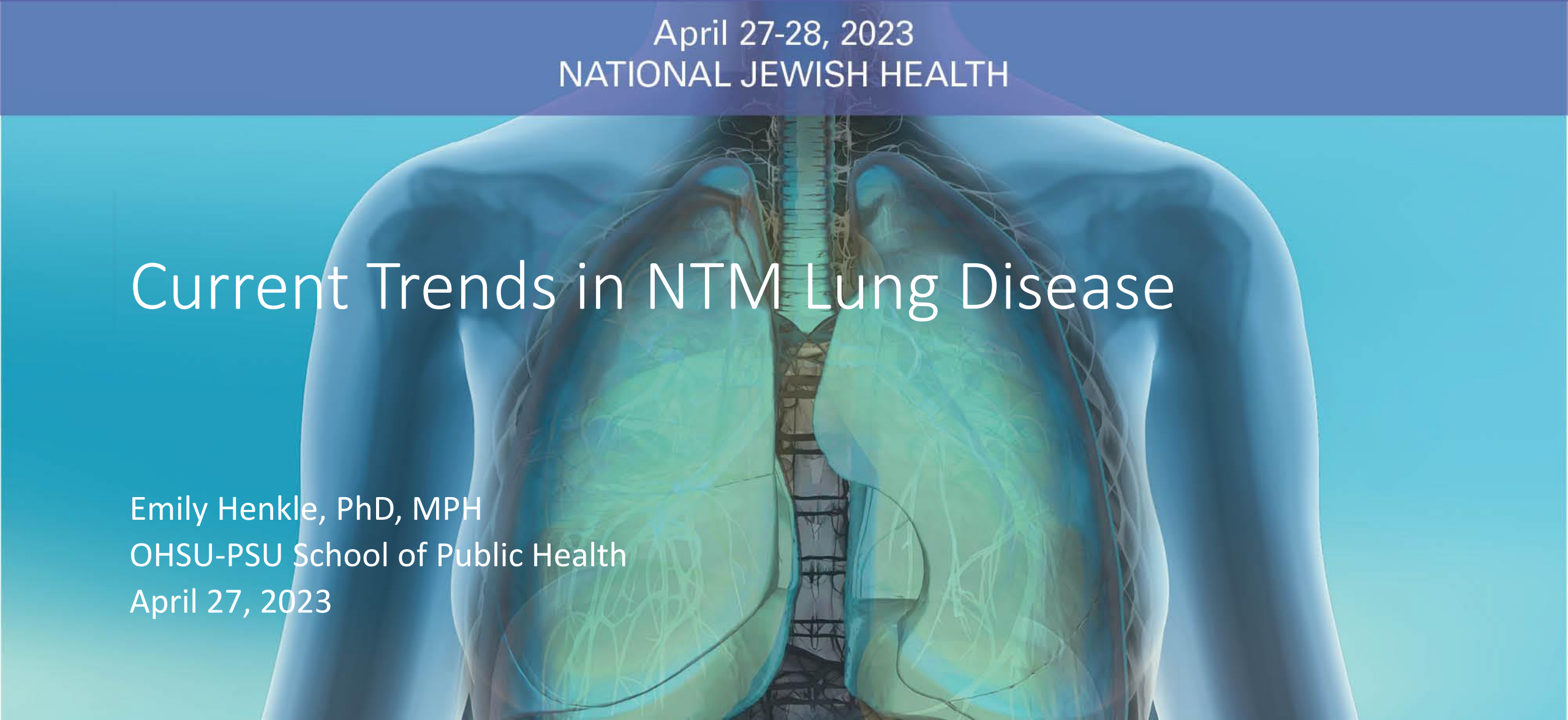
NTM Lecture Series for Providers

April 27-28, 2023
NATIONAL JEWISH HEALTH



Current Trends in NTM Lung Disease

Emily Henkle, PhD, MPH
OHSU-PSU School of Public Health
April 27, 2023

Disclosures

- Advisory Board/Consulting Fees AN2 Therapeutics
- Advisory Board MannKind Corp.

NTM-LD learning objectives

- Describe trends in the incidence and prevalence of NTM-LD
- Identify risk factors for NTM-LD

WHO definition of epidemiology

- Epidemiology is the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems. Various methods can be used to carry out epidemiological investigations: surveillance and descriptive studies can be used to study distribution; analytical studies are used to study determinants.

NTM Lung Disease (NTM-LD)

- NTM=nontuberculous mycobacteria
  - "MOTT" mycobacteria other than tuberculosis
  - "atypical" mycobacteria
  - Excludes *M. tuberculosis* complex*, M. leprae* (Hansen's Disease)
- Ubiquitous in soil, water
- *M. avium* complex (MAC) most common
- *M. abscessus*
- Rarely *M. xenopi, M. kansaii*

- Today: NTM-LD (also see as NTM-PD/PNTM), rare, chronic lung infection
- X- Extrapulmonary

Diagnosis of NTM-LD

Clinical Infectious Diseases
IDSA FEATURES

Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline

Charles L. Daley,[1,2,a] Jonathan M. Iaccarino,[3] Christoph Lange,[4,5,6,7,a] Emmanuelle Cambau,[8,a] Richard J. Wallace, Jr[9,a] Claire Andrejak,[10,11] Erik C. Böttger,[12] Jan Brozek,[13] David E. Griffith,[14] Lorenzo Guglielmetti,[8,15] Gwen A. Huitt,[1,2] Shandra L. Knight,[16] Philip Leitman,[17] Theodore K. Marras,[18] Kenneth N. Olivier,[19] Miguel Santin,[20] Jason E. Stout,[21] Enrico Tortoli,[22] Jakko van Ingen,[23] Dirk Wagner,[24] and Kevin L. Winthrop[25]

Table 2. Clinical and Microbiologic Criteria for Diagnosis of Nontuberculous Mycobacterial Pulmonary Disease[a]

Clinical	Pulmonary or Systemic Symptoms	
Radiologic	Nodular or cavitary opacities on chest radiograph, or a high-resolution computed tomography scan that shows bronchiectasis with multiple small nodules	Both Required
and	Appropriate exclusion of other diagnoses	
Microbiologic[b]	1. Positive culture results from at least two separate expectorated sputum samples. If the results are nondiagnostic, consider repeat sputum AFB smears and cultures **or** 2. Positive culture results from at least one bronchial wash or lavage **or** 3. Transbronchial or other lung biopsy with mycobacterial histologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture positive for NTM	

Source: Official ATS/IDSA statement [4].

Abbreviation: AFB, acid-fast bacilli; NTM, Nontuberculous mycobacteria.

[a]Expert consultation should be obtained when NTM are recovered that are either infrequently encountered or that usually represent environmental contamination. Patients who are suspected of having NTM pulmonary disease but do not meet the diagnostic criteria should be followed until the diagnosis is firmly established or excluded. Making the diagnosis of NTM pulmonary disease does not per se, necessitate the institution of therapy, which is a decision based on the potential risks and benefits of therapy for individual patients.

[b]When 2 positive cultures are obtained, the isolates should be the same NTM species (or subspecies in the case of *M. abscessus*) in order to meet disease criteria.

Laboratory data only

American Thoracic Society Documents

An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases

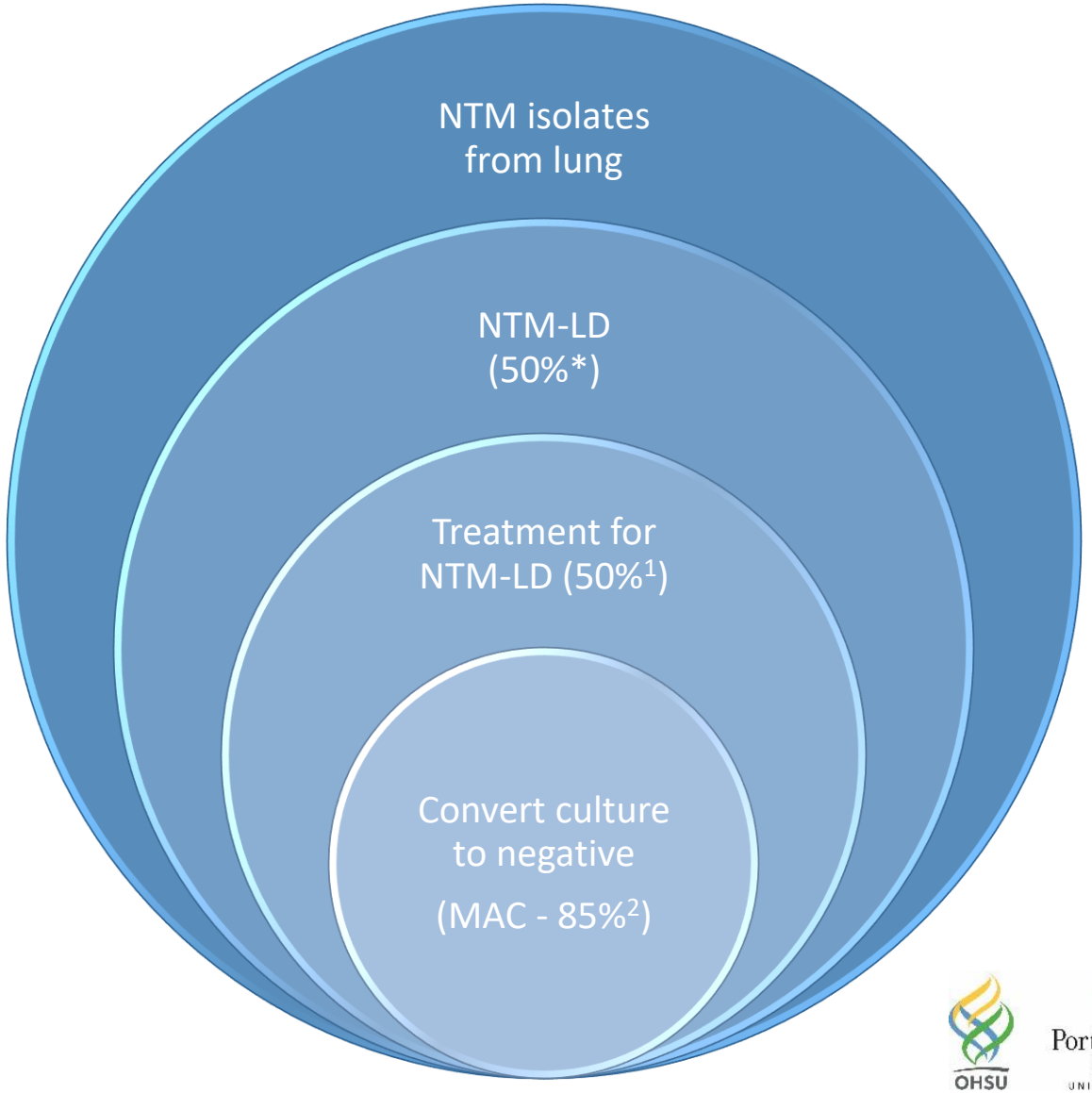
David E. Griffith, Timothy Aksamit, Barbara A. Brown-Elliott, Antonino Catanzaro, Charles Daley, Fred Gordin, Steven M. Holland, Robert Horsburgh, Gwen Huitt, Michael F. Iademarco, Michael Iseman, Kenneth Olivier, Stephen Ruoss, C. Fordham von Reyn, Richard J. Wallace, Jr., and Kevin Winthrop, on behalf of the ATS Mycobacterial Diseases Subcommittee

This Official Statement of the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) was adopted by the ATS Board Of Directors, September 2006, and by the IDSA Board of Directors, January 2007

Am J Respir Crit Care Med Vol 175. pp 367–416, 2007
DOI: 10.1164/rccm.200604-571ST
Internet address: www.atsjournals.org

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Natural history of MAC-LD



*Winthrop et al. AJRCCM 2010, Henkle et al. Annals ATS 2015

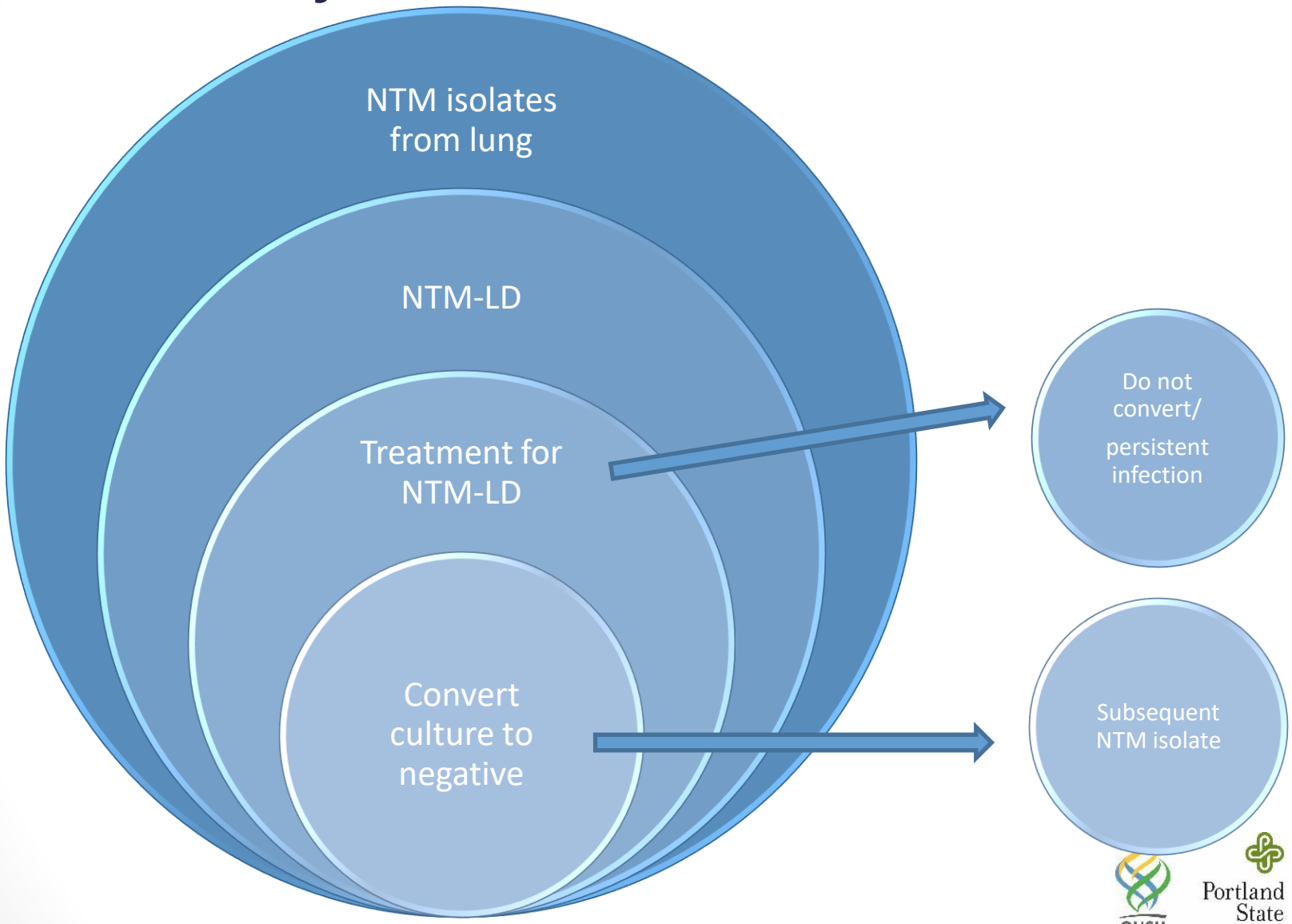
[1]Winthrop et al. AJRCCM 2010, Moon et al. Resp Med 2019

[2]Wallace et al. Chest 2014
Im et al. Chest 2022

Gaps: *M. abscessus*

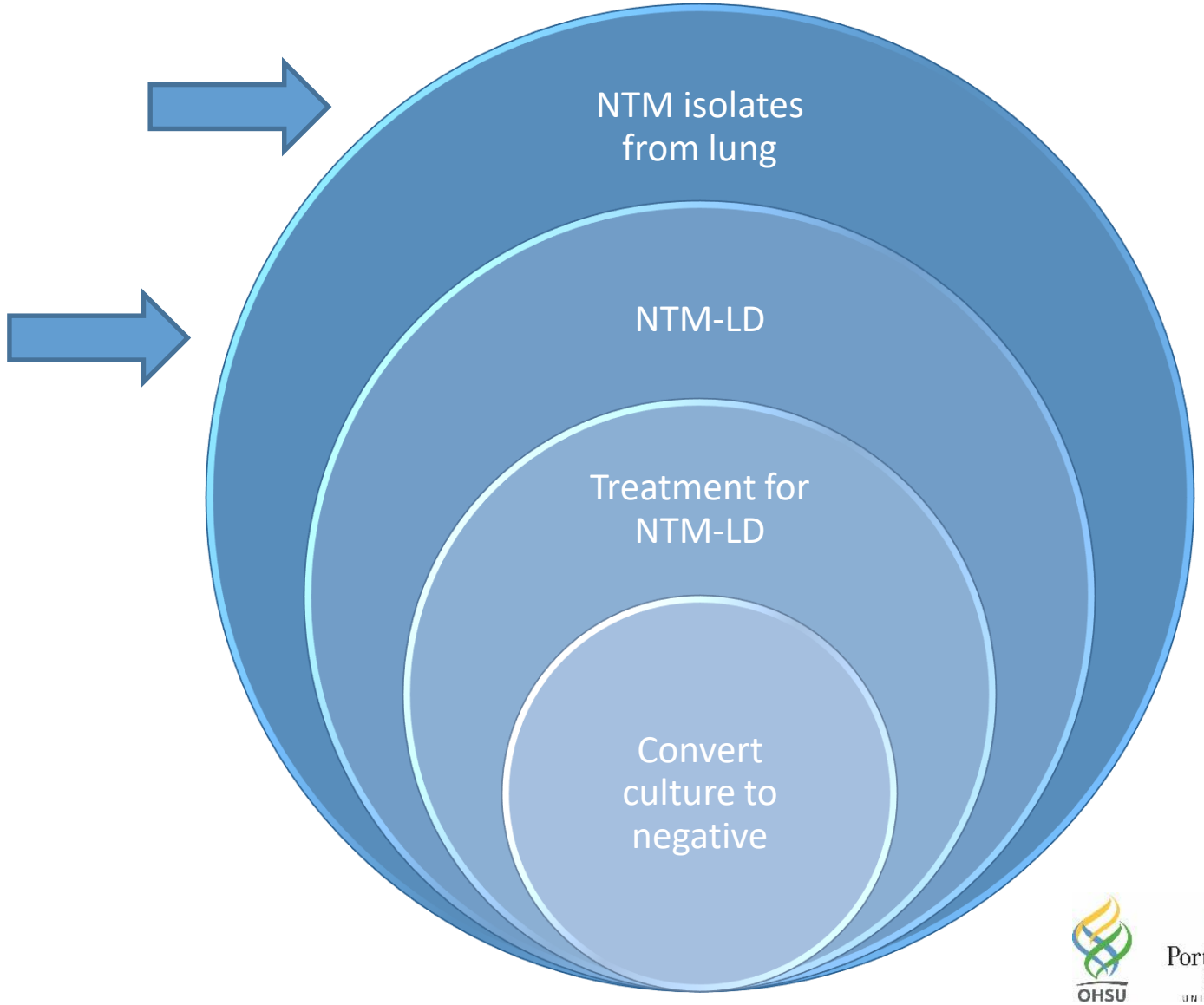
OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Natural history of NTM-LD



OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Incidence and Prevalence of NTM-LD



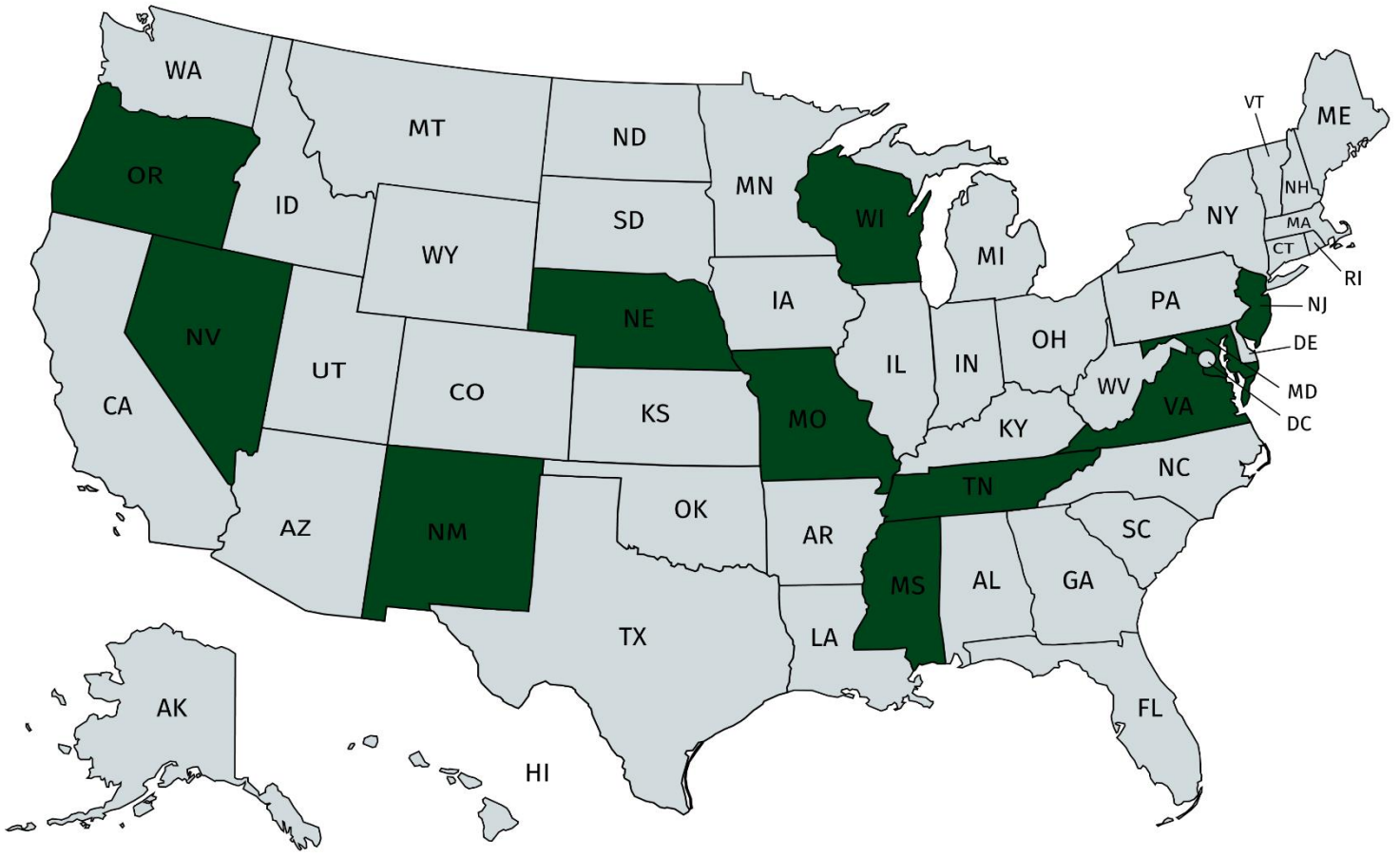
OHSU Portland State University SCHOOL OF PUBLIC HEALTH

SURVEILLANCE

Surveillance of NTM-LD

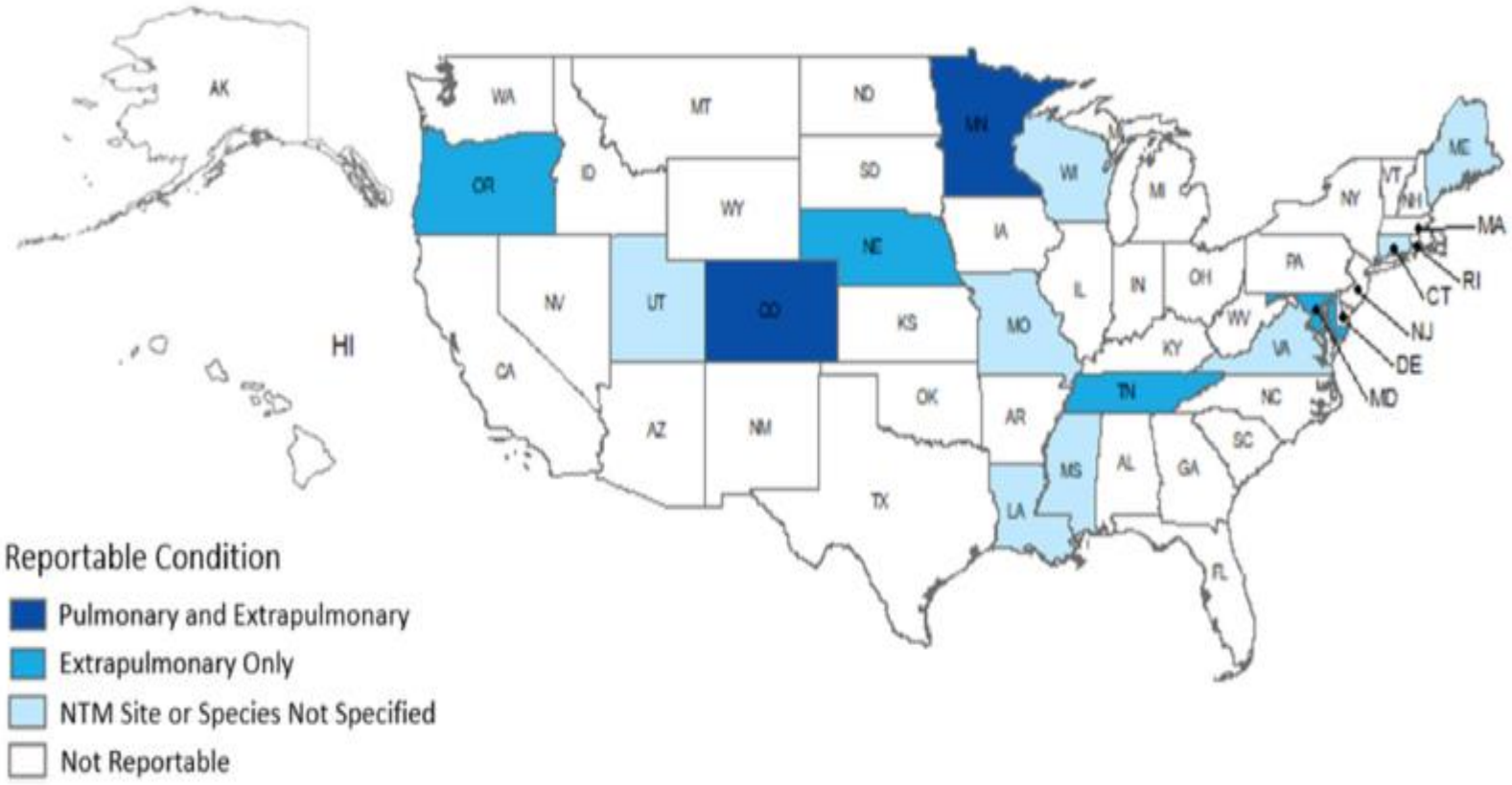
- Useful to track trends, identify clusters
- NTM considerations
  - Completeness of laboratory reporting/speciation
  - Meaning of single isolation?
    - ATS/IDSA microbiologic criteria- 2 sputum, 1 BAL/wash/biopsy
  - Chronic infection- once diagnosed, how long counted as case?
  - Exclude *M. gordonae*
- Accuracy of denominator?
- Clinical characteristics available?

States Requiring Reporting of NTM, 2017



N = 11 require reporting

States With Reporting of NTM, 2023



N = 14 with some form of NTM reporting

Mercaldo et al. 2023 Tuberculosis

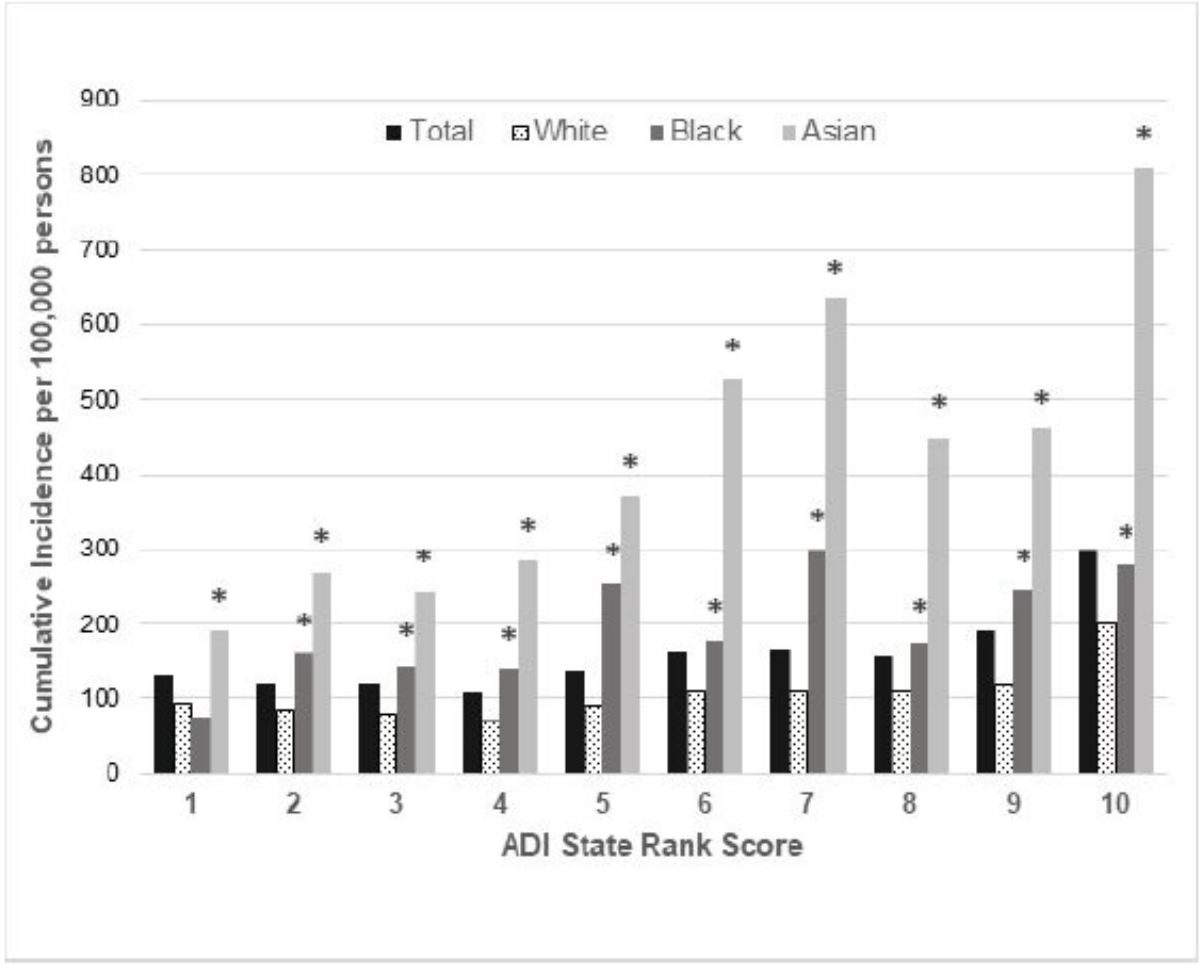
OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

NTM in Wisconsin 2011-2018

- Notifiable disease
- Over 8000 isolates from 6811 adults
  - 90.2% of isolates respiratory
    - MAC 76.4%
    - *M. chelonae-abscessus* group 7.3%
    - *M. xenopi* 9.4%
    - *M. kansasii* 3.7%
- Cumulative incidence 137/100,000 (134-141)
  - Similar male and female
  - Highest in Black (202 [184-219]/100,000) and Asian (238 [208-268]/100,000) populations
- Annual incidence stable

Vonasek et al. 2023 Annals ATS

NTM in Wisconsin 2011-2018 – Cumulative Incidence by Race and Area Deprivation Index Score



ADI Score: Kind AJH, Buckingham W. Making Neighborhood Disadvantage Metrics Accessible: The Neighborhood Atlas. *New England Journal of Medicine*, 2018. 378: 2456-2458. DOI: 10.1056/NEJMp1802313. PMCID: PMC6051533. AND University of Wisconsin School of Medicine Public Health. 2015 Area Deprivation Index v2.0. Downloaded from https://www.neighborhoodatlas.medicine.wisc.edu/ May 23, 2019.

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

CDC NTM Surveillance

https://www.cdc.gov/hai/eip/ntm.html

- Emerging Infections Program Healthcare-Associated Infections Community Interface (HAIC) NTM surveillance program piloted 2019-2020
  - Ongoing surveillance in four EIP sites
  - Data from this project will inform policy and prevention strategies to reduce NTM infections
  - First publication in press at Clinical Infectious Diseases
- **Objectives**
  - Describe the epidemiology of pulmonary and extrapulmonary NTM infections
  - Describe microbiologic characteristics of public health relevance
  - Evaluate antimicrobial susceptibility of organisms causing NTM infections
  - Characterize the molecular epidemiology of NTM
- **Case Definition**
  - Prevalent case: NTM identified from the same infection category (i.e., pulmonary or extrapulmonary) during the 12 months before the date of index specimen collection (DISC).
  - Incident case: no NTM were identified during the 12 months before the DISC.

CDC NTM Surveillance

Surveillance Areas		
Site	Estimated Population Under Surveillance: Pulmonary NTM	Estimated Population Under Surveillance: Extrapulmonary NTM
Colorado (5 counties)	2,835,257*	2,835,257*
Minnesota (2 counties)	1,816,164*	1,816,164*
New York (2 counties)	1,047,276	1,047,276
Oregon (3 counties PNTM; statewide ENTM)	1,832,634	4,217,737*

Surveillance Areas
*NTM reportable in the catchment area

CDC NTM Surveillance

- 6-month pilot results in press: Grigg et al. CID 2023
- Annualized prevalence 6.1/100,000
- N=231 NTM-LD cases defined by microbiologic criteria from 420 patients with pulmonary specimens
  - 87% had signs or symptoms
  - 63% female
  - 74% white, not (known to be) Hispanic (xx% missing)
  - 55% met (modified) ATS/IDSA disease criteria, 80% had clinician diagnosis
- 72% MAC
  - 48% treated with at least 1 antibiotic, 18% guideline-based therapy
- Exposure history limited
- Surveillance ongoing since 2021

POPULATION BASED STUDIES

Isolation prevalence

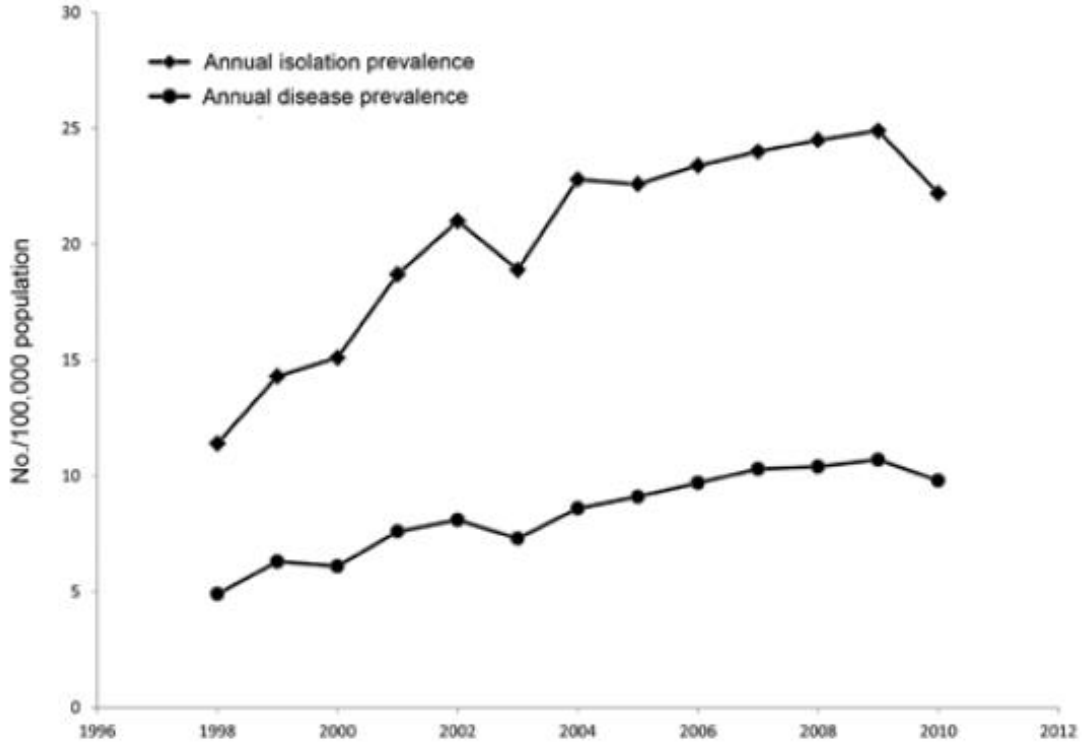


Figure. Annual isolation prevalence and disease prevalence per 100,000 persons of pulmonary nontuberculous mycobacteria, Ontario, Canada, 1998–2010.

Marras et al. EID 2013

OHSU Portland State UNIVERSITY | SCHOOL OF PUBLIC HEALTH

Oregon statewide study, 2007-2012

Henkle et al. Ann Am Thorac Soc Vol 12, No 5, pp 642–647, May 2015

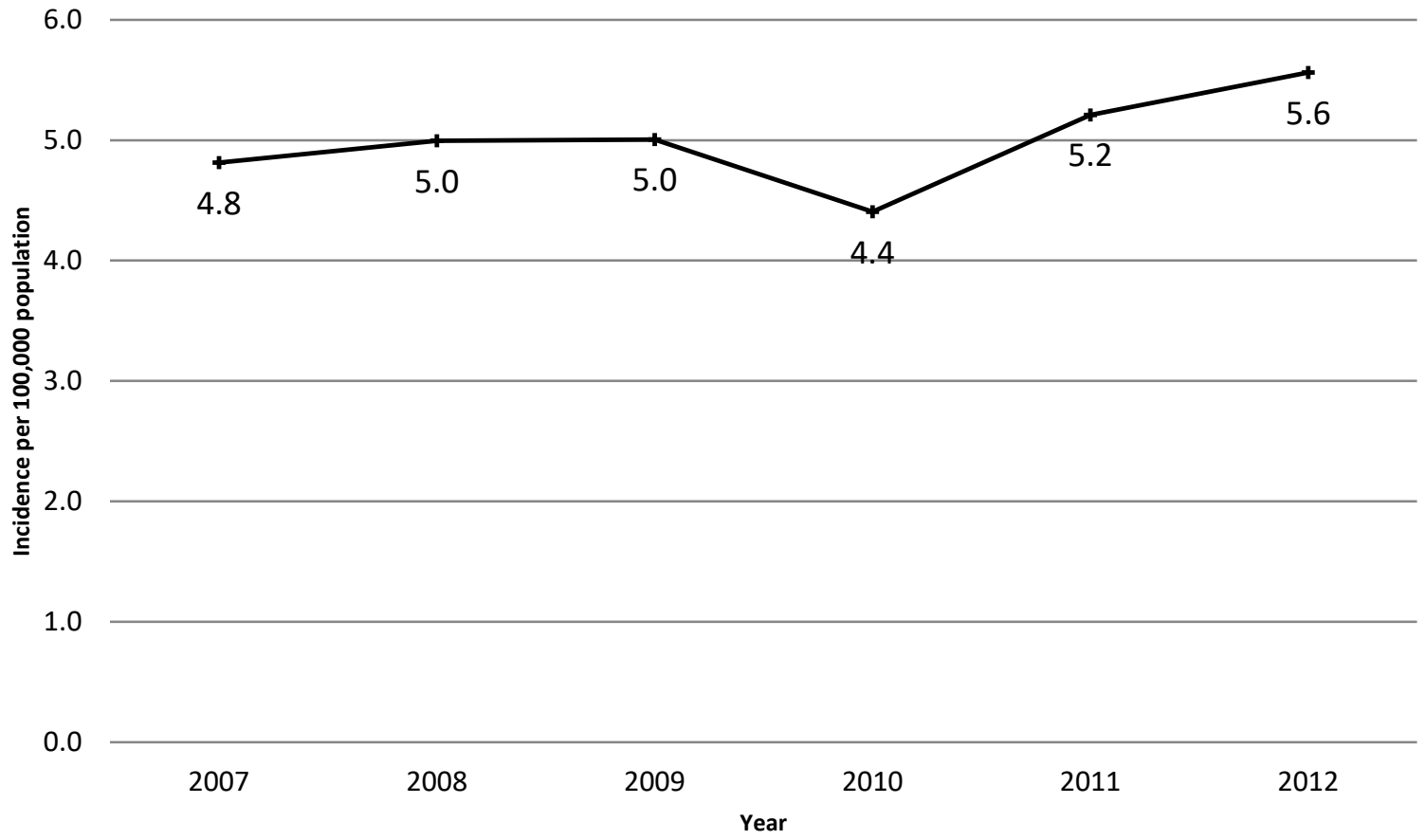
- Data source: all positive AFB lab results from 17 local/reference labs used in OR
- Case definition: ATS/IDSA microbiologic criteria, excluding *M. gordonae*
- Denominator: statewide population estimates
- Incidence and prevalence calculations
  - 2-year lag consider case “incident”

- 1146 pulmonary cases
- 57% BAL, 43% sputum
- 55% female
- Species
  - 85% MAC
  - 6% *M. abscessus/chelonae* complex
  - 1% each *M. chelonae*, *M. kansasii*, *M. lentiflavum*

OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

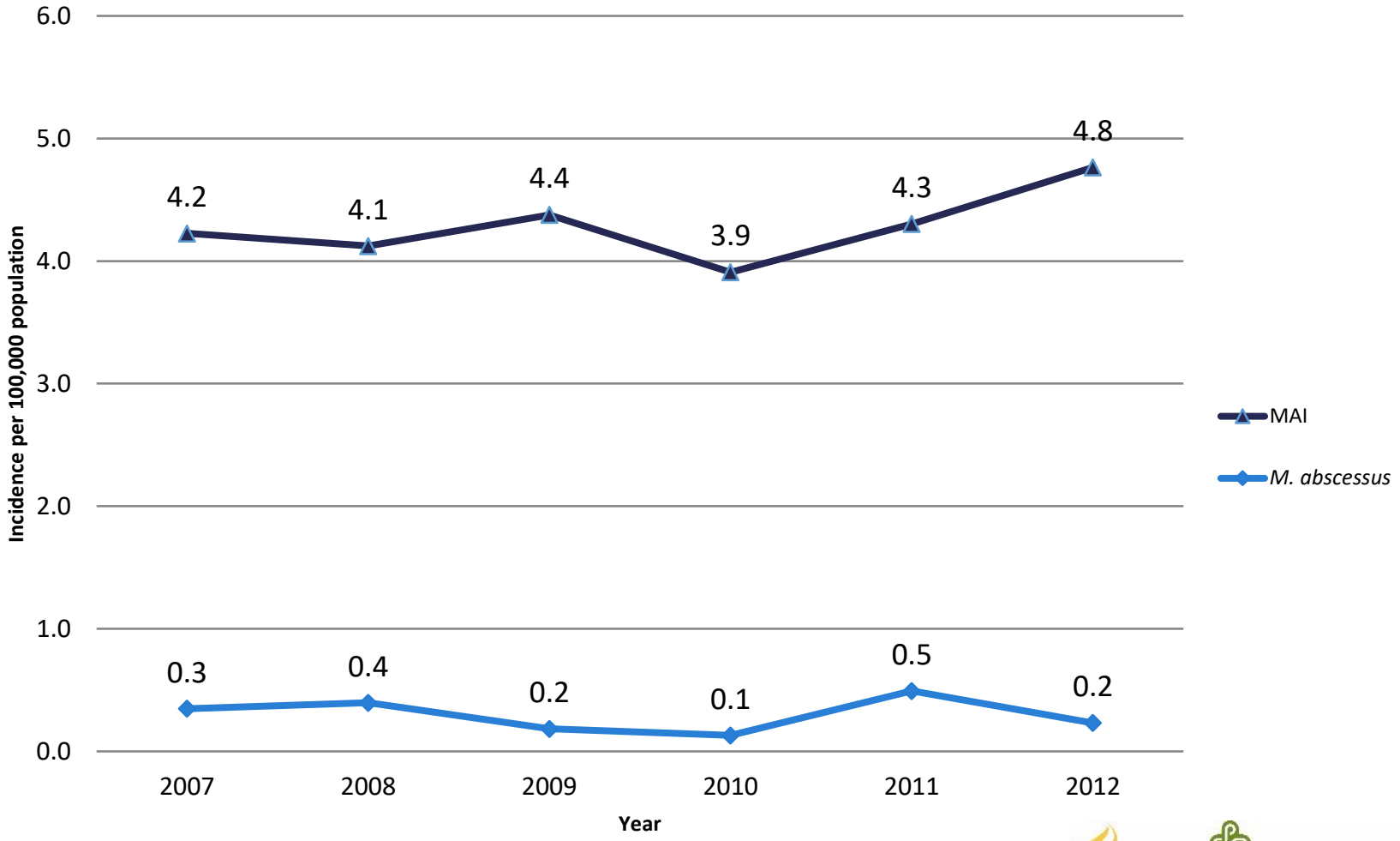
Incidence rate of NTM-LD, Oregon 2007-2012

Henkle et al. Ann Am Thorac Soc Vol 12, No 5, pp 642–647, May 2015



OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Incidence rates of MAI and *M. abscessus/chelonae* NTM-LD, Oregon 2007-2012.



Henkle et al. Ann Am Thorac Soc Vol 12, No 5, pp 642–647, May 2015

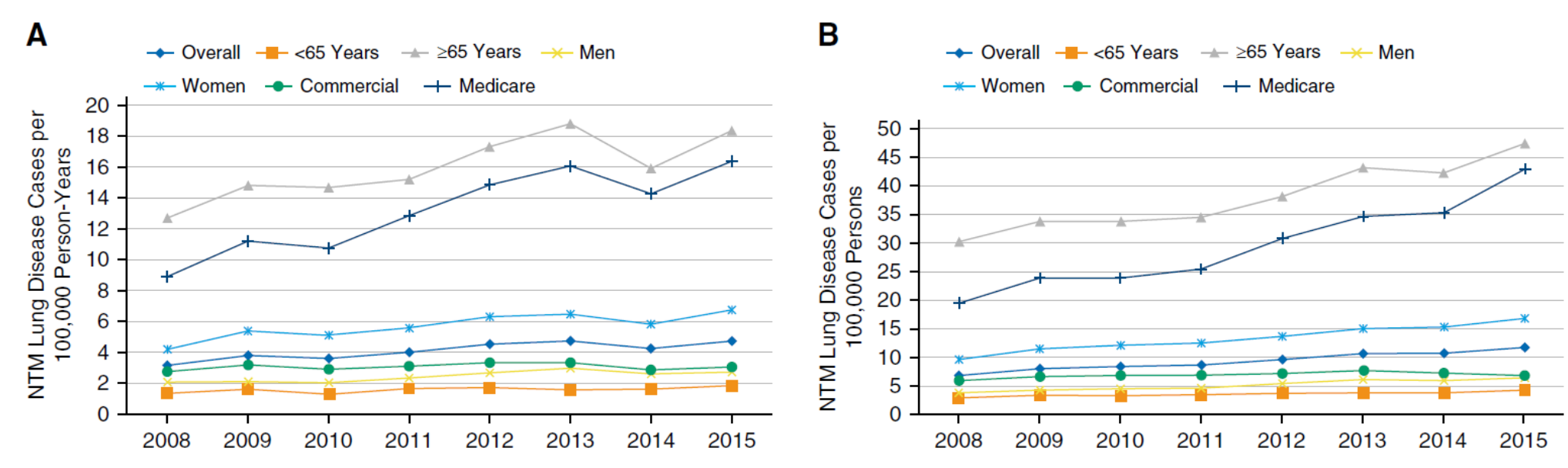
OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Annual prevalence of NTM-LD, North America

Geographic area	Disease definition	Annual isolation rate/ 100,000	Annual disease rate/ 100,000
Hawaii (Kaiser)	Microbiologic	44 (2013)	
US- Pacific Islands (2011)	Microbiologic	48 (2011)	
5 States (MO, MS, MD, OH, WI), NTM reporting	Microbiologic	8.7-13.9	n/a
North Carolina, 3 counties (2006-2010)	Microbiologic	9.4	
Oregon USA (2007-2012)	Microbiologic	12.7	5.9
USA: HMOs (CA, CO, PA, WA) (1997-2005)	Microbiologic	11.8	5.5
Ontario, Canada (1998-2010)	Microbiologic	22.2	9.8

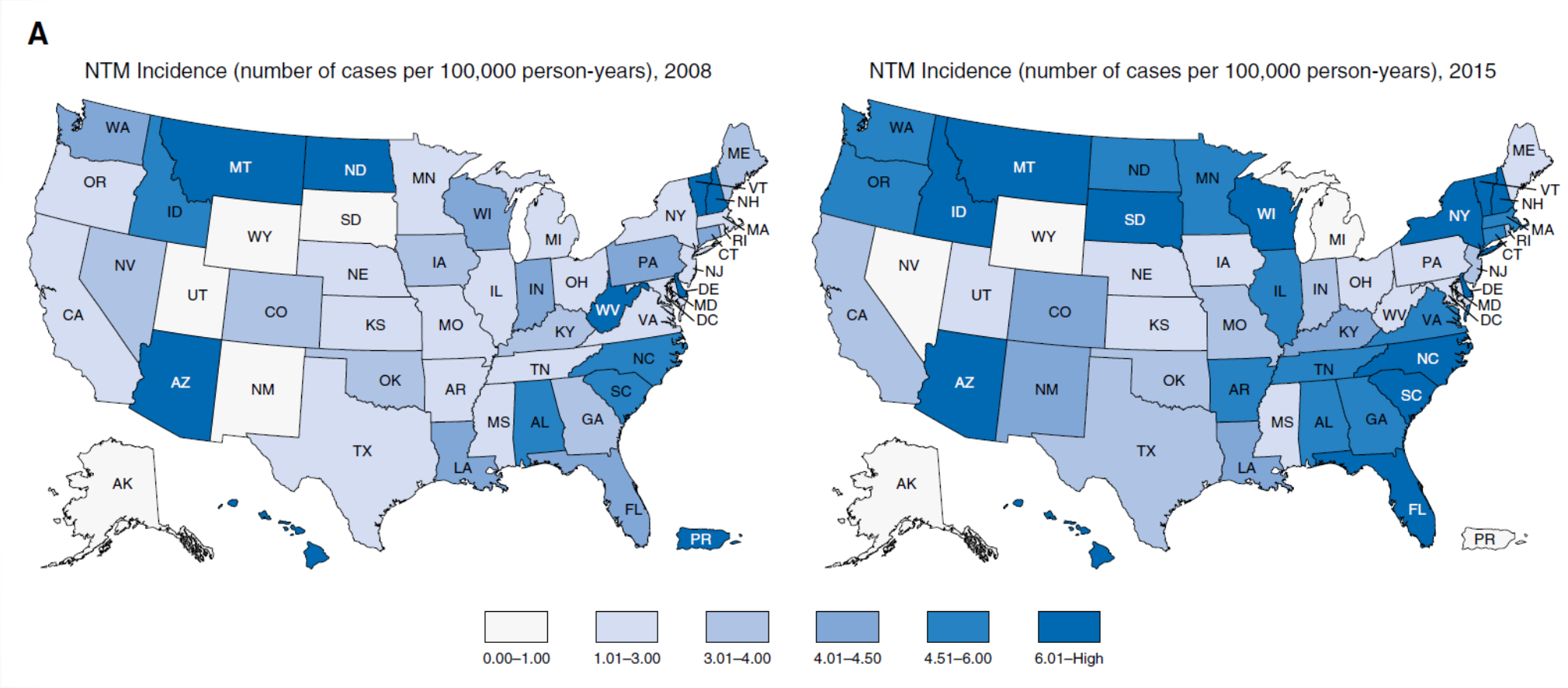
Prevots DR, Marras TK. Epidemiology of Human Pulmonary Infection with Nontuberculous Mycobacteria: a review. Clinics in Chest Medicine; 2015; 36:13-34

Yearly Incidence (A) and Prevalence (B) of NTM-LD 2008-2015



Winthrop et al. 2020 Annals ATS

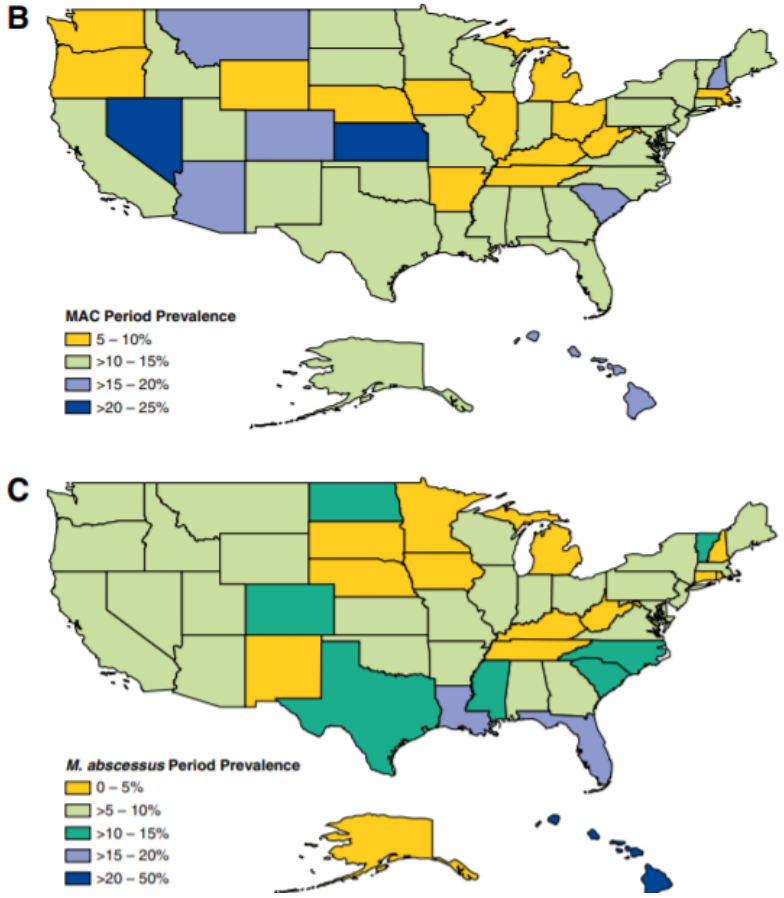
Geographic distribution of NTM-LD 2008-2015



Winthrop et al. 2020 Annals ATS

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Geographic variation in NTM prevalence among persons with cystic fibrosis: *M. abscessus* prevalence highest in the Southeast United States

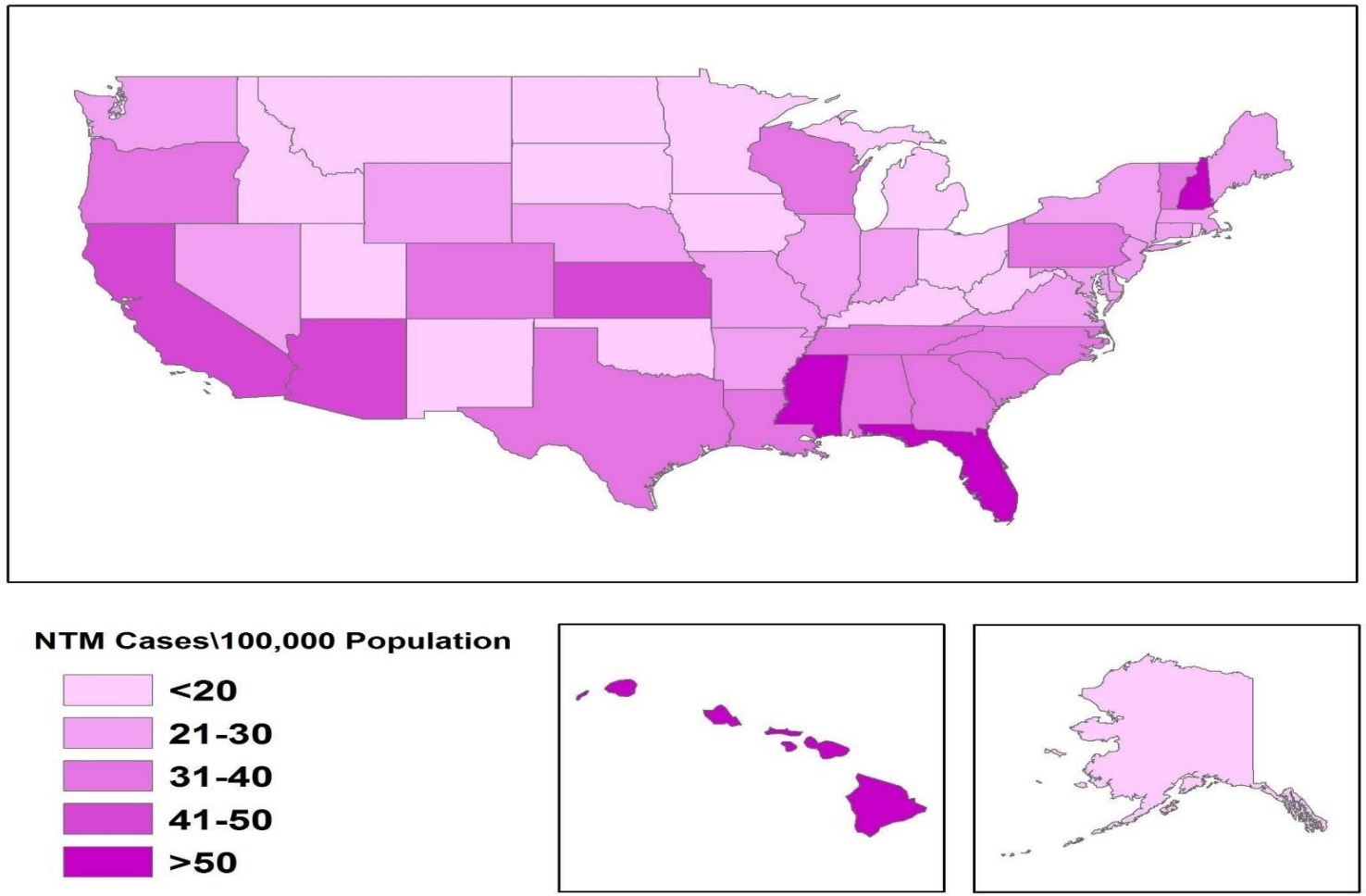


Tzou, Dirac, Becker, *et al.*: NTM Exposure and Pulmonary Disease

AnnalsATS Volume 17 Number 1 | January 2020

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Highest prevalence of NTM-LD in Hawai'i and Florida, 2010

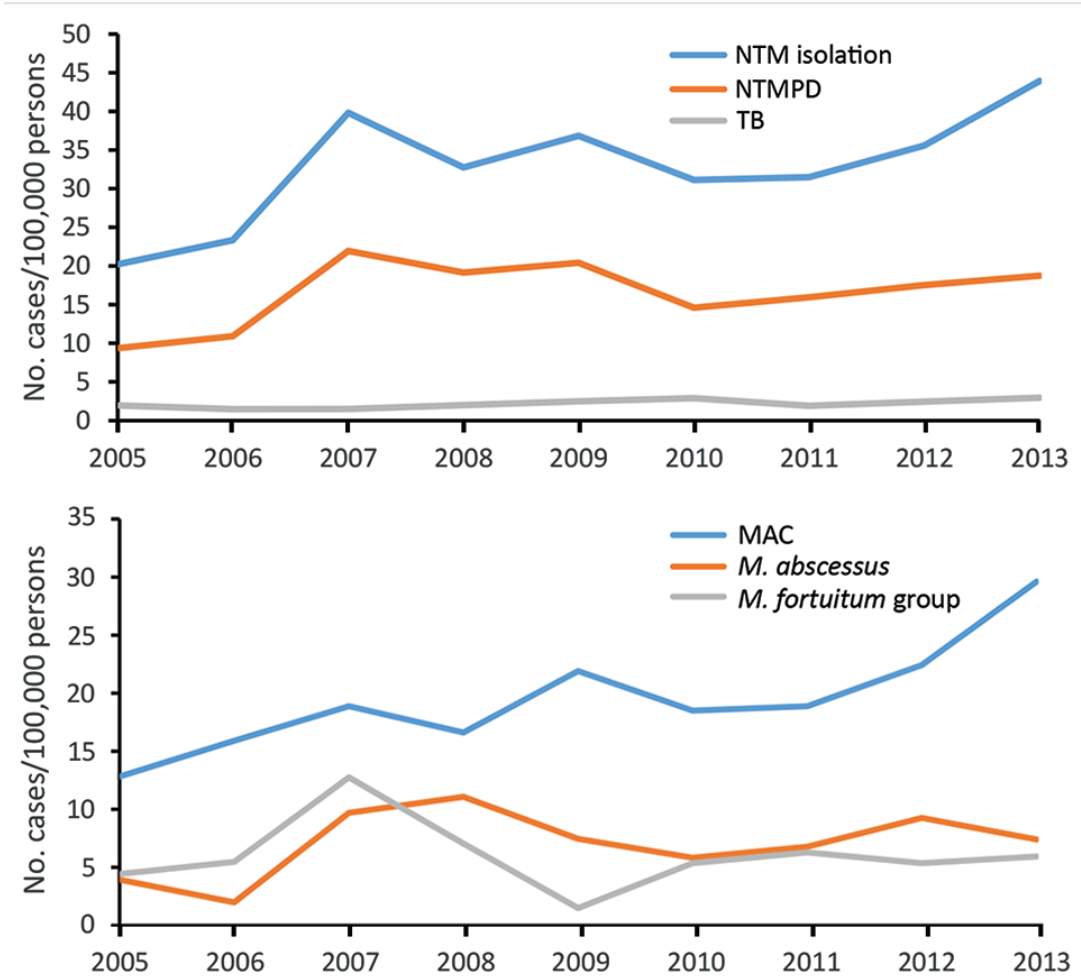


From Strollo et al: the burden of pulmonary NTM in the United States. Annals ATS 12; 2015: 1458-1464

OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Annual prevalence of pulmonary NTM isolation, NTM pulmonary disease, and TB (A) and annual prevalence of pulmonary NTM isolation by species (B) among a cohort of Kaiser Permanente Hawaii patients, Hawaii, 2005–2013.

Adjemian et al. Emerging Infectious Diseases Vol. 23, No. 3, March 2017



OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

AFB testing increased 3.2%/year and NTM positivity increased 4.5%/year, 2009-2015 (Cerner EHR database, 31 facilities)

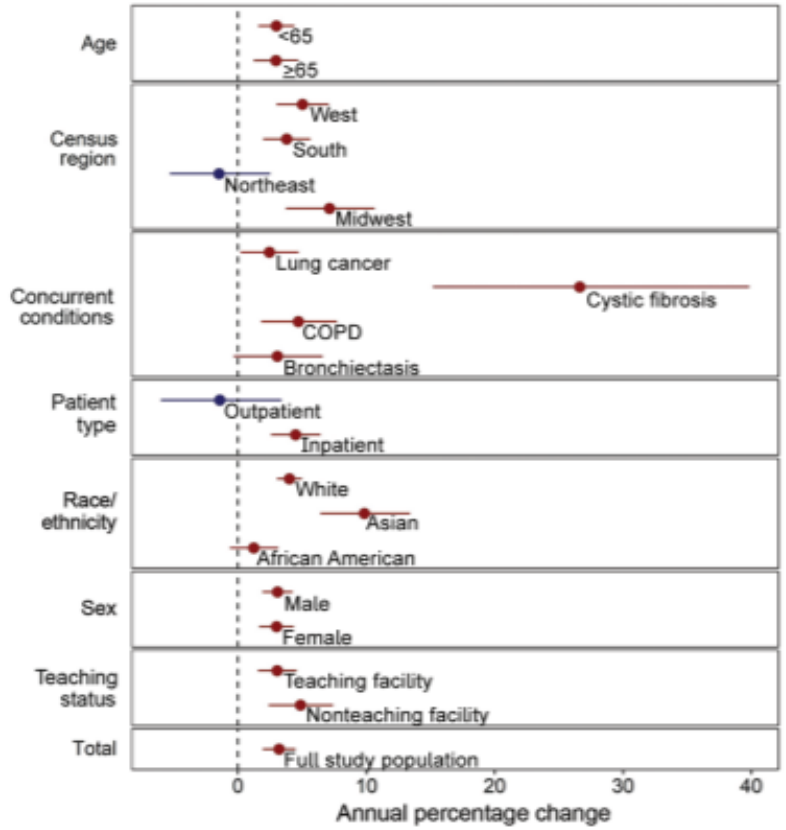


Figure 1. Annual percentage change in laboratory testing for acid-fast bacilli in 31 facilities, United States, 2009–2015

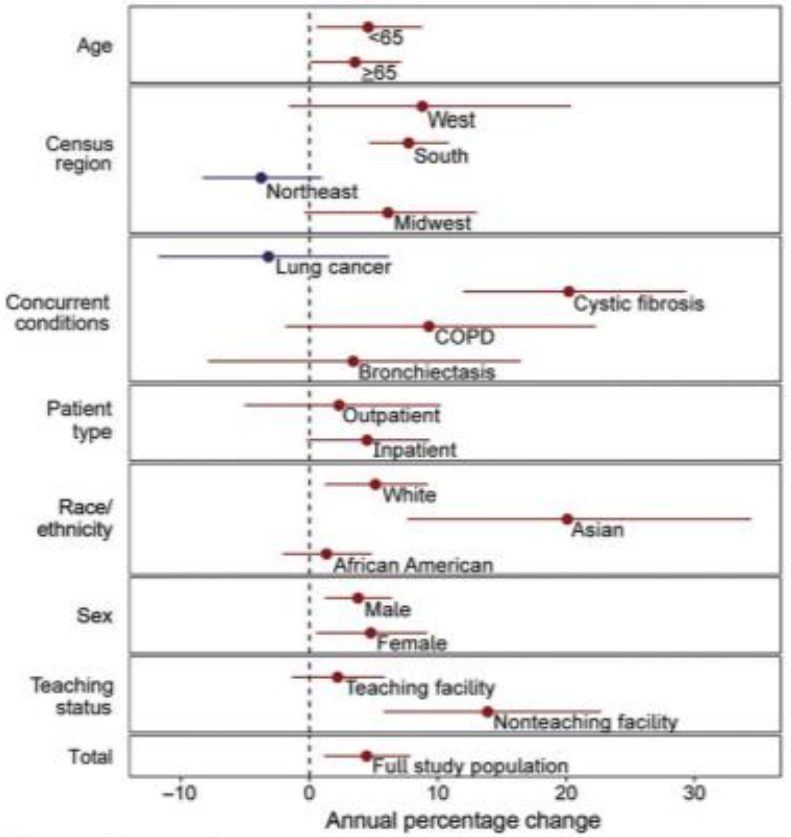


Figure 2. Annual percentage change in identified pathogenic nontuberculous mycobacteria (NTM) in 31 facilities, United States, 2009–2015. Red indicates increasing trends; blue indicates

Mycobacterial Testing Trends, United States, 2009–2015[1]

Samantha G. Dean, Emily E. Ricotta, Jonathan Fintzi, Yi Ling Lai,[2] Sameer S. Kadri, Kenneth N. Olivier, Adrian Zelazny, D. Rebecca Prevots

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 26, No. 9, September 2020

OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Positive predictive value and sensitivity of claims for NTM-LD

Table. Positive predictive value and sensitivity of ICD-9-CM diagnosis code–based case definitions for NTM infection in 2006–2014 Medicare data by using Bronchiectasis and NTM Research Registry as reference standard, United States*

NTM case definition†	No. participants with diagnosis-based Medicare claim for NTM infection	PPV (95% CI)‡	No. participants meeting BRR case definition for NTM infection§	Sensitivity (95% CI)¶
Primary definition: ICD-9-CM 031.0				
All clinician-given codes#	234	63.2 (57.1–69.4)	226	69.9 (63.9–75.9)
ID specialist– and pulmonologist-given codes only	205	65.4 (58.9–71.9)	226	61.5 (55.2–67.9)
ID specialist–given codes only	127	70.1 (62.1–78.0)	226	39.8 (33.4–46.2)
Pulmonologist-given codes only	133	60.9 (52.6–69.2)	226	36.7 (30.4–43.0)
Secondary definition: ICD-9-CM 031.0, requiring a second 031.0 claim >30 d but <12 m of first claim				
All clinician-given codes	122	72.1 (63.3–79.9)	226	41.6 (35.2–48.0)
ID specialist– and pulmonologist-given codes only	100	74.0 (64.3–82.3)	226	33.2 (27.1–39.7)
ID specialist–given codes only	45	82.2 (71.1–93.4)	226	16.4 (11.6–21.2)
Pulmonologist-given codes only	44	70.5 (57.0–83.9)	226	13.3 (30.4–43.0)

PPV ranges 61-82%; sensitivity ranges 13-70%

Ku et al. EID 2021

Claims underestimate NTM-LD

International Journal of Infectious Diseases 104 (2021) 398–406

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Predictive modeling of nontuberculous mycobacterial pulmonary disease epidemiology using German health claims data☆

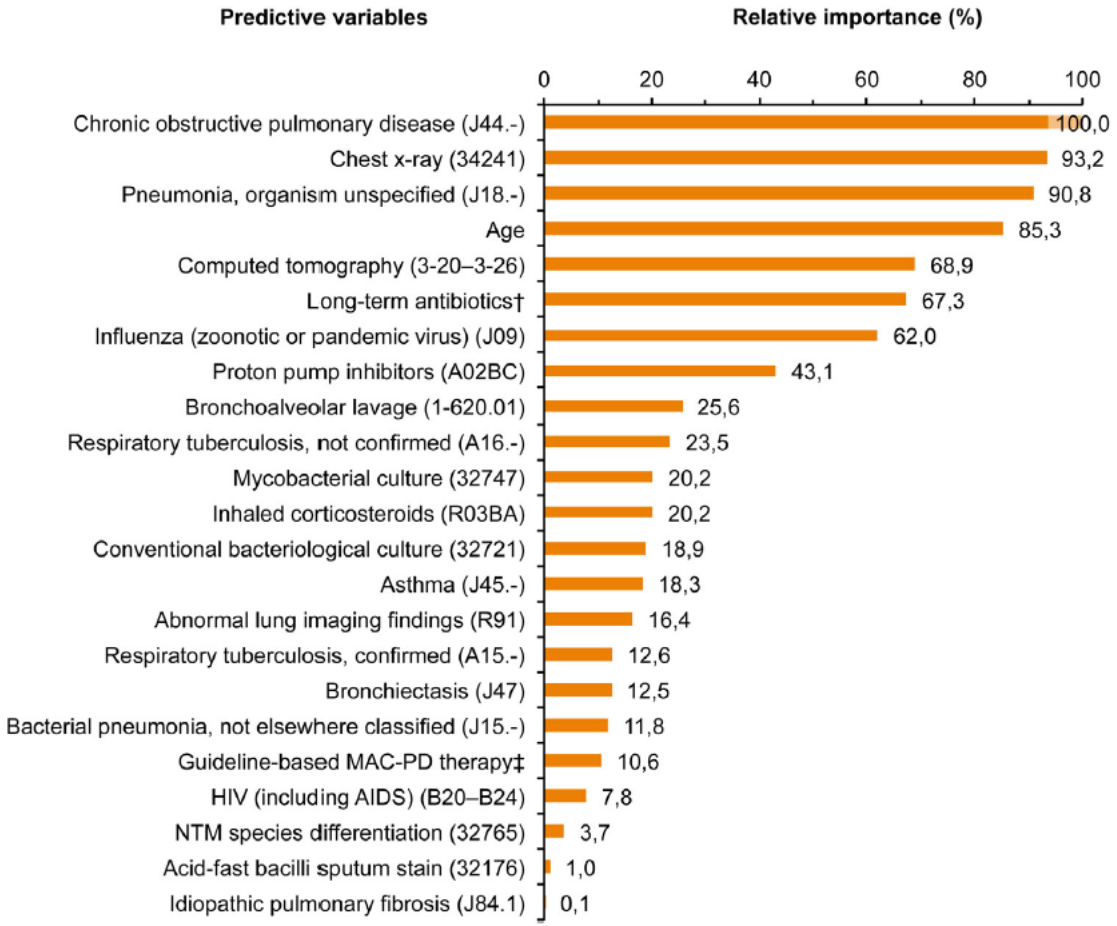
Felix C. Ringshausen[a,b,*], Raphael Ewen[a], Jan Multmeier[c], Bondo Monga[c,d], Marko Obradovic[e], Roald van der Laan[f], Roland Diel[b,g,h]

Table 2
Bivariate analysis of risk factors for NTM-PD: identification of highly significant variables between groups for entry into the prediction model ($p < 0.01$, each).

Characteristic	Coded NTM-PD (Group A) (N = 218)	Control group (Group B) (N = 218)	*P* value[a]
Mean (SD) age, years	61.4 (15.8)	52.6 (18.4)	<0.0001
Comorbidity (ICD-10 code)			
COPD (J44.-)	101 (46.3)	16 (7.3)	<0.0001
Influenza due to zoonotic or pandemic virus (J09)	84 (38.5)	11 (5.1)	<0.0001
Pneumonia, organism unspecified (J18.-)	67 (30.7)	<5[b]	<0.0001
Asthma (J45.-)	55 (25.2)	19 (8.7)	<0.0001
Pulmonary TB, not confirmed (A16.-)	30 (13.8)	0	<0.0001
Abnormal findings on diagnostic lung imaging (R91)	28 (12.8)	<5	<0.0001
Bacterial pneumonia, not elsewhere classified (J15.-)	23 (10.6)	0	<0.0001
Bronchiectasis (J47)	22 (10.1)	<5[b]	<0.0001
Pulmonary TB, confirmed by culture and/or histology (A15.-)	20 (9.2)	0	<0.0001
Idiopathic pulmonary fibrosis (J84.1)	8 (3.7)	0	0.0073
HIV (including AIDS) (B20–B24)	8 (3.7)	0	0.0073
Procedure (OPS or EBM code)			
Chest x-ray (34241)	101 (46.3)	18 (8.3)	<0.0001
Computed tomography (3-20–3-26)	88 (40.4)	11 (5.1)	<0.0001
Bronchoalveolar lavage (1-620.01)	33 (15.1)	0	<0.0001
Mycobacterial culture (liquid and solid medium) (32747)	33 (15.1)	0	<0.0001
Conventional bacteriological culture from respiratory specimens (32721)	30 (13.8)	0	<0.0001
NTM species differentiation (32765)	19 (8.7)	0	<0.0001
Acid-fast bacilli sputum stain (32176)	10 (4.6)	0	0.0018
Medication (ATC code)			
Proton-pump inhibitors (A02BC)	126 (57.8)	58 (26.6)	<0.0001
Long-term antibiotics[c]	112 (51.4)	37 (17.0)	<0.0001
Inhaled corticosteroids (R03BA)	33 (15.1)	<5[b]	<0.0001
Guideline-based MAC-PD therapy[d]	19 (8.7)	0	<0.0001

OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Claims underestimate NTM-LD



International Journal of Infectious Diseases 104 (2021) 398–406

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Predictive modeling of nontuberculous mycobacterial pulmonary [illegible]emiology using German health claims data☆

[illegible]usen[a,b,*], Raphael Ewen[a], Jan Multmeier[c], Bondo Monga[c,d], [illegible]c[e], Roald van der Laan[f], Roland Diel[b,g,h]

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Claims underestimate NTM-LD

International Journal of Infectious Diseases 104 (2021) 398–406

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Predictive modeling of nontuberculous mycobacterial pulmonary disease epidemiology using German health claims data☆

Felix C. Ringshausen[a,b,*], Raphael Ewen[a], Jan Multmeier[c], Bondo Monga[c,d], Marko Obradovic[e], Roald van der Laan[f], Roland Diel[b,g,h]

Table 4
Estimated prevalence and incidence of NTM-PD in 2016 (risk threshold >99%).

Estimation	Prevalence			Incidence		
	No. (%)	Rate†	Mean age	No. (%)	Rate[a]	Mean age
Coded NTM-PD	121 (0.004)	3.79	65.8	50 (0.002)	1.56	66.4
No coded NTM-PD	488 (0.015)	15.27	67.2	440 (0.014)	13.77	67.0
Coded and non-coded NTM-PD	609 (0.019)	19.05	67.0	490 (0.015)	15.33	67.0

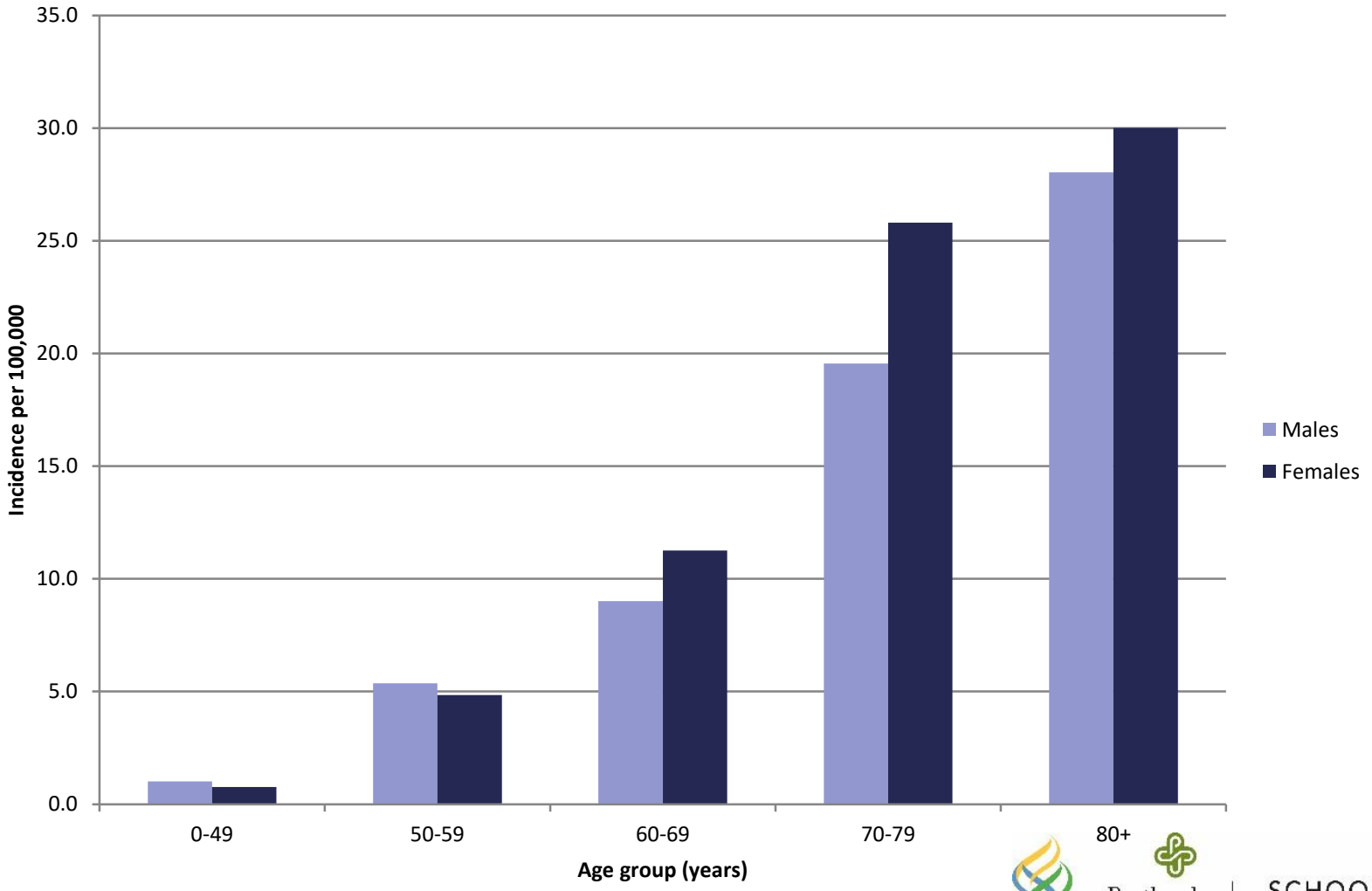
NTM-PD, nontuberculous mycobacterial pulmonary disease.
[a] Rate per 100,000 population.

Prevalence 5x higher, incidence 10x higher

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

RISK FACTORS

Average annual age- and sex- specific incidence of pulmonary NTM disease in Oregon, 2007-2012



Henkle et al. Ann Am Thorac Soc Vol 12, No 5, pp 642–647, May 2015

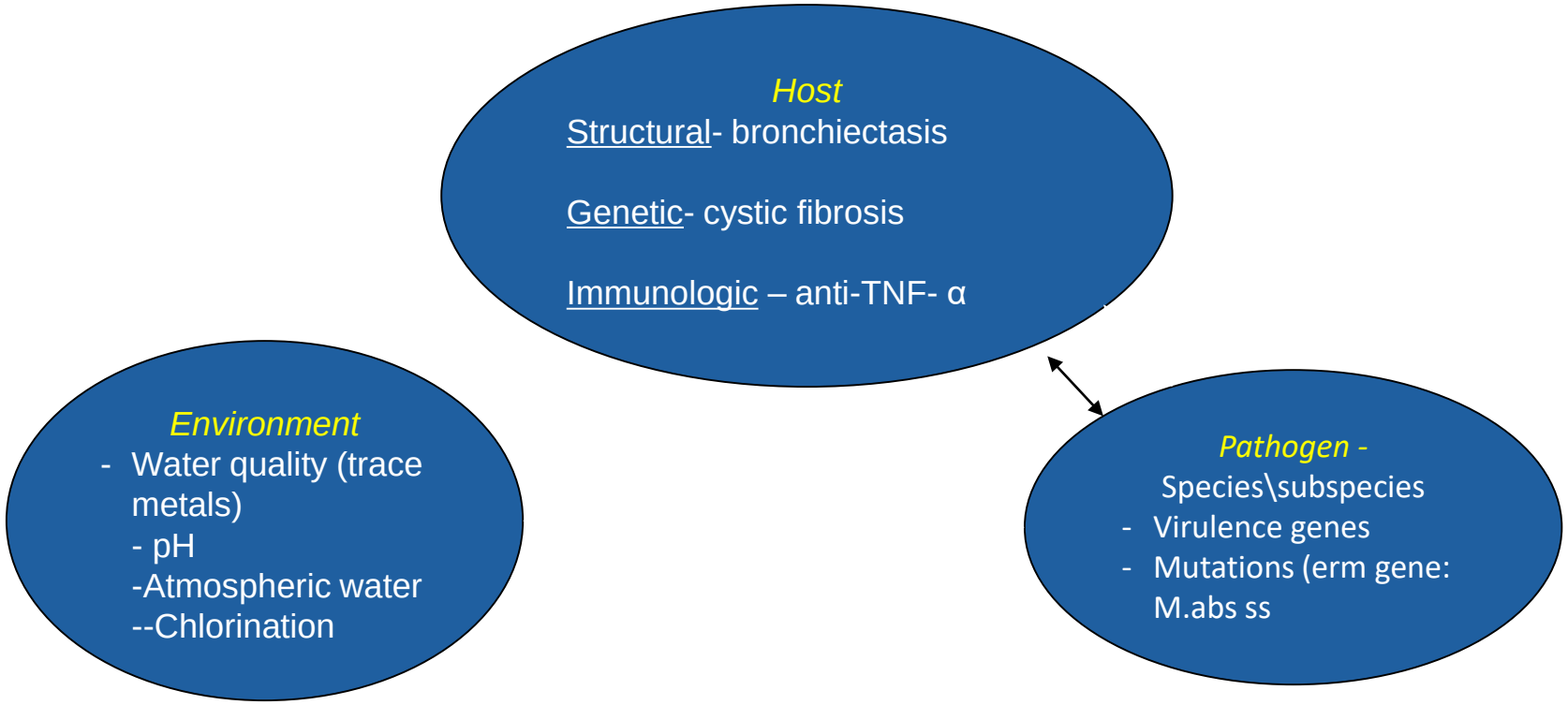
OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Risk factors – US Medicare population with bronchiectasis

Variables	Incident NTM-PD cohort	Bronchiectasis and no NTM-PD cohort	NTM-PD case definition 1[#]	IRR[¶]	95% CI
Overall	10289	161874	1600		
NTM-PD diagnosis at 6-months or later	5198	161874			
Sex					
Females	7972 (77.5)	102946 (63.6)	1880	1.81	1.72–1.91
Males	2317 (22.5)	58928 (36.4)	1040		
Age category					
65–69 years	2275 (22.1)	32696 (20.2)	1540		
70–74 years	2407 (23.4)	38010 (23.5)	1520	0.99	0.92–1.05
75–79 years	2447 (23.8)	36515 (22.5)	1620	1.05	0.98–1.12
⩾80 years	3160 (30.7)	54653 (33.8)	1690	1.09	1.03–1.16
COPD diagnosis					
COPD	3935 (38.2)	84072 (51.9)	1250	0.58	0.56–0.61
No COPD	6354 (61.8)	77802 (48.1)	2150		
Race and ethnicity					
American Indian or Alaska native	15 (0.1)	611 (0.4)	767	0.46	0.25–0.77
Asian/Pacific Islander	544 (5.3)	6296 (3.9)	2037	1.22	1.10–1.34
Black	211 (2.1)	8046 (4.9)	705	0.42	0.36–0.49
Hispanic	408 (4.0)	9607 (5.9)	985	0.59	0.52–0.66
Other	84 (0.8)	1231 (0.8)	1731	1.04	0.81–1.32
Unknown	15 (0.1)	327 (0.2)	1551	0.93	0.46–1.66
White (non-Hispanic)	9012 (87.6)	135,757 (83.9)	1671		

Schildknecht et al. ERJ 2022

NTM-LD Risk: Host-Environment-Pathogen



Risk factors: host factors – US population sample (4 HMOs)

TABLE 5. ASSOCIATED CONDITIONS AND SYMPTOMS CODED DURING THE 3 MONTHS BEFORE OR 6 MONTHS AFTER DETECTION OF A POSITIVE SPECIMEN, POSSIBLE AND DEFINITE CASES, THREE INTEGRATED HEALTH CARE DELIVERY SYSTEMS

Diagnosis or Symptom (*ICD9 code*)	Possible Cases	Definite Cases
Pulmonary nontuberculous mycobacteria (031.0)	638 (16)	488 (26.9)
Bronchiectasis (494, 494.0, 494.1)	628 (16)	427 (23.6)
Chronic obstructive pulmonary disease (496, 491)	1,256 (32.3)	511 (28.2)
Pneumonia, unspec (486)	1,224 (31.4)	603 (33.3)
Asthma (493.2, 493.9)	446 (11.5)	223 (12.3)
Other lung disease not elsewhere classified (518.89)	419 (10.8)	249 (13.7)
Malignancies (140-239, excluding 173)	838 (21.5)	454 (25)
Congestive heart failure (428.0)	422 (10.8)	188 (10.4)
Gastroesophageal reflux (530.81)	388 (10.8)	207 (11.4)
Cough (786.2)	916 (23.5)	508 (28)
Shortness of breath (786.05)	401 (10.3)	215 (11.9)
Hemoptysis (786.3)	443 (11.4)	264 (14.6)
Total	3,894	1,812

Prevots, Shaw, Strickland, *et al.*: NTM Prevalence

Am J Respir Crit Care Med Vol 182. pp 970–976, 2010

OHSU Portland State UNIVERSITY | SCHOOL OF PUBLIC HEALTH

Risk factors: host factors

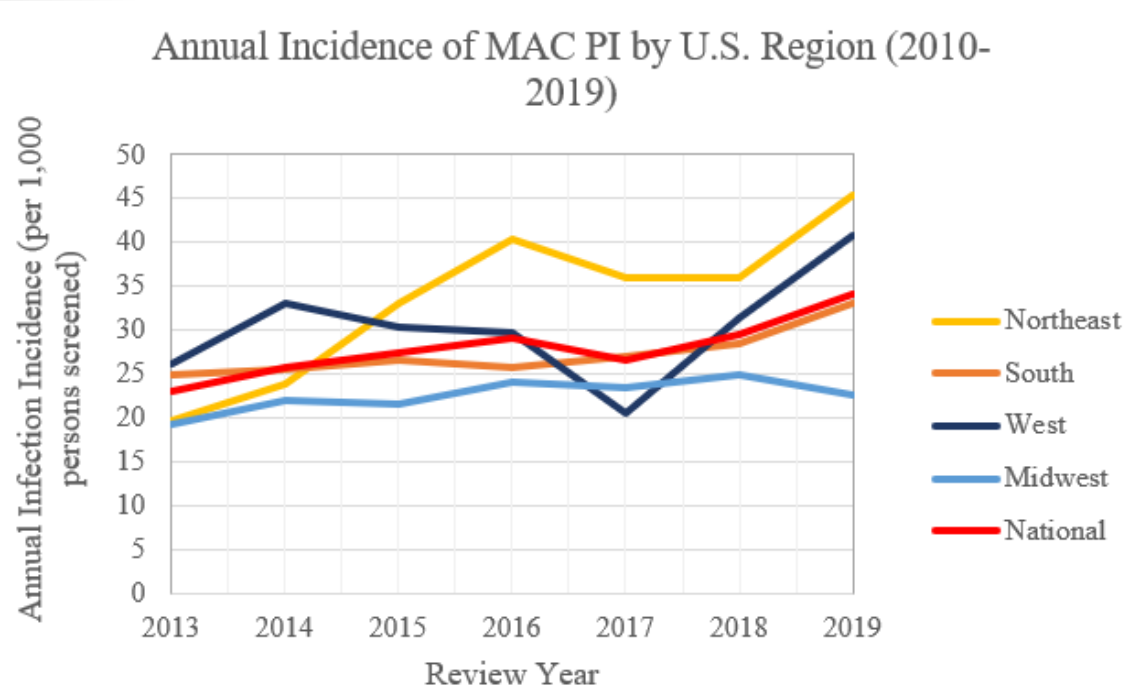
Host Factor	RR, OR, or Relative Prevalence
Lung Cancer	3.4
COPD	2-10
Bronchiectasis	44, 187.5
Thoracic skeletal abnormalities	5.4
Low body weight	9.1
Rheumatoid arthritis	1.5, 1.9
Immunomodulatory drugs/anti-TNF agents	2.2/1.6-2.9
Steroid use	1.6, 8
Gastroesophageal reflux disease	1.5, 5.3
Cystic Fibrosis	

adapted from: Prevots DR, Marras TK. Epidemiology of Human Pulmonary Infection with Nontuberculous Mycobacteria: a Review. Clinics in Chest Medicine; 2015; 36:13-34

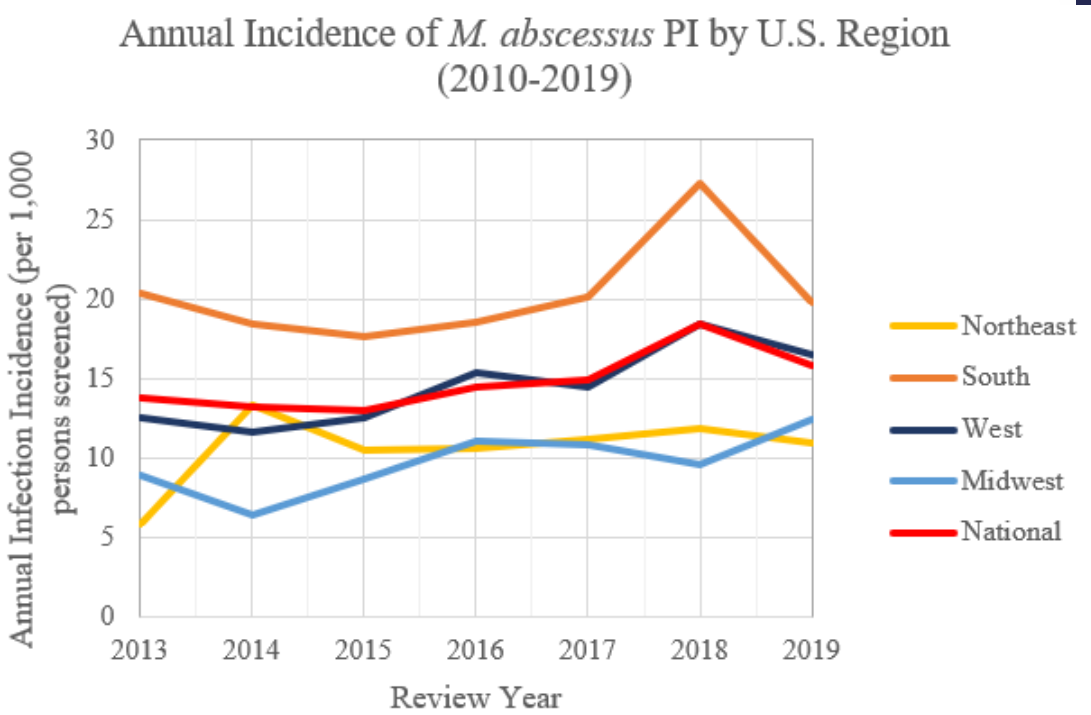
OHSU Portland State University SCHOOL OF PUBLIC HEALTH

a) Annual Incidence of MAC PI by U.S. Region (2010-2019) **b**) Annual Incidence of *M. abscessus* PI by U.S. Region (2010-2019)

a.



b.



Marshall, Mercaldo, Lipner, & Prevots (2023), unpublished data
source: Cystic Fibrosis Foundation Patient Registry

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Table 3: Annual percent change (APC) in NTM infection incidence among pwCF by species and U.S. region (2010-2019).

U.S. Geography	MAC (%)	*M. abscessus* (%)	Total NTM (%)
National	4.4*	3.9	3.5*
West	3.6	6.8	1.8
South	3.4	4.3	4.1*
Northeast	11.0*	2.7	**7.7***
Midwest	1.8	6.6	4.4*

Annual percent change (APC) in NTM infection incidence by NTM species and U.S. region.
*Significant APC ($p<0.05$)

Marshall, Mercaldo, Lipner, & Prevots (2023), unpublished data
source: Cystic Fibrosis Foundation Patient Registry

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

BMI and ethnic differences in NTM-LD, Hawaii

- Collaboration with Kaiser Permanente Hawaii
- n=505,202 beneficiaries, Kaiser Permanente Hawaii
- Population: 28 different ethnic categories
  - 48% “any” Asian
    - 20% Filipino
    - 13% Japanese
    - 7% Chinese
  - 26% “any” Native Hawaiian \ Pacific Islander
  - 44% “any” White

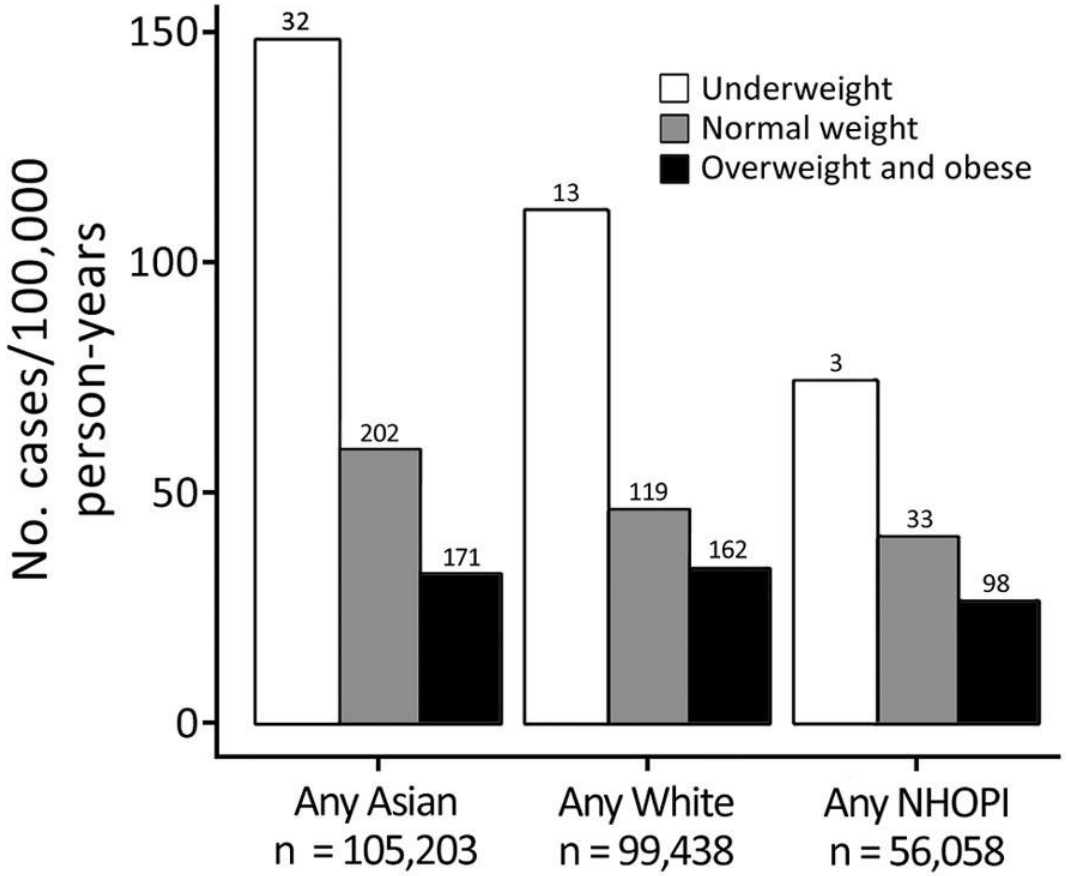


Figure. Nontuberculous mycobacterial pulmonary infection incidence among Kaiser Permanente Hawaii beneficiaries, by ethnicity and body mass index category, Hawaii, USA, 2005-2019. Numbers above bars indicate case count by BMI category. Underweight, <18.5 kg/m2; normal weight, 18.5 to <25 kg/m2; overweight/obese, >25 kg/m2. NHOPI, Native Hawaiian and Other Pacific Islander.

Blakney RA et al. Incidence of Nontuberculous Mycobacterial Pulmonary Infection, by Ethnic Group, Hawaii, USA, 2005–2019. Emerg Infect Dis. 2022;28(8):1543-1550.

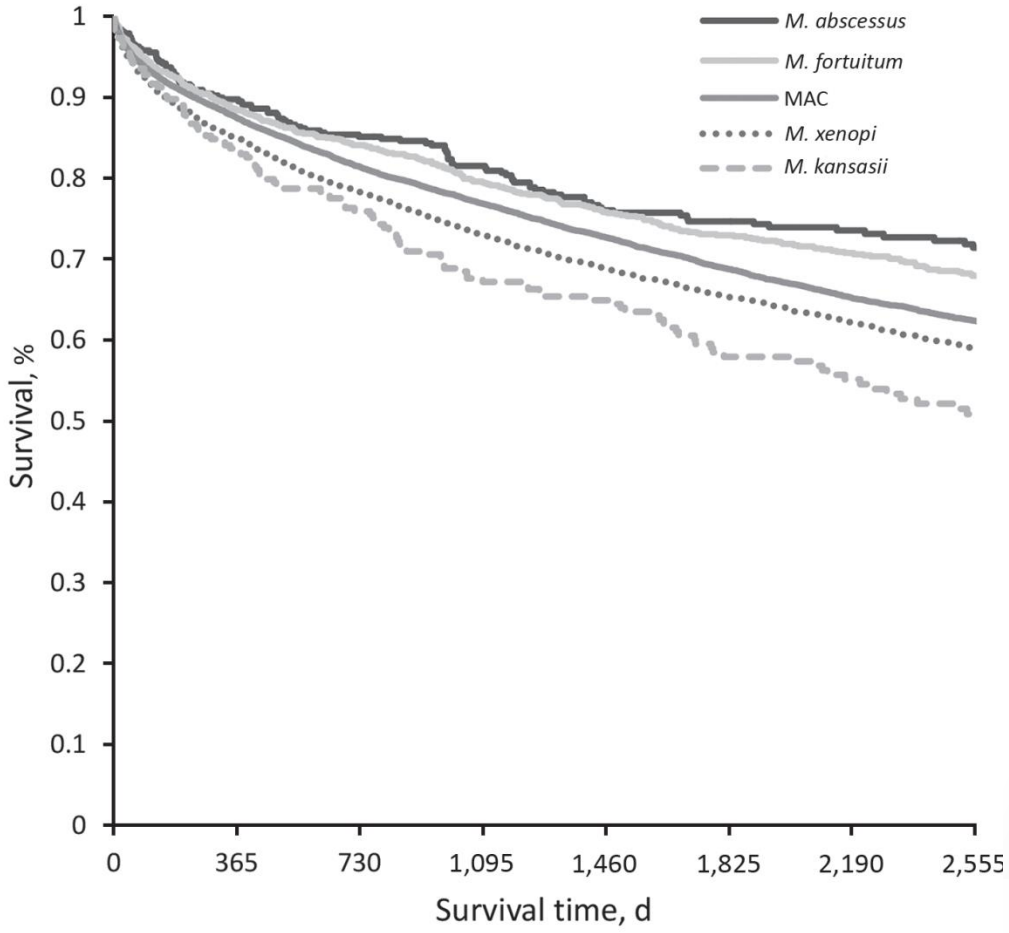
OHSU Portland State University SCHOOL OF PUBLIC HEALTH

MORTALITY

Mortality after NTM isolation

Marras et al. Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 23, No. 3, March 2017

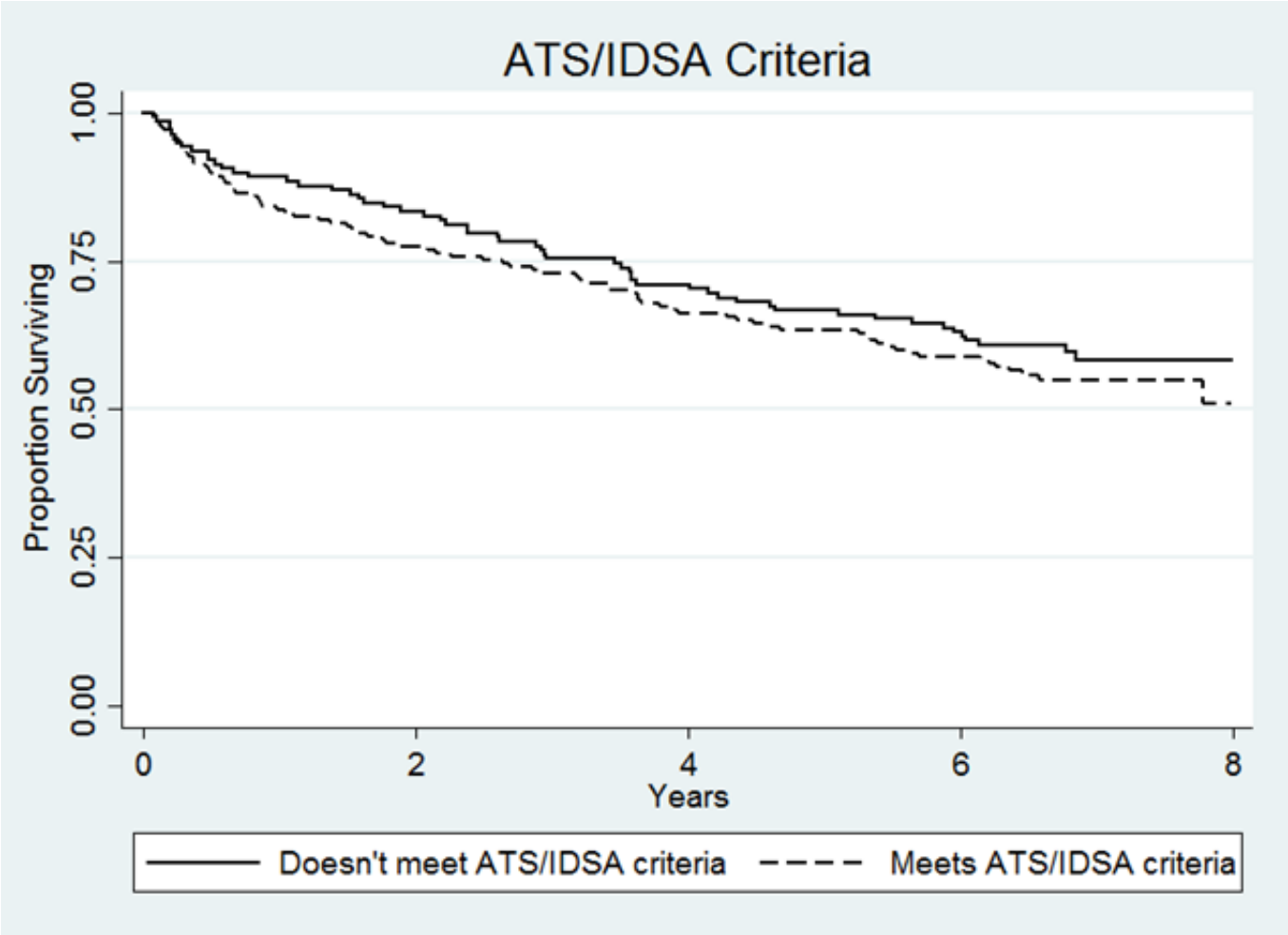
- Pulmonary isolation = 1, pulmonary disease = 2 positive cultures
- Overall increased risk of death NTM pulmonary isolation or disease vs. controls
- NTM disease species-specific (unadjusted) HR vs. controls range 1.25-1.84, except *M. kansasii* HR 2.5
- NTM disease adjusted HR 1.23 vs. NTM isolation



OHSU Portland State University | PUBLIC HEALTH

Mortality

Novosad et al. Ann Am Thorac Soc Vol 14, No 7, pp 1112–1119, Jul 2017



OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Mortality: Systematic review

Diel et al. BMC Infectious Diseases (2018) 18:206

- 14 studies
- 27% increase in mortality
- Factors associated with death
  - Male sex
  - Comorbidities/underlying lung disease
  - Fibrocavitary disease

Mortality following culture conversion

Im et al. Chest (2022) 1192-1200

TABLE 3] Effect of 6-Months or 12-Months Culture Conversion on Death in Patients With NTM-PD

Patient Group	Treatment for ≥ 6 mo (n = 712)[a]	Treatment ≥ 12 mo (n = 676)[a]
Death	n = 135	n = 116
HR of conversion within 6 or 12 mo for death		
Crude HR (95% CI, *P*)	0.46 (0.33–0.65, < .001)[b]	0.42 (0.29–0.61, < .001)[c]
Model 1, adjusted HR (95% CI, *P*)	0.51 (0.35–0.74, < .001)[b]	0.51 (0.33–0.78, .002)[c]
Model 2, adjusted HR (95% CI, *P*)	0.52 (0.35–0.76, < .001)[b]	0.52 (0.34–0.80, .003)[c]
Model 3, adjusted HR (95% CI, *P*)	0.52 (0.36–0.77, < .001)[b]	0.52 (0.34–0.81, .003)[c]

OHSU Portland State University | SCHOOL OF PUBLIC HEALTH

Challenges and gaps

- Surveillance/population-based data limited – most laboratory-based
- Prevention
- Natural history after treatment (mortality, recurrence)
- *M. abscessus*

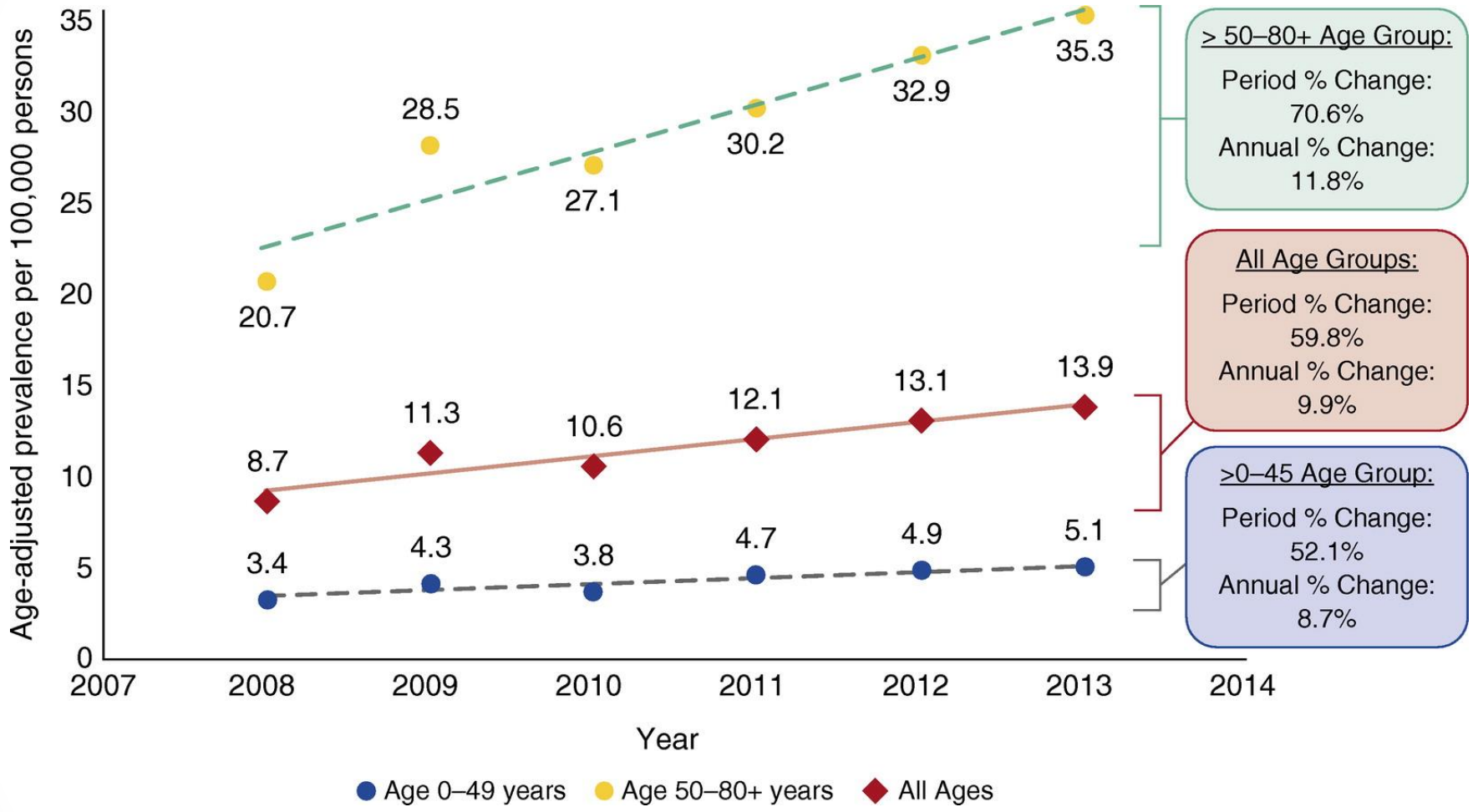
Summary

- Incidence and prevalence still increasing
- Rates increase with age; females higher than males
- Risk factors include bronchiectasis, COPD, lung & immunosuppressive conditions/medications
- Geographic variation in prevalence and species
  - Prevalence higher than TB, ranges from 6-???/100,000
- NTM-LD likely associated with increased mortality

Thank-you

OHSU Portland State University SCHOOL OF PUBLIC HEALTH

Average Age-Adjusted Annual Prevalence of Nontuberculous Mycobacteria Case Rate per 100,000 Persons, 5 States, 2008-2013*



*5 states: MD, MS, OH, MO, WI

Donohue et al *Annals ATS* 13, 2143-2150.