

Online Supplement

Original Research

Reproductive Lifespan and Adult-Onset Bronchiectasis in U.S. Postmenopausal Women: An Investigation of the Women's Health Initiative Cohort

Alexander I. Geyer¹ Shane J. Sacco² Aladdin H. Shadyab³ Mark L. Metersky²

¹Division of Pulmonary and Critical Care Medicine, Lenox Hill Hospital, Zucker School of Medicine at Hofstra University / Northwell Health, New York, NY, United States

²Department of Medicine, University of Connecticut School of Medicine, Farmington, Connecticut, United States

³Herbert Wertheim School of Public Health and Human Longevity Science and Division of Geriatrics, Gerontology, and Palliative Care, Department of Medicine, University of California San Diego, San Diego, California, United States

e-Appendix 1: Comorbidities related to bronchiectasis obtained from Medicare claims.

Comorbidity	ICD9	ICD10
Pulmonary conditions		
Asthma	493	J45
COPD	491, 492	J43, J44
Interstitial lung disease	515, 516	J82, J84, E70.331
Inhalational and other lung disorders due to external agents	500-508	J60-J70
Sarcoidosis	135	D86
Tuberculosis	011.9	A15, Z86.11
Non-tuberculous mycobacterial lung disease	031.0	A31.0
Gastrointestinal conditions		
GERD	530.81	K21
Inflammatory bowel disease	555, 556	K50, K51
Autoimmune conditions		
Rheumatoid arthritis	714	M05, M06, M08
Systemic connective tissue disorders	710	M30-M36
Hematologic malignancy		
Cancers of lymphatic or hematopoietic tissue	200-209, V10.6, V10.7	C81-C96, Z85.6, Z85.7
<i>Note. ICD=International Classification of Diseases.</i>		

e-Appendix 2. Multivariable-adjusted bronchiectasis incidence rates by reproductive characteristics overall and as modified by HT use.

	HT use		
	Total cohort	No	Yes
	aIR (/1000 PY)	aIR (/1000 PY)	aIR (/1000 PY)
Reproductive lifespan, years			
<30	1.73	1.61	1.79
30-34	1.70	1.45	1.83
35-39	1.70	1.48	1.82
≥40	1.53	1.25	1.70
Menopause age, years			
<40	1.78	1.70	1.82
40-44	1.58	1.40	1.66
45-49	1.68	1.37	1.85
50-54	1.53	1.25	1.69
≥55	1.49	1.28	1.58
Menarche age, years			
<12	1.82	1.72	1.89
≥12	1.55	1.33	1.71
<i>Note. aIR = Adjusted incidence rate. PY=Person-years. HT=Hormone therapy. All models were adjusted for age at Medicare enrollment, race, ethnicity, body mass index, smoking behaviors, surgical menopause, HT, oral contraceptive use, parity, and medical comorbidities (pulmonary, gastrointestinal, autoimmune, and malignancy).</i>			

e-Appendix 3: Study analyses utilizing two bronchiectasis diagnoses for case ascertainment as opposed to one

Table 1. Cohort characteristics overall and by reproductive lifespan.

Variable	Total cohort	Reproductive lifespan				p
		<30 yrs	30-34 yrs	35-39 yrs	≥40 yrs	
Age at WHI baseline, y, med (IQR)	63.0 (11.0)	64.0 (11.0)	64.0 (12.0)	62.0 (12.0)	64.0 (10.0)	<0.01
Race, % (n)						<0.01
Black or African American	7.0 (6675)	11.2 (1784)	6.9 (1282)	6.0 (2045)	5.9 (1564)	
Other race	5.2 (4912)	5.7 (900)	5.5 (1022)	5.1 (1755)	4.7 (1235)	
White or Caucasian	87.8 (83683)	83.1 (13201)	87.6 (16325)	88.9 (30568)	89.4 (23589)	
Ethnicity (Hispanic or Latina), % (n)	3.4 (3255)	3.9 (617)*	3.6 (674)	3.4 (1174)	3.0 (790)	0.01
Education, % (n)						<0.01
No school	<0.1 (44)	0.1 (14)	NR	NR	NR	
Grade school	1.0 (972)	1.6 (260)	NR	NR	NR	
High school	29.8 (28401)	37.2 (5912)	31.4 (5848)	27.8 (9551)	26.9 (7090)	
College degree	39.1 (37220)	39.3 (6235)	39.8 (7419)	39.3 (13508)	38.1 (10058)	
Advanced degree	30.1 (28633)	21.8 (3464)	27.6 (5138)	32.1 (11026)	34.1 (9005)	
Family income, % (n)						<0.01
\$0 to \$19,999	13.1 (12488)	17.8 (2826)	13.8 (2573)	11.4 (3935)	12.0 (3154)	
\$20,000 to \$49,999	45.3 (43129)	47.9 (7614)	45.7 (8506)	43.8 (15053)	45.3 (11956)	
\$50,000 to \$99,999	28.9 (27522)	24.4 (3869)	28.6 (5320)	30.7 (10541)	29.5 (7792)	
\$100,000 or more	10.3 (9836)	7.4 (1182)	9.5 (1778)	11.8 (4041)	10.7 (2835)	
Don't know	2.4 (2295)	2.5 (394)	2.4 (452)	2.3 (798)	2.5 (651)	
Body mass index, kg/m², med (IQR)	26.9 (7.1)	27.5 (7.1)	26.8 (7.0)	26.6 (6.9)	27.1 (7.3)	<0.01
Physical activity, min/wk, med (IQR)	145.0 (210.0)	135.0 (215.0)	145.0 (210.0)	145.0 (220.0)	150.0 (210.0)	<0.01
Alcohol use, drinks/wk, med (IQR)	0.4 (2.8)	0.2 (2.0)	0.4 (2.7)	0.4 (3.2)	0.4 (3.0)	<0.01
Smoking behavior, % (n)						<0.01
Former	42.5 (40519)	42.2 (6708)	43.0 (8008)	43.1 (14827)	41.6 (10976)	
Current	6.4 (6125)	8.7 (1380)	7.6 (1413)	6.3 (2173)	4.4 (1159)	
Surgical menopause, % (n)	15.9 (15113)	29.6 (4701)	20.4 (3802)	11.9 (4082)	9.6 (2528)	<0.01
HT, % (n)	57.8 (55104)	64.1 (10190)	61.4 (11437)	56.5 (19435)	53.2 (14042)	<0.01
Oral contraceptive, % (n)	41.5 (39491)	36.7 (5833)	42.5 (7911)	45.1 (15503)	38.8 (10244)	<0.01
Parity, % (n)						<0.01
One Child	8.6 (8174)	10.3 (1633)	9.0 (1672)	8.5 (2906)	7.4 (1963)	
Multiple Children	79.5 (75775)	75.4 (11978)	78.3 (14595)	79.6 (27355)	82.8 (21847)	
Comorbidities, % (n)						
Pulmonary	50.6 (48182)	53.9 (8564)	50.5 (9406)	48.6 (16689)	51.2 (13523)	<0.01
Gastrointestinal	35.8 (34128)	39.2 (6219)	36.4 (6773)	35.1 (12055)	34.4 (9081)	<0.01
Autoimmune	12.8 (12169)	14.0 (2229)	12.7 (2369)	12.1 (4171)	12.9 (3400)	<0.01
Malignancy	20.0 (19097)	19.9 (3167)	20.0 (3719)	19.4 (6681)	21.0 (5530)	>0.99

Note. NR=Not reported to comply with WHI reporting standards regarding small sample size. IQR=Interquartile range. HT=Hormone therapy.

2 **Table 2.** Cohort characteristics overall and by bronchiectasis occurrence.

Variable	Total cohort	Developed bronchiectasis		p
		Yes	No	
Age at WHI baseline, y, med (IQR)	63.0 (11.0)	64.0 (9.0)	63.0 (11.0)	>0.99
Race, % (n)				<0.01
Black or African American	7.0 (6675)	3.0 (35)	7.1 (6640)	
Other race	5.2 (4912)	5.6 (65)	5.2 (4847)	
White or Caucasian	87.8 (83683)	91.3 (1054)	87.8 (82629)	
Ethnicity (Hispanic or Latina), % (n)	3.4 (3255)	2.3 (27)	3.4 (3228)	0.93
Education, % (n)				<0.01
No school	<0.1 (44)	NR	NR	
Grade school	1.0 (972)	NR	NR	
High school	29.8 (28401)	25.6 (295)	29.9 (28106)	
College degree	39.1 (37220)	37.7 (435)	39.1 (36785)	
Advanced degree	30.1 (28633)	36.0 (416)	30.0 (28217)	
Family income, % (n)				<0.01
\$0 to \$19,999	13.1 (12488)	8.6 (99)	13.2 (12389)	
\$20,000 to \$49,999	45.3 (43129)	39.5 (456)	45.3 (42673)	
\$50,000 to \$99,999	28.9 (27522)	34.2 (395)	28.8 (27127)	
\$100,000 or more	10.3 (9836)	14.2 (164)	10.3 (9672)	
Don't know	2.4 (2295)	3.5 (40)	2.4 (2255)	
Body mass index, kg/m², med (IQR)	26.9 (7.1)	24.3 (6.0)	27.0 (7.1)	<0.01
Physical activity, min/wk, med (IQR)	145.0 (210.0)	150.0 (205.0)	145.0 (212.5)	0.03
Alcohol use, drinks/wk, med (IQR)	0.4 (2.8)	0.5 (3.7)	0.4 (2.7)	<0.01
Smoking behavior, % (n)				<0.01
Former	42.5 (40519)	49.2 (568)	42.4 (39951)	
Current	6.4 (6125)	4.4 (51)	6.5 (6074)	
Reproductive lifespan, y, % (n)				>0.99
<30	16.7 (15885)	16.6 (191)	16.7 (15694)	
30-34	19.6 (18629)	19.0 (219)	19.6 (18410)	
35-39	36.1 (34368)	35.9 (414)	36.1 (33954)	
≥40	27.7 (26388)	28.6 (330)	27.7 (26058)	
Surgical menopause, % (n)	15.9 (15113)	13.8 (159)	15.9 (14954)	>0.99
HT, % (n)	57.8 (55104)	63.4 (732)	57.8 (54372)	<0.01
Oral contraceptive, % (n)	41.5 (39491)	41.3 (477)	41.5 (39014)	>0.99
Parity, % (n)				>0.99
One Child	8.6 (8174)	8.6 (99)	8.6 (8075)	
Multiple Children	79.5 (75775)	79.1 (913)	79.5 (74862)	
Comorbidities, % (n)				
Pulmonary	50.6 (48182)	62.1 (717)	50.4 (47465)	<0.01
Gastrointestinal	35.8 (34128)	36.5 (421)	35.8 (33707)	>0.99
Autoimmune	12.8 (12169)	15.5 (179)	12.7 (11990)	0.10
Malignancy	20.0 (19097)	20.0 (231)	20.0 (18866)	>0.99

Note. NR=Not reported to comply with WHI reporting standards regarding small sample size. IQR=Interquartile range. HT=Hormone therapy.

Table 3. Multivariable-adjusted bronchiectasis risk by reproductive characteristics overall and by hormone therapy use.

	Total cohort		HT use			
			No		Yes	
	aHR	p	aHR	p	aHR	p
Reproductive lifespan, years		0.07		0.03		0.48
<30	Reference		Reference		Reference	
30-34	0.90 (0.72, 1.07)		0.84 (0.56, 1.13)		0.92 (0.70, 1.14)	
35-39	0.89 (0.74, 1.05)		0.86 (0.60, 1.11)		0.90 (0.71, 1.09)	
≥40	0.89 (0.73, 1.06)		0.74 (0.51, 0.98)		0.99 (0.77, 1.21)	
Menopause age, years		0.04		0.02		0.30
<40	Reference		Reference		Reference	
40-44	0.89 (0.67, 1.11)		0.87 (0.48, 1.27)		0.89 (0.62, 1.16)	
45-49	0.85 (0.66, 1.04)		0.83 (0.50, 1.17)		0.85 (0.62, 1.08)	
50-54	0.85 (0.66, 1.03)		0.74 (0.46, 1.03)		0.90 (0.67, 1.14)	
≥55	0.79 (0.60, 0.99)		0.74 (0.42, 1.06)		0.82 (0.57, 1.06)	
Menarche age, years		0.04 [†]		<0.01 [†]		0.69
<12	Reference		Reference		Reference	
≥12	0.83 (0.72, 0.95)		0.74 (0.57, 0.91)		0.89 (0.74, 1.05)	

Note. aHR=Adjusted approximate hazard ratio. HT=Hormone therapy. PY=Person-years. [†]both linear and non-linear ps<0.05. All models were adjusted for age at Medicare enrollment, race, ethnicity, body mass index, smoking behaviors, surgical menopause, hormone therapy, oral contraceptive use, and medical comorbidities (pulmonary, gastrointestinal, autoimmune, and malignancy).