Update on Infection Prevention and Control in Cystic Fibrosis

The 9th Annual Fleming Infection Prevention and Infectious Diseases Symposium

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Received honorariums for serving on Scientific Advisory Boards: Novartis, Gilead, AB Comm, Inc., Savara, Teva

Contract with Gilead

Learning Objectives

- Learn the current epidemiology of CF pathogens
- Consider routes of transmission of various CF pathogens
- Learn best practices to minimize the risks of acquisition and transmission of CF pathogens

Cystic Fibrosis Genetics

- Most common lethal genetic disease among Caucasians
- Autosomal recessive
- Mutation in cystic fibrosis transmembrane conductance regulator (CFTR) gene
- cAMP regulated chloride channel located in apical membrane of glandular epithelium
- Located long arm of chromosome #7
    - F508del most common mutation
    - 1700 identified mutations

Cystic Fibrosis Epidemiology

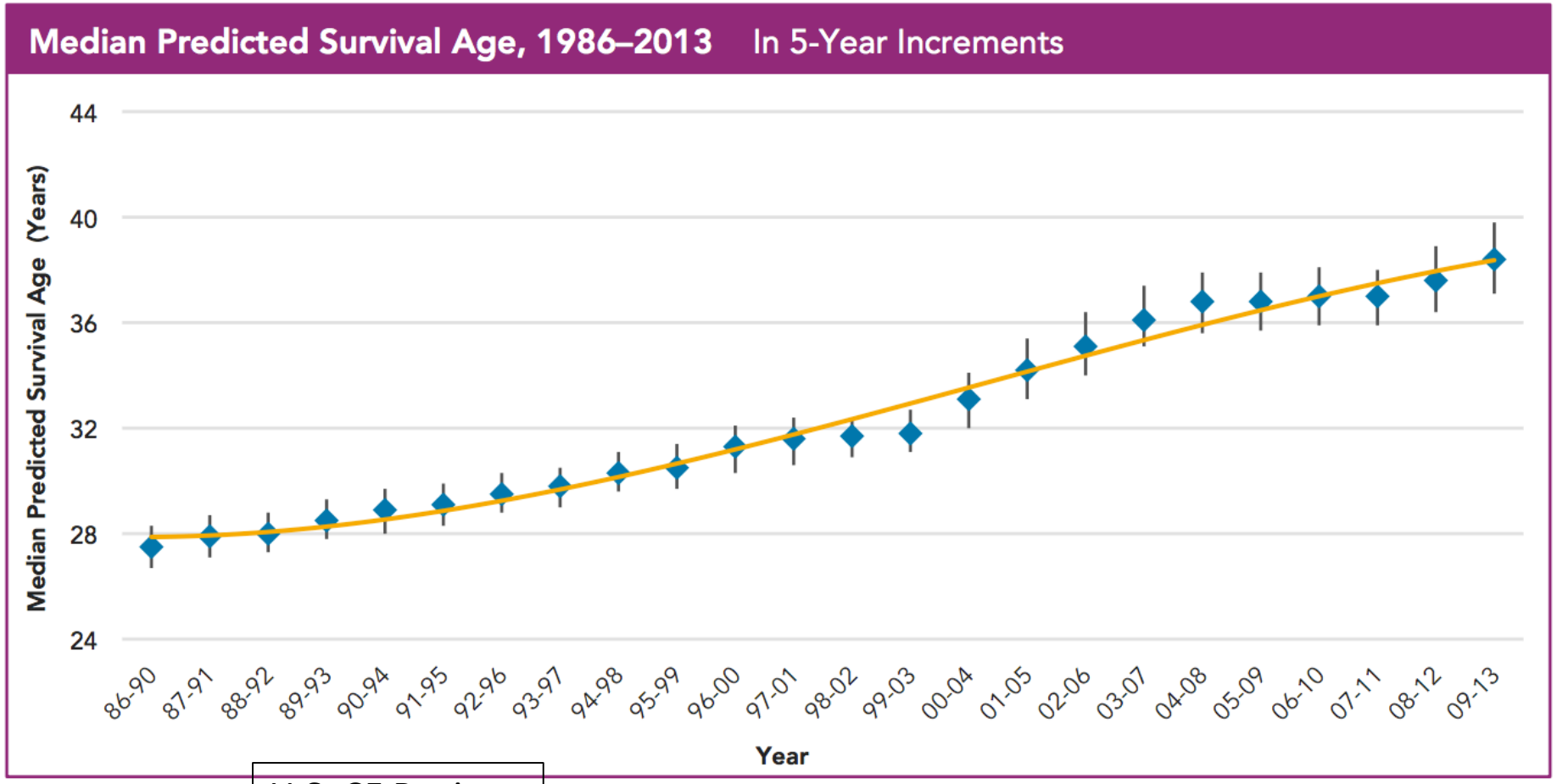
- 70,000 world wide
- 30,000 affected individuals in U.S.

- 1 in 3,200 live births among Caucasians
- 1 in 9,200 Hispanic
- 1 in 15,000 African Americans

- 1 in 25 carrier rate (unaffected)

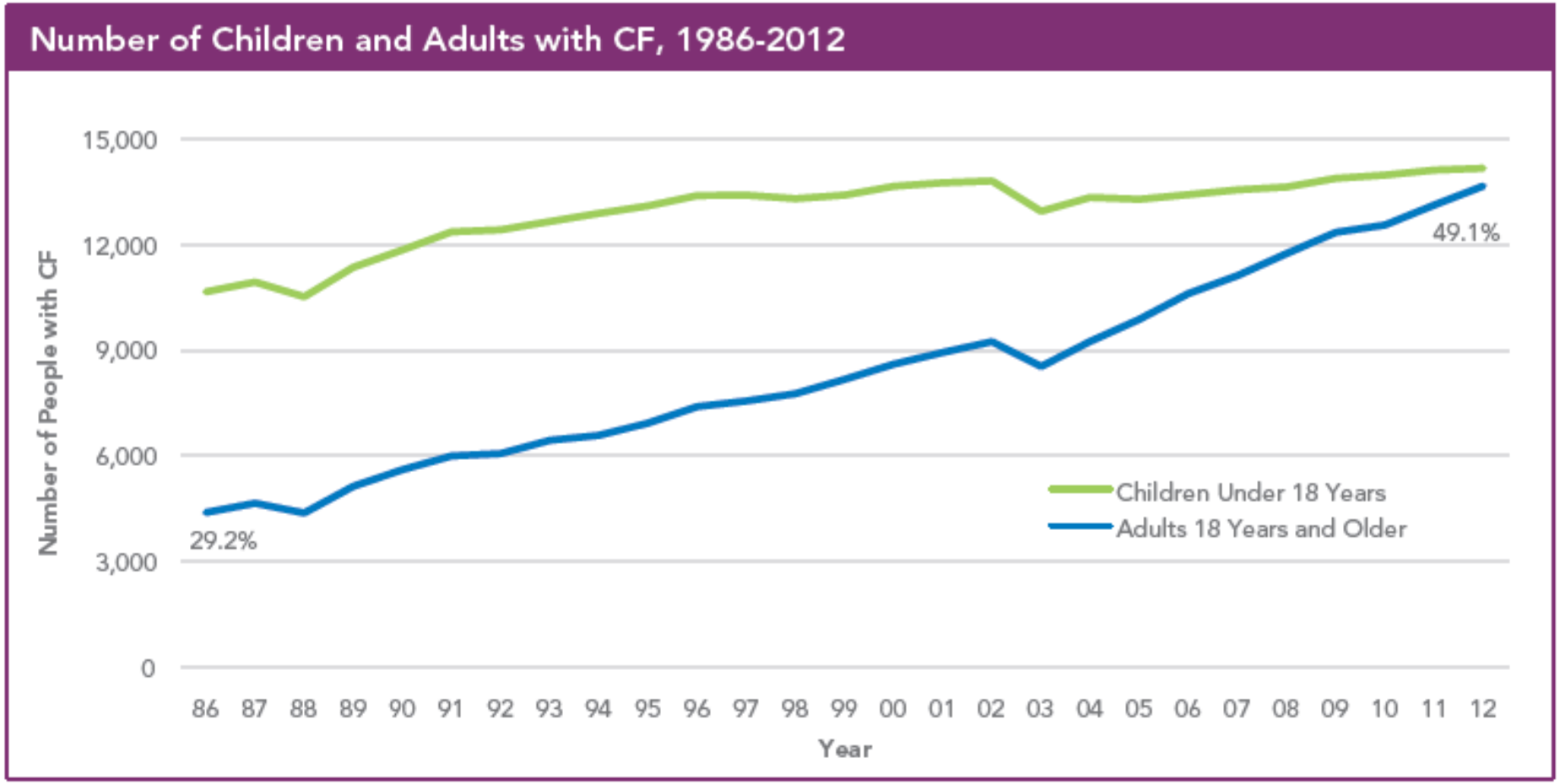
- 1,000 new cases per year
  - Newborn screening (NBS) in all states
  - >60% of patients detected by NBS.
  - 8% new diagnoses adults >18 years of age

Median Survival over time in U.S. Respiratory disease main cause of morbidity and mortality



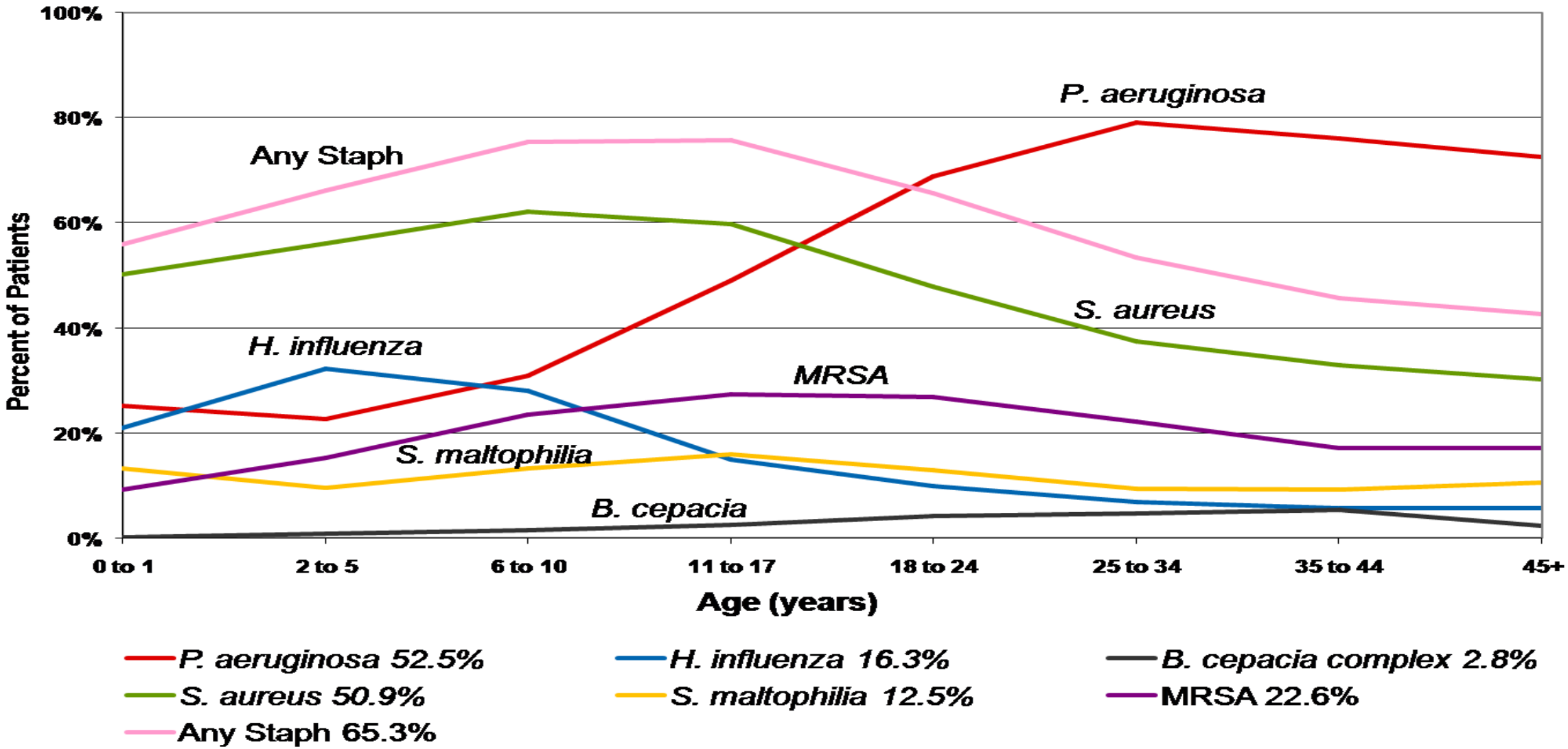
U.S. CF Registry

Half of patients with CF in U.S. are adults



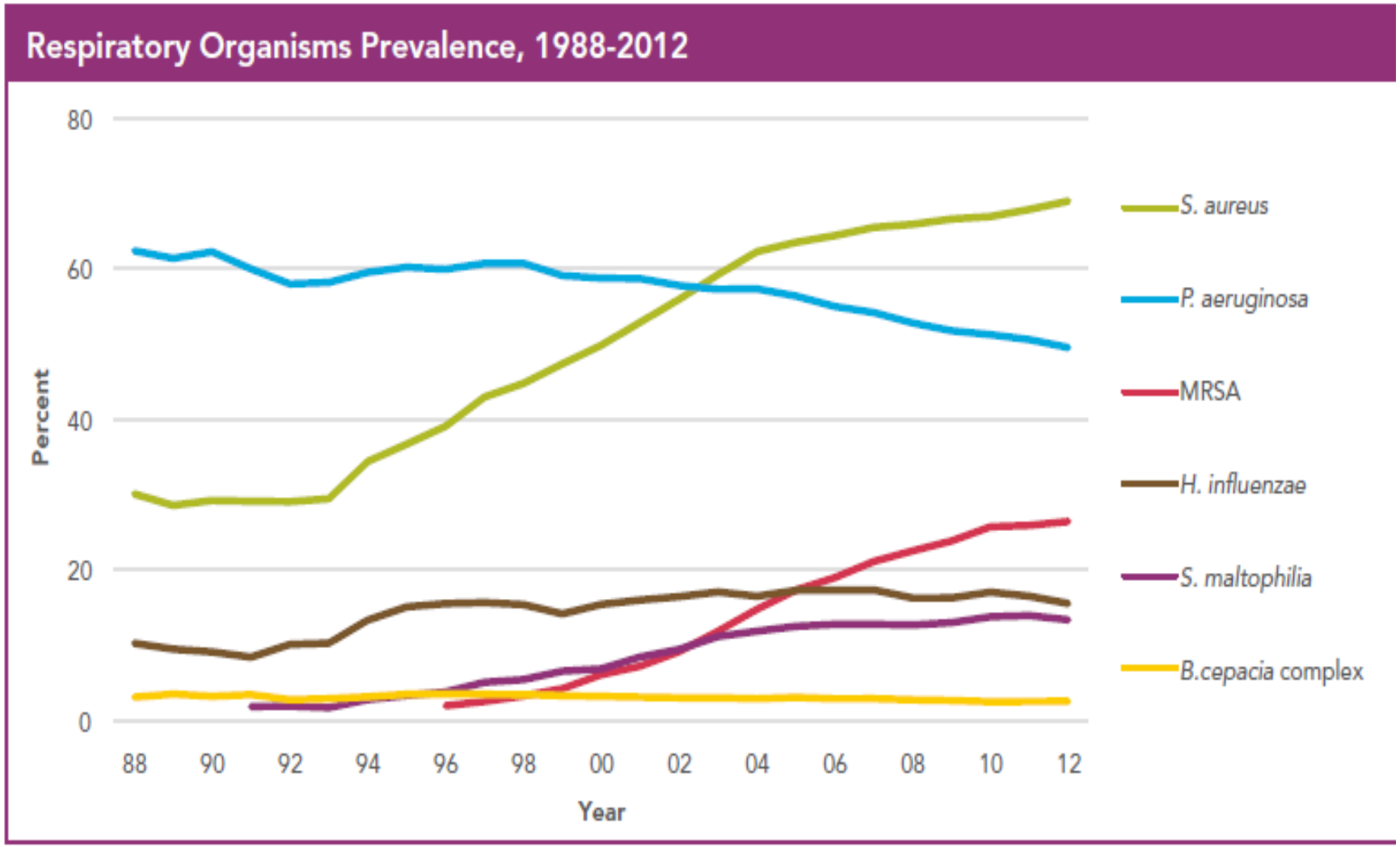
U.S. CF Registry

Age-Specific Prevalence of Respiratory Infections in CF Patients



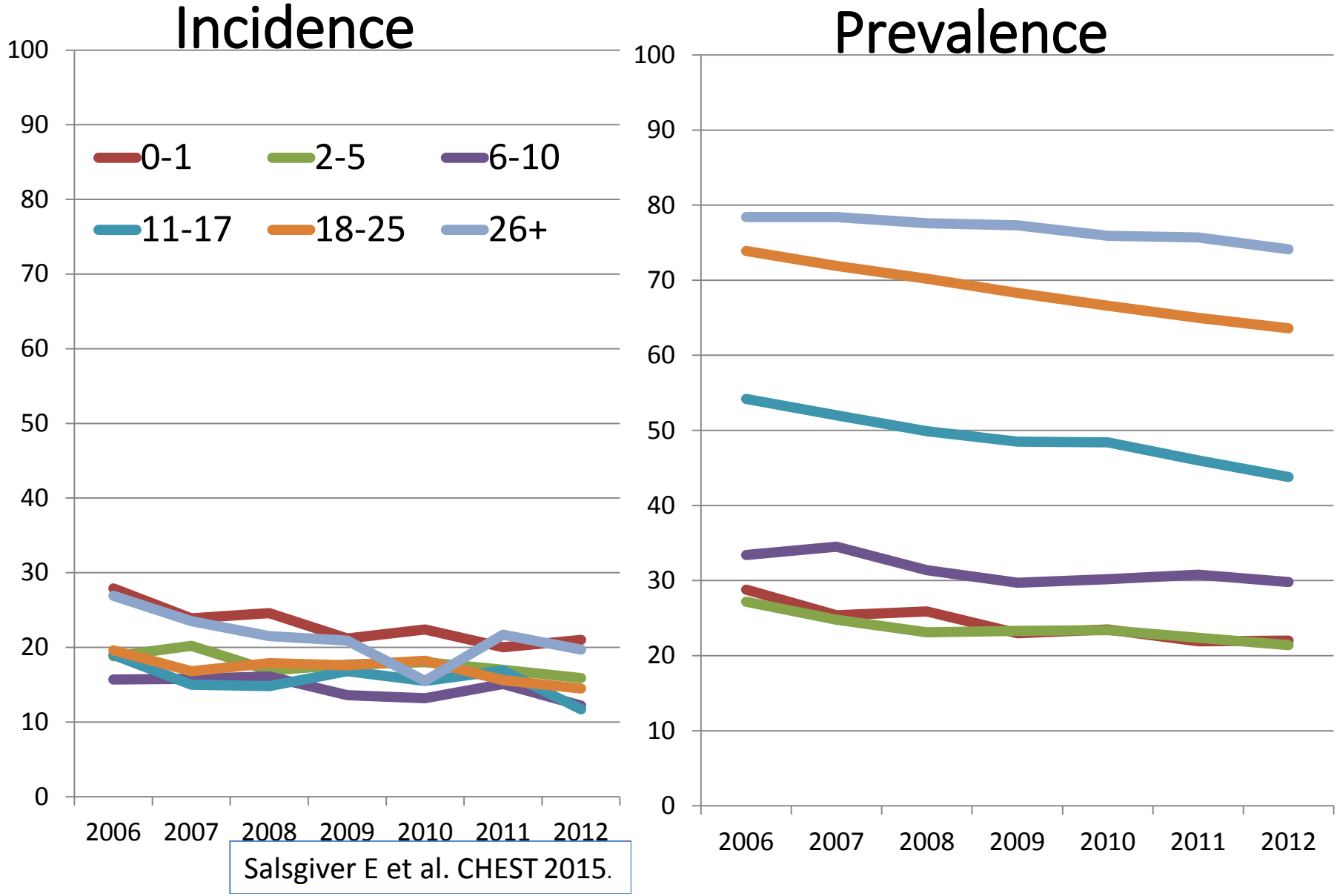
Source: Cystic Fibrosis Foundation Patient Registry, Annual Data Report

Changing Prevalence of CF Pathogens



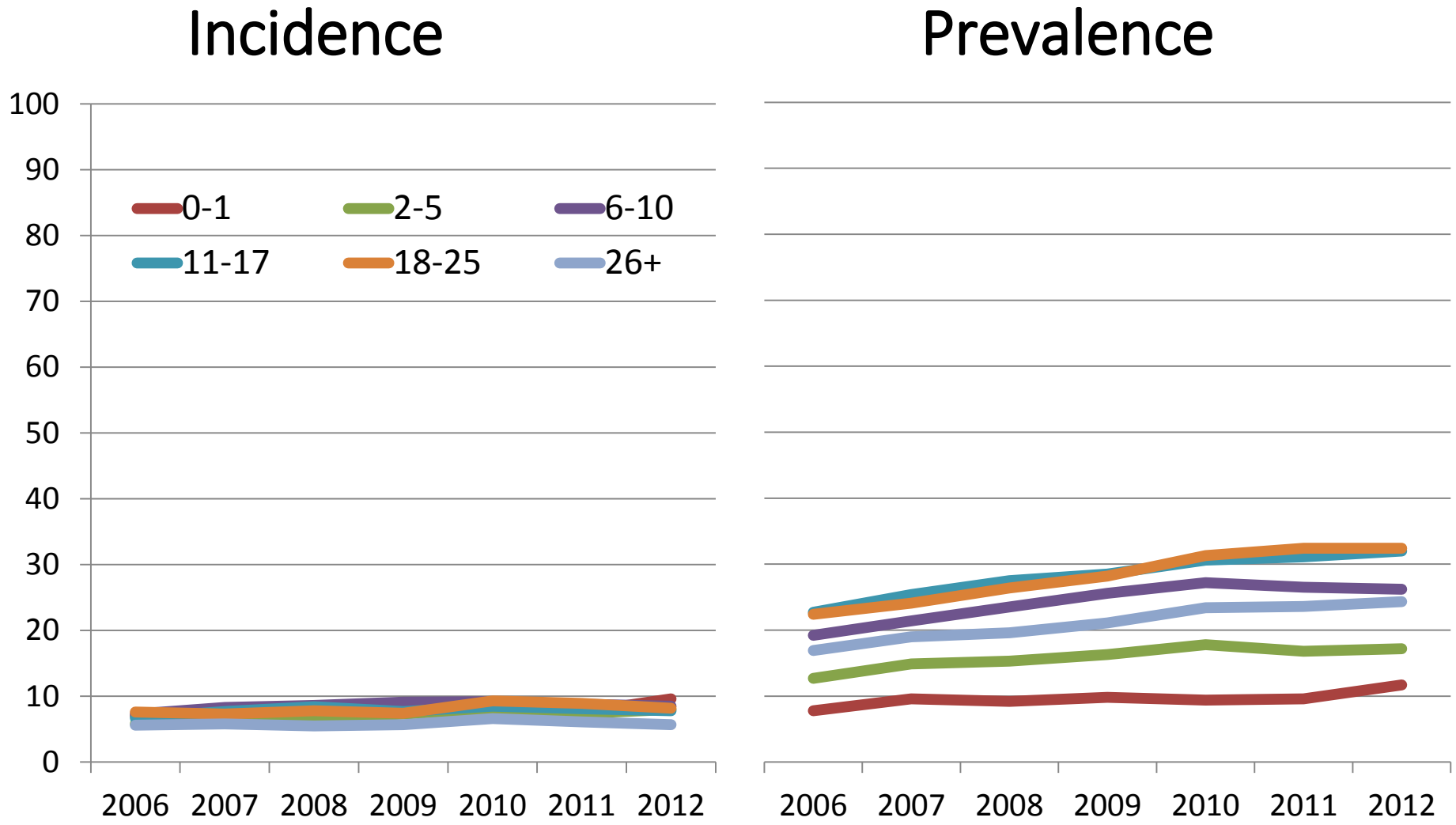
US CF Foundation Patient Registry, 2012

P. aeruginosa: 2006-2012

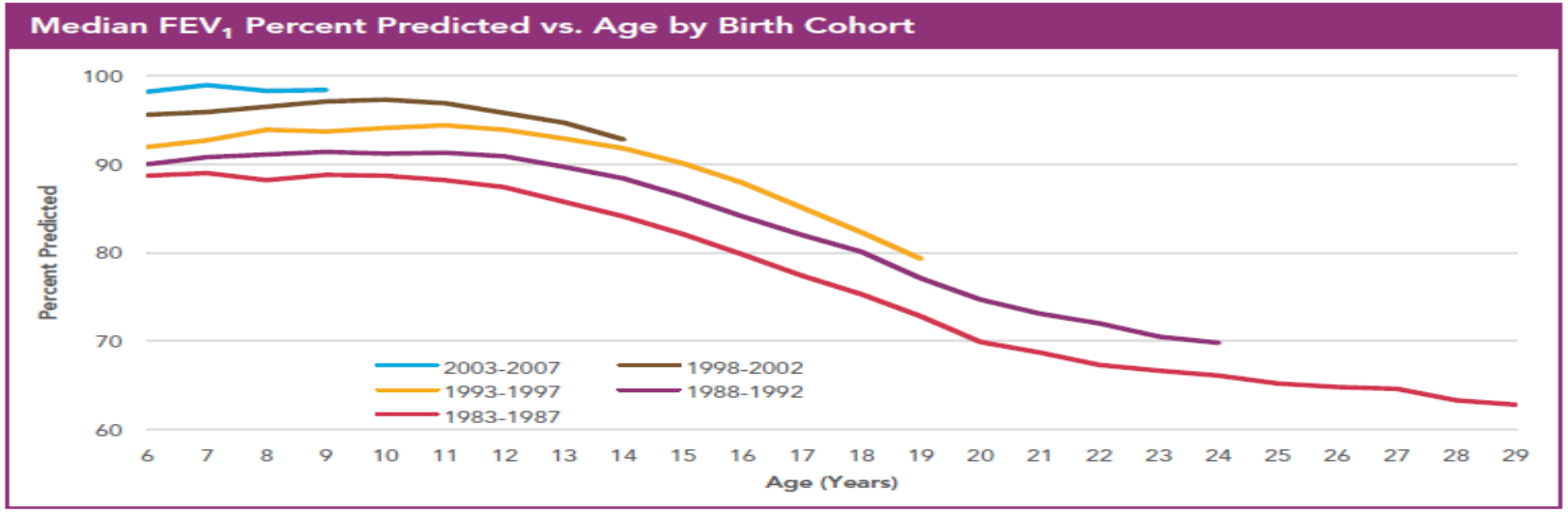


Salsgiver E et al. CHEST 2015.

MRSA, 2006-2012



Explaining Epidemiologic Changes?



- Improving lung function decreasing risk of infection
- Successful early eradication strategies for *P. aeruginosa*[1]
- Increase in community acquisition of MRSA[2]
- More rigorous infection prevention and control practices at CF centers[3,4]

[1]Treggiari et al. Arch Pediatr Adolesc Med. 2011;165(9):847–56.
[2] Dantes R, et al JAMA Intern Med 2013;173(21):1970-8
[3] **Saiman L**, et al. Infect Control Hosp Epid 2003;24(Suppl 5):S1-52
[4] Saiman et al. Infect Control Hosp Epidemiol. 2014;35 Suppl 1:S1-S67.

Discussion

- Changes to the CFFPR population during the study period
  - Increased number of patients identified by newborn screening

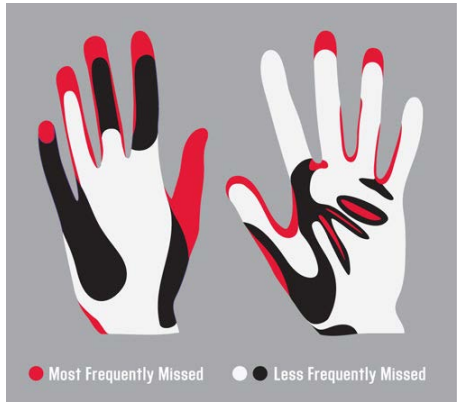
Major Routes of Transmission of CF Pathogens

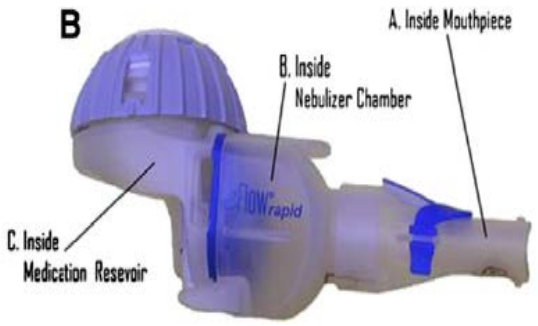
Siegel JD, et al and HICPAC. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings (www.cdc.gov/hicpac/pubs.html, accessed 3.1.2013 or Am J Infect Control 2007; 35 (suppl 2): S65-164)

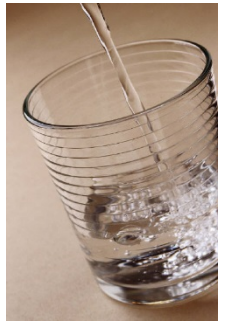
Indirect Contact Transmission

- Occurs when infectious agents are transferred through contaminated intermediate object or person

- ***Examples:*** Transfer of infectious agents via contaminated hands, contaminated respiratory therapy equipment, ommon items: eating utensils, drinking glass, toys, etc.







Siegel JD, et al and HICPAC. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings

Droplet Transmission

- Respiratory droplets carrying infectious agents travel from respiratory tract of infectious individual to susceptible mucosal surfaces of another person, generally over short distances (3-6 feet)

- Droplets generated by **coughing, sneezing** *OR* procedures, e.g., **pulmonary function tests** or **chest physiotherapy**

Festini F. Am J Infect Control 2010; 38: 244; Clifton IJ. Expert Rev Resp Med.2010; Wainwright CE. Thorax 2009; 64:926

Airborne Transmission

- Dissemination of droplet nuclei of **respirable size** containing infectious agents
- May remain *suspended in air* for prolonged periods of time and dispersed over long distances by air currents
- Inhaled by susceptible individuals without face-to-face contact with infectious individual

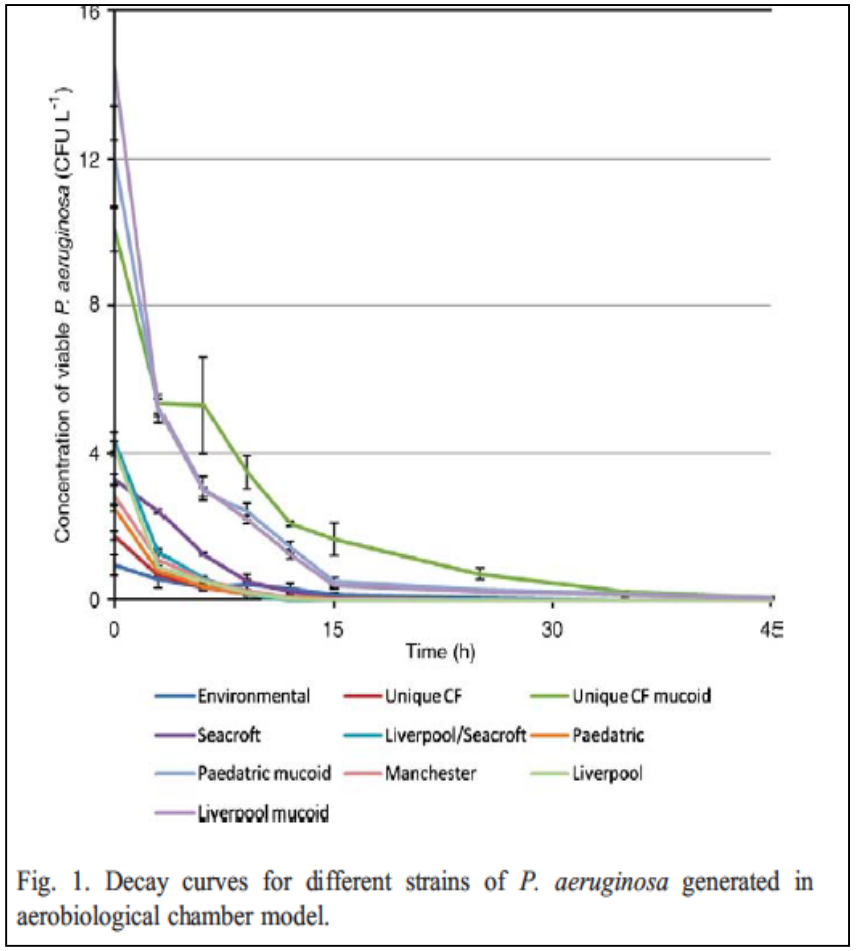


Fig. 1. Decay curves for different strains of *P. aeruginosa* generated in aerobiological chamber model.

Strain variation of *P. aeruginosa* in ability to remain suspended in air.

Clifton IJ. JCF 2010; 9:64

Evolving View of Droplet Transmission

- Data from:
  - Epidemiologic studies of outbreaks
  - Experimental studies
  - Aerosol dynamics
- Infectious droplets can remain suspended in the air 45 min. - 2 hrs.
- Experimental data from smallpox and SARS $\geq$ 6 ft.
- Experimental data in CF ~ 6 feet.

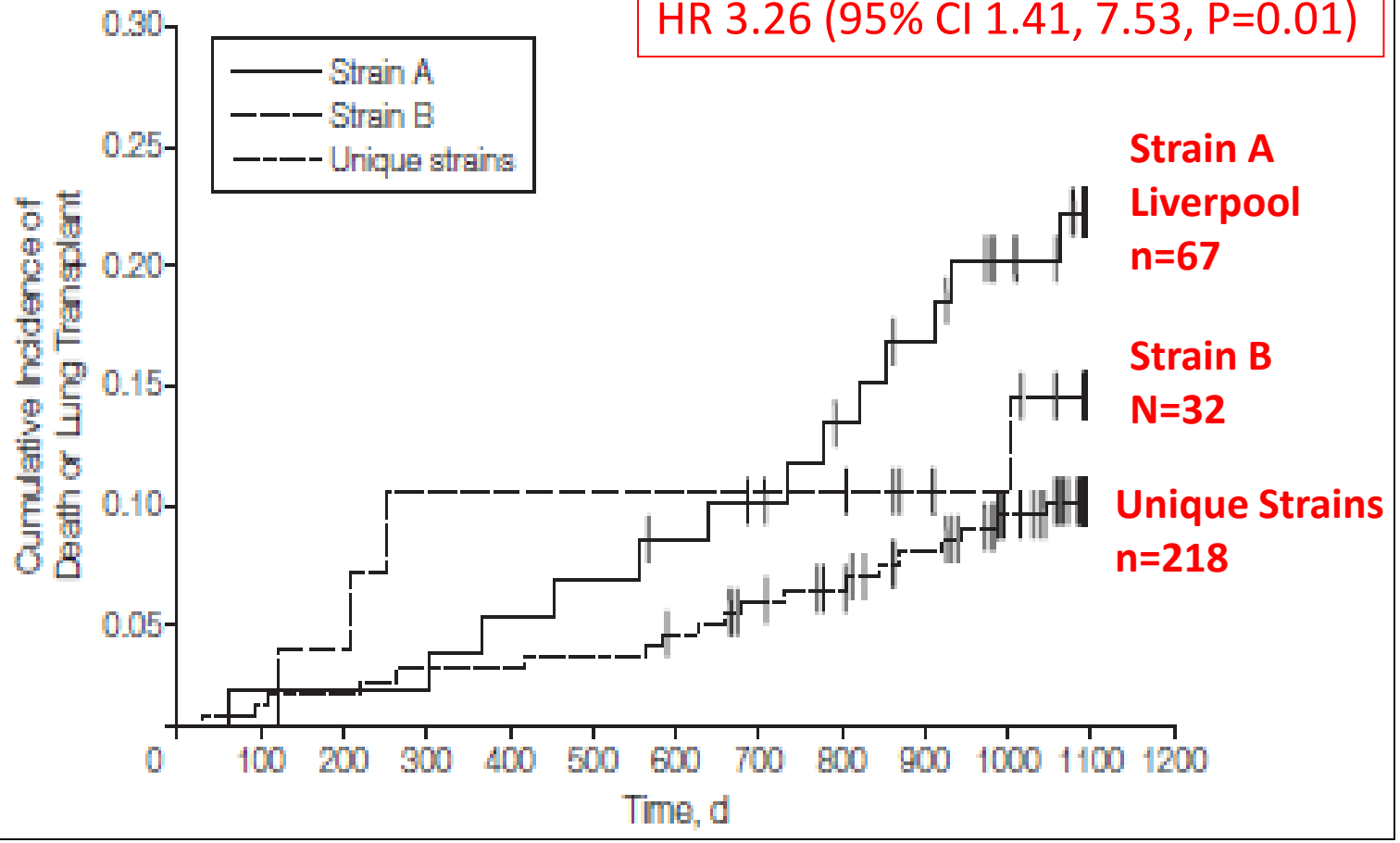
CDC. Isolation Guidelines 2007; Festini F. Am J Infect Control 2010; 38: 244;
Clifton IJ. Expert Rev Resp Med.2010; Wainwright CE. Thorax 2009; 64:926; Zuckerman J 2012

Transmission of CF Pathogens and Associated Morbidity and Mortality

Pseudomonas aeruginosa

Liverpool Strain and Increased Risk of Mortality/ Transplant

Figure 3. Comparison of Time to Death or Lung Transplant



Aaron S, et al. JAMA 2011

Transmission of Multi-resistant *P. aeruginosa* (MRPA), Houston

- **2006:** average MRPA in U.S. 16% vs. 30.1% in Houston
- **2004-2009 PA strains:** 32 of 71 (45%) patients had strains with >95% similarity, aka Houston-1
- **12** more hospital-days year before Houston-1 acquisition
- **Improved** IP&C practices in clinic and hospital reduced acquisition

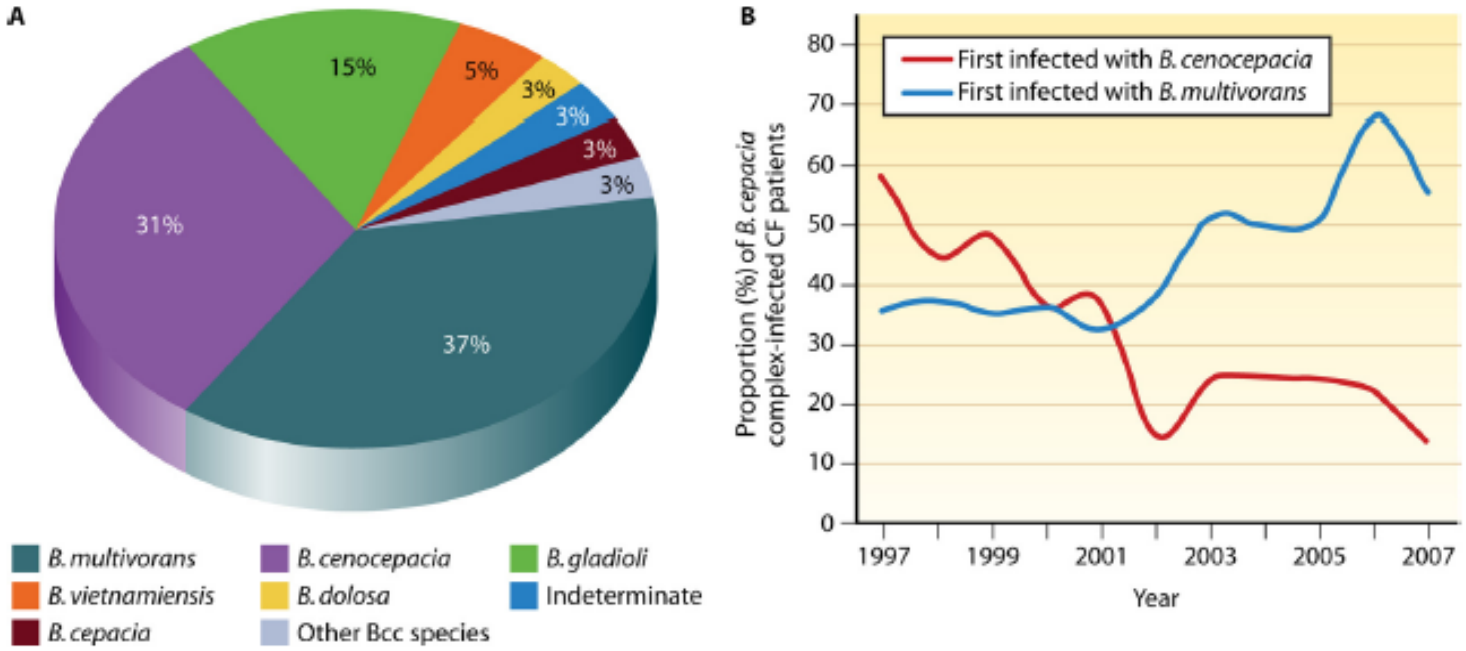
Logistic regression for variables associated with Houston-1 strain

	Strata	P	OR 95% CI
Age		0.66	
Days from clinic visit	≤ 60 61-120 >120	0.33 0.5 0.15	
Days from hospitalization	≤ 90 91-180 181-365	0.04* 0.11 0.51	4.02* 1.1-14.7

Luna RA, et al. J Clin Microbiol 2013; 51: 1237

Burkholderia dolosa

Distribution of *Burkholderia* spp., U.S.

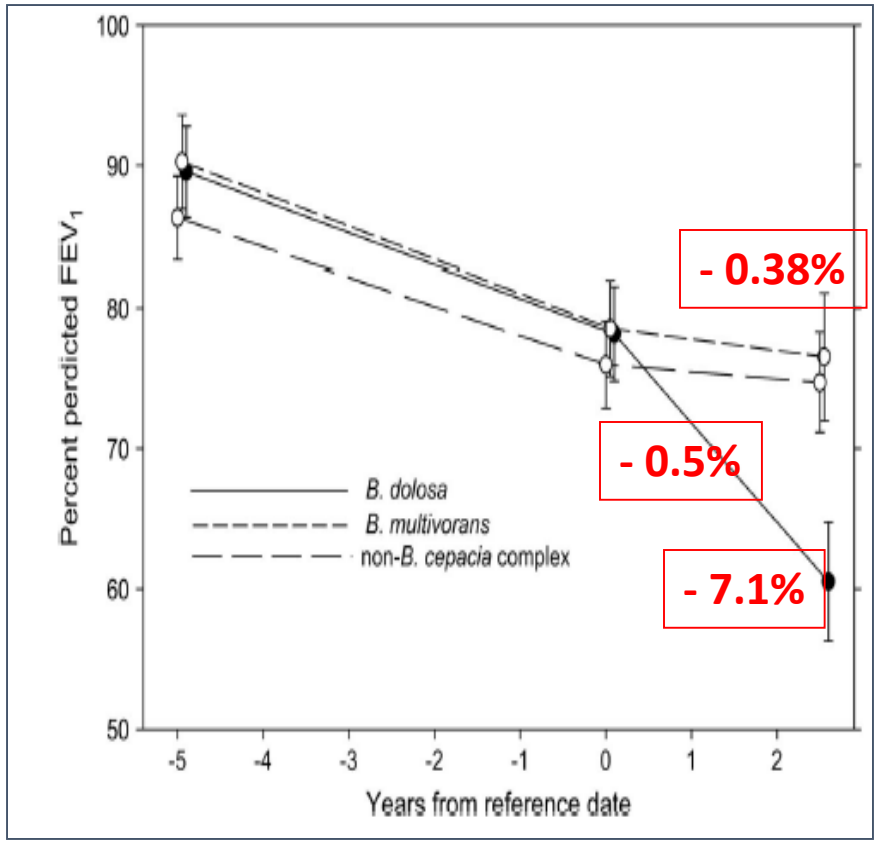


- *B. cenocepacia* and *B. multivorans* most common 1997-2007
- *B. multivorans* now more frequent than *B. cenocepacia*

LiPuma JJ Clin Microbiol Rev 2010

B. dolosa: Morbidity and Mortality

- Case-control study
  - 31 *B. dolosa*
  - 24 *B. multivorans*
  - 58 age-, sex-matched controls
- Increased decline lung function
- Increased 18-month mortality
  - 13% *B dolosa*
  - 7% *B. multivorans*
  - 3% controls

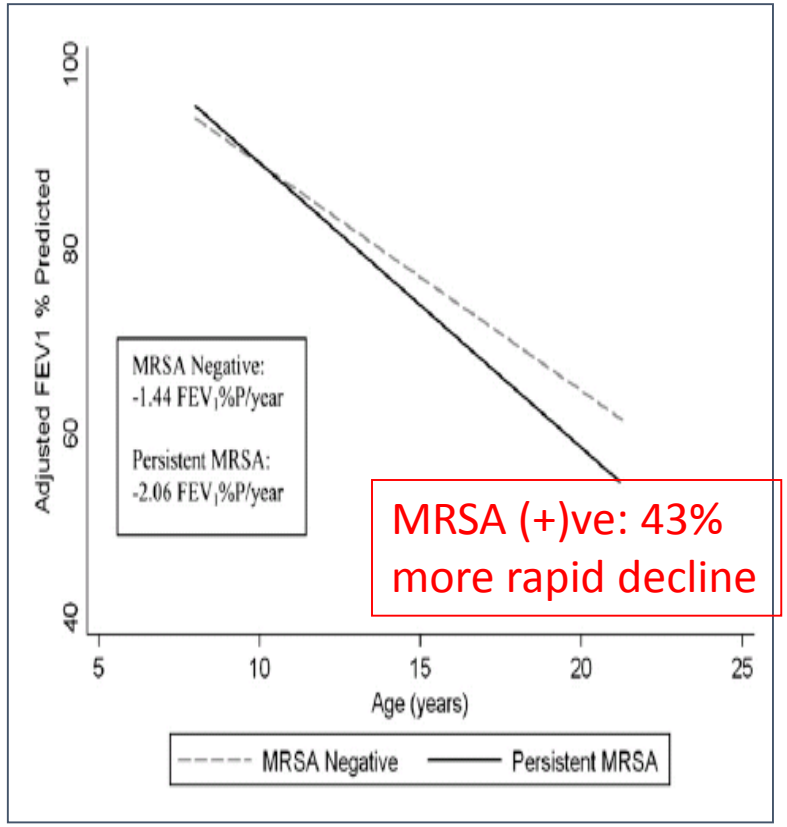


Kalish LA, et al. Am J Resp Crit Care Med 2006;15:421-425.

MRSA

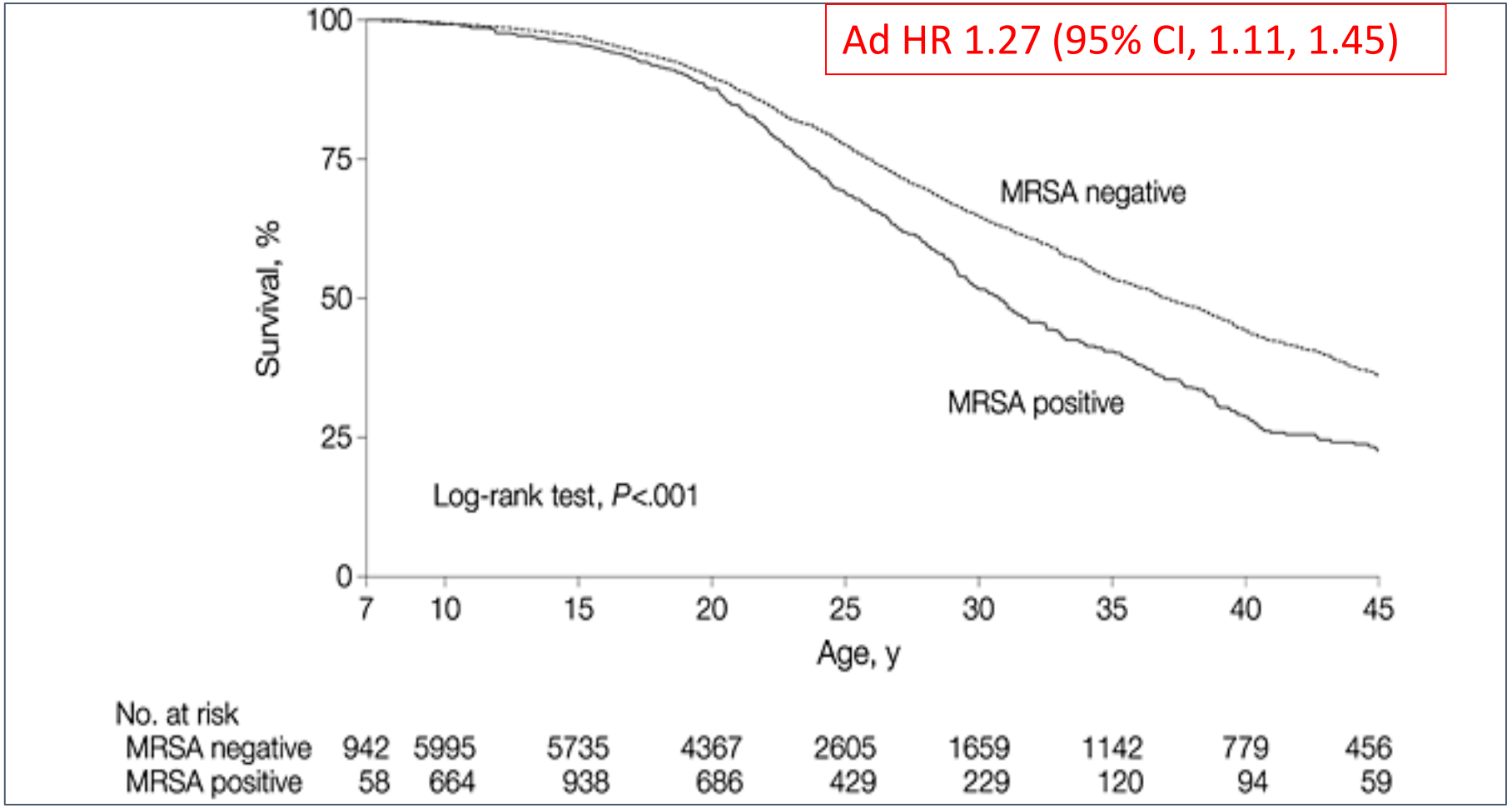
MRSA Impact: CFF Patient Registry, 1996-2003

- Mean 5.3 years follow-up
  - 1,732 *persistently* (+)ve
  - 13,922 *never* MRSA
- 8-21 year olds
  - (+)ve MRSA FEV_1 71.0%
  - Never MRSA FEV_1 79.6%



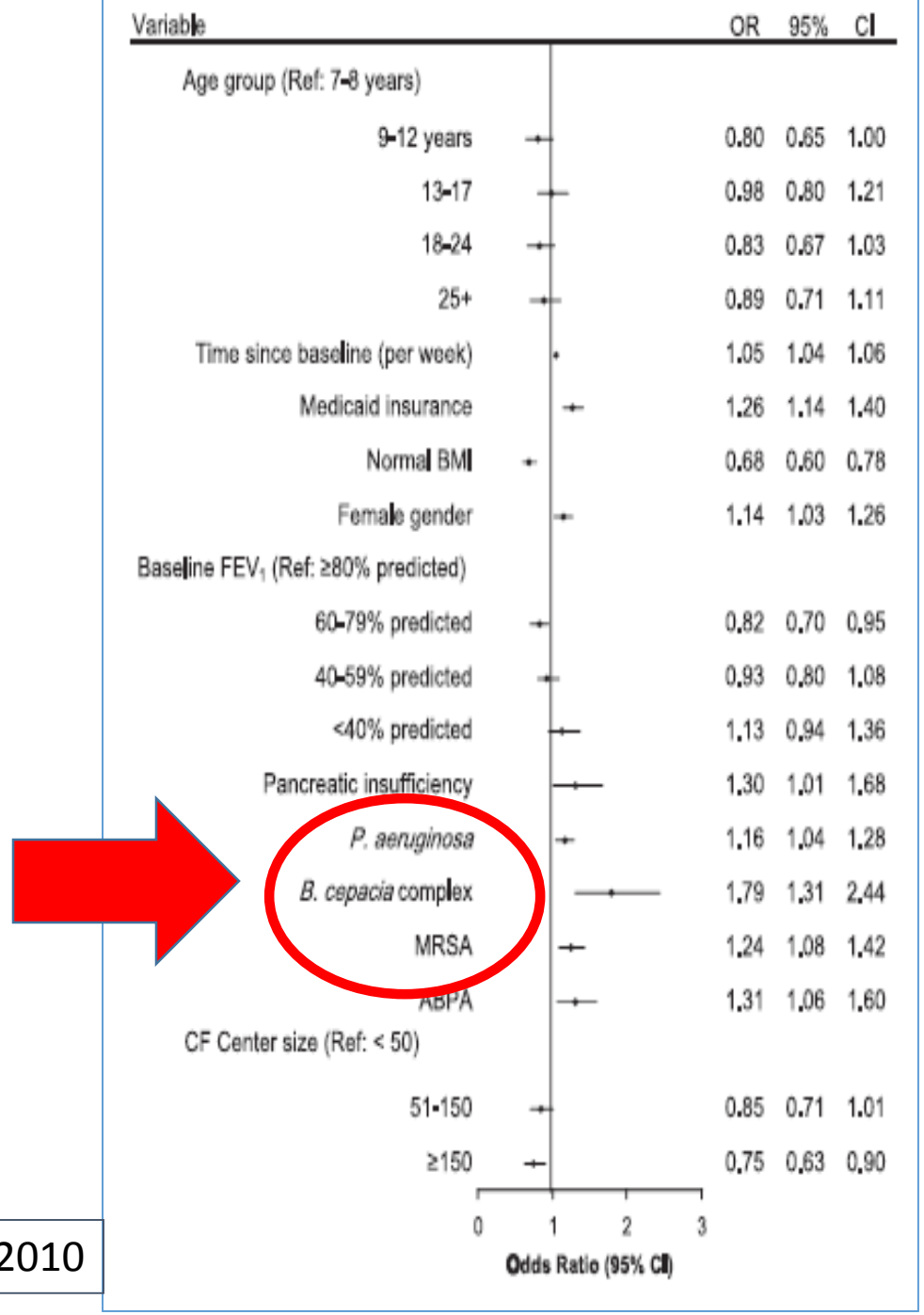
Dasenbrook EC et al. Am J Resp Crit Care Med 2008

Impact of MRSA on Survival (N = 19,833)



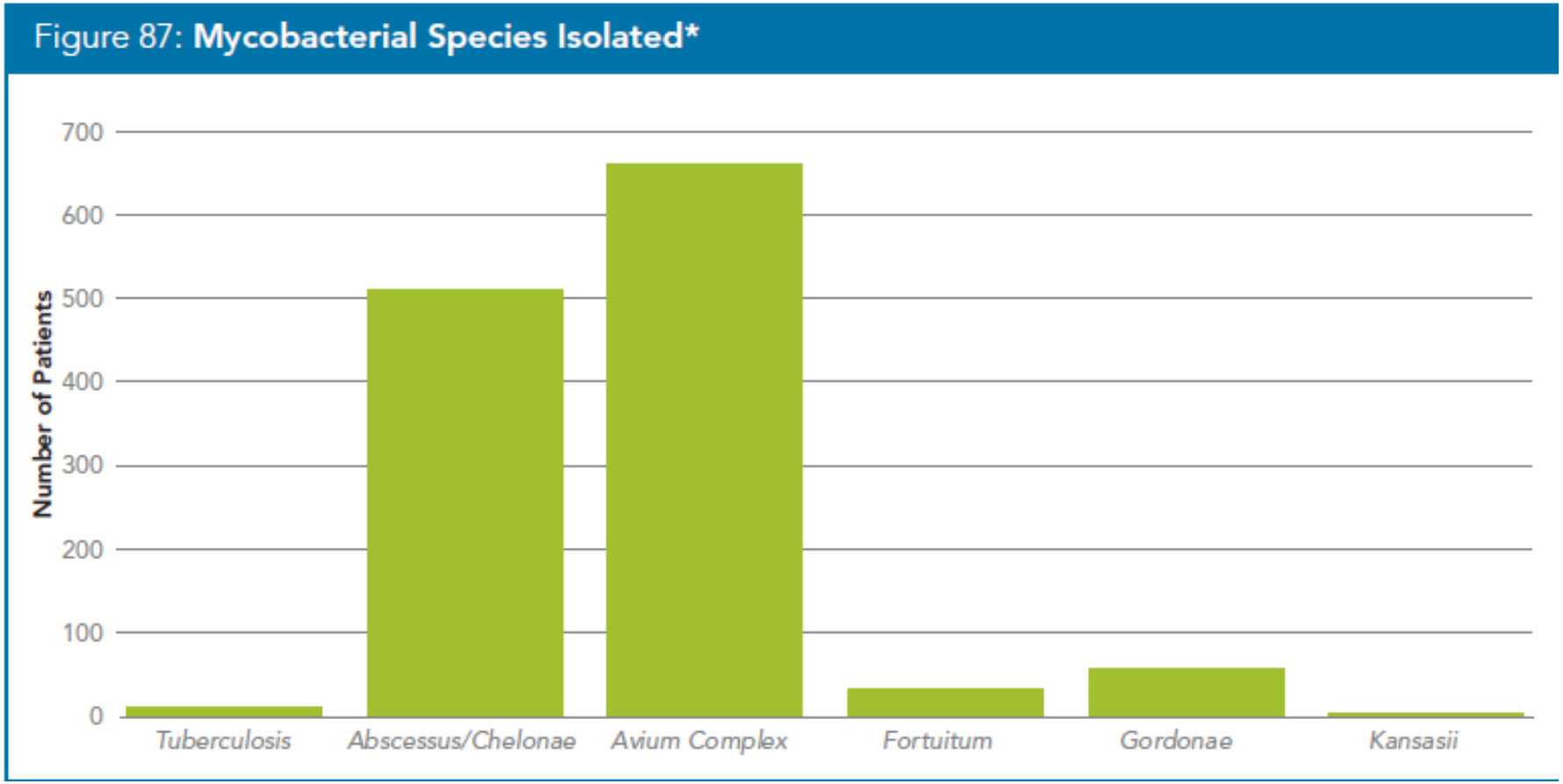
Dasenbrook, E. C. et al. JAMA 2010;303:2386-2392.

Pseudomonas, Burkholderia, and MRSA: Adversely impact recovery of FEV_1 in Exacerbations



Sanders DB, et al. Am J Resp Crit Care Med 2010

NTM Epidemiology
CFF Patient Registry



Epidemiology of NTM in CF

- Described since 1970's
- Variable prevalence 2-28%

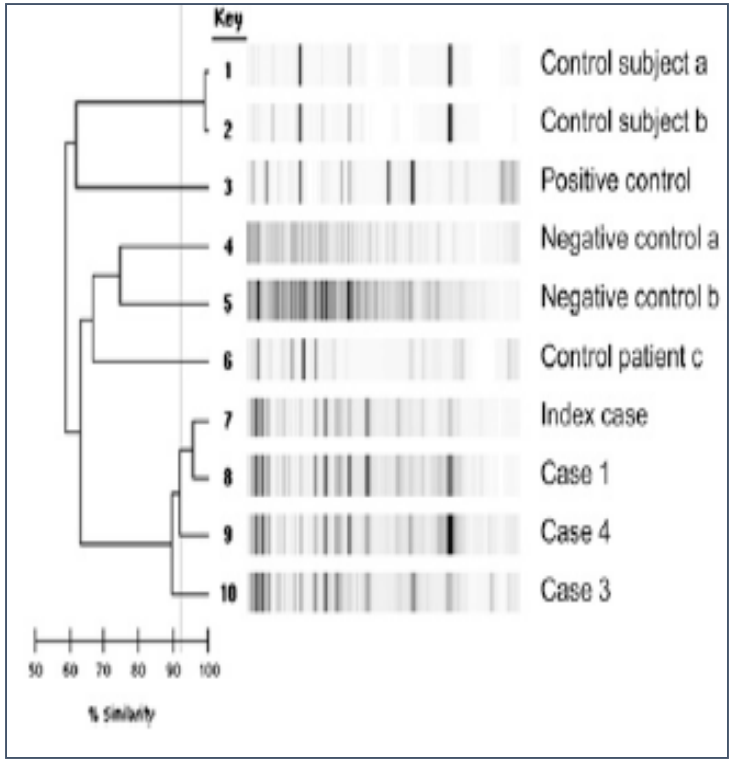
Country	Patients	Species (%)
US	986	MAC (72%) *M. abscessus* (16%)
France	385	*M. abscessus* (39%) MAC (21%) *M. gordonae* (18%)
Israel	186	*M. Simiae* (41%) *M. Abscessus* (31%) MAC (14%)

Olivier K Am J Resp Dis Crit Care Med 2003; Pierre-Audigier C et al. J Clin Microbiol 2005; Levy I et al. Emerg Infect Dis 2008

M. abscessus subspecies *massiliense*

- **Index case**: CF adult with multi-drug resistant *M. absessus ssp. massiliense* for 7 years
  - Transfer to clinic: AFB 4+ smear (+)ve

- **Transmission:** 4 additional CF adults (+)ve next 8 months
- 4/5 overlapping CF clinic days
- 3/5 died

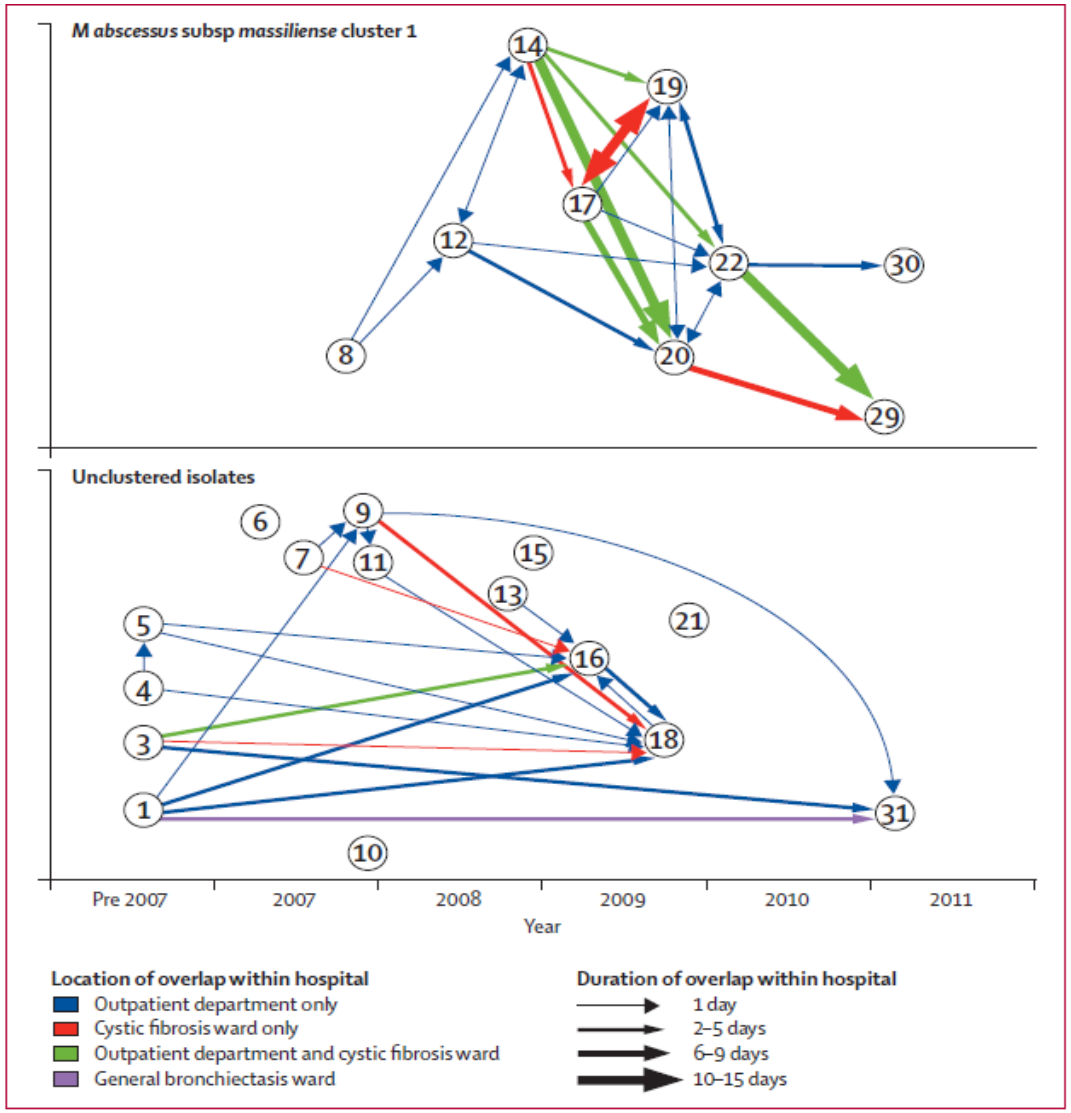


Aitken ML, et al. Am J Respir Crit Care Med 2012;185(2):231-232.

M. abscessus ssp. *massiliense*

- **Whole genome sequencing**
  NTM isolates, 2007-2011)
- 31 patients (+) *M. abscessus*
  - 13 subsp. *abscessus* (6-patient cluster)
  - 15 subsp. *massiliense* (2 clusters of 9 and 2 patients)

- **9 patient *massiliense* cluster**
  - More hospital exposure (10.8 vs. 1.2 d, p= 0.01)
  - CF inpatient ward (5.7 vs. 1.5 d, p=0.01)
  - CF clinic (3.9 vs. 2.3 d, p=0.02)
  - Hospitalized same time as infected patient (4.2 vs. 0.6 d, p=.005)



Bryant JM, et al. Lancet 2013; 381: 1551
Johnston DI, et al. J Hosp Infect 2016;94(2):198-200
Kapnadak SG, et al. Am J Infect Control 2016;44(2):154-59

Role of Healthcare Environment

- *P. aeruginosa* in room air samples
  - obtained when waking up or after physiotherapy
  - 12/22 (55%) infected patients
  - 6/12 (50%) genetically identical to sputum strains
- Liverpool Epidemic Strain
  - 5/8 (63%) air samples in CF clinic hallway
- Non-epidemic *P. aeruginosa*
  - 3/15 (20%) PFT machine surface
- *Pseudomonas* and *S. aureus*
  - 13.6% of sites in CF clinics contaminated
  - hands (7%), exam room air (8%), environmental surfaces (1%)
  - No differences in adults vs. children; routine vs. sick visit

Ferroni A., et al. J Cystic Fibrosis 2008; 7: 477.
Panagea S. et al., J Hosp Infect 2005;59:102-107
Zuckerman H et al. J Cystic Fibrosis 2009; 8:186

Hands of People with CF, USA

- 74 patients hands cultured prior to performing alcohol hand hygiene at start of clinic visit
  - Hand hygiene reduced hand contamination
  - But…patients' hands contaminated at visit end

Zuckerman JB, et al. J Cystic Fibrosis 2009; 8:186

KEY RECOMMENDATIONS

RECOMMENDATION KEY MESSAGES

- ❑Whenever feasible, provided ***choices*** for implementation strategies in healthcare settings.
- ❑Emphasized treating all people with CF the same…***regardless of respiratory tract cultures***. Assume all people with CF could have transmissible pathogens in respiratory tract secretions.
- ❑No longer recommending different care practices for those infected with *Burkholderia cepacia complex*
- ❑Recommendations for non-healthcare settings and for healthcare professionals with CF intended to ***provide education to help make informed choices***.

Use Principles of Adult Education

- **Increase Knowledge of all providers**
  - Perceive relevance of information to their personal situation
  - Flexible
  - Encourage networking, critical analysis, self-reflection on practice, opportunities for open questioning
  - Increase awareness of guidelines
  - **Repeated exposures to information**
  - Educational materials that include **“WHY”**
- **Increase Skills**
  - Observations
  - Return demonstrations
- **Acknowledge Impact of Attitudes**
  - Reflect individual beliefs, professional and personal life experiences
  - Must believe practice change directly benefits themselves or patients

Matlow AG. AJIC 2012; 40: 260 [environmental service workers]; Ferguson PE. BMT 2010;45:656 [pt./families]; (Miroballi Y, Pediatric Pulm 2012;47:144 [CF patients and families].

Partner with Local IP&C Teams

- **Both teams** are data analysis/data driven
- **Expertise of IP&C Teams**
  - Implementation, prioritization and staging of recommendations, if appropriate
  - Identifying appropriate stakeholders, including C suite
  - Monitoring adherence to practices and providing feedback
  - Apply experience with improving hand hygiene, respiratory hygiene, environmental cleaning, transmission precautions, and collaborations with microbiology lab
- Audits of hand hygiene and cleaning practices
- Use existing tools for monitoring cleaning effectiveness
  - www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html

Eckstein BC. BMC ID 2007; 7: 61; Hayden MK 2006; CID 2006; 42:1552;
Otter JA. ICHE 2011; 32: 687; Harris A. CID 2008; 46:686, Boyce JM. ICHE 2011; 32: 1187

Hand Hygiene (HH)

- Improve HH among Healthcare Providers:
  - Prior to patient contact or after contact with body fluids or inanimate objects, e.g., equipment
  - Make improvement institutional priority
  - Make supplies readily accessible
- Improve HH among people with CF and families

CDC HH Guidelines 2002; WHO HH Guidelines 2003;

Use of Gowns, Gloves, Masks

- Gowns and gloves
  - **Staff** wear when caring for all people with CF in hospital and ambulatory care areas
  - **Patients and families** do ***not*** wear gowns and gloves
- Masks
  - **All people with CF** wear surgical masks (if tolerated)
  - Staff ***only*** wear surgical masks if suspected pathogen spread by droplets, e.g., influenza or pertussis
  - Staff ***only*** wear N95 masks if suspected airborne pathogen, e.g., TB or measles
- 6 foot rule

Knibbs LD, et al. Thorax 2014;69(8):740-45.
Driessche KV, et al. Am J Respir Crit Care Med 2015;192:897-99.

Implementing Contact Precautions

- Pediatric CF center, USA (n=180)
- Measure pathogen revalence before and after all staff wore gowns and gloves for all CF patients
- Change in *P. aeruginosa* prevalence
  - 30% → 21% ($p<0.001$)
- Change in MRSA prevalence
  - 10.8% → 8.7% ($p=0.008$)

Savant AP et al. BMJ Qual Saf 2014;Suppl 1:i73-80

Transmission Precautions for Non-tuberculous Mycobacteria

Insufficient evidence to place people with CF who are infected with NTM on Airborne Precautions, i.e., negative pressure room.

Johnston DI et al. J Hosp Infect 2016;94(2):198-200.
Kapnadak SG et al. Am J Infect Control 2016;44(2):154-9.
Harris KA, et al. Clin Infect Dis 2015;60(7):1007-16.

Scheduling CF Clinics

Insufficient evidence to routinely scheduling CF clinics based on specific pathogens isolated from respiratory tract cultures.

4 Options for Performing PFTs

1. In exam room at beginning of clinic visit
2. In a negative pressure room (Airborne Infection Isolation Room = AIIR)
3. In PFT lab with either portable or integrated high-efficiency particulate [HEPA] filters
4. In PFT lab without HEPA filtration, allowing 30 minutes to elapse before next person with CF enters PFT lab.

Zuckerman J et al. *Am J Resp Crit Care Med* 2015;191(5):598-601.

Psychosocial Impact IP&C Guidelines

- Centers should anticipate specific concerns regarding psychosocial impact of implementing IP&C recommendations
- Identify strategies to minimize negative impact

Somayaji R et al. BMC Pulm Med 2015;15:138.
Bowmer G et al. J Cystic Fibrosis 2017;16(1):146-50
Jain M, et al. Chest 2014;145:678-80
Shepherd SL et al. Chest 2014;145(4):680-83.

CF Foundation- and CF Center-sponsored Indoor Events

- Only one person with CF attend CFF- or CF Center-sponsored ***indoor events*** (e.g., CF Education Days) unless they live in the same household.

- ***Develop and utilize alternative CF education programs***, (e.g., videotapes, video-conferencing, CD-ROM web-based learning, Apps)

Cross-infection Policy

Guidance for people with cystic fibrosis at events and meetings

- ✓ **UK CF Trust** "…it is our policy for only one person with CF to be present…at an indoor event organised by Trust staff or its volunteer branches, groups, and committees… www.cysticfibrosis.org.uk/about-cf/living-with-cystic-fibrosis/cross-infection.aspx

Cystic Fibrosis Fibrose kystique Canada

- ✓ **CF Canada** "For indoor events, a provision has made for organizers to invite one person with CF to attend." www.cysticfibrosis.ca/en/aboutUs/infectionControlPolicy

*CHEST JOURNAL

- ✓ Sponsored Pro-Con debate on this recommendation

Jain M et al. and Shephard SL et al. Chest 2013, Oct 17

BALANCING INFECTION PREVENTION AND CONTROL WITH QUALITY OF LIFE

Updated Executive Summary

- http://www.cff.org/Care/Clinical-Care-Guidelines/Infection-Prevention-and-Control-Clinical-Care-Guidelines/Infection-Prevention-and-Control-Clinical-Care-Guidelines/

Summary and Conclusions

- The epidemiology of CF pathogens is changing; most notably the incidence and prevalence of *P. aeruginosa* are decreasing with the incidence and prevalence of MRSA are increasing
- Infection prevention and control may be reducing acquisition of some CF pathogens.
- New knowledge mandated new guidance for IP&C practices for CF.
- To be effective at preventing transmission of CF pathogens, IP&C has to be understood and practiced by everyone.
- Research directions suggested by recommendations with ***insufficient evidence.***

Questions, Comments, Thoughts, Concerns????