algorithm.[8] Population attributable risk of mortality or institutionalization was estimated using prevalence and risk estimates from pooled analyses when available or from individual studies.[9] Remaining life expectancy for older persons with each syndrome[10] and relative risks of all-cause mortality in older populations with each syndrome were estimated. Life expectancy was estimated as area under the survival curves. When available in the studies, sex- and race-specific regression coefficients were applied.

RESULTS

Of the 2,374 publications screened, 509 publications from 123 studies were eligible. The majority of the studies were well-designed national surveys. Detailed descriptions of the studies are available in the full text report.[11]

Definitions and Prevalence

Each syndrome had multiple definitions, and in some cases, the concepts underlying the various syndromes overlapped. For example, frailty measures, based on

accumulation of deficits, often included disability and comorbidity. The definitions of the syndromes and their component parts, summarized in Table 1, varied widely. The definitions, in turn, affected the prevalence of the specific condition.

Multiple Comorbidities

In accordance with the National Institute on Aging Task Force on Comorbidity,[12] comorbidity was defined as co-occurrence of preexisting age-related health conditions or diseases in reference to an index disease and multimorbidity as the co-occurrence of two or more diseases or active health conditions (e.g., aggregate of co-equals) that may or may not be linked by a causal relationship or with no consistent dominant index disorder. Neither definition considers severity of the diseases or conditions or the quality of health care in managing diseases.

Cognitive Impairment

Cognitive impairment was defined as deterioration in memory or executive function, difficulty learning new information or recalling previously learned information, and other disturbances of cognitive function such as aphasia, apraxia, and agnosia.[10] The most common definition of cognitive impairment required a subjective complaint of memory impairment with objective memory impairment, normal general cognitive function, and intact activities of daily living (ADLs) and instrumental activities of daily living (IADLs).[13,14]

Frailty

Frailty definitions were categorized as phenotype and accumulation of deficits.[15] Phenotype definitions use the biological syndrome model of frailty, measuring weight loss, fatigue, exhaustion, weakness, low physical activity, slowness, and mobility impairment.[16] Accumulation-of-deficit measures use the burden model of frailty, including symptoms, diseases, conditions, and disability.[17]

Disability

Disability was defined as having difficulty with or requiring help with ADLs (dressing, hygiene, bathing, toileting, transferring, ambulating, feeding, and grooming) or IADLs (telephoning, shopping, preparing meals, housekeeping, transportation, medication, and financial management).

Malnutrition

Studies defined malnutrition as unintended weight loss or low body mass index (BMI). Among biochemical markers, low blood albumin levels, anemia, and deficit of micronutrients identified malnourished older people. Several studies used composite nutritional scores based on self-reported dietary intake and habits to identify malnourished older persons.[18] Of biological markers that may be related to malnutrition, red cell distribution width is a quantitative measure of variability in the size of circulating erythrocytes, with higher values reflecting greater heterogeneity in cell sizes. It is typically high in older persons with malnutrition, iron deficiency, or B12 or folate deficiency.[11]

Impaired Homeostasis

Few studies examined the prevalence of impaired homeostasis in older persons. The National Health and Nutrition Examination Surveys (NHANES) defined impaired homeostasis in older persons using an allostatic load score as high C-reactive protein (CRP), interleukin (IL)-6, aldosterone, urinary cortisol, epinephrine, and norepinephrine and low albumin.[19]

Chronic Inflammation

Few studies reported the prevalence of unspecified chronic inflammation in older persons, including high CRP,[20] IL-6, and tumor necrosis factor alpha.[21]

Sarcopenia

The association between sarcopenia and mortality was examined in one study, which showed that, even though older people with greater muscle density had a lower risk of death, sarcopenia was not associated with mortality.[22]

Association Between Syndromes and Mortality

The associations between each syndrome and mortality were compared to identify the strength of the associations with survival in older persons. The estimates of the association varied depending on definitions of comorbidities, population subgroups, definitions of the outcomes, and adjustment for correlated contributing factors. In most instances, the studies did not correct for the effects of possible simultaneous other factors, including the presence of other syndromes. Definitions of comorbidities differed between studies. For instance, the Women's Health and Aging Study adjusted for a number of chronic diseases;[23] the Norwood-Montefiore Aging Study adjusted for depression, cognitive impairment, and self-perceived health;[24] the Glostrup Aging Study adjusted for individual diseases;[25] and a study of a Medicaid home- and community-based care program[26] and the Longitudinal Study on Aging[27] were adjusted for self-reported health status and number of medical conditions.

Multiple Comorbidities

The significant association between multiple comorbidities and poor survival was consistent across the studies. Older persons with comorbidities had 32% to 112% greater mortality. The magnitude of the association was dose responsive, with 85% greater mortality for older persons with four to five diseases and 112% for those with six or more chronic conditions. The magnitude of the association decreased with the time of follow-up, from 100% greater at 10 years (OR = 2.0, 95% CI = 1.4–2.82) to 59% greater at 15 years of follow-up (OR = 1.59, 95% CI = 1.1–2.25).[25] Polypharmacy was significantly associated with mortality in two studies.[28,29] Older persons with poor perceived health had a greater risk of death in all studies that examined the association [pooled relative risk (RR) = 2.04, 95% CI = 1.81–2.31]. Of various definitions of multimorbid conditions, comorbidity scores and poor perceived health demonstrated a strong association with poor survival.

Cognitive Impairment

Cognitive impairment was associated with a significantly higher risk of mortality in all studies examining this association. The largest relative increases, 250% in women and 280% in men, were found in the Canadian Study of Health and Aging, which defined cognitive impairment as a score of less than 78 on the Modified Mini-Mental State examination (3MS) scale.[30] The association was dose responsive, with a 4% relative increase in mortality for a 1-point decrease in 3MS score.[31] The studies that estimated RR or hazard rate ratios found 37%[24,28] and 61%[32,33] relative increases in risk of death.

Older women (pooled RR = 1.37, 95% CI = 1.11–1.69) but not men (pooled RR = 1.20, 95% CI = 0.79–1.82) with MMSE scores less than 24 had a significant risk of death. Men and women with severe cognitive impairment (MMSE score <18) were at higher risk of death.

Dementia was associated with a significantly higher risk of mortality in the majority of the studies that examined this association. Overall, dementia was associated with 163% greater odds of death (pooled OR = 2.63, 95% CI = 2.17–3.2).[34]

Frailty

Frailty was associated with mortality in a number of studies with varying definitions. The strength of the association was cumulative in relation to the number of components[35] and dose responsive, with a greater risk in those with more frailty components.[36,37] The association generally persisted over long follow-up periods.[16,36]

The association was significant in men and women. Frail older men had a greater risk of death of 105% to 251% according to phenotype definitions and of 65% to 356% according to accumulation deficit definitions. Older frail women had greater mortality in different studies and with definitions of frailty.

Disability

In general, individuals with ADL disabilities were at higher risk of death (OR = 1.9–86.8) than those with IADL disabilities (OR = 1.5–6.6). Those with more ADL disabilities had a higher risk of death than those with fewer. Severe ADL disabilities were associated with the highest risk of death at 72 months (OR = 30.0, 95% CI = 18.0–51.0)[27] and at 24 months (OR = 86.8, 95% CI = 39.4–190.8),[38] followed by those with moderate ADL disabilities, in whom the risk of death had an OR of 8.6 (6.6–11.0) at 72 months[27] and 14.1 (9.2–21.6) at 24 months.[38] The lowest risk of death was when the study outcome was reported as any ADL disability (OR = 1.9, 95% CI = 1.2–2.7).[39]

The risk of death associated with IADL disabilities was high when at least one IADL disability was reported.[27,38] Those with severe IADL disability had a slightly higher risk of death (OR = 1.64–2.2) than those with moderate IADL disability (OR = 1.46–1.72).

When disability was measured on a continuous scale, a 1-unit increase in disability score and risk of death was the same whether the scale measured ADLs, IADLs, or both. Men with ADL disabilities had a slightly higher risk of death than women.[40] Women have greater discrepancies in years of expected active life remaining than men if they have an ADL or IADL disability.[41]

Malnutrition

The association between mortality and malnutrition was consistent across the studies and different definitions of malnutrition. Low BMI was the strongest predictor of mortality in older persons.

Of biological markers of malnutrition, one meta-analysis of individual participant data from seven community-based studies of 11,827 older adults found that red blood cell distribution width demonstrated a strong and significant association with mortality in all age, sex, and race subgroups.[42] Routinely measured as a part of complete blood count, a red cell distribution width greater than 15% was associated with a 151% greater risk of death [hazard rate (HR) = 2.51, 95% CI = 2.16–2.91].[42] Very low and very high pre-albumin levels (transthyretin <258 or >316 mg/L) were also associated with greater mortality.[43,44]

Several studies analyzing composite measures of malnutrition and chronic inflammation in older persons found a significant positive association with mortality. Older people with the highest levels of alpha-1-acid glycoprotein and the lowest levels of transthyretin had the highest risk of death—364% greater in women and 586% greater in men.[44] A high prognostic inflammatory and nutritional index was associated with greater risk of death in older men but not women.[44]

Impaired Homeostasis

Individual studies demonstrated a significant association between mortality and indicators of impaired homeostasis. The association between impaired homeostasis and clinical outcomes varied depending on the definitions of exposure and the population studied.

A change in either direction of BMI (HR = 1.34, 95% CI = 1.03–1.75), pulse pressure (HR = 1.34, 95% CI = 1.03–1.74), and fasting plasma glucose (HR = 1.56, 95% CI = 1.17–2.08) was associated with a greater risk of mortality in an elderly Italian cohort.[45]

Allostatic load is a summary measure that addresses impaired homeostasis; it consists of multiple abnormalities including dyslipidemia, chronic inflammation, low albumin levels, low aldosterone and high stress hormone levels, high blood pressure and waist-to-hip ratio, and high glycosylated hemoglobin. The MacArthur Studies of Successful Aging demonstrated a significant association between high allostatic load and mortality after adjustment for health conditions and socioeconomic status.[46] The same study found 27% greater odds of death (OR = 1.27, 95% CI = 1.04–1.54) in adults with a high stress hormone index.[46]

Chronic Inflammation

Studies consistently found significant associations between chronic inflammation and poor survival. Among common definitions of chronic inflammation, IL-6 and CRP were associated with higher mortality in older persons. Older

persons with high IL-6 levels had a 42% greater risk of death (pooled RR = 1.42, 95% CI = 1.16–1.74). Older persons with high CRP had a 42% greater risk of death (pooled 1.42, 95% CI = 1.29–1.55). Among other individual markers of chronic inflammation, a combination of high CRP with low albumin (HR = 4.98, 95% CI = 2.25–11.01)[44] or with high fibrinogen levels (HR = 9.56, 95% CI = 4.34–21.1)[47] had the strongest association with mortality.

Modeling Survival

Table 2 shows the prevalence and multivariate-adjusted RR of mortality for the various syndromes and the population attributable risk (PAR). The latter is the combination of prevalence and RR. The prevalence shown here differs somewhat from those in Table 1 because different studies were used. Table 2 includes only studies that also examined mortality.

More than 15% of deaths were attributable to moderate ADL disability; 7.5% to 16.4% of deaths were attributable to multiple comorbidities and 7.2% to high CRP. Using the PAR, it was estimated that preventing frailty could delay 3% to 5% of deaths in older persons. Prevention of cognitive impairment could result in delaying 5% to 6% of deaths in older persons. Overall, when PAR with three to four diseases, phenotype definition of frailty, cognitive impairment, chronic inflammation, low BMI, and high allostatic load are summed, approximately 26% of deaths in older persons can be attributed to the geriatric syndromes examined.

The prevalence and risk of mortality are almost inversely related. The prevalence of accumulation deficit frailty (which uses many components) was higher than phenotype frailty (which uses only a few components), whereas the RR of mortality was higher for phenotype frailty. The same negative association is seen for more-severe forms of the same syndrome. Prevalence of severe cognitive impairment and dementia was lower, but the risk of mortality was higher than that of mild cognitive impairment. A negative association between prevalence of a syndrome and its effect on mortality was evident across all syndromes.

The data shown in Figure 1 represent a merger of several data sets to yield general trends about the effect of geriatric syndromes on survival. Impaired homeostasis has the most dramatic effect. Table 3 shows these effects more explicitly. Some factors have a much greater influence on survival than others. The greatest effect comes from the large difference in impaired homeostasis (allostatic load). Malnutrition exerts twice the influence of factors such as multiple comorbidities and frailty. The size of the effect differs according to age and thus life expectancy. The effects are sizable for those aged 65 to 74 but diminish with age. In the old-old, particularly past age 90, the added value of factoring in conditions and syndromes to predict mortality beyond 1 year is minimal.

DISCUSSION

Survival models vary according to complexity, selection of predictors, and time course. Some models strive for simplicity, with a few easily measured variables, many or all of which could be gained by culling administrative data. Clinicians can use a few basic geriatric parameters to identify whether a patient has a higher or lower than normal risk. For the purpose of evaluating the benefit of preventive services, a simpler approach, based on some crude classifications of average life expectancy (based on age and sex) may prove more informative than more-complex models.[48,49] There is some hope that electronic health records may ultimately be able to perform sophisticated calculations of multiple risk factors, but for the moment, simpler seems better.

Age is a good general predictor of survival, but syndromes play some role. In this analysis, the evidence is mixed. Adding syndromic information is informative for younger old persons, but it adds little insight for the very old. The syndromes with the strongest link to mortality are the rarest. In clinical settings, clinicians' concerns are with individual prognosis based on absolute risk. In that

Table 2. Prevalence and Risk of Mortality Associated with Geriatric Syndromes

Syndrome	Prevalence, %	Relative Risk	Population Attributable Risk, %
Multiple morbidities			
3–4 diseases*	31†	1.3–2.1	7.5–16.4
Poor health	3†	2.1†	1.5
Mini-Mental State Examination score			
<24*	17*	1.4–1.6	4.6–6.4
<15	8†	2.2	4.1
Frailty			
Accumulation deficit	24†	1.2†	3.1
Phenotype	14†	2†	4.8
Disability in activities of daily living			
Moderate	16.1–20.5	14.1	15.8
Severe	6.0–7.8	86.8	6.9
Low body mass index	2†	2†	1.2
Impaired homeostasis	1	5	1.1
High C-reactive protein	24	1.4†	7.2

* Ranges of the estimates from individual studies.

† Pooled estimates with random effects models.

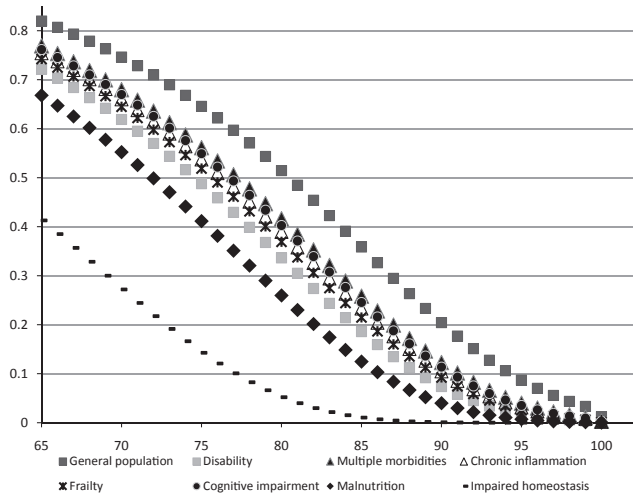

Figure 1. Survival in older persons in the general population and with geriatric syndromes (effect of relative risk of mortality). Vertical axis = probability of survival. Horizontal axis = age. Dots = probability of survival until the next year for adults aged 65 and older from the general population and with geriatric syndromes. At age 65, the order of syndromes with the lowest to highest relative risk of mortality is multiple morbidities, cognitive impairment (Mini-Mental State Examination score <24), chronic inflammation (high C-reactive protein), frailty (phenotype), disability (activities of daily living), malnutrition (low body mass index), and impaired homeostasis.

light, the estimation of life expectancy was based on the U.S. Life Tables, which incorporate average survival of older adults with different diseases and syndromes. Life expectancy was calculated assuming the same RR across the remaining life span.[11] To examine overall effects of different syndromes on mortality in adults aged 65 and older, numbers of deaths per 1,000 were estimated from individual studies that provided death rates in persons with and without different syndromes.[8] It was estimated that, in frail older persons, 459 per 1,000 died within 1 to 2 years of follow-up.[50,51] Disability in ADLs and IADLs is the strongest predictor of mortality.

Within 3 years, 500 to 600 older persons with malnutrition, 351 with cognitive impairment, and 534 with severe dementia died per 1,000 older persons.[52–54] Within 5 years, 490 elderly persons with malnutrition, 513 with frailty, 530 with high CRP, and 827 to 941 with vascular dementia died per 1,000 older persons.[30,55–57] Frailty and cognitive impairment were associated with 400 to 800 deaths per 1,000 during more than 5 years of follow-up.[16,31,58] Such estimations may not reflect mortality in age, sex, or race subgroups but demonstrate the burden of geriatric syndromes.

Some basic relationships hold regardless of the measure used. They can be summarized as follows.

- For informing prevention considerations at a societal level, PAR may be helpful. PAR represents the product of prevention and risk size. Absolute risk provides more information for individualized decision-making in clinical settings. Clinicians want to know how much a given strategy will improve outcomes in a given patient.
- Simpler measures that reflect the severity of individual diseases, such as indicators of advanced dementia, or the overall effect of multiple conditions and assessments of overall health also identify the fewer and sicker patients at higher risk of mortality. They add modestly to the RR of mortality provided by age and sex alone but account for a more population-based mortality burden because of their high prevalence. Simple indicators, such as gait speed, also hold promise.[59]
- Advanced dementia appears to confer significantly added mortality risk, but it is typically associated with more comorbidity.
- How syndromes are defined inversely affects their prevalence and their effect on survival. More-inclusive definitions will foster higher prevalence rates but lesser effects.

Greater uniformity in measuring syndromes like these would facilitate interpretation by clinicians who may not appreciate the effects of the actual structure on the findings.

Table 3. Differences in Remaining Life Expectancy in Older Persons Between the General Population and Individuals with Selected Geriatric Syndromes

		Geriatric Syndromes							
Age	Remaining Life Expectancy in the General Population	Multiple Morbidities (>3 Diseases)	Inflammation (High C-Reactive Protein)	Frailty (Phenotype)	Cognitive Impairment (Mini-Mental State Examination Score <24)	Frailty (Accumulation Deficit)	Low Body Mass Index	Allostatic Load	Disability in Activities of Daily Living
65	18.4	−2.2	−2.8	−3.2	−2.5	−1.1	−5.4	−10.3	−3.9
70	14.9	−2.0	−2.5	−2.8	−2.2	−1.0	−4.8	−8.9	−3.4
75	11.7	−1.7	−2.1	−2.5	−1.9	−0.9	−4.1	−7.5	−3.0
80	8.9	−1.4	−1.8	−2.1	−1.6	−0.7	−3.4	−6.0	−2.5
85	6.5	−1.1	−1.4	−1.6	−1.3	−0.6	−2.7	−4.7	−2.0
90	4.6	−0.8	−1.1	−1.2	−1.0	−0.4	−2.0	−3.5	−1.5
95	2.8	−0.5	−0.6	−0.7	−0.6	−0.2	−1.2	−2.2	−0.9
100	0.4	−0.1	−0.1	−0.1	−0.1	−0.1	−0.2	−0.4	−0.2

Limitations

These estimates address the effects of selected syndromes. They do not assume the presence or absence of underlying medical conditions. The added predictive power of these syndromes in the presence of disease was not specifically tested. Most older people live with multiple chronic diseases. Outcomes are worse with greater numbers of diseases.[12] Some syndrome measures use diseases as part of their formulation. Many of the remaining syndromes probably represent intermediate states between specific diseases and survival. When thinking about prevention, clinicians can use the syndromes as summary proxies for various conditions.

In conclusion, complex survival models add little value to more simply measured and calculated models. In making prognostic judgments, clinicians may do well by simply using standard survival tables and placing patients into crude risk categories, such as those used by the Centers for Disease Control and Prevention, that group mortality forecasts into three levels.[1] Measures of the effect of conditions and syndromes on overall health and functioning provide greater discrimination between individual patients for assessing risk of poor survival. Survival associations appear to be relatively consistent across short- and long-range models. The added information that complex survival models provide over simple remaining life expectancy is greater for younger individuals. More remains to be understood about how interventions, such as exercise, can change the predicted clinical courses for persons with these syndromes.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Epidemiological Studies of Older Adults.

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