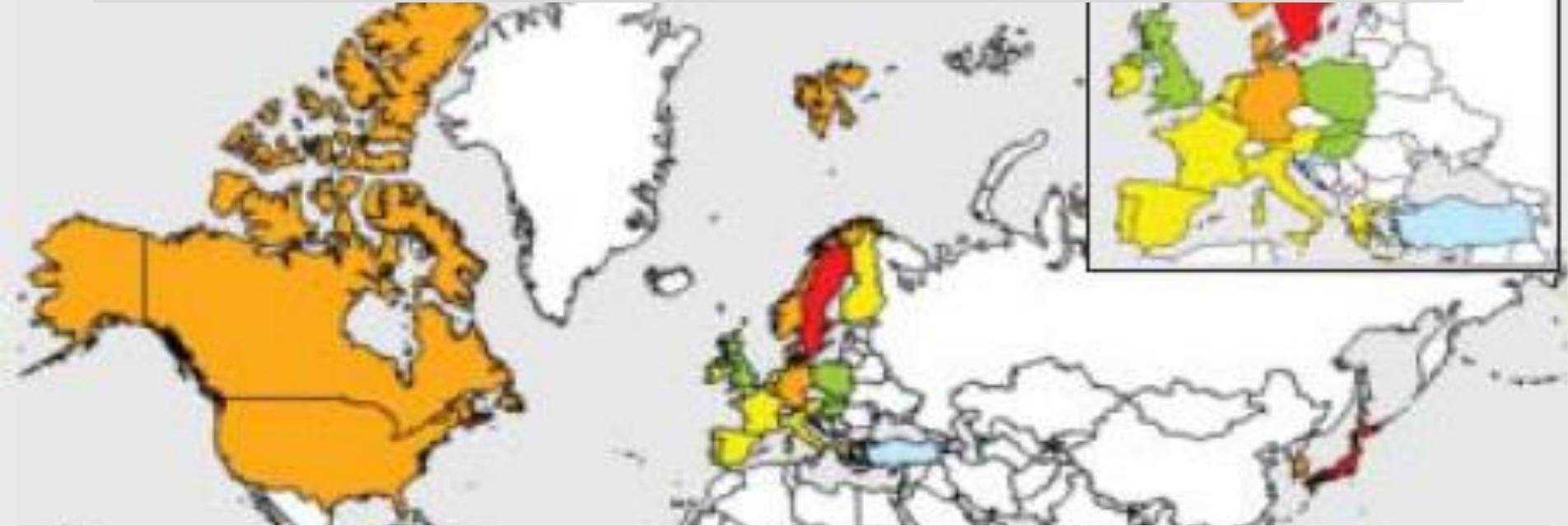


Epidemiology Around the World

North America



NTMir & UTHealth Physician/Patient Conference

Grapevine, TX

May 17, 2019



Ted Marras, MD FRCPC MSc



Toronto Western Hospital / University Health Network

Epidemiology NTM: North America

- *Objectives*

- Frequency – overall and by species
- Geography
- Temporal trends
- Mortality

Epidemiology NTM: North America

- *Questions & challenges*

What do we want to measure?

- All patients with “disease”

Microbiology

Clinical

+ Radiological

= Disease

How do we measure it?

- Population-based



Not reportable

Annual Rates of NTM-PD

-North America, population based

Study	Region	Frequency*
Adjemian, AJRCCM 2012	Medicare (≥ 65 y) 1997-2007	~ 47
Marras, EID 2013	Ontario, population, 1998-2010	9.8
Prevots, AJRCCM 2010	Four US HMO / IHCDSSs, 1994-2006	5.5
Cassidy, CID 2009	Oregon, population, 2005-6	5.6
Adjemian, EID 2017	Hawaii, single large HMO, 2005-13	~ 18
Winthrop, ATS 2017	US national managed care claims database, 2008-15	11.7
Median (range)		9.8 (5.5-18)

*Annualized prevalence / 100,000; average or final year of study; excludes *M. gordonae*

NTM population burden

- Period prevalence

Period Prevalence / Cumulative Incidence

Study	Methods	
Winthrop, AJRCCM 2010 (Oregon, 2005-6)	Portland tri-county Clinical record review	2-year PP All ages = 8.6/100,000 ≥ 50 yrs = 20.4/100,000
Prevots, AJRCCM 2010 (4 US IHCDs, 1994-2006)	Four US IHCDs ATS micro definition with some validation	3-year CI <60 yr ~ 4/100,000 60-69 yr ~ 40/100,000 70-79 yr ~ 100/100,000 ≥ 80 yr ~ 220/100,000
Adjemian, AJRCCM 2012 (Medicare 1997-2007)	Representative 5% Medicare sample (≥ 65 yr) - ICD9	<u>≤11-year PP</u> ≥ 65 yrs = 112/100,000
Adjemian, Ann ATS 2017 (Hawaii 2005-13)	Single large HMO ATS micro	9 year PP >65 yrs ~ 350/100,000 50-65 yrs ~ 100/100,000
Marras, EID 2013 (Ontario, 2006-10)	Province-wide ATS micro	5-year PP All ages = 41.3/100,000

NTM epidemiology

- North America – disease by species

Study	N	Most Common Species			
New York City, single institution, 2000-4 (Bidle, EID 2008)	81	MAC (80%)	RGM (9%)	<i>xenopi</i> (6%)	<i>kansasii</i> (5%)
Oregon, state-wide, 2007-12 (Henkle, Ann ATS 2015)	1,146	MAC (86%)	<i>abscessus</i> / <i>cheloneae</i> (7%)	<i>kansasii</i> (1.2%)	<i>fortuitum</i> (<1%)
Four US HMO / IHCDSSs, 1994-2006 (Prevots AJRCCM 2010)	1,865	MAC (80%)	<i>abscessus</i> / <i>cheloneae</i> (12%)	<i>fortuitum</i> (6%)	<i>kansasii</i> (6%)
Charlottesville VA, single institution, 2001-9 (Satyanarayana, BMC ID 2011)	83	MAC (69%)	<i>kansasii</i> (5%)	<i>xenopi</i> (5%)	<i>abscessus</i> (4%)
Hawaii, state-wide, 2005-2013, single HMO (Adjemian EID 2017)	254	MAC (67%)	<i>abscessus</i> (18%)	<i>fortuitum</i> (16%)	
Ontario, province-wide, 2010 (Marras, EID 2013)	1,294	MAC (64%)	<i>xenopi</i> (23%)	<i>abscessus</i> (3%)	<i>fortuitum</i> (3%)

MAC – *M. avium* complex

RGM – rapidly growing mycobacteria

NTM epidemiology

- North America – disease by species

Study	N	Most Common Species			
New York City, single institution, 2000-4 (Bidle, EID 2008)	81	MAC (80%)	RGM (9%)	<i>xenopi</i> (6%)	<i>kansasii</i> (5%)
Oregon, state-wide, 2007-12 (Henkle, Ann ATS 2015)	1,146	MAC (86%)	<i>abscessus</i> / <i>cheloneae</i> (7%)	<i>kansasii</i> (1.2%)	<i>fortuitum</i> (<1%)
Four US HMO / IHCDSSs, 1994-2006 (Prevots AJRCCM 2010)	1,865	MAC (80%)	<i>abscessus</i> / <i>cheloneae</i> (12%)	<i>fortuitum</i> (6%)	<i>kansasii</i> (6%)
Charlottesville VA, single institution, 2001-9 (Satyanarayana, BMC ID 2011)	83	MAC (69%)	<i>kansasii</i> (5%)	<i>xenopi</i> (5%)	<i>abscessus</i> (4%)
Hawaii, state-wide, 2005-2013, single HMO (Adjemian EID 2017)	254	MAC (67%)	<i>abscessus</i> (18%)	<i>fortuitum</i> (16%)	
Ontario, province-wide, 2010 (Marras, EID 2013)	1,294	MAC (64%)	<i>xenopi</i> (23%)	<i>abscessus</i> (3%)	<i>fortuitum</i> (3%)

MAC – *M. avium* complex

RGM – rapidly growing mycobacteria

NTM epidemiology

- North America – disease by species

Study	N	Most Common Species			
New York City, single institution, 2000-4 (Bidle, EID 2008)	81	MAC (80%)	RGM (9%)	<i>xenopi</i> (6%)	<i>kansasii</i> (5%)
Oregon, state-wide, 2007-12 (Henkle, Ann ATS 2015)	1,146	MAC (86%)	<i>abscessus</i> / <i>chelonae</i> (7%)	<i>kansasii</i> (1.2%)	<i>fortuitum</i> (<1%)
Four US HMO / IHCDSSs, 1994-2006 (Prevots AJRCCM 2010)	1,865	MAC (80%)	<i>abscessus</i> / <i>chelonae</i> (12%)	<i>fortuitum</i> (6%)	<i>kansasii</i> (6%)
Charlottesville VA, single institution, 2001-9 (Satyanarayana, BMC ID 2011)	83	MAC (69%)	<i>kansasii</i> (5%)	<i>xenopi</i> (5%)	<i>abscessus</i> (4%)
Hawaii, state-wide, 2005-2013, single HMO (Adjemian EID 2017)	254	MAC (67%)	<i>abscessus</i> (18%)	<i>fortuium</i> (16%)	
Ontario, province-wide, 2010 (Marras, EID 2013)	1,294	MAC (64%)	<i>xenopi</i> (23%)	<i>abscessus</i> (3%)	<i>fortuitum</i> (3%)

MAC – *M. avium* complex

RGM – rapidly growing mycobacteria

NTM epidemiology

- North America – disease by species

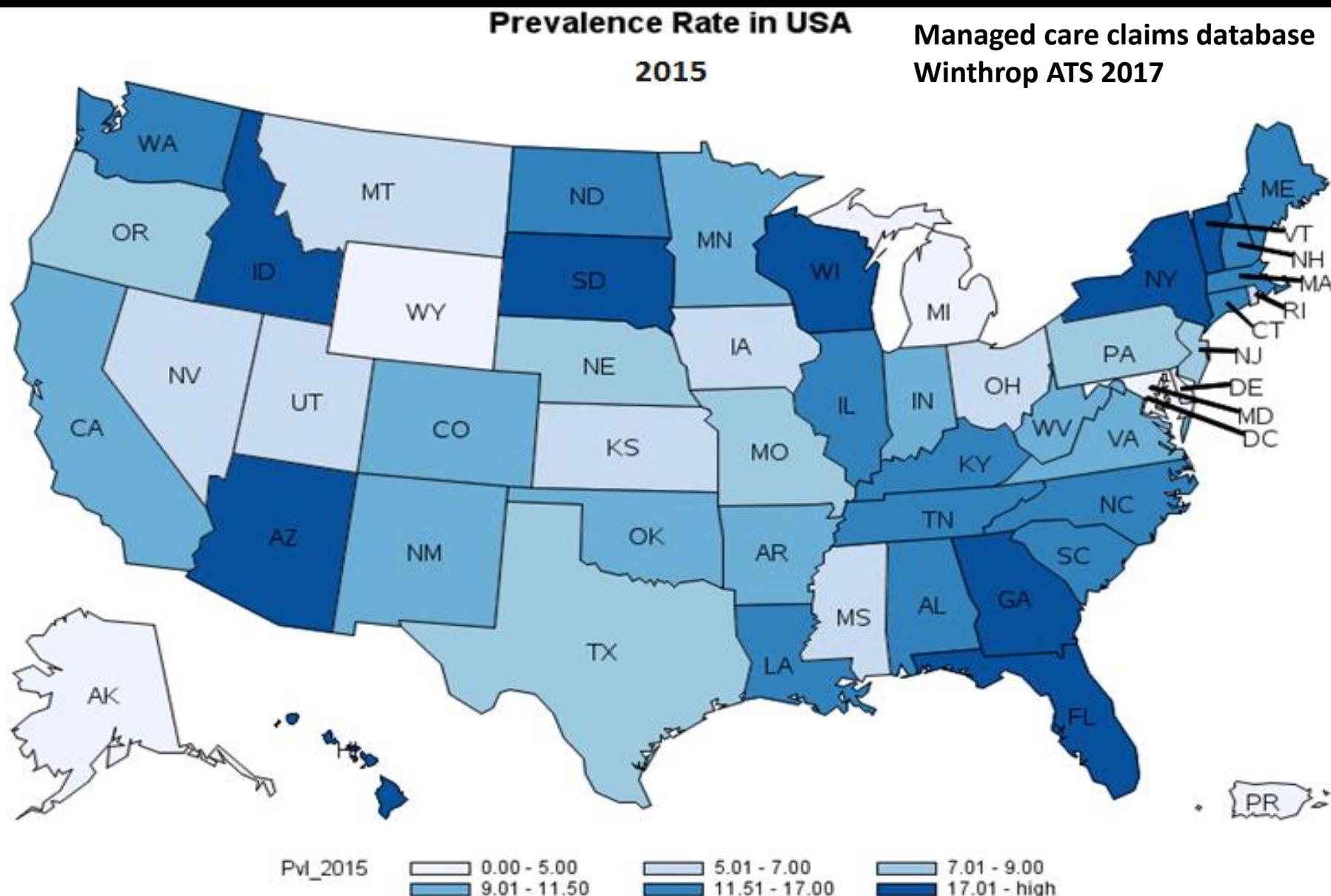
Study	N	Most Common Species			
New York City, single institution, 2000-4 (Bidle, EID 2008)	81	MAC (80%)	RGM (9%)	<i>xenopi</i> (6%)	<i>kansasii</i> (5%)
Oregon, state-wide, 2007-12 (Henkle, Ann ATS 2015)	1,146	MAC (86%)	<i>abscessus</i> / <i>chelonae</i> (7%)	<i>kansasii</i> (1.2%)	<i>fortuitum</i> (<1%)
Four US HMO / IHCDSSs, 1994-2006 (Prevots AJRCCM 2010)	1,865	MAC (80%)	<i>abscessus</i> / <i>chelonae</i> (12%)	<i>fortuitum</i> (6%)	<i>kansasii</i> (6%)
Charlottesville VA, single institution, 2001-9 (Satyanarayana, BMC ID 2011)	83	MAC (69%)	<i>kansasii</i> (5%)	<i>xenopi</i> (5%)	<i>abscessus</i> (4%)
Hawaii, state-wide, 2005-2013, single HMO (Adjemian EID 2017)	254	MAC (67%)	<i>abscessus</i> (18%)	<i>fortuium</i> (16%)	
Ontario, province-wide, 2010 (Marras, EID 2013)	1,294	MAC (64%)	<i>xenopi</i> (23%)	<i>abscessus</i> (3%)	<i>fortuitum</i> (3%)

MAC – *M. avium* complex

RGM – rapidly growing mycobacteria

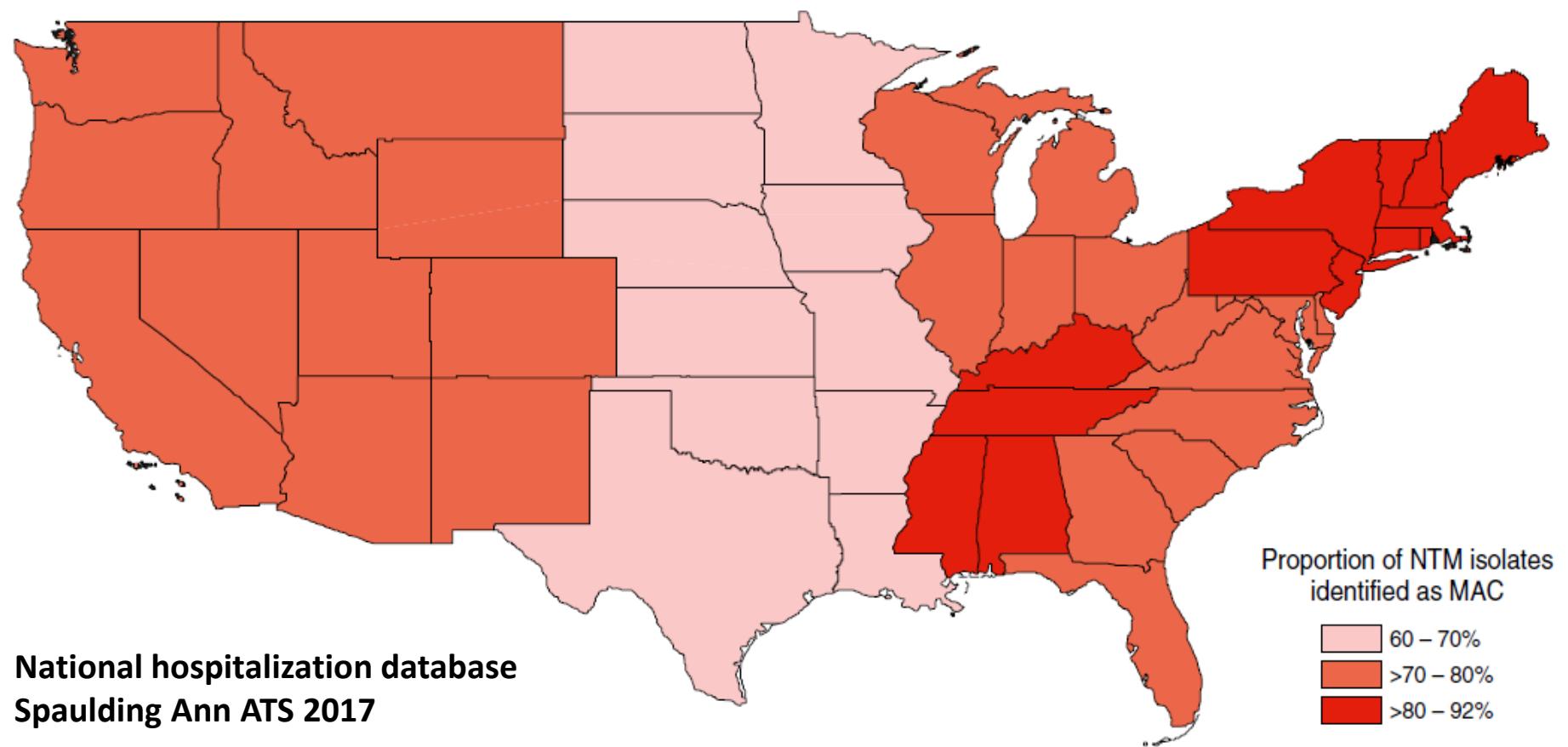
NTM epidemiology - geography

- North America – all NTM



NTM epidemiology - geography

- North America – species distribution



Recent temporal disease trends

- North America

Study / Region / Cased definition	Annual increase
Prevots AJRCCM 2010 (4 US IHCDS, 1994-2006) - <i>Micro + ICD9</i>	2.6-2.9% (prevalence)
Alhouqani, Chest 2012 (Ontario, Canada, 2003-2008) - <i>ATS micro</i>	10% (MAC prevalence)
Adjemian, AJRCCM 2012 (US Medicare '97-'07) - <i>ICD9</i>	8.5% (prevalence)
Henkle, AnnATS 2015 (Oregon, state-wide, 2007-2012) - <i>ATS micro</i>	2.2% (incidence)
Adjemian, Ann ATS 2017 (Hawaii state-wide, single HMO, 2005-2013) - <i>ATS micro</i>	9.6% (prevalence)
US managed care claims database, 2008-2015 (Winthrop ATS 2017) – <i>ICD-9/10</i>	5.2% (incidence) 7.5% (prevalence)
Median (range)	3.7 (2.2-5.2)
	Prevalence
	8.5 (2.8-10)

Survival in NTM-PD

- Population-based

Study	Population	Comparison	Mortality risk HR (95% CI)
Marras et al. EID 2017	Ontario, Canada (all, 2001-2013) n=8,469 ATS micro criteria	Uninfected general pop. Matched 1:1 by age, sex, propensity score	1.63 (1.56-1.70)
Marras et al. Resp Med 2018	US managed care insurance database (2007-2016) n=2,005 Claims-based (≥ 2 claims, $\geq 30d$ apart)	Uninfected ,same coverage period Matched 3:1 by age, sex MV adjustment: demographics, comorbidity	2.06 (1.52-2.79)
Marras et al. ID week 2018	Medicare 2008-2015 n=38,981 ICD-9/10 (≥ 2 codes, $\geq 30d$ apart)	Uninfected, same coverage period Matched 2:1 by age, sex MV adjustment: demographics, comorbidity, Charlson CI	1.30 (1.25-1.35)

Epidemiology NTM: North America

- Summary

- **Frequency** → moderate (MAC, *M. abscessus*, others)
- **Geography** → drives variability
- **Temporal trends** → rising
- **Mortality** → substantial