Supplementary Methods S1. Other Measurements.

Age, race/ethnicity, and education were assessed via self-administered questionnaires at baseline, and marital status, smoking status, and usual alcohol consumption were updated via self-administered questionnaires at every study visit.[1] Participants reported history of myocardial infarction, angina, heart failure, hypertension, diabetes, prostate cancer (51% treated with surgery, 29% with radiation only, 14% with hormones only, and 6% were not treated), stroke, Parkinson's disease, osteoporosis, osteoarthritis, and thyroid disease. Multimorbidity was defined as the cumulative number of ten common chronic diseases.[2] All participants were administered the Geriatric Depression Scale (GDS)[3] and Medical Outcomes Study Short Form (SF-12).[4] Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE).[5] Cognitive function was assessed using the Modified Mini Mental State Examination (3MS) and the Trail Making Test part B (Trails B)[6,7] and cognitive impairment defined as 3MS<80 and/or Trails B > 226 seconds. Comprehensive prescription medication use was coded from labels on pill packets and canisters brought in by the participant, and medications to treat LUTS (α-antagonist, 5α-reductase inhibitor, or anti-cholinergic) were identified using the Iowa Drug Information System (IDIS).[8] Men were asked if a doctor had told them they "have or had an enlarged prostate (benign prostatic hyperplasia)" and if so, they were asked if they received "Surgery", "Prescription medications", or "Other" treatments for this condition, which was used to define self-reported BPH surgery. Tests of physical function included maximum grip strength (measured bilaterally using a hand-held Jamar dynamometer) and walk speed (time in seconds to walk 6 meters at usual pace expressed as m/sec). Study staff measured height using wall-mounted Harpenden stadiometers. Weight was measured with a digital scale or with a standard regularly calibrated balance beam scale. Height and weight measurements were used to calculate

a standard body mass index (BMI). Waist circumference was measured at the narrowest part of the torso using a standard tape measure. We identified men with phenotypic frailty, as proposed by Fried et al[9,10], using five criterion collected in the Cardiovascular Health Study and adapted for the MrOS cohort[11]: shrinking/sarcopenia (unintentional weight loss of ≥5% since prior visit; mean time since prior visit = 2.3 years), weakness (grip strength in the lowest quintile stratified by BMI), exhaustion (assessed via SF-12 or Geriatric Depression Scale), slowness (walk speed in the lowest quintile stratified by standing height), and low physical activity (PASE score in the lowest quintile).

Supplemental Table 1. Association of LUTS severity at baseline with incident mobility limitation, ADL limitation, and cognition-dependent task limitation after adjusting for potential mediators.*

	MV Adjusted + Multimorbidity[‡]	MV Adjusted + LUTS Medication Use	MV Adjusted + Frailty Phenotype Components[§]	MV Adjusted + Self-Reported General Health Status	MV Adjusted + Geriatric Depression Scale
	Risk Ratio (95% CI)[†]		Risk Ratio (95% CI)[†]	Risk Ratio (95% CI)[†]	Risk Ratio (95% CI)[†]
Incident Mobility Limitations Overall LUTS Severity (AUASI)					
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	1.35 (1.12, 1.64)	1.27 (1.04, 1.54)	1.21 (1.00, 1.46)	1.28 (1.06, 1.54)	1.28 (1.06, 1.55)
Severe (20-35)	2.02 (1.51, 2.69)	1.79 (1.33, 2.41)	1.60 (1.20, 2.13)	1.59 (1.19, 2.13)	1.53 (1.12, 2.09)
Incident ADL Limitations Overall LUTS Severity (AUASI)					
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	1.31 (1.04, 1.66)	1.34 (1.05, 1.71)	1.23 (0.97, 1.57)	1.25 (0.99, 1.58)	1.26 (0.99, 1.59)
Severe (20-35)	1.63 (1.08, 2.45)	1.65 (1.09, 2.51)	1.25 (0.80, 1.94)	1.34 (0.88, 2.03)	1.24 (0.81, 1.91)
Incident Cognition-dependent Task Limitations Overall LUTS Severity (AUASI)					
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	0.72 (0.47, 1.11)	0.72 (0.47, 1.13)	0.69 (0.44, 1.10)	0.71 (0.46, 1.08)	0.66 (0.43, 1.02)
Severe (20-35)	1.34 (0.70, 2.55)	1.33 (0.70, 2.52)	1.32 (0.65, 2.67)	1.17 (0.61, 2.26)	0.86 (0.41, 1.79)

ADL activities of daily living; AUASI American Urological Association Symptom Index; LUTS lower urinary tract symptoms; MV multivariable

*   Mobility limitation defined as having any difficulty or inability for either walking 2–3 blocks or climbing 10 steps. ADL limitation defined as having any difficulty or inability for bathing or showering and transfers in and

out of beds or chairs. Cognition-dependent task limitation defined as having any difficulty or inability to manage money or medications.

†   Risk ratios and 95% confidence intervals calculated using Poisson regression adjusted for age, site, and history of myocardial infarction or angina, heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, prostate cancer, and stroke or Parkinson's disease plus potential mediators.

‡   Multimorbidity defined as the cumulative number of the following chronic medical conditions: stroke, Parkinson's disease, myocardial infarction, angina, chronic obstructive pulmonary disease, heart failure, diabetes mellitus, osteoporosis, osteoarthritis, hyperthyroidism or hypothyroidism (0, 1, 2, and ≥3).

§   Frailty phenotype components include shrinking (≥5% weight loss since prior visit; yes/no), grip strength (continuous in kg), gait speed (continuous in m/s), Physical Activity Scale for the Elderly score (continuous), and exhaustion (categorical responses to SF-12 question that asks "Did you have a lot of energy?").

Supplemental Table 2. Association of lower urinary tract symptoms (LUTS) severity at baseline with incident cognition-dependent task limitation*.

	AUASI Score Range[†]	# Incident Limitation /Total (%)	Age and site-Adjusted	Multivariable[§] Adjusted	
			Risk Ratio (95% CI)[‡]	Risk Ratio (95% CI)[‡]	*P* value
Clinical LUTS Categories					
None/Mild	0-7	60/1512 (4.0)	Ref.	Ref.	0.16
Moderate	8-19	32/1045 (3.0)	0.77 (0.50, 1.17)	0.73 (0.48, 1.12)	
Severe	20-35	10/159 (6.3)	1.50 (0.78, 2.89)	1.34 (0.70, 2.57)	
Total AUASI					
Tertile 1	0-4	27/930 (2.9)	Ref.	Ref.	0.15
Tertile 2	5-10	44/972 (4.5)	1.61 (1.01, 2.57)	1.58 (0.99, 2.51)	
Tertile 3	11-35	31/814 (3.8)	1.27 (0.76, 2.11)	1.24 (0.75, 2.04)	
Storage Subscore					
Tertile 1	0-3	38/1228 (3.1)	Ref.	Ref.	0.23
Tertile 2	4-6	33/848 (3.9)	1.33 (0.85, 2.10)	1.35 (0.86, 2.11)	
Tertile 3	7-15	31/640 (4.9)	1.49 (0.94, 2.37)	1.44 (0.91, 2.29)	
Voiding Subscore					
Tertile 1	0-1	44/1108 (3.9)	Ref.	Ref.	0.67
Tertile 2	2-4	27/732 (3.7)	0.87 (0.55, 1.38)	0.89 (0.56, 1.40)	
Tertile 3	5-20	31/876 (3.6)	0.85 (0.54, 1.34)	0.81 (0.52, 1.28)	

*   Defined as having any difficulty or inability to manage money or medications.

†   American Urological Association Symptom Index (AUASI) score range is 0 to 35 and equals the sum of 2 validated subscores based on symptom type: storage (urgency, frequency, nocturia) and voiding (intermittency, weak stream, straining, incomplete emptying). Higher score indicates more frequent symptoms. Total AUASI score was categorized using clinically validated thresholds for none/mild (0-7), moderate (8-19), and severe (20-35) LUTS and approximately into equal fourths (quartiles). Storage and voiding subscores were categorized approximately into equal thirds (tertiles) of the subscore distribution.

‡   Risk ratios and 95% confidence intervals calculated using Poisson regression. *P* values calculated using the Wald test.

§   Adjusted for age, site, and history of myocardial infarction or angina, heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, prostate cancer, and stroke or Parkinson's disease.

Supplemental Table 3. Sensitivity analyses of association of overall LUTS severity at baseline with incident mobility limitation, ADL limitation, and cognition-dependent task limitation.*

	Expanded Multivariable[†] Adjusted Model	Inverse Probability of Censoring Weighted[§] Model	Restricted to Men without Urinary Incontinence	Restricted to Men without Cognitive Impairment[‖]
	Risk Ratio (95% CI)[‡]	Risk Ratio (95% CI)[‡]	Risk Ratio (95% CI)[‡]	Risk Ratio (95% CI)[‡]
Incident Mobility Limitations Overall LUTS Severity (AUASI)				
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	1.40 (1.15, 1.70)	1.34 (1.11, 1.63)	1.31 (1.06, 1.63)	1.39 (1.12, 1.73)
Severe (20-35)	2.07 (1.55, 2.76)	2.02 (1.52, 2.68)	1.89 (1.29, 2.78)	1.93 (1.38, 2.70)
Incident ADL Limitations Overall LUTS Severity (AUASI)				
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	1.29 (1.02, 1.64)	1.32 (1.04, 1.67)	1.30 (0.99, 1.70)	1.46 (1.13, 1.90)
Severe (20-35)	1.62 (1.07, 2.45)	1.70 (1.13, 2.56)	1.62 (0.96, 2.75)	1.52 (0.95, 2.43)
Incident Cognition-dependent Task Limitations Overall LUTS Severity (AUASI)				
None/Mild (0-7)	Ref.	Ref.	Ref.	Ref.
Moderate (8-19)	0.67 (0.43, 1.06)	0.76 (0.50, 1.16)	0.74 (0.46, 1.18)	0.79 (0.45, 1.42)
Severe (20-35)	1.58 (0.83, 3.02)	1.35 (0.71, 2.57)	1.63 (0.78, 3.42)	1.68 (0.74, 3.83)

ADL activities of daily living; AUASI American Urological Association Symptom Index; LUTS lower urinary tract symptoms

* Mobility limitation defined as having any difficulty or inability for either walking 2–3 blocks or climbing 10 steps. ADL limitation defined as having any difficulty or inability for bathing or showering and transfers in and

out of beds or chairs. Cognition-dependent task limitation defined as having any difficulty or inability to manage money or medications.

† Adjusted for age, site, and history of myocardial infarction or angina, heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, prostate cancer, and stroke or Parkinson's disease, education, race/ethnicity, marital status, body mass index, waist circumference, alcohol intake, smoking, and physical activity.

‡ Risk Ratios and 95% confidence intervals calculated using Poisson regression.

§ Coefficients adjusted for informative censoring using inverse probability of censoring weighting (IPCW) whereby observations were re-weighted using all measured covariates listed in Table 1.

|| Cognitive impairment defined as Teng 3MS<80 and/or Trails Making Test Part B > 226 seconds.

Supplemental Table 4. Association of AUASI score at baseline with incident mobility limitation, ADL limitation, and cognition-dependent task limitation, stratified by age tertile.
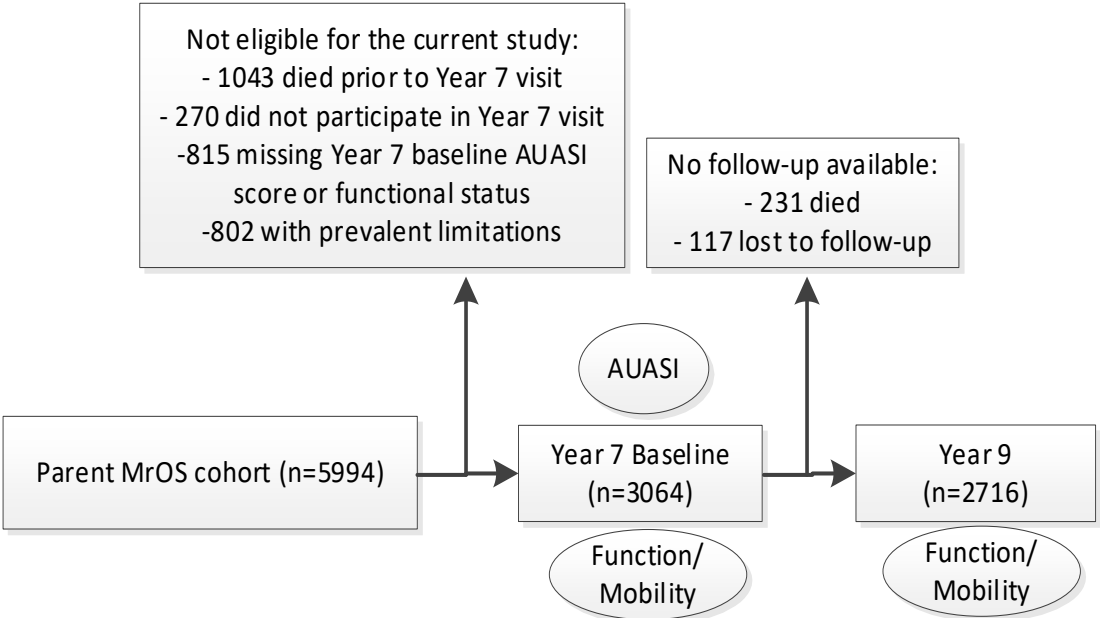
AUASI Quartile (Score Range)	Age Tertile 1 (71-76 years; n =1102)			Age Tertile 2 (77-80 years; n =721)			Age Tertile 3 (81-98 years; n =893)		
	# Incident Limitation /Total (%)	Risk Ratio (95% CI)[‡]	*P* value	# Incident Limitation /Total (%)	Risk Ratio (95% CI)[‡]	*P* value	# Incident Limitation /Total (%)	Risk Ratio (95% CI)[‡]	*P* value
Incident Mobility Limitation*									
Q1: 0-3	13/291 (4.5)	Ref.	0.001	11/203 (5.4)	Ref.	0.03	46/218 (21.1)	Ref.	0.09
Q2: 4-7	28/337 (8.3)	1.75 (0.94, 3.25)		19/212 (9.0)	1.57 (0.78, 3.17)		56/251 (22.3)	1.07 (0.76, 1.50)	
Q3: 8-12	25/248 (10.1)	2.14 (1.12, 4.10)		18/161 (11.2)	1.80 (0.87, 3.73)		45/199 (22.6)	1.02 (0.71, 1.47)	
Q4: 13-35	38/226 (16.9)	3.18 (1.74, 5.81)		25/145 (17.2)	2.67 (1.37, 5.21)		70/225 (31.2)	1.40 (1.02, 1.93)	
Incident ADL Limitation*									
Q1: 0-3	13/291 (4.5)	Ref.	0.08	8/203 (3.9)	Ref.	0.02	33/218 (15.1)	Ref.	0.49
Q2: 4-7	14/337 (4.2)	0.88 (0.42, 1.84)		13/212 (6.2)	1.45 (0.63, 3.36)		44/251 (17.5)	1.13 (0.75, 1.70)	
Q3: 8-12	13/248 (5.2)	1.11 (0.53, 2.34)		13/161 (8.1)	1.90 (0.79, 4.54)		32/199 (16.1)	0.99 (0.64, 1.54)	
Q4: 13-35	21/226 (9.3)	1.88 (0.97, 3.64)		20/145 (13.8)	3.07 (1.40, 6.73)		47/225 (20.9)	1.30 (0.87, 1.96)	
Incident Cognition-Dependent Limitation*									
T1: 0-4	2/389 (0.5)	Ref.	0.10	6/246 (2.4)	Ref.	0.86	19/295 (6.4)	Ref.	0.12
T2: 5-10	9/399 (2.3)	3.79 (0.83, 17.37)		7/277 (2.5)	1.09 (0.39, 3.06)		28/296 (9.5)	1.50 (0.85, 2.66)	
T3: 11-35	9/314 (2.9)	5.04 (1.14, 22.35)		7/198 (3.5)	1.33 (0.48, 3.66)		15/302 (5.0)	0.83 (0.42, 1.63)	

ADL activities of daily living; AUASI American Urological Association Symptom Index; Q quartile; T tertile

* Mobility limitation defined as having any difficulty or inability for either walking 2–3 blocks or climbing 10 steps. ADL limitation defined as having any difficulty or inability for bathing or showering and transfers in and out of beds or chairs. Cognition-dependent task limitation defined as having any difficulty or inability to manage money or medications.

† Risk Ratios and 95% confidence intervals calculated using Poisson regression models adjusted for age, site, and history of myocardial infarction or angina, heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, prostate cancer, and stroke or Parkinson's disease. *P* values calculated using the Wald test.

Supplemental Figure 1. Study flowchart.

Not eligible for the current study:
- 1043 died prior to Year 7 visit
- 270 did not participate in Year 7 visit
- 815 missing Year 7 baseline AUASI score or functional status
- 802 with prevalent limitations

No follow-up available:
- 231 died
- 117 lost to follow-up

AUASI

Parent MrOS cohort (n=5994)

Year 7 Baseline (n=3064)

Year 9 (n=2716)

Function/ Mobility

Function/ Mobility

AUASI American Urological Association Symptom Index

Supplemental Figure 2. 2-year risk of new cognition-dependent task limitation by tertile of AUASI score, stratified by age.
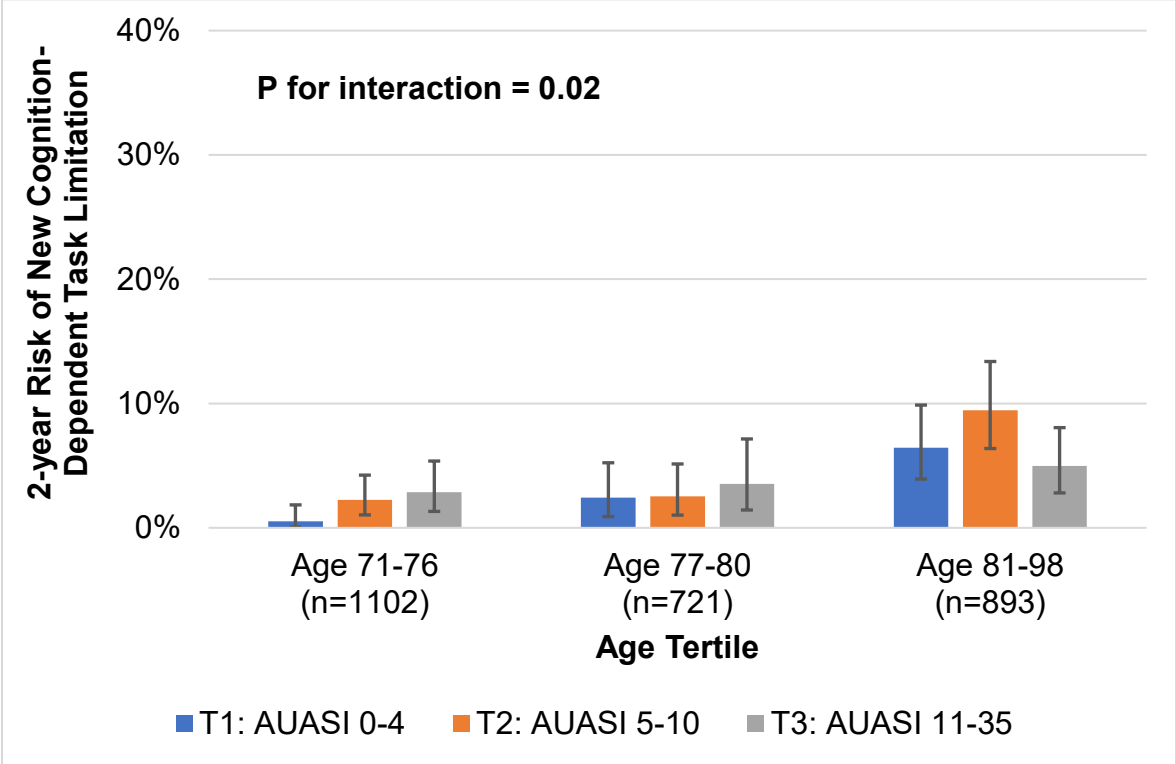
AUASI American Urological Association Symptom Index; T tertile

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