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Infection Prevention and Control Guideline for Cystic Fibrosis: 2013 Update

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Source: *Infection Control and Hospital Epidemiology*, Vol. 35, No. S1, Cystic Fibrosis Foundation Guideline (August 2014), pp. S1-S67

Published by: Cambridge University Press on behalf of The Society for Healthcare Epidemiology of America

Stable URL: <https://www.jstor.org/stable/10.1086/676882>

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## CYSTIC FIBROSIS FOUNDATION GUIDELINE

# Infection Prevention and Control Guideline for Cystic Fibrosis: 2013 Update

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Received March 3, 2014; accepted March 5, 2014; electronically published July 1, 2014.

*Infect Control Hosp Epidemiol* 2014;35(S1):S1-S67

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DOI: 10.1086/676882

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### EXECUTIVE SUMMARY

#### INTRODUCTION

The 2013 Infection Prevention and Control (IP&C) Guideline for Cystic Fibrosis (CF) was commissioned by the CF Foundation as an update of the 2003 Infection Control Guideline for CF.<sup>1</sup> During the past decade, new knowledge and new

challenges provided the following rationale to develop updated IP&C strategies for this unique population:

1. ***The need to integrate relevant recommendations from evidence-based guidelines published since 2003 into IP&C practices for CF.*** These included guidelines from the Centers for Disease Control and Prevention (CDC)/Healthcare Infection Control Practices Advisory Committee (HICPAC), the World Health Organization (WHO), and key professional societies, including the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA). During the past decade, new evidence has led to a renewed emphasis on source containment of potential pathogens and the role played by the contaminated healthcare environment in the transmission of infectious agents. Furthermore, an increased understanding of the importance of the application of implementation science, monitoring adherence, and feedback principles has been shown to increase the effectiveness of IP&C guideline recommendations.

2. ***Experience with emerging pathogens in the non-CF population has expanded our understanding of droplet transmission of respiratory pathogens and can inform IP&C strategies for CF.*** These pathogens include severe acute respiratory syndrome coronavirus and the 2009 influenza A H1N1. Lessons learned about preventing transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant gram-negative pathogens in non-CF patient populations also can inform IP&C strategies for CF.

3. As the use of molecular technologies increased throughout the past decade, there is ***an improved understanding of the epidemiology of newer CF pathogens that are increasing in prevalence and are associated with increased morbidity and mortality.*** Such pathogens include MRSA, *Mycobacterium abscessus*, new species in the *Burkholderia cepacia* complex (eg, *Burkholderia dolosa*), and epidemic clones of *Pseudomonas aeruginosa* (eg, the Liverpool epidemic strain).

#### METHODS FOR DOCUMENT DEVELOPMENT

An interdisciplinary committee of healthcare personnel with expertise in CF, 3 parents of children with CF, and an adult with CF determined the scope of the guideline, reviewed the evidence (including that from a systematic review), and developed and voted anonymously on specific recommendations. Whenever appropriate, this guideline has integrated relevant recommendations from the 2003 Infection Control Guideline for CF and from other existing IP&C guidelines.

The focus of the updated guideline is to provide recommendations to prevent individuals with CF from transmitting and/or acquiring respiratory tract pathogens from others with CF in ambulatory care and inpatient settings. Recommendations for nonhealthcare settings represent efforts to respond to questions and concerns voiced by people with CF and their caregivers and, thus, are intended to educate the CF community about potential risks and to help people with CF and their families and friends make informed choices in their

personal lives. Recommendations for nonhealthcare settings are not intended to be enforced by healthcare personnel.

This guideline is intended for use by all healthcare personnel involved with the care of people with CF and the IP&C teams that support CF care centers in the United States. The recommendations for healthcare settings apply to inpatient settings, CF clinics and other ambulatory care areas, diagnostic and therapeutic areas, and all clinical research activities. Successful and consistent implementation of IP&C practices must include the ongoing participation of people with CF and their families as well as auditing the IP&C practices of healthcare personnel and feedback about their performance.

***The goal of this guideline is to reduce substantially the risk of transmission and acquisition of CF pathogens,*** while recognizing that the risk is unlikely to reach zero.

A draft of the guideline was made available to the CF and IP&C communities for review, and all comments were considered by the committee. This guideline was reviewed and endorsed by SHEA and by the Association for Professionals in Infection Control (APIC).

#### RECOMMENDATIONS

The recommendations are divided into 7 sections.

- I. Core recommendations, intended for all people with CF (including following lung or liver transplantation) in all settings
- II. Recommendations for microbiology and molecular epidemiology
- III. Recommendations for CF clinics and other ambulatory settings
- IV. Recommendations for inpatient settings
- V. Recommendations for nonhealthcare settings
- VI. Recommendations for healthcare personnel with CF
- VII. Recommendations regarding the psychosocial and medical impact of IP&C

To facilitate use of the guideline, the relevant sections of "Background Information Supporting the Recommendations" (**Sections I–III**) and strategies to reduce transmission and acquisition of pathogens (**Sections IV–VII**) are provided with each recommendation. The recommendations emphasize that healthcare personnel, people with CF, and their family and friends receive education about IP&C that fosters understanding of the rationale for the recommendations.

The recommendations highlight the importance of partnering with local IP&C teams to facilitate implementation and the use of existing audit and feedback tools to monitor adherence to IP&C practices. The recommendations emphasize source containment of the respiratory secretions of people with CF, appropriate use of personal protective equipment, and cleaning and disinfection to prevent acquisition of CF pathogens from the contaminated healthcare environment. Furthermore, the CF community is encouraged to share best practices, written policies, quality improvement

initiatives, educational materials, strategies for non-face-to-face interactions among individuals with CF, and outcome studies related to IP&C practices.

The key recommendations in this document that are new for the CF community are as follows:

1. Develop strategies to monitor adherence to IP&C practices by healthcare personnel and provide them with feedback for improvement.
2. Partner with IP&C teams to implement the recommendations in this guideline, especially those that are likely to be followed in areas of the facility that are not dedicated only to people with CF.
3. Implement *Contact Precautions* (ie, wear a gown and gloves) when caring for all people with CF, regardless of respiratory tract culture results, in both ambulatory and inpatient settings.
4. Separate all people with CF from others with CF, regardless of their respiratory tract culture results, at least 6 feet (2 meters) in all settings, to reduce the risk of droplet transmission of CF pathogens.
5. All people with CF and their family members and friends should perform appropriate hand hygiene (with either alcohol-based hand rub or antimicrobial soap and water) when there is the potential for contamination of hands with pathogens. Contamination of hands may occur when entering and exiting a CF clinic, clinic exam room, or hospital room or from respiratory secretions after coughing, performing pulmonary function tests, or performing chest physiotherapy.
6. All people with CF, regardless of respiratory tract culture results, should wear a surgical (also called procedure or isolation) mask when in a healthcare setting to reduce the risk of transmission or acquisition of CF pathogens.
7. Perform pulmonary function tests (PFTs) to reduce transmission from one person with CF to another person with CF by performing the test in one of the following ways:
  - In the exam room at the beginning of the clinic visit, allowing 30 minutes to elapse between CF patients;
  - In a negative pressure room (airborne infection isolation room);
  - In a PFT laboratory with high-efficiency particulate (HEPA) filters; or
  - In a PFT laboratory without HEPA filters, allowing 30 minutes to elapse between individuals with CF.
8. Updated recommendations for care of nebulizers in the hospital.
9. Only 1 person with CF may attend a CF Foundation-sponsored indoor event.

### I–III. Background Information Supporting the Recommendations

#### I. CF Microbiology and Molecular Typing

The recommendations for processing CF respiratory tract specimens in the 2003 Infection Control Guideline for CF<sup>1</sup>

are endorsed in the updated guideline. Several molecular typing strategies are reviewed, with a focus on newer technologies, such as whole-genome sequencing. The importance of international efforts in understanding the molecular epidemiology of CF pathogens is discussed, as is the need to use molecular epidemiology as one tool to monitor the success of IP&C strategies. An update on the epidemiology of CF pathogens is provided, with an emphasis on gram-negative pathogens, including *Burkholderia* spp., small colony variant *S. aureus*, and nontuberculous mycobacteria (NTM). This section also emphasizes the importance of surveillance strategies to assess the impact of therapeutic interventions, to identify potential outbreaks, and to monitor the success of IP&C strategies.

#### II. Routes of Transmission of CF Pathogens

In this section, as in the 2003 Infection Control Guideline for CF, the importance of contact and droplet transmission is emphasized. While the precise routes of transmission are unclear for every acquisition, data support transmission by direct contact with infectious secretions; indirect contact with infectious secretions through contaminated intermediate objects, such as healthcare surfaces, equipment, or the hands of healthcare personnel; and/or infectious droplets. New data are provided demonstrating that droplets can travel as far as 6 feet (2 meters), the complexities of droplet transmission are described, and the potential role played by droplet nuclei in transmission of CF pathogens is discussed.

#### III. Potential Sources of CF Pathogens

In this section, as in the 2003 Infection Control Guideline for CF, it is again emphasized that the source of CF pathogens is often unknown and that many individuals with CF are infected with unique strains. However, molecular epidemiology tools have expanded the evidence that people with CF can share epidemic strains of *P. aeruginosa*, *Burkholderia* spp., MRSA, and *M. abscessus*. Less commonly, strains of other gram-negative pathogens (eg, *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, *Ralstonia*, *Cupriavidus*, and *Pandora* spp.) may be shared by people with CF. The adverse clinical impact of epidemic strains is highlighted. The sources of and role played by filamentous fungi in CF lung disease (eg, *Aspergillus* spp.) are also considered.

While transmission of CF pathogens among people with CF is very well described, transmission of CF pathogens from individuals without CF to individuals with CF appears to be almost exclusively limited to respiratory viral pathogens. Acquisition of CF pathogens from animals has not been described. In contrast, acquisition from the natural environment (ie, soil, organic matter, and water) is feasible given the ecologic niches of some CF pathogens. The potential for acquisition of CF pathogens from contaminated healthcare environmental sources, including water, surfaces, equipment, air, and products, is also discussed.

#### IV. Strategies to Reduce Transmission and Acquisition of CF Pathogens

This section is divided into 9 subsections that describe IP&C strategies and the rationale for implementing them for all people with CF, including those who have undergone lung or liver transplantation. The subsections include **education strategies** for healthcare personnel and for people with CF and their families, including audits and feedback for healthcare personnel performance; **hand hygiene** for healthcare personnel, people with CF, and their families; **use of personal protective equipment**, including the appropriate use of gowns and gloves by healthcare personnel for all interactions with people with CF; mask use by healthcare personnel as per CDC recommendations; mask use by individuals with CF; **cleaning and disinfection** of the healthcare environment and equipment, including recommendations for nebulizer care; **CF clinic** strategies, including recommendations for performing pulmonary function testing; **transmission-based precautions** for hospitalized people with CF; **construction and renovation**; and **strategies for nonhealthcare settings** (eg, camps, indoor and outdoor events, and schools).

Three additional sections have been developed: “Healthcare Personnel with CF” (**Section V**), which provides the recommendation that people with CF who are interested in healthcare professions should seek advice from their CF care teams about lower-risk options on the basis of their health status; “Psychosocial and Medical Impact of Transmission-Based Isolation Precautions” (**Section VI**), in which the unintended consequences of transmission precautions in both CF and non-CF patient populations as well as strategies to mitigate these are described, including developing non-face-to-face methods of communicating among people with CF; and “Challenges to Implementation of IP&C Recommendations” (**Section VII**), in which challenges experienced by healthcare personnel and by individuals with CF and their families—as well as strategies to overcome them—are discussed.

#### TABLES, FIGURES, AND RESEARCH AGENDA

Tables are provided to supplement the text. These include (1) the population, intervention, comparison, and outcome (PICO) questions the committee developed for the systematic review; (2) a review of the grading systems used; (3) the species in the *B. cepacia* complex; (4) examples of hand hygiene opportunities for healthcare personnel, people with CF, and their families; (5) indications for use of personal protective equipment by healthcare personnel, people with CF, and their families; (6) strategies to enhance the effectiveness of environmental cleaning in healthcare settings; (7) strategies for CF clinics to minimize risk of transmission of potential pathogens; (8) strategies to minimize the adverse psychosocial impact of isolation precautions; (9) knowledge, attitudes, and practice barriers related to implementing IP&C in CF; and (10) strategies to enhance implementation of IP&C in CF. Two figures are also presented: the age-specific prevalence of

CF pathogens in 2012 in the United States, and the changing prevalence of CF pathogens in the United States from 1988 to 2012.

A research agenda is proposed to address some of the unresolved IP&C issues for the CF community, including, for example (1) the role played by small colony variant *S. aureus*; (2) the frequency of shared strains of CF pathogens, including *P. aeruginosa* and NTM in the United States; (3) the routes of transmission of *M. abscessus*; (4) the role played by specific niches for CF pathogens in the natural environment; (5) continued efforts to define best IP&C practices for CF; (6) continued efforts to assess and overcome challenges to implementation of IP&C; and (7) additional research into the unique needs of healthcare personnel with CF.

#### SUMMARY

In summary, epidemiologic studies have shown that pathogens, other than *Burkholderia* spp., can be transmitted among individuals with CF, resulting in adverse clinical outcomes, including increased morbidity and mortality. The updated guideline is a response to new knowledge and new challenges in both IP&C and CF. **The primary objective of the guideline is to provide recommendations to reduce the risk of transmission and acquisition of CF pathogens by individuals with CF and to provide a more comprehensive understanding of effective strategies to optimize safety for this unique population.**

#### INTRODUCTION

In 2003, the Cystic Fibrosis (CF) Foundation published recommendations for infection prevention and control (IP&C) in an effort to reduce the risk of acquisition and transmission of pathogens among people with CF.<sup>1</sup> However, both IP&C and CF are dynamic disciplines, and during the past decade new knowledge and new challenges necessitated the development of updated IP&C strategies for this unique population.

**1. IP&C experiences in the general population can provide insight into strategies for people with CF.** Numerous evidence-based guidelines for IP&C and clinical practice guidelines have been published since 2003 by the Centers for Disease Control and Prevention (CDC)/Healthcare Infection Control Practices Advisory Committee (HICPAC), the World Health Organization (WHO), and professional societies, including the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA). These guidelines contain relevant recommendations for people with CF (see Table 1 for the most relevant guidelines).<sup>2–13</sup>

In addition, each year the CDC/Advisory Committee on Immunization Practices (ACIP) updates the recommendations for immunizations in children and adults and the recommendations for the prevention of influenza for the upcoming season; these recommendations are published in *Morbidity and Mortality Weekly Report (MMWR)*.<sup>14</sup> Relevant

TABLE 1. Infection Prevention and Control Guidelines Published since 2003

Guideline	Organization	Reference
Guidelines for Environmental Infection Control in Health-Care Facilities, 2003	CDC/HICPAC	2
Guidelines for Preventing Health-Care–Associated Pneumonia, 2003	CDC/HICPAC	3
Guidelines for Preventing the Transmission of <i>Mycobacterium tuberculosis</i> in Health-Care Settings, 2005	CDC/NCHHSTP	4
Management of Multidrug-Resistant Organisms in Health Care Settings, 2006	CDC/HICPAC	5
Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings, 2007	CDC/HICPAC	6
Disinfection and Sterilization in Health-Care Facilities, 2008	CDC/HICPAC	7
Strategies to Prevent Transmission of Methicillin-Resistant <i>Staphylococcus aureus</i> in Acute Care Hospitals, 2008	IDSA/SHEA	8
Guidelines on Hand Hygiene in Healthcare, 2009	WHO	9
Infection Prevention for Outpatient Settings: Minimum Expectations for Safe Care, 2011	CDC/HICPAC	10
Immunization of Health-Care Personnel: Recommendations of the Advisory Committee on Immunization Practices	CDC/ACIP	11
Infection Prevention and Control in Residential Facilities for Pediatric Patients and Their Families, 2013	SHEA	12
Clinical Practice Guideline for Vaccination of the Immunocompromised Host, 2013	IDSA	13

NOTE. ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; HICPAC, Healthcare Infection Control Practices Advisory Committee; HIV, human immunodeficiency virus; IDSA, Infectious Diseases Society of America; NCHHSTP, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; SHEA, Society for Healthcare Epidemiology of America; STD, sexually transmitted diseases; TB, tuberculosis; WHO, World Health Organization.

recommendations from both IP&C guidelines and ACIP recommendations have been integrated into this updated IP&C guideline for people with CF. Furthermore, during the past decade new evidence has led to a renewed emphasis on source containment of potential pathogens, the role played by the contaminated healthcare environment in transmitting infectious agents, and an increased understanding of the importance of implementation science, monitoring adherence, and feedback principles to enhance the effectiveness of IP&C practices as detailed throughout this document.

**2. Experience with emerging pathogens can inform IP&C strategies for CF.** The severe acute respiratory syndrome coronavirus (SARS-CoV) and the 2009 influenza A H1N1 pandemic expanded our understanding of droplet transmission of infectious agents.<sup>6,14,15</sup> While the incidence of healthcare- and community-associated infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) has been decreasing in adults in the United States in recent years,<sup>16</sup> a similar trend has not been observed among children.<sup>17</sup> Additionally, multidrug-resistant gram-negative pathogens continue to emerge and are increasing in healthcare settings,<sup>18</sup> which has heightened the awareness of healthcare personnel and the public of the importance of preventing patient-to-patient transmission of multidrug-resistant organisms (MDROs).<sup>5,19,20</sup>

**3. Changes in the demographic characteristics of the CF population and in the epidemiology of CF pathogens during the past decade have implications for IP&C.** The median predicted life expectancy of people with CF has increased to 41 years of age.<sup>21</sup> In the United States and in many other countries, the number of adults with CF is comparable to or has surpassed the number of children with CF. Newborn

screening for CF is now mandated in all 50 states in the United States. Newer CF pathogens are increasing in prevalence and are associated with increased rates of morbidity and mortality among individuals with CF. Such pathogens include MRSA,<sup>22,23</sup> *Mycobacteria abscessus*,<sup>24</sup> *Burkholderia do-losa*,<sup>25</sup> new species in the *Burkholderia cepacia* complex,<sup>26</sup> epidemic clones of *Pseudomonas aeruginosa* (eg, the Liverpool epidemic strain [LES]),<sup>27–29</sup> and others.<sup>30</sup> Thanks to the increasing use of molecular typing, strains that are shared among people with CF continue to be identified, suggesting that new strategies beyond those recommended in the 2003 Infection Control Guideline for CF are needed to improve the implementation of IP&C practices and to reduce the transmission of CF pathogens.

While extraordinary advances have been made in the treatment of CF, including the use of potentiators and correctors aimed at correcting the abnormal CF transmembrane conductance regulator (CFTR),<sup>31</sup> the CF and the IP&C communities must continue to prioritize minimizing the risk of acquisition and transmission of CF pathogens. To update the 2003 Infection Control Guideline for CF, the CF Foundation assembled an interdisciplinary committee to (1) review existing literature and present new knowledge that served as the basis for the updated IP&C practice recommendations; (2) assess the relevance of existing guidelines and integrate appropriate recommendations, including those from the 2003 Infection Control Guideline for CF; (3) craft updated recommendations; and (4) address strategies to improve implementation of IP&C practices, including education and overcoming challenges to implementation.

The process the committee undertook to complete its tasks,

including the systematic review, is described below. The groups of updated IP&C recommendations are as follows: (I) core recommendations for all people with CF (including following lung or liver transplantation) in all settings; (II) recommendations for microbiology and molecular epidemiology; (III) recommendations for CF clinics and other ambulatory care settings; (IV) recommendations for inpatient settings; (V) recommendations for nonhealthcare settings; (VI) recommendations for healthcare personnel with CF; and (VII) recommendations for the psychosocial and medical impact of IP&C. To facilitate use of the guideline, the relevant sections of “Background Information Supporting the Recommendations” (*Sections I–III*) and strategies to reduce transmission and acquisition of pathogens (*Sections IV–VII*) are provided for each recommendation as supporting rationale.

This guideline is intended for use by all healthcare personnel involved with the care of people with CF and the IP&C teams that support CF care centers in the United States. The recommendations for healthcare settings are intended to be implemented in CF clinics and other ambulatory care areas, in inpatient settings, in diagnostic and therapeutic areas, and during all clinical research activities. The recommendations for nonhealthcare settings presented in this updated guideline are not intended to be enforced by healthcare personnel but instead represent efforts to respond to questions and concerns voiced by people with CF and their caregivers and to provide education about the potential risks associated with various activities or exposures. People with CF and their families and friends will then be better prepared to make informed choices in their personal lives.

## METHODS FOR DOCUMENT DEVELOPMENT

### COMMITTEE STRUCTURE

In March 2011, the CF Foundation requested volunteers to participate in developing an update of the 2003 Infection Control Guideline for CF. The 21-member interdisciplinary committee consisted of 4 infectious disease specialists (all of whom had expertise in IP&C and CF microbiology), 4 pulmonologists, 4 nurses, 1 respiratory therapist, 1 infection preventionist, 3 parents of children with CF, 1 adult with CF, 1 social worker, and 2 CF Foundation staff members (a pulmonologist and a nurse).

In November 2011, the committee assembled and developed the scope of the guidelines by identifying clinical questions to be addressed, using the population, intervention, comparison, and outcome (PICO) format.<sup>32</sup> To evaluate the published evidence for answers to these questions, the CF Foundation commissioned an evidence review from a Johns Hopkins University team under the leadership of an epidemiologist (K.A.R.) with experience in conducting systematic reviews, including those assessing interventions used in the CF population. The PICO questions used to guide the evidence search are presented in Table 2.

### SYSTEMATIC REVIEW PROCESS

For the systematic review, searches of PubMed, Embase, and the Cochrane Central Register of Controlled Studies were conducted by the Johns Hopkins University research team in June 2012. Searches of reference lists for all eligible articles and Cochrane reviews were also completed. Committee members provided additional potentially eligible studies. Studies performed in the CF population were sought preferentially, but studies conducted in other populations considered relevant were also reviewed. Two independent reviewers screened search results for eligible studies. Details about eligible studies were abstracted and a report, including evidence tables and qualitative synthesis, was submitted to the CF Foundation and disseminated to the committee.

Additionally, the Johns Hopkins University research team identified relevant guidelines and Cochrane reviews through searches (completed in August 2012) of the National Guidelines Clearinghouse, United Kingdom CF Trust website, CF Foundation guidelines database, the Cochrane Library, and lists provided by the committee chairs. Details from these sources, including recommendation statements, were abstracted and provided to the committee.

### RESULTS OF THE SYSTEMATIC REVIEW

The search identified 16 eligible articles reporting 15 unique studies. These included 4 before-and-after studies, 4 cross-sectional studies, and 7 nonconcurrent cohort studies, but these studies provided insufficient evidence to use the US Preventive Services Task Force grading system that has been used for other recent CF practice guidelines.<sup>33,34</sup> The systematic review team also abstracted 2,403 recommendation statements from 47 relevant IP&C guidelines. Evidence tables can be obtained from the CF Foundation on request ([resources@cff.org](mailto:resources@cff.org)).

### PROCESS FOR INCLUSION OF RECOMMENDATIONS

Each recommendation from the 2003 Infection Control Guideline for CF was reviewed for continued relevance and modified if clarification was needed or if new data were available. The grade of evidence from the 2003 Infection Control Guideline for CF was retained. Relevant recommendations from other CF practice guidelines were included verbatim. Relevant recommendations from other guidelines developed for non-CF populations by other expert professional organizations, including CDC/HICPAC, SHEA, IDSA, WHO, APIC, and ACIP were also included, and their grade of evidence was retained without a vote by the committee (Table 3).<sup>1,9</sup> New recommendations that had not been published previously were developed by the committee. Inclusion of the recommendations was determined by anonymous voting. At least 80% approval by the committee members (ie, consensus) was set as the threshold for acceptance of new recommendations, relevant recommendations from the 2003 Infection



TABLE 2. Population, Intervention, Comparison, and Outcome (PICO) Clinical Questions Developed for the Guideline for Infection Prevention and Control in Cystic Fibrosis (CF): 2013 Update

**Microbiology**

1. Does identification of **small colony variant *Staphylococcus aureus*** versus not performing identification of small colony variant *S. aureus* affect clinical outcomes of people with CF experiencing exacerbation?

**Transmission: Personal Protective Equipment**

- 2a. What is the evidence for benefit or harm of **people with CF wearing masks** in the healthcare setting versus not wearing masks?
- 2b. What is the evidence for benefit or harm of **healthcare providers wearing masks** versus not wearing masks when caring for people with CF?
- 3a. What is the evidence for benefit or harm of **people with wearing gowns** versus not wearing gowns in healthcare settings?
- 3b. What is the evidence for benefit or harm of **healthcare providers wearing gowns** versus not wearing gowns when caring for people with CF?
- 4a. What is the evidence for benefit or harm of **people with CF wearing gloves** versus not wearing gloves in healthcare settings?
- 4b. What is the evidence for benefit or harm of **healthcare providers wearing gloves** in healthcare setting versus not wearing gloves among people with CF?

**Transmission: Distance for Droplets**

5. What is the evidence that **more than 3 feet** distance between people with CF **versus 3 feet or less** is required to prevent droplet transmission?

**Transmission: Methicillin-Resistant *S. aureus* (MRSA)**

- 6a. What is the evidence that **separation versus nonseparation reduces MRSA transmission from people without CF** who have skin and soft-tissue infection (SSTI) to prevent respiratory tract infection in people with CF?
- 6b. What is the evidence that **separation versus nonseparation of people with CF with MRSA** respiratory tract infections reduces MRSA transmission to others with CF?
- 6c. What is the evidence that **separation versus nonseparation of people with CF with MRSA** respiratory tract infections reduces MRSA transmission and prevents SSTI in people without CF?

**Transmission: Nonhealthcare Settings**

7. What is the evidence that **restriction versus nonrestriction** reduces transmission of CF pathogens in **indoor and/or outdoor nonhealthcare settings** where more than 1 person with CF is present (eg, fund-raising events, cystic fibrosis chapter offices, pharmaceutical company venues, Great Strides)?
- 8a. What is the evidence among people with CF that **restriction versus nonrestriction** reduces transmission of CF pathogens from **leisure activities involving soil and plants** (eg, gardening and lawn care)?
- 8b. What is the evidence that among people with CF **restriction versus nonrestriction** reduces transmission of CF pathogens from **leisure activities involving aquatic settings**, hot tubs, swimming pools, and natural bodies of water?

**Transmission: Animals**

- 9a. What is the evidence that among people with CF **restriction versus nonrestriction** reduces transmission of CF pathogens from **pet therapy**?
- 9b. What is the evidence that among people with CF **restriction versus nonrestriction** reduces transmission of CF pathogens from **personal pets or farm animals**?

**Transmission: Healthcare Personnel with CF**

10. What is the evidence that a healthcare provider with CF should be **restricted versus not restricted** from working with people with CF to prevent **transmission of CF pathogens from a healthcare provider with CF** to his or her patients and vice versa?

**Transmission: Scheduling CF Clinic Visits**

11. What is the evidence that **scheduling CF clinic visits on the basis of pathogen status** (separate clinic times) **versus not scheduling CF clinic visits on the basis of pathogen status** (no separate clinic times) reduces transmission of CF pathogens?

**Cleaning Respiratory Equipment**

- 12a. What is the evidence for cleaning and disinfecting **respiratory equipment** of people with CF **after each use** versus some other frequency for cleaning to prevent contamination and transmission of CF pathogens in the **hospital**?
- 12b. What is the evidence for cleaning and disinfecting **respiratory equipment** of people with CF **after each use** versus some other frequency for cleaning to prevent contamination and transmission of CF pathogens in the **home**?
- 12c. What is the evidence for cleaning and disinfecting **respiratory equipment** of people with CF with one **method** versus another method for cleaning to prevent contamination and transmission of CF pathogens in the **hospital**?
- 12d. What is the evidence for cleaning and disinfecting **respiratory equipment** of people with CF with one **method** versus another method for cleaning to prevent contamination and transmission of CF pathogens in the **home**?

Control Guideline for CF, or relevant recommendations from other guidelines developed for non-CF populations.

The CDC/HICPAC guidelines and the WHO hand hygiene guideline cited in this document used a unique HICPAC grad-

ing system that was used for HICPAC guidelines published before 2009. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system<sup>35</sup> was adopted for use by CDC/HICPAC/ACIP in 2009<sup>36,37</sup> and is

TABLE 3. Grading Systems Used in the Updated Infection Prevention and Control (IP&amp;C) Guidelines for Cystic Fibrosis (CF), 2013

Source of recommendation	Grading strategy	Comments
2003 Infection Control Guideline for CF <sup>1</sup> <b>and</b> CDC HICPAC guidelines <sup>2,3,5-7,10</sup> <b>and</b> WHO Guidelines on Hand Hygiene in Healthcare, 2009 <sup>9</sup>	<i>Category IA</i>	Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies
	<i>Category IB</i>	Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale
	<i>Category IC</i>	Required for implementation, as mandated by federal and/or state regulation or standard
	<i>Category II</i>	Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale
	<i>No recommendation</i>	<i>Unresolved issue</i> ; <sup>a</sup> practices for which insufficient evidence or no consensus regarding efficacy exist
Systematic review	Not applicable	Limited evidence was found by the systematic review conducted for the 2013 IP&C guideline; thus, the grading of evidence was not used
2013 Updated IP&C Guideline for CF	% agreement Certainty: low	≥80% agreed with statement by anonymous voting <80% agreed with statement by anonymous voting and thus insufficient evidence exists to recommend for or against

NOTE. CDC, Centers for Disease Control and Prevention; HICPAC, Healthcare Infection Control Practices Advisory Committee; WHO, World Health Organization.

<sup>a</sup> The *unresolved issue* category was not included in the 2009 WHO hand hygiene guidelines.

used by more than 70 organizations worldwide. However, the GRADE system can result in IP&C guidelines that are more likely to include expert consensus compared with guidelines developed for specific treatment regimens that have randomized clinical trials as their evidence base. Limitations of the GRADE system that may impact developing IP&C guidelines include (1) questions for which little or no evidence is available on which to base a recommendation, (2) little or no requirement for evidence given the high probability of a recommendation's success, and (3) difficulty assessing the strength of evidence from studies performed in varying populations with varying study designs.<sup>37,38</sup> The evidence base for this updated guideline had similar limitations; thus, the recommendations in this guideline are often based on expert consensus.

#### EXTERNAL REVIEW

In May 2013, the CF Foundation made a draft of the updated guideline available for comment to the CF community, including the teams at CF care centers and people with CF. Infection preventionists and healthcare epidemiologists were also notified of the availability of the document for comment. All comments were considered by the committee, and the recommendations and background information were revised as appropriate. This guideline was reviewed and endorsed by SHEA and by APIC.

## UPDATED RECOMMENDATIONS FOR IP&C IN CF

### I. CORE RECOMMENDATIONS

The CF Foundation recommends implementation of the following core IP&C recommendations to minimize the risk of transmission and acquisition of pathogens among *all* people with CF, including following lung or liver transplantation, in all settings.

#### *Education/Adherence Monitoring for Healthcare Personnel, People with CF, and Families*

1. The CF Foundation recommends that all healthcare personnel caring for people with CF (eg, the CF care team, inpatient staff, environmental services staff, research staff, and staff in diagnostic and therapeutic areas, including pulmonary function test [PFT] laboratories, radiology, phlebotomy, operating room, and physical therapy) receive education regarding IP&C for CF, using principles of adult learning. Education should be repeated at intervals each center deems appropriate.

*Source of supporting evidence:* 2003 CF IP&C guideline, *Category II*; 2006 MDRO guideline, *Category IB*; 2007 transmission guideline, *Category IB*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.2; IV.B

2. The CF Foundation recommends that the CF care team develop strategies to monitor adherence to IP&C practices by healthcare personnel and provide feedback. Feedback to the CF care team includes immediate feedback to an individual when a lapse in practice is observed and feedback to the entire CF care team of trends of overall adherence rates at regular intervals (eg, quarterly) on the basis of consistency of practices.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB; 2006 MDRO guideline, Category IB; 2007 transmission guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.B; IV.E.1

3. The CF Foundation recommends that all people with CF and their families receive education regarding IP&C for CF, using age appropriate tools and reading/language level appropriate to the target audience. Involve people with CF and their families in the development of educational programs and implementation of recommended practices. Education should be repeated at intervals each center deems appropriate.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.B

#### **Partnering with Institutional IP&C Teams**

4. The CF Foundation recommends that CF care teams collaborate with their institutional IP&C teams to implement the recommendations in this guideline.

*Source of supporting evidence:* 2006 MDRO guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* I.D; IV.B; IV.E.1, 2; IV.F

5. The CF Foundation recommends that CF care teams collaborate with their institutional IP&C teams to develop protocols, checklists, and audits to standardize implementation of practices for the following:

- a. Single-patient-use, disposable items
- b. Cleaning and disinfecting multiuse items (eg, patient care equipment, oximeters, iPads and similar tablets, and computers)
- c. Cleaning and disinfecting surfaces in the healthcare environment (eg, CF clinics, PFT rooms, hospital rooms, and sinks and showers)

*Source of supporting evidence:* 2008 disinfection and sterilization guideline, Category II; <http://www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html>

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.2; IV.E.2; IV.F.6, 7

6. The CF Foundation recommends ensuring that dust containment during renovation and construction and water-

leak remediation policies and practices are followed according to institutional and national guidelines in all ambulatory care areas and inpatient settings where people with CF receive care.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB/IC; 2003 CDC environmental guideline, Category IB/IC

**2013 IP&C guideline consensus: 100%**

*Sections in the text:* III.D.3; IV.H

7. The CF Foundation recommends that healthcare personnel assume that *all* people with CF could have pathogens in respiratory tract secretions that are transmissible to other people with CF.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IA

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.F.1; IV.G

#### **Practices for Healthcare Personnel**

8. The CF Foundation recommends that all healthcare facilities caring for people with CF ensure ready availability of alcohol-based hand rub or antimicrobial soap and water in all patient rooms, PFT rooms, and waiting areas.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IA; 2009 WHO and 2002 hand hygiene guidelines, Category IA

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.B; IV.F.3

9. The CF Foundation recommends that healthcare personnel perform *hand hygiene* (either using alcohol-based hand rub or washing hands with antimicrobial soap and water), as per CDC and WHO guidelines, in the following clinical situations:

- a. Before entering the room and when leaving the room of any patient
- b. Before and after direct contact with any patient
- c. Before putting gloves on and after removing gloves, for both sterile and nonsterile procedures
- d. After contact with patient's skin, mucous membranes, respiratory secretions, or other body fluids
- e. After contact with inanimate objects (including medical equipment) in the vicinity of the patient that may be potentially contaminated with respiratory secretions

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IA; 2009 WHO and 2002 hand hygiene guidelines, Category IA

*Sections in the text:* IV.C; IV.F.3

10. The CF Foundation recommends that healthcare personnel should not wear artificial fingernails or nail extenders when having direct contact with people with CF.

Source of supporting evidence: 2002 HICPAC hand hygiene, Category IA for high-risk patients; 2009 WHO hand hygiene, Category IA for all patients  
Sections in the text: IV.C

11. The CF Foundation recommends that healthcare personnel should disinfect their stethoscopes before and after use on each patient in accordance with institutional IP&C policies. Stethoscopes that remain in the patient's room and are dedicated for use only for that patient do not need to be disinfected before and after use.

Source of supporting evidence: 2006 MDRO guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

Sections in the text: III.D.2; IV.E.2; IV.F.7; IV.G

12. The CF Foundation recommends that healthcare personnel caring for people with CF should *not* be routinely screened for MRSA colonization unless they are epidemiologically linked to a cluster of MRSA infections in accordance with institutional IP&C policies and national guidelines.

Source of supporting evidence: 2006 MDRO guideline, Category IB

Sections in the text: III.B.2

### Isolation Precautions

13. The CF Foundation recommends that all healthcare personnel implement *Contact Precautions* (ie, wear a gown and gloves) when caring for all people with CF regardless of respiratory tract culture results, in ambulatory and inpatient settings.

Source of supporting evidence: 2007 transmission guideline, Category IB/IC

**2013 CF IP&C guideline consensus: 100%**

Sections in the text: II.A; IV.D.1; IV.G

14. The CF Foundation does not recommend that healthcare personnel wear a mask *routinely* when caring for people with CF. However, the CF Foundation recommends mask use per CDC guidelines, as follows:

- Surgical (procedure, isolation) masks are worn by healthcare personnel caring for any patient under *Droplet Precautions* with suspected or confirmed pathogens that are transmitted by the droplet route (eg, adenovirus, rhinovirus, influenza virus, or *Mycoplasma pneumoniae*).
- Masks and eye protection should be worn by healthcare personnel if splashes or sprays of respiratory tract secretions are anticipated as per *Standard Precautions*.
- N-95 respirators (masks) or powered air-purifying respirators (PAPRs) are worn by healthcare personnel caring for any patient under *Airborne Precautions* (in an airborne infection isolation room [AIIR]) for suspected or confirmed infection with *Mycobacterium tuberculosis*.

Source of supporting evidence: 2003 CF IP&C guideline, Category IA; 2007 transmission guideline, Category IB; 2007 transmission guideline, Category IB; 2005 tuberculosis (TB) transmission guideline

Sections in the text: II.C; IV.D.2; IV.G

15. The CF Foundation recommends placing people with CF who are acid-fast bacilli (AFB) smear positive *for the first time* under *Airborne Precautions* (AIIR requirements: negative-pressure single room, more than 12 air exchanges per hour, air exhausted to the outside) in ambulatory and inpatient settings until *M. tuberculosis* infection has been excluded. Alternatively, in geographic locations with a very low incidence of TB, a risk assessment that includes the likelihood of exposure to individuals with TB (eg, travel or visitors from high-prevalence areas) may be used to guide the use of AIIRs. Consult with institutional IP&C staff and/or infectious disease physicians.

Source of supporting evidence: 2003 CF IP&C guideline, Category IA; 2005 *M. tuberculosis* transmission guideline; 2007 transmission guideline, Category IA/IC

**2013 CF IP&C guideline consensus: 100%**

Sections in the text: IV.D.2; IV.G

16. The CF Foundation concludes that there is insufficient evidence at the time of publication of this document for or against placing people with CF who are infected with NTM under *Airborne Precautions*.

**2013 CF IP&C guideline, certainty: low**

Sections in the text: III.A.5; III.D.2; IV.G

### Practices by People with CF and Family Members/Friends

17. The CF Foundation recommends that all people with CF, *regardless of their respiratory tract culture results*, be separated by at least 6 feet (2 meters) from other people with CF in all settings, to reduce the risk of droplet transmission of CF pathogens. This does not apply to members of the same household.

**2013 CF IP&C guideline consensus: 100%**

Sections in the text: II.A; II.B; II.C; III.D.2; IV.F.1, 2

18. The CF Foundation recommends that all people with CF and their family members/friends perform hand hygiene (with either alcohol-based hand rub or antimicrobial soap and water) when there is potential for contamination of hands with pathogens, such as the following:

- Entering and exiting CF clinics, clinic exam rooms, or hospital rooms
- Hands become contaminated with respiratory secretions (eg, after coughing or performing PFTs or chest physiotherapy)

Source of supporting evidence: 2003 CF IP&C guideline, Category IA

**2013 CF IP&C guideline consensus: 100%**

Sections in the text: II.A; IV.C; IV.F.3

19. The CF Foundation does *not* recommend that people with CF wear gowns or gloves in CF clinics, in other ambulatory healthcare settings, or while hospitalized.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.C; IV.D.1

20. The CF Foundation recommends that people with CF be instructed to follow *Respiratory Hygiene* practices to contain their secretions when coughing or sneezing (ie, cough into a tissue, immediately discard soiled tissue into a trash receptacle, and perform hand hygiene after disposing of soiled tissues). A covered trash receptacle with a foot pedal is preferred.

*Source of supporting evidence:* 2003 CF IP&C guideline,

*Category II*; 2007 transmission guideline, *Category IB*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.A; IV.D.2; IV.F.4

21. The CF Foundation recommends that all people with CF wear a surgical (procedure, isolation) mask when in a healthcare facility to reduce the risk of transmission or acquisition of CF pathogens. Masks should be worn throughout the facility, including in restrooms. Masks should *not* be worn during pulmonary function testing, in the clinic exam room, or in the patient's hospital room. If the optimal size mask is not available (eg, for small infants), use the smallest mask available. If a mask is not tolerated by an individual with CF who is having respiratory distress, encourage that person to follow *Respiratory Hygiene* practices. Masks should be changed when wet.

*Source of supporting evidence:* 2007 transmission guideline,

*Category IB*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; IV.F.4

22. The CF Foundation recommends that all people with CF who *do not* live in the same household avoid activities and risk factors that are associated with transmission of CF pathogens in nonhealthcare and healthcare settings, including the following:

- a. Social contact between people with CF
- b. Physical contact between people with CF (eg, handshakes, kissing, and intimate contact)
- c. Car rides with another person with CF
- d. Sharing hotel rooms with another person with CF
- e. Fitness class with another person with CF

Activities that all people with CF, including those who live in same household, should avoid include the following:

- a. Sharing personal items (eg, toothbrush and drinking utensils) with another person with CF
- b. Sharing respiratory therapy equipment

*Source of supporting evidence:* 2003 CF IP&C guideline,

*Category IA*; 2013 residential facility guideline

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.A.1; IV.I

23. The CF Foundation recommends that

- a. Tap water or well water that meets local public health standards, distilled water, or bottled water may be used by people with CF
  - i. For *drinking*
  - ii. For *bathing*
  - iii. For *cleaning* nebulizers and other respiratory equipment (eg, airway clearance devices, spacers, and neti pots) if followed by *disinfection*
  - iv. For the water needed for *heat disinfection* (eg, boiling, microwaving, and steam sterilizing)
- b. Only *sterile* water be used for nasal rinses (eg, neti pots), filling of humidifier reservoirs, and as a final rinse of respiratory equipment (eg, after cold disinfection)

**2013 IP&C guideline consensus: 100%**

*Sections in the text:* III.D.1; III.D.2; IV.E.3; IV.E.4

### *Immunizations/Influenza Chemoprophylaxis*

24. The CF Foundation recommends that, as per CDC/ACIP recommendations, all healthcare personnel (unless there is a medical contraindication to immunization) should be immunized or have evidence of immunity to mumps, measles, rubella, varicella, pertussis (Tdap), and hepatitis B and receive an annual influenza immunization.

*Source of supporting evidence:* MMWR 2013;62(RR-07):1–

43; <http://www.cdc.gov/vaccines/schedules/index.html>

*Sections in the text:* IV.I.5

25. The CF Foundation recommends that, as per CDC/ACIP recommendations, all people with CF and their family members/close contacts receive recommended vaccines at the recommended schedule, age, dose, and route of administration unless there is a medical contraindication.

*Source of supporting evidence:* MMWR 2013;62(RR-07):1–

43; <http://www.cdc.gov/vaccines/schedules/index.html>

*Sections in the text:* IV.I.5

26. The CF Foundation recommends use of antiviral chemoprophylaxis or treatment (eg, oseltamivir) for prevention or treatment of influenza according to ACIP recommendations.

*Source of supporting evidence:* 2003 CF IP&C guideline, *Cat-*

*egory 1A*; <http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm> (2012–2013 season)

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.I.5

### *Research Settings*

27. The CF Foundation recommends that for all research activities, people with CF, their family members/friends, and healthcare personnel follow relevant IP&C recommendations for that healthcare setting.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.A

## II. RECOMMENDATIONS FOR MICROBIOLOGY AND MOLECULAR EPIDEMIOLOGY

In addition to the microbiology recommendations for processing CF respiratory specimens described in the 2003 Infection Control Guideline for CF, the CF Foundation recommends implementation of the following recommendations:

### Review Center-Specific Microbiology Data

28. The CF Foundation recommends that all CF centers obtain and review center-specific quarterly surveillance reports (eg, data from the local clinical microbiology laboratory or the CF Foundation Patient Registry) of the incidence and prevalence of respiratory tract pathogens at their centers. This review should be conducted in collaboration with institutional IP&C teams and microbiology laboratory directors.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB; 2006 MDRO guideline, Category IB  
**2013 CF IP&C guideline consensus: 100%**  
*Sections in the text:* I.D; IV.F.1

### Molecular Typing

29. The CF Foundation recommends that CF isolates of *Burkholderia* spp. be sent to the laboratory at the University of Michigan (US) for confirmation of identification, speciation, and molecular typing, as follows:

- a. All initial isolates from every patient
- b. At least 1 isolate per patient per year
- c. Any isolates suspected of being associated with transmission or an outbreak
- d. Any other nonfermenting gram-negative organism for which species identification remains equivocal after routine analysis should be sent for confirmation of identification

CF Foundation *Burkholderia cepacia* Research Laboratory and Repository  
 University of Michigan  
 8323 MSRB III, SPC 5646  
 1150 West Medical Center Drive  
 Ann Arbor, MI 48109-0646  
 Tel: 734-936-9767; fax: 734-764-4279; e-mail: jlipuma@umich.edu

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB  
**2013 CF IP&C guideline consensus: 100%**  
*Sections in the text:* I.B; III.A.1

30. The CF Foundation recommends that molecular typing of *B. cepacia* complex isolates and other microorganisms (eg, *P. aeruginosa* and NTM) be performed when epidemiologically indicated (eg, suspected patient-to-patient transmission).

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IA; 2006 MDRO guideline, Category IB  
**2013 CF IP&C guideline consensus: 100%**  
*Sections in the text:* I.B; I.D; III.A

31. The CF Foundation recommends that molecular typing be performed using an appropriate genotyping method (eg, pulsed-field gel electrophoresis, random-amplified polymorphic DNA polymerase chain reaction [PCR], repetitive sequence-based PCR, or multilocus sequence typing).

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IA; 2006 MDRO guideline, Category IB  
**2013 CF IP&C guideline consensus: 100%**  
*Sections in the text:* I.B; III.A.2; III.A.4; III.A.5

### Surveillance

32. The CF Foundation and European CF Society (ECFS) recommend that screening cultures for NTM should be performed annually in individuals with a stable clinical course. Culture and smears for AFB from sputum should be used for NTM screening.

In the absence of clinical features suggestive of NTM pulmonary disease, individuals who are not capable of spontaneously producing sputum do not require screening cultures for NTM. The CF Foundation and ECFS recommend against the use of oropharyngeal swabs for NTM screening.

*Source of supporting evidence:* 2013 NTM in CF guideline  
**2013 IP&C guideline consensus: 100%**  
*Sections in the text:* I.C.5; III.A.5

33. The CF Foundation concludes that there is insufficient evidence at the time of publication of this document to recommend criteria by which to consider a person with CF who previously had *Burkholderia* species isolated from respiratory tract cultures to be *Burkholderia*-free.

**2013 IP&C guideline, certainty: low**  
*Sections in the text:* IV.F.1

## III. RECOMMENDATIONS FOR CF CLINICS AND OTHER AMBULATORY CARE SETTINGS

In addition to the core recommendations, the CF Foundation recommends implementing the following recommendations in CF clinics and other ambulatory care areas, including those clinics where people with CF who have undergone lung or liver transplantation are followed.

### Scheduling in CF Clinics

34. The CF Foundation recommends that CF clinics schedule and manage people with CF in ways to minimize time in common waiting areas. Such strategies include the following:

- a. Stagger clinic schedule
- b. Place people with CF *regardless of their respiratory culture results* in an exam room immediately on arrival to the clinic
- c. Use a pager system or personal cell phone to alert people with CF that an exam room is available
- d. Keep a person with CF in one exam room while the CF care team rotates through the exam room

- e. Do not share common items (eg, clinic computer and toys), and request that people with CF bring their own recreational items to clinic appointments

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; III.D.2; IV.F.1, 2, 7

35. The CF Foundation recommends that infants under 2 years of age be separated from other people with CF in CF clinics until adequate infection control education has been provided to and is understood by the caregivers.

*Source of supporting evidence:* 2009 CF Foundation guideline Management of Infants with CF Consensus, *certainty: low; benefit: moderate*

*Sections in the text:* II; III.A; IV.B; IV.F.1, 2, 7

36. The CF Foundation recommends that all newly diagnosed people with CF be separated from other people with CF in CF clinics until adequate IP&C education has been provided to and is understood by newly diagnosed individuals and their caregivers.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; III.A; IV.B; IV.F.1, 2

37. The CF Foundation concludes that there is insufficient evidence at the time of publication of this document for or against *routinely* scheduling CF clinics *on the basis of specific pathogens* isolated from respiratory tract cultures.

**2013 CF IP&C guideline, certainty: low**

*Sections in the text:* III.A; IV.F.1

### ***Pulmonary Function Testing***

38. The CF Foundation recommends that PFTs be performed in one of the following ways:

- In the exam room at the beginning of the clinic visit
- In a negative-pressure room (AIIR)
- In a PFT laboratory with either portable or integrated HEPA filters
- In a PFT laboratory without HEPA filtration, allowing 30 minutes to elapse before the next person with CF enters the PFT laboratory

**2013 IP&C guideline consensus: 100%**

*Sections in the text:* II.E; III.D.2; IV.A; IV.F.6

### ***Environmental Practices***

39. The CF Foundation recommends that exam rooms be cleaned and disinfected between patients using a 1-step process and Environmental Protection Agency (EPA)–registered hospital-grade disinfectant/detergent designed for house-keeping in accordance with institutional IP&C policies.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.2; IV.F.7

### ***Designing a New CF Clinic***

40. The CF Foundation recommends that the leadership staff of CF centers collaborate with the institutional IP&C and planning design and construction departments when designing a new CF clinic to ensure a design that includes the following:

- Provision for management of people with CF who require *Airborne Precautions*
- Appropriate number of exam rooms
- Single-person restrooms
- Adequate space for personal protective equipment (eg, masks, gowns, and gloves) *at the point of use*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II.E; III.D.2; IV.F; IV.G

## **IV. RECOMMENDATIONS FOR INPATIENT SETTINGS**

In addition to the core recommendations, the CF Foundation recommends implementing the following recommendations in inpatient settings, including those units where people with CF who have undergone lung or liver transplantation are located.

### ***Room Placement***

41. The CF Foundation recommends that people with CF be placed in a single-patient room. Only people with CF who live in the same household may share a hospital room.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II; 2006 MDRO guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; IV.G

42. The CF Foundation recommends placing people with CF who are solid-organ transplant recipients in a single-patient room in accordance with institutional policy and national guidelines. There is insufficient evidence to recommend for or against *Protective Environment* (ie, positive pressure room and HEPA filtration) for solid-organ recipients.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II; 2007 transmission guideline, *no recommendation, unresolved issue*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; IV.G

### ***Practices for People with CF and Their Families***

43. The CF Foundation recommends evaluating people with CF on a case-by-case basis in accordance with institutional IP&C policies for participation in activities outside the

hospital room (eg, walking in the hallway, going to the playroom, physical therapy, exercise room, or school room) *only when no other person with CF is present* and under the supervision of a trained staff member.

Considerations include the capability of a person with CF to contain his or her respiratory tract secretions, age, endemic levels of pathogens in an individual center, and adherence to the following practices:

- a. Perform hand hygiene and put on a mask immediately before leaving patient rooms
- b. After a person with CF has left a hospital activity room, clean surfaces and touched items with an EPA-registered hospital disinfectant/detergent

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB/II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; IV.E.1; VI

44. The CF Foundation recommends that all people with CF perform all respiratory interventions (eg, aerosol therapy, airway clearance, and collection of respiratory tract cultures) in the patients' rooms. If 2 people with CF who live in the same household are sharing a room, these procedures should be performed when the second person is not in the room, whenever possible.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; II.C; II.D; II.E; III.D.2

45. The CF Foundation recommends that airway clearance devices (eg, flutter, acapella, pep device, and therapy vest) be for single-patient use only, in accordance with institutional IP&C policies.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.2; IV.A; IV.G

46. The CF Foundation recommends following institutional IP&C policies for the use of masks, gowns, and gloves by individuals who are visiting hospitalized people with CF.

*Source of supporting evidence:* 2007 transmission guideline, no recommendation, unresolved issue

**2013 IP&C guideline consensus: 100%**

*Sections in the text:* II; IV.D.1; IV.D.2

### Care of Nebulizers in the Hospital

47. The CF Foundation recommends the following:

- a. Nebulizers are for single-patient use only
- b. Aseptic technique is always followed when handling the nebulizer and dispensing medications
- c. Single-dose vials of medication used in nebulizers are

always preferred

- d. Handheld *disposable* nebulizers are managed as follows:
  - i. After each use, rinse out residual volume with sterile water and wipe mask/mouthpiece with an alcohol pad
  - ii. Discard the nebulizer every 24 hours
- e. Handheld *reusable* nebulizers (eg, home equipment) are managed as follows:
  - i. After each use, clean, disinfect, rinse with sterile water (if applicable, following cold disinfection method), and air dry away from sink
  - ii. After each use, the nebulizer can be reprocessed (eg, by steam sterilization) if the reprocessing is performed according to the manufacturer's instructions and the CF Foundation recommendations for home care (rec. 59) and if the nebulizer can be returned to the patient in time for the next treatment

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II; 2003 pneumonia guidelines, Category IB; 2008 sterilization and disinfection guidelines, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.2; IV.E.2

### Animals

48. The CF Foundation recommends that people with CF can participate in animal-assisted ("pet") therapy in accordance with institutional policies.

*Source of supporting evidence:* 2003 environmental guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.C

### Designing New Inpatient Facilities

49. The CF Foundation recommends that the leadership staff of CF centers collaborate with the institutional IP&C and the planning, design, and construction departments when designing a new inpatient unit to ensure a design that

- a. Provides an adequate number of single-patient rooms to care for people with CF
- b. Includes a provision for people with CF who require possible *Airborne Precautions*
- c. Provides access to exercise during hospitalization (eg, adequate space for exercise equipment)
- d. Provides adequate space for personal protective equipment (eg, masks, gowns, and gloves) *at the point of use*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* I.C.5; II.D; IV.D.1; IV.D.2; IV.G; VI

### V. RECOMMENDATIONS FOR NONHEALTHCARE SETTINGS

In addition to the core recommendations, the CF Foundation recommends implementing the following recommendations in nonhealthcare settings.



### Families with More than 1 Person with CF

50. The CF Foundation recommends that it is preferable that people with CF who live in the same household perform airway clearance with only 1 person with CF in the room during treatment.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; II.C; II.D; II.E

### Events and Activities

51. The CF Foundation recommends against CF-specific camps or CF-specific educational retreats for groups of people with CF. Only 1 individual with CF should attend any camp or educational retreat unless they live in the same household.

However, family members who do not have CF may attend educational retreats. People with CF are encouraged to participate in camps and sports with non-CF individuals.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category IB

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; III.A; IV.I.1

52. People with CF and their parents or legal guardians are *not* obligated to disclose the diagnosis of CF or the results of respiratory tract cultures to school or day care personnel. However, the CF Foundation recommends disclosure so that school or day care personnel can be made aware of the importance of IP&C principles and practices for the protection of students with CF and can make the recommended accommodations. Such information must be maintained as confidential medical information unless the person with CF and/or parent or legal guardian choose to make this information known.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 95%**

*Sections in the text:* II; III.A; IV.I.4

53. The CF Foundation recommends that people with CF attending the same day care and/or school should *not* be in the same room at the same time unless they live in the same household. The CF Foundation recommends education of day care/school personnel on the principles of IP&C for CF so they can work with people with CF and/or parents or legal guardians to develop strategies to minimize contact *between* people with CF (eg, assignment to separate classrooms and separation during other scheduled common activities, including lunch, physical education, and recess).

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.I.4

54. The CF Foundation recommends that only 1 person with CF attend CF Foundation–sponsored, healthcare-sponsored, or CF center–sponsored *indoor events* (eg, CF Education Days) unless they live in the same household, to reduce the risk of person-to-person transmission of CF pathogens.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; III.A; IV.I.2

55. The CF Foundation recommends developing and utilizing alternative CF education programs, (eg, videotapes, video conferencing, CD-ROM web-based learning, and apps) that do not require face-to-face meetings among people with CF.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.B; IV.I.1; IV.I.2; VI

56. The CF Foundation recommends that people with CF can attend CF Foundation–sponsored, healthcare-sponsored, or CF center–sponsored *outdoor events* (eg, Great Strides) providing they maintain a distance of at least 6 feet (2 meters) from others with CF.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* II; III.A; IV.I.3

### MRSA

57. The CF Foundation recommends that people with CF should avoid direct contact with people with skin and soft-tissue infections caused by MRSA *unless* wounds are covered, hand hygiene is performed frequently, personal items (eg, towels) are not shared, sports equipment is cleaned between use, and cleaning protocols for environmental surfaces are established to reduce the risk of MRSA transmission.

*Source of supporting evidence:* CDC guidance (<http://www.cdc.gov/mrsa/prevent/personal.html>)

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.B.2

58. The CF Foundation recommends that people with CF and respiratory cultures positive for MRSA should *not* be restricted from contact with people without CF in congregate settings (eg, sports teams, classrooms, and the workplace) if the person with CF performs appropriate hand and respiratory hygiene.

*Source of supporting evidence:* CDC guidance (<http://www.cdc.gov/mrsa/prevent/personal.html>)

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.A.4; III.B.2

### Nebulizers: Cleaning and Disinfecting

59. The CF Foundation recommends that the following steps be performed for nebulizers used in the home as soon as possible after each use:

- a. *Clean* the nebulizer parts with dish detergent soap and water
- b. *Disinfect* the nebulizer parts using *one* of the following methods:

*Heat methods:*

- a. Place in boiling water and boil for 5 minutes
- b. Place in a microwave-safe receptacle submerged in water and microwave for 5 minutes
- c. Use a dishwasher if the water is more than or equal to 70°C or 158°F for 30 minutes
- d. Use an electric steam sterilizer

*Cold methods:*

- a. Soak in 70% isopropyl alcohol for 5 minutes
- b. Soak in 3% hydrogen peroxide for 30 minutes
  - i. Rinse off the cold-method disinfectant using sterile water, not tap water; the *final rinse* must be with sterile or filtered (less than or equal to 0.2-micron filter) water
  - ii. Air dry the nebulizer parts before storage

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.1; IV.E.3

60. The CF Foundation recommends that nebulizers used in the home should *not* be disinfected with acetic acid (vinegar), bleach solutions, or benzalkonium chloride (eg, “Control III”).

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.E.3

### *Leisure Activities*

61. The CF Foundation recommends that people with CF should limit prolonged and/or repeated exposure to activities that generate dust from soil and organic matter (eg, gardening and lawn mowing) to decrease exposure to potential soilborne pathogens (eg, *Burkholderia* spp. and *Aspergillus* spp.).

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* IV.D.1

62. The CF Foundation recommends that people with CF should avoid exposure to construction and renovation activities that generate dust to decrease exposure to potential pathogens (eg, *Aspergillus* spp.).

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.1; III.D.3

63. The CF Foundation recommends that people with CF can swim in pools or water parks with adequate disinfection (eg, chlorination).

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.1

64. The CF Foundation recommends that people with CF avoid activities in hot tubs, whirlpool spas, and stagnant water.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.D.1

65. There is insufficient evidence at the time of publication of this document for the CF Foundation to recommend for or against people with CF avoiding activities in natural bodies of water that are not stagnant (eg, ocean, ponds, and hot springs).

**2013 CF IP&C guideline, certainty: low**

*Sections in the text:* III.D.1

### *Contact with Pets or Farm Animals*

66. The CF Foundation recommends that people with CF perform hand hygiene after changing the litter, handling feces, cleaning and disinfecting the cages or fish tanks of their pets, or interacting with farm animals.

*Source of supporting evidence:* <http://www.cdc.gov/healthypets/>

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.C

67. The CF Foundation recommends that people with CF avoid cleaning stalls, pens, or coops.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.C

## VI. RECOMMENDATIONS FOR HEALTHCARE PERSONNEL WITH CF

In addition to the core recommendations, the CF Foundation recommends implementing the following recommendations for healthcare personnel with CF.

68. The CF Foundation recommends that healthcare personnel with CF should not provide care for other people with CF.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III.A; V

69. The CF Foundation recommends that people with CF interested in a career in healthcare receive counseling from their CF care team regarding specialty areas wherein job duties minimize the risk of transmission or acquisition of potential pathogens.

*Source of supporting evidence:* 2003 CF IP&C guideline, Category II

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text:* III; V

70. The CF Foundation recommends that healthcare personnel with CF consider informing their employers' workforce health and safety department about their diagnosis of CF to ensure that job duties are assigned and care practices

are adopted that minimize the risk of acquisition or transmission of potential pathogens. This disclosure is legally required to be kept confidential.

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: V*

71. The CF Foundation recommends that when it is known that a healthcare provider with or without CF is infected/colonized with MRSA, work assignments should be made according to local hospital policy.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: V*

72. The CF Foundation recommends that healthcare personnel with CF be assigned to care for patients without CF on a case-by-case basis, considering health- and behavior-related factors, such as

- a. Frequency and severity of coughing episodes, quantity of sputum production during these episodes, and ability to contain respiratory tract secretions;
- b. Ability to use barrier precautions and adhere to IP&C guidelines, Centers for Medicare & Medicaid Services, HICPAC, and CDC guidelines; and
- c. Risk of transmission of pathogens by healthcare personnel with CF in the context of specific job duties.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: III.A; V*

## VII. RECOMMENDATIONS FOR PSYCHOSOCIAL AND MEDICAL IMPACT OF IP&C

The CF Foundation recommends implementing the following recommendations to reduce the psychosocial impact of IP&C for people with CF, their families, and healthcare personnel.

73. The CF Foundation recommends educating, when appropriate, friends, teachers, employers, and coworkers about the rationale for the IP&C recommendations.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: IV.B; VI*

74. The CF Foundation recommends identifying CF center-specific concerns for the potential psychosocial impact of the IP&C guideline for people with CF in the hospital, clinic, community, school, and home and strategies, *including an available counselor*, to minimize the negative impact.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: VI*

75. The CF Foundation recommends that the CF care team inform people with CF and their parents or legal guardians of their microbiologic status. People with CF and their parents or legal guardians will then determine whom they will inform.

*Source of supporting evidence: 2003 IP&C guideline, Category II*

**2013 IP&C guideline consensus: 100%**

*Sections in the text: IV.I.1; IV.I.4; VI*

76. The CF Foundation recommends collaboration with the child life staff to ensure individualized programs consistent with the recommended IP&C guidelines.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: IV.B; VI*

77. The CF Foundation recommends making accommodations (eg, providing entertainment, enhancing communication with the outside world, facilitating visits with non-CF individuals, and adapting child life programs) to relieve the psychosocial stress of inpatient and outpatient IP&C guidelines without placing people with CF at risk for transmission or acquisition of pathogens.

*Source of supporting evidence: 2003 CF IP&C guideline, Category II*

**2013 CF IP&C guideline consensus: 100%**

*Sections in the text: VI*

## BACKGROUND INFORMATION SUPPORTING THE RECOMMENDATIONS

### I. CF MICROBIOLOGY AND MOLECULAR TYPING

#### I.A. General Microbiology Methods

The 2003 Infection Control Guideline for CF provided detailed recommendations for obtaining and processing CF respiratory tract specimens that were endorsed by the American Society for Microbiology and the National Committee for Clinical Laboratory Standards (now the Clinical and Laboratory Standards Institute).<sup>1</sup> Others have supported these recommendations.<sup>39,40</sup> Furthermore, review of the protocols of clinical microbiology laboratories in the United States obtained in 2003–2004 demonstrated excellent adherence to the 2003 Infection Control Guideline for CF recommendations for processing CF specimens.<sup>41</sup> Thus, the majority of clinical laboratories processing the CF respiratory tract specimens have standardized their techniques, use appropriate selective media and prolonged incubation, and identify gram-negative organisms to the species level. The CF Foundation recommends continued use of the methods described in the 2003 Infection Control Guideline for CF for *when to perform* respiratory tract cultures, *how to transport* specimens, and the use of *selective media*.<sup>1</sup> A detailed description of processing lower respiratory tract specimens for NTM will be provided

in a joint CF Foundation and ECFS guideline (B.C.M., written personal communication, April 2013).

The committee reviewed the following microbiology topics but agreed not to develop revised recommendations in the updated guidelines: (1) ***The relative merits of different types of respiratory tract specimens.*** The positive and negative predictive values of deep throat specimens or oropharyngeal specimens for the lower airway specimens have been studied with varying results, presumably due to the different patient populations and pathogens studied.<sup>42</sup> The yield of induced sputum relative to upper airway specimens has also been assessed in research settings, and induced sputum generally yields more potential pathogens.<sup>43</sup> The 2003 Infection Control Guideline for CF recommendations for processing all types of respiratory tract specimens (throat, sputum, or bronchoalveolar lavage) continues to be appropriate. (2) ***The relative merits of different frequencies of respiratory tract cultures.*** Cultures of the respiratory tract can detect new pathogens, guide therapy, monitor the success of eradication strategies, and distinguish transient versus persistent colonization/infection. However, more frequent surveillance is associated with increased incidence and prevalence of CF pathogens.<sup>44</sup> The 2003 Infection Control Guideline for CF recommendation for quarterly cultures—or more frequently if clinically indicated—continues to be supported by published studies.<sup>45</sup> (3) ***The role played by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry platforms for identification of gram-negative bacilli from patients with CF.*** Several studies have found an advantage of this technology for rapid identification of pathogens that require many days using traditional phenotypic and genomic sequencing methods.<sup>46–48</sup> However, this technology is not widely available in the United States. (4) ***The relative merits of susceptibility testing to guide treatment of CF pathogens.*** Recent studies have questioned the clinical utility of performing routine susceptibility testing.<sup>49,50</sup> Nonetheless, antimicrobial susceptibility can distinguish methicillin-susceptible *S. aureus* (MSSA) from MRSA, identify unique multidrug-resistance patterns, and has been crucial for epidemiologic investigations. For example, CF clinicians were alerted to the transmission of epidemic strains of *P. aeruginosa* due to the emergence of ceftazidime-resistant,<sup>51</sup> colistin-resistant,<sup>52</sup> or multidrug-resistant strains.<sup>30,53</sup> Thus, susceptibility testing is still recommended as per the 2003 Infection Control Guideline for CF. (5) ***Clinical implications of the CF microbiome.*** The reader is referred to several recent studies for information on this increasingly important topic.<sup>54–57</sup>

## I.B. Molecular Typing Methodologies

### Overview

While earlier methods for typing bacteria from the respiratory tract of individuals with CF for epidemiologic purposes were based primarily on comparison of phenotypic (physical) features, molecular methods using analysis of the genetic content

of bacteria are now preferred. Compared with phenotypic methods, genotyping methods are more reproducible and provide greater discriminatory power in differentiating epidemiologically related strains from unrelated strains. Further attributes of the ideal genotyping system include ease of use, low cost, and unambiguous interpretation.<sup>58–60</sup>

### Random-Amplified Polymorphic DNA (RAPD)

RAPD typing is based on PCR amplification of random sections of the bacterial genome.<sup>61</sup> The amplified DNA segments are separated by gel electrophoresis, and the resulting banding pattern is compared with that of other bacteria visually or by means of computer-imaging software. Bacterial isolates with a high level of similarity in RAPD pattern are considered indistinguishable or highly likely to be the same strain.

### Repetitive-Element PCR (rep-PCR)

Another PCR-based genotyping method relies on the amplification of certain repetitive genetic elements found within the bacterial genome. A frequently used target for such rep-PCR typing is a genetic element referred to as the BOX A1R element (so-called BOX-PCR typing).<sup>62</sup> As with RAPD, the DNA banding patterns of bacterial isolates revealed by rep-PCR are compared; those with a highly similar pattern are considered highly likely to be related.

### Pulsed-Field Gel Electrophoresis (PFGE)

PFGE has been a mainstay of bacterial genotyping for the past 2 decades. PFGE evaluates genetic polymorphisms within the entire bacterial genome by macrorestriction, a technique that extracts genomic DNA from bacterial cells and then cleaves the DNA into large fragments using a restriction enzyme. These DNA fragments are separated by size using gel electrophoresis. The resulting banding pattern is compared among bacterial isolates; those with highly similar patterns are considered highly likely to be related.<sup>60</sup>

### Multilocus Sequence Typing (MLST)

MLST has become a preferred method for bacterial genotyping.<sup>63</sup> This method measures DNA sequence variations in a set of housekeeping genes that are present in all strains of a given species and characterizes strains by their unique allelic profiles. For each housekeeping gene of interest, the different sequences found within a bacterial species are designated as distinct alleles. For each isolate, the alleles identified for each of the housekeeping genes define the allelic profile or sequence type (ST). Compared with PFGE and PCR-based genotyping methods, MLST has distinct advantages, as it yields unambiguous, reproducible results that can be compared between laboratories. Public-access ST databases make MLST particularly well suited to global studies of the epidemiology of CF pathogens.<sup>64</sup>

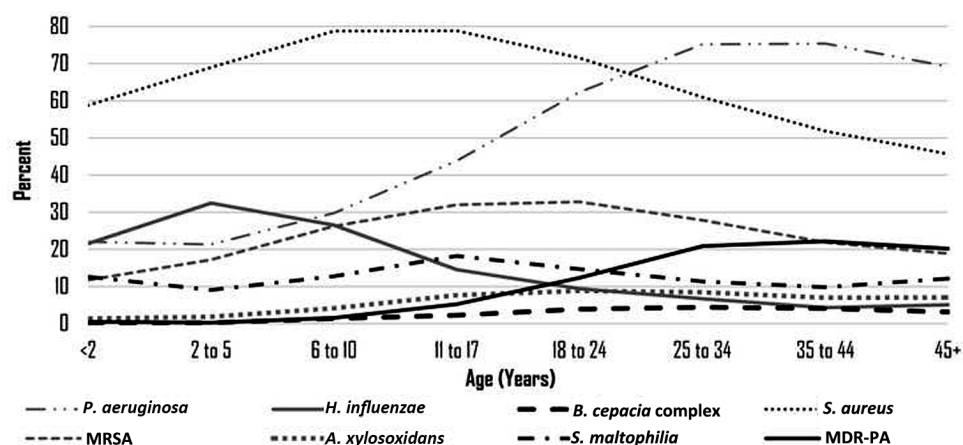


FIGURE 1. Age-specific prevalences of respiratory organisms, 2012. Age-specific prevalences of *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Haemophilus influenzae*, *Achromobacter xylosoxidans*, *Burkholderia cepacia* complex, *Stenotrophomonas maltophilia*, *Staphylococcus aureus*, and multidrug-resistant *Pseudomonas aeruginosa* (MDR-PA) among patients with cystic fibrosis in the United States in 2012 are shown. These data reflect an analysis of the US Cystic Fibrosis Foundation Patient Registry.

## Whole-Genome Sequencing

Most recently, whole-genome sequencing has been used to help define the epidemiology of bacterial pathogens for which conventional molecular typing may not have the resolution to accurately analyze population structure. Notably, whole-genome sequencing was used to assess transmission of NTM between individuals with and without CF.<sup>65,66</sup> The slow mutation rate of NTM is another reason for the need for whole-genome sequencing methods with these pathogens.

## Summary

Several molecular typing strategies have been developed that have been instrumental in documenting shared strains of CF pathogens and identifying potential environmental sources, as described below. It is likely that whole-genome sequencing will become more widely used to delineate the epidemiology of some pathogens, such as NTM and MRSA, while other strategies, such as MLST, will continue to be used for *Burkholderia* and *Pseudomonas* spp. National CF organizations in Canada, the United States, and several countries in the European Union have established research and referral laboratories for molecular typing of CF bacterial isolates that interact with one another through international networks, such as the International *Burkholderia cepacia* Working Group.<sup>67</sup> Such interactions help determine whether bacterial strains are found in more than 1 country, and thanks to the efforts of these laboratories, our understanding of the molecular epidemiology of CF pathogens has greatly expanded, as described further below.

In addition to its use in outbreak investigations, molecular typing is a critical tool in active surveillance programs and in monitoring the success of IP&C strategies. It should be emphasized, however, that molecular typing is best used to augment conventional shoe-leather epidemiology, since most

genotyping methods are not performed routinely in diagnostic clinical microbiology laboratories and active surveillance using molecular methods is not a component of routine CF care in the United States.

## I.C. Epidemiology of CF Pathogens

### I.C.1. Overview

The CF Foundation Patient Registry (CFFPR) is an invaluable source of data to further our understanding of the epidemiology of CF pathogens. The CFFPR has improved data collection for CF microbiology by creating numerous drop-down menus for both common and emerging pathogens. The CF Foundation provides annual data on the epidemiology of CF pathogens, as shown for 2012 in Figure 1.<sup>68</sup> *S. aureus* is the most common CF pathogen in the first 2 decades of life. While MSSA is more prevalent than MRSA, the prevalence of MRSA is highest in 11–24-year-olds. *P. aeruginosa* is detected in more than 20% of young infants, and nearly 80% of adults are infected with this pathogen. The prevalence of multidrug-resistant gram-negative organisms, including *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, and *B. cepacia* complex, increases with age.

The CF Foundation analyzed the changing prevalence of CF pathogens from 1988 to 2012, as shown in Figure 2.<sup>68</sup> Several pathogens, including MRSA, *S. aureus*, and *S. maltophilia*, have increased during this time. The explanation for these increases is unknown. It is likely that improved microbiology laboratory processing and data collection have improved our ability to detect and report these microorganisms, but increasing longevity, antimicrobial selective pressure, and potentially person-to-person transmission may also contribute to these findings. In contrast, the prevalence of *P. aeruginosa* and *B. cepacia* complex has decreased, which suggests

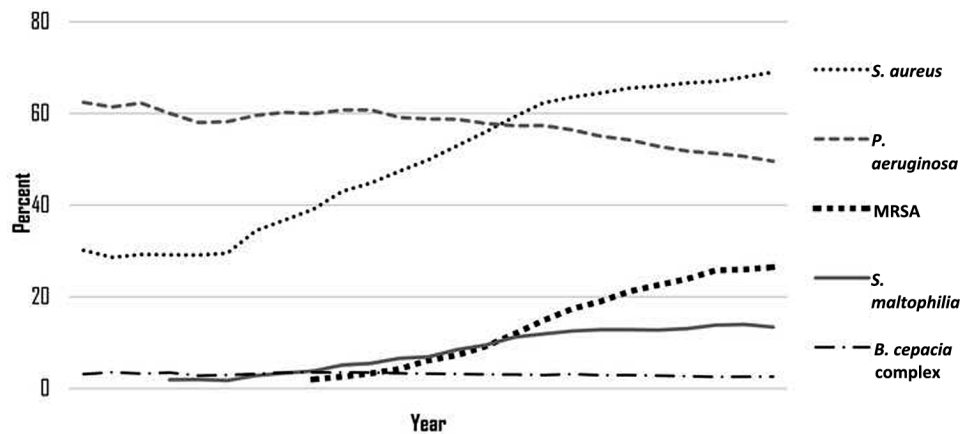


FIGURE 2. Respiratory organism prevalences, 1988–2012. Prevalences of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Stenotrophomonas maltophilia*, and *Burkholderia cepacia* complex among patients with cystic fibrosis in the United States of all ages from 1988 to 2012 are shown. These data reflect an analysis of the US Cystic Fibrosis Foundation Patient Registry.

that treatment paradigms, including early eradication strategies for *P. aeruginosa* and improved IP&C, may have influenced the epidemiology of these CF pathogens. The following sections provide a brief overview of the epidemiology of selected CF pathogens. Potential sources of these pathogens, including person-to-person transmission, are discussed in **Section III**.

#### I.C.2. *Burkholderia* spp.

At present, the *B. cepacia* complex consists of 18 distinct yet closely related species (Table 4).<sup>69–80</sup> The frequency of detection of these species in people with CF varies considerably, although *Burkholderia cenocepacia* and *Burkholderia multi-*

*vorans* are most common.<sup>26,81</sup> *Burkholderia gladioli* is the third most frequently isolated *Burkholderia* species among CF patients in the United States.<sup>26</sup> However, while *B. gladioli* are phenotypically quite similar to the species in the *B. cepacia* complex, it is not a member of the *B. cepacia* complex.<sup>82</sup>

#### I.C.3. Other Gram-Negative Species

The *Burkholderia* Reference Laboratory and Repository at the University of Michigan has expanded our understanding of the epidemiology of less commonly isolated gram-negative organisms in CF, including *Ralstonia* spp. (eg, *R. picketti* and *R. paucula*) and *Pandoraea* spp.<sup>26</sup> Readers are referred to several excellent reviews that have highlighted the recent epidemiology of CF pathogens.<sup>26,81,83</sup>

#### I.C.4. Small Colony Variant (SCV) *S. aureus*

In the past several years, there has been increasing interest in the clinical and therapeutic implications of SCVs of *S. aureus* in CF. *S. aureus* persists in the airways of people with CF for years and can develop a hypermutator phenotype that promotes adaptive changes, including SCVs, thought to facilitate survival of this organism within the CF airway.<sup>84,85</sup> SCVs are detected visually on laboratory agar plates and exhibit slower growth rates due to metabolic defects (eg, thymidine biosynthesis deficiency<sup>86</sup>), and they therefore require special susceptibility testing. However, the testing method has not been standardized by the Clinical and Laboratory Standards Institute.

Several potential clinical implications of SCV strains have been proposed. SCV strains of *S. aureus* are thought to have increased resistance to the innate immune system and increased resistance to antibiotics.<sup>85,87,88</sup> In vitro, SCVs have an increased ability to infect normal and CF airway epithelial cells.<sup>89</sup> In non-CF patients, SCV *S. aureus* are associated with

TABLE 4. *Burkholderia cepacia* Complex

Species name	Former genomovar designation	Year identified and/or named	Reference(s)
<i>B. cepacia</i>	I	1950, 1997	69, 74
<i>B. multivorans</i>	II	1997	74
<i>B. cenocepacia</i>	III	1997, 2003	73, 74
<i>B. stabilis</i>	IV	1997, 2000	74, 75
<i>B. vietnamiensis</i>	V	1995, 1997	74, 80
<i>B. dolosa</i>	VI	2001, 2004	79
<i>B. ambifaria</i>	VII	2001	70
<i>B. anthina</i>	VIII	2002	71
<i>B. pyrrocinia</i>	IX	2002	71
<i>B. ubonensis</i>	...	2000, 2008	76, 77
<i>B. latens</i>	...	2008	76
<i>B. diffusa</i>	...	2008	76
<i>B. arboris</i>	...	2008	76
<i>B. seminalis</i>	...	2008	76
<i>B. metallica</i>	...	2008	76
<i>B. contaminans</i>	...	2009	72
<i>B. lata</i>	...	2009	72
<i>B. pseudomultivorans</i>	...	2013	78

chronic or recurrent infections, such as endocarditis and osteomyelitis.<sup>86,90</sup>

SCV strains have been isolated from 8% to 33% of individuals with CF who are infected with *S. aureus*.<sup>91-93</sup> SCV *S. aureus* are associated with older age, coinfection with *P. aeruginosa*, lower lung function,<sup>92</sup> and treatment with antibiotics, specifically trimethoprim-sulfamethoxazole. In vitro, SCV strains can be induced by exoproducts expressed by *P. aeruginosa*.<sup>94</sup>

Recently, a causal relationship was suggested between the emergence of SCV *S. aureus* and a decline in lung function. In a CF center in the United States, 100 children with CF, of whom 24 had SCV *S. aureus*, were followed for an average of 1.7 years.<sup>95</sup> Those with SCV strains had lower lung function at the beginning and end of the study, but they had a similar rate of pulmonary exacerbations. Notably, 33% of the children with SCV strains did not have normal-colony *S. aureus* strains, which suggests that these children would not have been identified as infected with *S. aureus* had SCV strains not been sought.<sup>95</sup> In addition, 2 pairs of subjects had the same SCV strains, suggesting possible transmission of SCVs between children with CF.

Currently, it is unknown how many clinical laboratories have instituted methods to detect SCV strains of *S. aureus*, and there are no standardized methods for detection and susceptibility testing. Additional studies are needed to further describe the epidemiology of SCV *S. aureus* as well as the treatment and IP&C implications for CF. Furthermore, SCVs of other bacteria, including *Pseudomonas*,<sup>93,96</sup> *Stenotrophomonas*,<sup>97</sup> and *B. cepacia* complex,<sup>98</sup> have been described in people with CF.

### I.C.5. Nontuberculous Mycobacteria

Among the NTM are several opportunistic human pathogens, including *Mycobacterium intracellulare* and the species in the *Mycobacterium avium* complex (MAC; *M. avium* subsp. *avium*, *M. avium* subsp. *silvaticum*, and *M. avium* subsp. *paratuberculosis*).<sup>99</sup> The rapid-growing NTM species include those in the *M. abscessus* complex. Although the taxonomy of the *M. abscessus* complex was uncertain at the time of publication, currently 3 closely related subspecies are described: *M. abscessus* subsp. *abscessus*, *M. abscessus* subsp. *massiliense*, and *M. abscessus* subsp. *bolletii*.<sup>100,101</sup>

The prevalence of NTM in people with CF varies between countries and centers and appears to be increasing. The 2 most common species of NTM seen in individuals with CF are MAC and *M. abscessus*. Although MAC is more prevalent in North America, *M. abscessus* is more common in Europe and Israel.<sup>102-104</sup> In France, MAC was detected in older patients with less severe disease.<sup>104</sup> Thus, it appears that MAC and *M. abscessus* may target different subpopulations of people with CF.

### I.C.6. *Aspergillus* spp.

People with CF are at increased risk for colonization with filamentous fungi. The most frequently identified filamentous fungi are *Aspergillus fumigatus*, *Scedosporium apiospermum*, and *Aspergillus terreus*.<sup>105</sup> Less common fungi include *Aspergillus flavus*, *Aspergillus nidulans*, *Exophiala dermatitidis*, *Scedosporium prolificans*, *Penicillium emersonii*, and *Acrophialophora fusispora*. People with CF are at risk for allergic bronchopulmonary aspergillosis (ABPA), but many do not fulfill the clinical criteria for a diagnosis of ABPA.<sup>106-109</sup> Furthermore, criteria for initiation of antifungal therapy in individuals with positive *Aspergillus* cultures are incompletely defined.<sup>110</sup> In addition, invasive infection due to *Aspergillus* may occur, especially after lung transplantation.<sup>111</sup>

### I.D. Surveillance Strategies for CF Pathogens

Routine real-time surveillance for epidemiologically significant microorganisms is recommended in acute care settings to understand endemic rates and to identify outbreaks as soon as possible.<sup>5</sup> Regulatory requirements from state health departments and priorities established by local IP&C departments determine specific surveillance strategies. Local clinical microbiology laboratories are crucial partners to ensure accurate and meaningful data. Examples of pathogens for which surveillance is performed in hospitalized patients without CF, under defined circumstances, include MRSA, vancomycin-resistant enterococci (VRE), gram-negative bacilli resistant to carbapenem agents (CRE), and *Clostridium difficile*.

Routine surveillance for CF pathogens at individual CF centers can be used to track and trend the incidence and prevalence of specific microorganisms. Surveillance can assist centers in measuring the efficacy of both IP&C measures and other treatment strategies, such as early eradication. As described above, molecular typing is an invaluable tool for assessing potential patient-to-patient transmission, but it is not yet available routinely. Surveillance data for particular species can be generated by local clinical microbiology laboratories or by the CFFPR.

The CF community is continually challenged by the changing epidemiology of CF pathogens. Not only have new pathogens emerged, but the epidemiology of classic CF pathogens has changed thanks to new treatment strategies (eg, early eradication of *P. aeruginosa*) and improved microbiologic detection and identification. To remain vigilant, surveillance strategies that assess the impact of therapeutic interventions, identify potential outbreaks, and monitor the success of IP&C practices must be integrated into CF care.

## II. ROUTES OF TRANSMISSION OF CF PATHOGENS

### II.A. Contact and Droplet Transmission

Several routes of transmission have been described for CF pathogens, including **direct contact** with infectious respira-

tory secretions (eg, by kissing), **indirect contact** with an intermediate object contaminated with infectious respiratory secretions (eg, hands, environmental surfaces, or shared equipment), and infectious **droplets** from the respiratory tract that can travel in the air a distance of 3–6 feet (1–2 meters). These routes of transmission are summarized in Table 5. Bacterial and viral pathogens can remain viable on hands or inanimate surfaces for minutes, hours, or even days.<sup>112,113</sup>

Since publication of the 2003 Infection Control Guideline for CF, several studies conducted in people with and without CF who are infected with viral or bacterial pathogens have expanded our understanding of droplet transmission and now challenge the 3-foot rule. These studies include epidemiologic data collected during outbreaks of influenza<sup>114,115</sup> and SARS in non-CF individuals,<sup>116–118</sup> experimental and observational studies performed in people with CF,<sup>119–121</sup> and studies of the dynamics of infectious aerosols.<sup>119,122,123</sup>

## II.B. Classic View of Droplet Transmission

In the classic view of droplet transmission, infectious respiratory droplets (more than 5  $\mu\text{m}$  in diameter) are expelled by one person onto the mucous membranes of the nose, mouth, or conjunctivae of another susceptible person within 3 feet.<sup>124</sup> Infectious droplets are generated by coughing, sneezing, or talking or during such procedures as suctioning, intubation, chest physiotherapy, or pulmonary function testing. Infectious droplets remain suspended in the air for a short time, generally minutes, and can contaminate horizontal environmental surfaces, equipment, and the hands of patients

and healthcare personnel. Droplets are contrasted with much smaller droplet nuclei (less than 3.3  $\mu\text{m}$  in diameter), which can travel farther, remain suspended in the air for longer periods of time, do not require face-to-face contact for transmission, and are directly inhaled into the respiratory tract. Thus, pathogens transmitted by droplet nuclei do not require individuals to be in close proximity but do require them to share common air space.

## II.C. Emerging View of Droplet Transmission

New data have challenged the classic view of droplet transmission. Infectious droplets containing influenza virus and SARS-CoV traveled 3–6 feet.<sup>6,114,116,118</sup> Aerosols of droplet nuclei from patients infected with influenza can be generated during intubation and suctioning. Droplet size and distance traveled can be affected by (1) environmental factors (eg, humidity, temperature, air currents, and number of air changes per hour in a room), (2) agent factors (eg, infectious load, transferability, survivability, infectivity, and contagiousness), and (3) host factors (eg, susceptibility and behavior).<sup>122,123</sup>

In CF, several recent studies have explored the dynamics of droplet transmission. In an experimental model, subjects with CF infected with *P. aeruginosa* coughed into a chamber, and both droplets and smaller droplet nuclei containing viable organisms were collected as far as 6 feet from the subjects.<sup>121</sup> CF pathogens were recovered from the air collected 6 feet from CF subjects who were performing PFTs,<sup>125</sup> and *P. aeruginosa* was recovered from the air in hospital rooms, rooms after chest physiotherapy was performed, the hospital cor-

TABLE 5. Modes of Transmission of Potential Pathogens in Cystic Fibrosis

Type of transmission	Mode of transmission	Examples of respiratory tract pathogens	Source
Contact transmission	Direct or indirect contact with infectious secretions	MRSA <i>Pseudomonas aeruginosa</i> <i>Burkholderia</i> spp. Respiratory syncytial virus	Hands of healthcare workers Shared toys Contaminated respiratory therapy equipment or surfaces
Droplet transmission	Infectious droplets containing pathogens	MRSA <i>P. aeruginosa</i> <i>Burkholderia</i> spp. Influenza virus Rhinovirus Adenovirus <i>Mycoplasma</i> <i>Bordetella pertussis</i>	Infectious droplets (general size, >0.5 $\mu\text{m}$ ; distance, 3–6 feet [1–2 meters]) travel from respiratory tract of infected person to nasal mucosa, conjunctiva, or mouth of susceptible person during coughing, sneezing, or chest physiotherapy
Airborne transmission	Droplet nuclei arising from desiccation of droplets containing pathogens	<i>Mycobacterium tuberculosis</i> Varicella zoster virus Measles virus SARS-CoV	Airborne dissemination of droplet nuclei in respirable range that remain infectious over time and distance; may occur for some pathogens that are usually transmitted by the droplet route under unusual circumstances

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*; SARS-CoV, severe acute respiratory syndrome coronavirus.



TABLE 6. Relative Frequency of Shared Strains of Different Cystic Fibrosis Pathogens

Species	Frequency <sup>a</sup>	Reference(s)
<i>Pseudomonas aeruginosa</i>	+++	27, 28, 30, 130–132
<i>Burkholderia</i> spp.	+++	27, 133–135
Methicillin-susceptible <i>Staphylococcus aureus</i>	+	136, 137
Methicillin-resistant <i>S. aureus</i>	++	138, 139
<i>Stenotrophomonas maltophilia</i>	+	140, 141
<i>Achromobacter xylosoxidans</i>	+	142–144
<i>Mycobacterium avium</i> complex	None described	102
<i>Mycobacterium abscessus</i> subsp. <i>massiliense</i>	+	66, 129, 145

<sup>a</sup> Frequency (+ to +++) is based on the relative number of published reports.

ridor, and a CF clinic.<sup>126,127</sup> Factors associated with generating infectious droplets are unknown, as exacerbations, sick versus well CF clinic visits, and age were not predictive of the rate of recovery from air samples.<sup>125,128</sup>

#### II.D. Potential Role of Droplet Nuclei

Most recently, the potential for person-to-person droplet and/or droplet nuclei transmission of *M. abscessus* subsp. *massiliense* has been suggested.<sup>66,129</sup> Transmission in one center was halted by simultaneous implementation of multiple IP&C strategies, including separation of people with CF infected with this pathogen, increased microbiologic surveillance, enhanced environmental cleaning, mask use by individuals with CF, and the use of negative pressure rooms among adults with CF.<sup>129</sup> (See **Section III.A.5** for a more detailed description of NTM transmission.)

#### II.E. Paradigm for Transmission of Respiratory Pathogens

In an effort to explain observations made during the 2003 SARS epidemics, the following paradigm was proposed to describe the potential for transmission of respiratory tract pathogens by both infectious droplets and droplet nuclei under different conditions:<sup>117</sup> (1) **Obligate transmission** is that which occurs under natural conditions (eg, transmission of *M. tuberculosis* by droplet nuclei). (2) **Preferential transmission** is that which occurs when one route is the usual route but another route has been described; for example, transmission of the measles virus (rubeola) usually occurs by inhalation of droplet nuclei that are deposited in distal airways, but infectious droplets may also transmit the measles virus. (3) **Opportunistic transmission** is that which can occur when a pathogen usually transmitted by droplets can be transmitted by droplet nuclei (eg, influenza transmitted by aerosols of droplet nuclei) under unusual environmental conditions, such as intubation. Future studies may help define the applicability of this paradigm to CF pathogens.

#### Summary

In summary, CF pathogens can be transmitted by direct or indirect contact with infectious secretions, objects contaminated with infectious secretions, or infectious droplets. Recent data suggest that infectious droplets may travel as far as 6

feet (2 meters) from individuals with CF. While detection of infectious droplets is not confirmatory of patient-to-patient transmission, it is highly suggestive of the potential for such transmission. The potential for people with CF to generate droplet nuclei has been demonstrated in experimental models, but the relevance of these observations for transmission, including that of *M. abscessus* subsp. *massiliense*, has not been established and should be studied.

### III. POTENTIAL SOURCES OF CF PATHOGENS

#### III.A. Person-to-Person Transmission among People with CF

The source of CF pathogens is often unknown, and many individuals with CF are infected with unique strains of *P. aeruginosa* or *Burkholderia* spp. However, the molecular tools described above have expanded the evidence that people with CF can acquire CF pathogens from others with CF in both healthcare and nonhealthcare settings. **These are the primary transmission and acquisition events targeted by the recommendations in this guideline.** The relative frequency of shared strains of different CF pathogens is shown in Table 6.<sup>27,28,30,66,102,129–145</sup>

##### III.A.1. *Burkholderia* spp.

**B. cenocepacia.** Several methods have been used to genotype *Burkholderia* to define the epidemiology of infections in people with CF.<sup>61,146–150</sup> In the late 1980s, genotyping studies identified common strains in multiple individuals receiving care at the same CF centers, suggesting person-to-person spread.<sup>149</sup> More compelling evidence soon followed. Transmission of *B. cepacia* complex was described at a CF educational retreat<sup>134</sup> and among people with CF attending summer camps.<sup>151</sup> Outbreaks were also reported within CF centers.<sup>135</sup>

Among so-called epidemic strains, the ET12 (electrophoretic type 12) strain was prevalent in eastern Canada and the United Kingdom.<sup>152,153</sup> The Midwest strain and the PHDC (Philadelphia–Washington, DC) strain were identified in people with CF in the Midwest and mid-Atlantic regions of the United States, respectively.<sup>154–157</sup> The ST04 strain (RAPD type 04) was identified in people with CF in western Canada, and the CZ1 strain (now referred to as ST32) was identified in

most individuals infected with *Burkholderia* at the Prague CF center in the Czech Republic.<sup>158–160</sup> Other *B. cenocepacia* strains have been shared among multiple individuals with CF in various Italian CF centers.<sup>161,162</sup>

**Other species of *B. cepacia* complex.** Shared strains from other species in the *B. cepacia* complex have been reported and generally involved smaller numbers of patients.<sup>133,161,163,164</sup> A notable exception is *B. dolosa* strain SLC6, which was identified in an outbreak in a US CF center and associated with deterioration in lung function and increased mortality.<sup>25,133</sup> The Glasgow strain of *B. multivorans* was identified in an outbreak among people with CF in the city in the early 1990s.<sup>133,165</sup>

However, the majority of *Burkholderia*-infected CF patients harbor genotypically distinct strains. *B. multivorans* and *B. gladioli* account for more than half of the *Burkholderia* infections in the United States, but it is uncommon that multiple individuals with CF share strains belonging to these 2 species. Thus, the majority of new *Burkholderia* infections in people with CF currently involve the acquisition of strains from independent sources, most likely the natural environment, as will be discussed further in **Section III.D.1** below.<sup>166,167</sup>

**Clinical impact of epidemic *Burkholderia* spp.** Poor outcomes, including more rapid clinical decline, decline in lung function, and increased mortality both before and after lung transplantation<sup>165,168</sup> have been associated with certain strains of *B. cepacia* complex. Outcomes from the Canadian and US CF patient registries demonstrated a 2.5-fold increase in the relative risk of death in people with CF who are infected with *B. cepacia* complex.<sup>169,170</sup> Overwhelming infection (the *cepacia* syndrome) has been reported with species of *B. cepacia* complex other than *B. cenocepacia*, including *B. multivorans*<sup>164</sup> and *B. dolosa* SLC6.<sup>25</sup> Both single-center and multicenter studies suggest that poor outcomes with *B. cepacia* complex may be related to species, and such strains as *B. cenocepacia* ET12 have been associated with the worst outcomes.<sup>171</sup> Among 29 lung transplant recipients infected with *B. cenocepacia* ( $n = 16$ ), *B. multivorans* ( $n = 11$ ), and *B. vietnamiensis* ( $n = 2$ ), all of the deaths occurred in those infected with *B. cenocepacia*.<sup>172</sup>

### III.A.2. *P. aeruginosa*

**Shared *P. aeruginosa* strains.** Early strain-typing studies demonstrated that individuals with CF infected with *P. aeruginosa* harbored distinct strains, presumably acquired from the natural environment.<sup>61,173,174</sup> Shared strains between siblings were well documented,<sup>175–177</sup> and in 1986 a report from Denmark described the spread of a multidrug-resistant *P. aeruginosa* strain in a CF care center.<sup>178</sup> In 1996, PFGE analysis of isolates recovered during an antibiotic trial identified a  $\beta$ -lactam-resistant strain of *P. aeruginosa* infecting 55 children at a CF center in Liverpool, United Kingdom.<sup>51</sup> Other reports described shared or epidemic *P. aeruginosa* strains in the United Kingdom and Australia.<sup>53,179–181</sup> PFGE analysis of 1,225

*P. aeruginosa* isolates recovered from people with CF receiving care in 31 treatment centers in the United Kingdom demonstrated that 28% of those infected harbored a strain shared with at least 1 other person with CF.<sup>173</sup> The 2 most prevalent strains accounted for more than 20% of the isolates examined. Some strains, including the Liverpool and Midlands 1 epidemic strains, were widely distributed and identified in 48% and 29% of CF treatment centers, respectively.

In Melbourne, Australia, a strain first detected in children with CF<sup>181</sup> was subsequently identified in half of the individuals with CF who were infected with *P. aeruginosa* in Sydney.<sup>180</sup> This strain, now referred to as the Australian epidemic strain 1 (AES-1), has also been identified in Brisbane.<sup>179</sup> The Australian epidemic strain 2 (AES-2) is even more common in Brisbane,<sup>182</sup> while the Australian epidemic strain 3 (AES-3) is common in Tasmania.<sup>183</sup> In Copenhagen, Denmark, PFGE and genomic DNA sequence analyses identified 2 major *P. aeruginosa* clones that have been common among and likely transmitted among people with CF for more than 2 decades.<sup>131</sup> In the Netherlands, MLST analysis of 443 *P. aeruginosa* isolates recovered from 265 individuals with CF in 2 CF centers identified 2 strains (designated ST406 and ST497) in 15% and 5% of the patients.<sup>184</sup> Furthermore, 60% of the individuals studied harbored a strain also found in at least 2 other individuals.

Strains common to large numbers of people with CF cared for in North America have also been described. In Vancouver, Canada, RAPD and PFGE were used to analyze *P. aeruginosa* isolates recovered between 1981 and 1999 from 174 individuals with CF; 157 distinct strains were identified, 123 of which were unique to individual patients.<sup>130</sup> Several strains were shared by clusters of 2, 3, or 4 individuals, and 2 strains were shared by 21 and 18 individuals. More recently, in Ontario, Canada, MLST was used to analyze *P. aeruginosa* isolates recovered from 446 individuals with CF.<sup>28</sup> The LES was identified in 15% of these individuals, while a second strain (designated ST439) was found in 7%. The route by which the LES was transmitted to people with CF in Canada is unknown.

In the United States, the presence of epidemic *P. aeruginosa* strains remains uncertain, as very few genotyping studies of isolates from large numbers of people with CF have been performed. In Houston, rep-PCR typing identified a multidrug-resistant *P. aeruginosa* strain in 32 (45%) of 71 children with CF; this strain, designated Houston 1, appears to be distinct from other epidemic *P. aeruginosa* strains (J.J.L., written personal communication, October 2013).<sup>30</sup> Compared with other strains, new infection with the Houston 1 strain was significantly more likely to occur in those children hospitalized within the 90 days prior to infection. In addition, compared with those infected with other strains, those with the Houston 1 strain spent 12 more days in the hospital in the year prior to acquisition. The authors found that following adoption of recommendations from the 2003 Infection Control Guideline for CF, transmission was halted. Furthermore,

*P. aeruginosa* strains from participants in an antibiotic trial who were cared for at 18 CF centers in the United States were evaluated with MLST; at each center, shared strains were noted in 0%–71% of participants, and 15 of 18 centers had participants with shared strains.<sup>132</sup>

Most epidemic strains of *P. aeruginosa* have had a multi-drug-resistant phenotype, which facilitated their recognition. The presence of epidemic strains without an unusual or noteworthy phenotype might be difficult to detect. Active surveillance of sufficiently large numbers of isolates is required to monitor the presence and ongoing transmission of shared strains of *P. aeruginosa*. Such surveillance is not currently a component of routine CF care in the United States.

**Routes of transmission and reservoirs of *P. aeruginosa*.** The epidemiologic and microbiologic basis for epidemic *P. aeruginosa* strains remains poorly understood,<sup>27</sup> and it is unclear whether all epidemic *P. aeruginosa* strains have comparable capacity for patient-to-patient transmission. Strain differences in the production of infectious droplets or droplet nuclei that remain suspended in the air under experimental conditions may explain the differences in efficiency of transmission of epidemic *P. aeruginosa* strains.<sup>119</sup>

Infections with a shared strain<sup>130,173,179</sup> are highly suggestive of patient-to-patient transmission, particularly as institution of IP&C measures halted transmission.<sup>30,185</sup> While acquisition from a common source is also a possibility, surveillance of inpatient and outpatient settings have not detected a reservoir for shared strains.<sup>51,53</sup> Strains that are more widely distributed (ie, found in multiple CF care centers) might suggest contact among individuals with CF from different centers or, possibly, acquisition from the natural environment, as described below in **Section III.D**.

**Clinical impact of epidemic *Pseudomonas*.** The LES has developed increasing antibiotic resistance,<sup>186</sup> and some epidemic strains of *Pseudomonas* are associated with clinical deterioration.<sup>185–188</sup> The LES has been associated with an increased risk of death or lung transplantation during 3 years of follow-up and/or decline in lung function.<sup>28</sup> Furthermore, those infected with the LES had a worse quality of life, including worse treatment burden, physical functioning, and respiratory symptoms, compared with those individuals infected with nonepidemic strains.<sup>189</sup>

### III.A.3. Other Gram-Negative Bacteria

Several other nonfermenting gram-negative bacteria can cause intermittent or chronic infection in people with CF. Among these, *S. maltophilia*, *Achromobacter* spp., *Ralstonia* spp., *Cupriavidus* spp., and *Pandora* spp. are the most common.<sup>26,190</sup>

***S. maltophilia*.** In the United States, 33 (80%) of 41 individuals with CF infected with *S. maltophilia* harbored genetically distinct strains, and 4 clusters (each of 2 individuals) were detected, suggesting either patient-to-patient spread or acquisition from a common environmental source.<sup>140</sup> Among

183 *S. maltophilia* isolates obtained from a multicenter antibiotic trial conducted in the United States, only 3 instances of shared strains were found.<sup>143</sup> More recently, 110 isolates recovered from 50 individuals with CF were studied, and 5 distinct strains were identified that were each shared by 2 or 3 patients.<sup>141</sup> Thus, while there is some evidence for shared strains of *S. maltophilia* and possible patient-to-patient transmission, most infections in people with CF appear to result from independent acquisition, most likely from non-health-care-associated environmental sources or as a result of antimicrobial selective pressure.

***A. xylosoxidans*.** *A. xylosoxidans* is an opportunistic pathogen that causes healthcare-associated infections, including bacteremia, meningitis, pneumonia, endocarditis, peritonitis, osteomyelitis, urinary tract infection, and endophthalmitis, in vulnerable hosts, including neonates, burn victims, and other immunocompromised patients.<sup>191–193</sup>

Among 341 individuals with CF in the United States infected with *Achromobacter*, 42% were infected with *A. xylosoxidans*, and 23.5% were infected with *Achromobacter rhulandii*.<sup>190</sup> In 2 small single-center studies, *Achromobacter*-infected individuals each harbored genotypically distinct strains.<sup>194,195</sup> However, there is some evidence that *Achromobacter* spp. are shared by people with CF. A CF center in the United States reported that 9 (36%) of 25 *Achromobacter*-infected individuals harbored the same strain of *A. xylosoxidans*.<sup>142</sup> In the same multicenter antibiotic trial described above, 92 *Achromobacter* isolates were analyzed, and 5 instances of shared strains (2 individuals each) were detected.<sup>143</sup> In Athens, Greece, 5 of 9 individuals with CF infected with the same strain of *A. xylosoxidans* were close social contacts.<sup>196</sup> In a multicenter study conducted in Belgium, 2 clusters of *A. xylosoxidans* strains were identified (one consisted of 4 individuals, and the other consisted of 10 individuals).<sup>144</sup> Thus, there is some evidence of shared strains of *A. xylosoxidans* and a suggestion of possible patient-to-patient transmission.

***Ralstonia*, *Cupriavidus*, and *Pandora* spp.** Several of the 15 species in the genus *Ralstonia*, including *R. pickettii*, *R. mannitolilytica*, and *R. insidiosa*, have been recovered from people with CF.<sup>197</sup> In the United States, 25 (66%) of 38 individuals infected with *Ralstonia* species had *R. mannitolilytica*; 9 had *R. pickettii*, 2 had *R. gilardii*, 1 had *R. taiwanensis*, and 1 had a *Ralstonia* species that could not be classified.<sup>198</sup> Several of the 14 species included in the genus *Cupriavidus*,<sup>199</sup> including *C. pauculus*,<sup>200</sup> *C. gilardii*,<sup>201</sup> *C. respiraculi*,<sup>202</sup> and *C. taiwanensis*,<sup>203</sup> have also been recovered from people with CF.<sup>199</sup> Among isolates obtained in the United States from 2004 to 2008, *Ralstonia* and *Cupriavidus* species were recovered from 72 and 73 CF patients, respectively.<sup>26</sup> *R. mannitolilytica* accounted for 60% of *Ralstonia* species, while *C. respiraculi* was the most common (53%) *Cupriavidus* species identified. Genotyping analyses of these isolates have not identified a strain common to more than 1 person with CF (J.J.L., unpublished data, October 2013).

The genus *Pandoraea*, first described in 2000, is currently comprised of 9 species, all of which have been recovered from persons with CF.<sup>204,205</sup> Among the 74 individuals with CF in the United States with *Pandoraea* species recovered between 2004 and 2008, *P. apista*, *P. phoenicis*, and *P. sputorum* accounted for approximately equal proportions of isolates.<sup>26</sup> In Denmark, a *P. apista* strain spread among 6 children with CF attending a winter camp, and most subsequently experienced a significant deterioration in lung function.<sup>206</sup>

### III.A.4. *S. aureus*

**Shared MSSA strains.** *S. aureus* is normal skin flora and commonly colonizes the anterior nares. In 2003–2004, the anterior nares of approximately 35% of children in the United States without CF aged 1–19 years were colonized with *S. aureus*,<sup>207</sup> and *S. aureus* can also be recovered from 48% of oropharyngeal swabs of healthy children 18 years of age and younger.<sup>208</sup> In Germany, the anterior nares of 72 individuals with CF aged 1–25 years and 72 age-matched non-CF controls as well as 128 family members of 38 children with CF and 79 family members of 23 children without CF were studied to compare the frequency of *S. aureus* colonization.<sup>209</sup> A significantly greater prevalence of nasal carriage of *S. aureus* (66%) was found among those with CF who had *not* been treated with antistaphylococcal antibiotics during the 4 weeks preceding culture, compared with those recently treated (29%) or those without CF (32%). The proportion of family members colonized with *S. aureus* was similar among CF (32%) and non-CF (35%) families. PFGE analyses indicated that colonized individuals within the same family often shared the same *S. aureus* strain, indicating that *S. aureus* can be transmitted within families. The genome types found in people with CF and their families were also noted in the community.

Colonization does not usually have consequences, but it is a risk factor for subsequent disease in people with and without CF; isolates colonizing the anterior nares and disease-producing isolates typically have the identical genotype.<sup>209–212</sup> In people with CF, airway infection may be intermittent or chronic.<sup>91,213–216</sup> Chronic infection of the airways with the same clone can persist for several years.<sup>91,209,213</sup>

Shared strains of *S. aureus* among individuals with CF are well documented. Four typing methods were used to compare MSSA strains recovered from individuals with CF before and after attendance at a 4-week summer camp.<sup>136</sup> Four of 20 patients acquired a strain noted in another camper at the start of camp, consistent with patient-to-patient transmission. In St. Louis, 2 episodes of transmission of MSSA between siblings with CF in which transmission to the younger siblings resulted in considerable morbidity have also been reported.<sup>137</sup>

**Shared MRSA strains.** In 2003–2004, the anterior nares of approximately 1.3% of children in the United States without CF aged 1–19 years were colonized with MRSA.<sup>207</sup> In Australia, healthcare-associated transmission of MRSA among people with CF and the spread of MRSA from patients

without CF to individuals with CF hospitalized in the same ward at the same time have been reported.<sup>138</sup> In Leeds, United Kingdom, individuals with CF infected with MRSA spent more time in the hospital in the year prior to initial isolation of MRSA than age- and sex-matched uninfected control subjects with CF (19.8 vs 5.5 days;  $P < .001$ ).<sup>217</sup>

The molecular epidemiology of MRSA has also been studied to (1) understand the relative contribution of community versus traditional healthcare-associated clones, (2) compare the types of MRSA strains in CF versus non-CF individuals, and (3) assess the frequency of shared strains. In Dallas and Chicago, 88% of strains from children without CF were staphylococcal chromosomal cassette *mec* (SCC*mec*) type IV (so-called community-associated strains), while 65% of MRSA strains from children with CF were SCC*mec* type II (so-called traditional healthcare-associated strains); MRSA strains more recently acquired in children with CF were more likely to be SCC*mec* type IV.<sup>218</sup> In addition, the distribution of MLST clonal complexes (CCs), which are closely associated with SCC*mec* types, was different among CF versus non-CF isolates. Among CF isolates, 71% were CC5, 26% were CC8, and 3% were CC1, whereas among non-CF isolates, 89% were CC8, 4% were CC5, and 7% were CC1. While the reasons for differences in the molecular epidemiology of MRSA strains between non-CF versus CF individuals are unclear, the presence of common strains in the CF population suggest patient-to-patient transmission and/or potential virulence factors that facilitate colonization and infection in CF.

In Chapel Hill, North Carolina, similar findings were noted, as 72% of individuals with CF were infected with SCC*mec* type II strains, while only 17% were infected with SCC*mec* type IV strains.<sup>219</sup> The latter group consisted of younger individuals. In a multicenter study conducted in the United States from 2008 to 2010, SCC*mec* type II strains were more common than SCC*mec* type IV strains, accounting for 71% of MRSA isolates, and 84% of SCC*mec* type IV strains that harbored Panton-Valentine leukocidin were USA300, the most common community-associated MRSA clone.<sup>220</sup>

In a multicenter study conducted in Italy, MLST analysis revealed common types in multiple individuals with CF attending multiple CF centers.<sup>139</sup> Twenty-nine strains from 6 CF centers were identified as ST8 SCC*mec* type IV (USA), and 26 strains from 6 CF centers were identified as ST5 SCC*mec* type I (also a healthcare-associated clone initially reported from the United Kingdom). Thus, epidemic lineages of MRSA from around the world have been identified in the CF population in Italy. It is not clear why the SCC*mec* type I and II strains predominate among individuals with CF at a time when SCC*mec* type IV predominates in non-CF populations. It is likely that more sensitive testing (eg, rep-PCR<sup>221</sup> or whole-genome sequencing) will provide more precise information about the extent of person-to-person transmission of MRSA.<sup>222,223</sup>

**Clinical impact of MRSA.** Recent reports have demonstrated that chronic infection with MRSA is associated with

increased morbidity and mortality. In a study using the CFFPR, when compared with 13,922 individuals with CF without chronic MRSA infection, 1,732 individuals chronically infected with MRSA had an increased rate of decline in lung function (decline in FEV<sub>1</sub> % predicted 1.44% per year vs 2.06% per year, respectively).<sup>22</sup> Similar findings have been reported by others.<sup>224-226</sup> In addition, MRSA has also been associated with increased mortality; in a cohort study of 19,833 individuals reported to the CFFPR with at least 2 years of follow-up, those with MRSA had a 1.27 higher risk of death when adjusted for severity of disease.<sup>23</sup>

### III.A.5. Nontuberculous Mycobacteria

**Shared NTM strains.** Until recently, there was little evidence for shared strains of NTM species among individuals with CF.<sup>102,227</sup> In a multicenter study conducted in the United States, most of the 140 NTM isolates appeared to be distinct by single-locus (*hsp65*) sequence analysis.<sup>102</sup> Among 14 NTM-infected individuals with CF included in a study in Sweden, a shared strain was found only in 1 pair of siblings.<sup>228</sup>

However, a recent report from the United States described the use of rep-PCR and PFGE typing to show the apparent spread of a strain of *M. abscessus* subsp. *massiliense* from a chronically infected adult with CF to 4 others attending the same clinic in Seattle.<sup>129</sup> The index case and 2 others died within several months of becoming infected. Similarly, typing of 41 strains of *M. abscessus* complex from 17 individuals with CF in the United Kingdom using a novel variable-number tandem repeat scheme and an automated rep-PCR system found that most were persistently infected with a single clone, but some shared strains; no differences in clinical outcomes linked to specific strains was reported.<sup>145</sup> In another recent report of NTM transmission, whole-genome sequencing and single-nucleotide polymorphism analysis were used to characterize 168 *M. abscessus* complex isolates from 31 individuals at a CF care center in the United Kingdom.<sup>66</sup> Two clusters (1 consisting of 9 individuals and 1 consisting of 2 individuals) of *M. abscessus* subsp. *massiliense* were identified, with epidemiologic evidence of opportunities for person-to-person spread within the hospital setting. The strains from Seattle and the United Kingdom outbreaks are highly related and are also related to strains causing soft-tissue infections in Brazil.<sup>229</sup> However, it is currently unknown why these strains from around the world are related. A third outbreak of *M. abscessus* occurred from 2009 to 2011 at a pediatric CF center in Hawaii, in which 9 (55%) of 17 children were infected with the same strain as identified by PFGE.<sup>230</sup> An investigation conducted in conjunction with the Department of Health revealed that the PFT laboratory was the most likely source of transmission, as the infected patients performed PFTs at the same time in very close proximity.

**Clinical impact of NTM.** *M. abscessus* in particular is challenging to treat and may be associated with rapid clinical deterioration and poor outcomes after lung transplanta-

tion.<sup>231-233</sup> A multicenter prospective study conducted more than a decade ago showed no association between *M. abscessus* and decline in lung function,<sup>102</sup> but a longer single-center study showed that chronic *M. abscessus* infection was associated with an excess decline of 0.78% predicted FEV<sub>1</sub> per year.<sup>66,234</sup>

### Summary

In summary, epidemiologic studies have shown that individuals with CF can share the same strain of several CF pathogens. For decades, person-to-person transmission of *Burkholderia* spp. has been described, while person-to-person transmission of *P. aeruginosa* has been increasingly recognized in CF centers worldwide. MRSA strains detected in people with CF have been identified as epidemic clones, causing both healthcare- and community-associated infections in both CF and non-CF populations. Thus, studies of transmission of MSSA and MRSA are confounded by the fact that such species commonly colonize and infect people without CF. Most recently, compelling evidence of person-to-person transmission of *M. abscessus* has been described. Currently, the route(s) of transmission, including the potential for transmission by droplet nuclei, and the role played by mycobacterial virulence factors are under investigation. Multicenter studies, core laboratories, and use of advanced molecular methodologies are needed to understand the frequency and routes of transmission of mycobacteria in persons with CF. Epidemic strains of *Burkholderia*, *Pseudomonas*, and *M. abscessus* as well as infection with MRSA have been associated with increased morbidity and mortality. Use of higher resolution typing, such as whole-genome sequencing, is needed in future studies to provide a more precise understanding of the dynamics of transmission.

### III.B. Acquisition from People without CF

#### III.B.1. *P. aeruginosa* and *Burkholderia* spp.

Approximately 10% of people without CF may have gastrointestinal tract colonization with *P. aeruginosa*. *P. aeruginosa* is a well-described opportunistic pathogen of immunocompromised non-CF individuals, including oncology patients, burn victims, and ventilated patients.<sup>235-237</sup> To our knowledge, there is only 1 case report of transmission of *P. aeruginosa* to the non-CF household members of a person with CF. Both parents of a 22-year-old woman with CF, infected with the LES, developed pneumonia caused by this strain.<sup>238</sup> Both were carriers of abnormal CFTR, but neither had CF.

*B. cepacia* complex strains do not colonize people without CF<sup>239</sup> but can cause infections in individuals who are immunocompromised, including those with chronic granulomatous disease or solid-organ transplantation.<sup>240,241</sup> To our knowledge, there is only 1 case report describing hospital transmission of *Burkholderia* from a non-CF individual with

chronic respiratory failure to multiple patients with and without CF.<sup>242</sup>

### III.B.2. *S. aureus*

Unlike other CF pathogens, both MSSA and MRSA can colonize and infect non-CF individuals, including household members and other close contacts. Thus, there is the potential for acquisition of *S. aureus* in healthcare and community settings from people without CF. Furthermore, as described above, healthcare- and community-associated MRSA strains can infect people with CF.<sup>218,220</sup> Definitive evidence of transmission of MRSA, particularly community-associated strains, may be confounded by the observation that relatively few clones have been described, and highly sensitive molecular techniques have been used only in recent years.

#### **MRSA colonization and infections in non-CF patients.**

For decades, MRSA infection and colonization in patients without CF were exclusively associated with hospitalization, chronic care facilities, or dialysis units.<sup>243</sup> Beginning in the late 1990s, MRSA infections began to occur in the community setting in previously healthy individuals, so-called community-onset or community-acquired MRSA (CA-MRSA).<sup>244</sup> Skin and soft-tissue infections are the most common manifestation of CA-MRSA, but necrotizing pneumonia, bone infections, and sepsis are also described.<sup>245-248</sup> A recent meta-analysis assessing MRSA colonization of the anterior nares in children described a prevalence of 5.4% in hospitalized children and 3% in children in the community, suggesting that MRSA colonization is relatively common in the general population.<sup>249</sup>

**Transmission from non-CF patients.** To our knowledge, there is only 1 report describing healthcare-associated transmission of MRSA from patients without CF to patients with CF. In Australia, transmission of MRSA from patients without CF to individuals with CF hospitalized in the same ward at the same time was described.<sup>138</sup> However, the authors did not describe the routes of transmission and the IP&C strategies that were in place.

**CF households.** In a multicenter study of children with CF with MRSA in New York, non-CF household members had anterior nares colonization with the same strain of MRSA (14.7% vs 1.6% of case vs control household members).<sup>215</sup> While the direction of transmission is unknown, it is likely that the non-CF family member acquired MRSA from his or her child with CF. No staphylococcal infections occurred in household members.

**Healthcare personnel.** The anterior nares of healthcare personnel without CF may be colonized with MRSA. However, routine screening is not recommended, unless healthcare personnel are epidemiologically associated with ongoing transmission.<sup>20,250-252</sup> In contrast, healthcare personnel without CF who develop symptomatic MRSA infections (eg, draining wounds, sinusitis with drainage, and superinfection of chronic dermatitis) should be placed on administrative leave,

treated until no longer infectious, and obtain clearance from the facility's occupational health service before returning to work.<sup>5,8</sup>

#### **Other nonhealthcare settings, including sports teams.**

Participation in sports has been identified as a risk factor for the development of MRSA colonization and infection in the non-CF community, presumably due to skin colonization, skin abrasions, intimate contact between players, and poor hygiene.<sup>253,254</sup> MRSA has been detected both in the environment (eg, locker room, strength and conditioning equipment, and whirlpool equipment) and in samples obtained from athletes (eg, nose, skin sites, and shoes).<sup>254-258</sup> In addition, outbreaks of MRSA skin and soft-tissue infections have been reported among members of sports teams.<sup>255,259-267</sup> However, to our knowledge there are no reports of transmission of MRSA from a person with CF on a sports team to another athlete without CF or vice versa. Thus, there are no data to support exclusion of an individual with CF with MRSA in their respiratory tract from participation in sports.

The CDC has developed recommendations to prevent MRSA transmission among athletes and in athletic facilities.<sup>268</sup> They include the following: (1) **improve hygiene among athletes** by covering and containing wounds, showering after participating in sports activity, washing and drying uniforms after each use, not sharing personal items (eg, razors), and reporting possible infections to the team physician, athletic trainer, school nurse, or primary care doctor so that treatment can be initiated promptly; (2) **clean and disinfect athletic facilities**, including showers, using appropriate cleaning and disinfection measures; and (3) **exclude athletes with MRSA wound infections from participation if wounds cannot be completely covered or if a healthcare provider determines that the infection poses a risk to the individual with the infection.** Athletes with MRSA infections should not use common-use water facilities or pools until the infection has resolved.

### III.B.3. Respiratory Viruses

Viral respiratory pathogens, including respiratory syncytial virus (RSV), rhinovirus, and influenza virus, pose a risk to people with CF. In adults and children with CF, viral infections can trigger pulmonary exacerbations,<sup>269-272</sup> particularly influenza virus<sup>271,273</sup> and rhinovirus.<sup>269,270</sup> Exacerbations in which a virus is identified are associated with worse clinical severity compared with viral exacerbations.<sup>274</sup> As sensitive viral detection methods like real-time PCR become increasingly available and identify a broader range of viruses,<sup>275</sup> the role played by other viral pathogens (eg, coronavirus and human metapneumovirus) in CF exacerbations will be further elucidated.

### Summary

Transmission of gram-negative bacterial pathogens between people with CF and people without CF is very rare. Given

the recent observations that people with CF are infected with community-associated MRSA, it is feasible that some transmission of *S. aureus* is occurring between people with and without CF. Further studies are needed to assess the extent to which this occurs. In contrast, it is highly likely that viral pathogens are frequently transmitted between people with and without CF, given the annual community outbreaks of seasonal viruses and the high transmissibility of these agents.

### III.C. Acquisition from Animals

**Overview of zoonotic infection.** More than 800 microorganisms can cause zoonotic infections, defined as pathogens transmitted from animals to humans or from humans to animals. The CDC's National Center for Emerging and Zoonotic Infectious Diseases is charged with preventing disease and disabilities from such infections.<sup>276</sup> People with CF can have opportunities for close contact with animals, including with personal pets, service animals, and pet therapy animals as well as farm animals and animals in petting zoos.

**Pets.** A few reports have addressed transmission of pathogens from animals to people with CF and from people with CF to animals.<sup>277–281</sup> Following lung transplantation, *Bordetella bronchiseptica* pneumonia developed in 2 children with CF who acquired this pathogen from ill pet dogs, and 1 child died.<sup>278–280</sup> *B. bronchiseptica* was also detected in the respiratory tract of a child with CF who acquired this organism from an ill kitten, and this child had no adverse effects following treatment.<sup>280</sup> The LES of *P. aeruginosa* was transmitted from a 54-year-old man with CF to his pet cat; the cat developed respiratory symptoms.<sup>281</sup> The reptile collection of a person with CF was cultured and not found to harbor potential CF pathogens.<sup>277</sup>

MRSA colonization and infections have been described in dogs, cats, rabbits, hamsters, guinea pigs, turtles, chinchilla, and birds.<sup>282,283</sup> Outbreaks of MRSA have been described in animal hospitals, and both hospital- and community-associated strains have been identified. Most of these are sporadic infections, but when outbreaks occurred, they are thought to reflect initial transmission from people to animals.<sup>282,283</sup> There are limited data on the frequency of MRSA transmission from animals to humans, and there are no published data describing this phenomenon in people with CF.

*Mycobacterium marinum* skin and soft-tissue infections have been linked to cutaneous exposure to fish tanks.<sup>284</sup> Infections have occurred in both immunocompetent and immunocompromised patients, including transplant recipients.<sup>285</sup> Risk factors included exposure to fish tanks, the presence of open skin lesions during the cleaning of fish tanks, fishing, and exposure to aquarium water. There are no published reports of *M. marinum* infections in individuals with CF linked to fish tank exposure.

The CDC has several IP&C recommendations for people who own pets that are relevant for people with CF who own pets.<sup>286</sup> These recommendations emphasize using hygienic principles to prevent zoonotic infections, including (1) hand

hygiene, (2) disinfecting cages or tanks, (3) appropriate preventive care for pets, (4) prompt assessment of ill pets by a veterinarian, and (5) wearing gloves while cleaning fish tanks. Handling of reptiles is not recommended for any individuals at risk of serious complications of *Salmonella* infections.

**Pet therapy and service animals.** Many institutions, particularly children's hospitals, have introduced pet therapy programs that allow pets that have been certified to be free of certain infections to visit patients in healthcare settings. Recommendations for such programs include (1) training programs for the dogs and their owners, (2) stringent criteria for animal vaccinations and cleanliness, and (3) criteria for eligible patients.<sup>287,288</sup> The importance of hand hygiene before and after contact with the animals is emphasized. Patients under *Transmission-Based Precautions*, those with animal allergies, or children frightened by animals are generally excluded from participation. To date, there are no reports of transmission of potential pathogens from pet therapy animals to people with CF. People with CF can participate in such programs as per local institutional policies.

Service animals represent unique interactions between people and animals by providing guidance and support for both physical and emotional disabilities. There are no published reports of transmission of potential pathogens from service animals to people with CF. People with CF can participate in such programs when instituted as per relevant state and federal guidelines.<sup>289</sup>

**Farm animals.** Farm animals have been associated with several types of zoonotic infections. Farm animals have been linked to transmission of viral pathogens to humans, most notably influenza virus from pigs (<http://www.who.int/topics/influenza/en/>) and coronavirus.<sup>290</sup> Animal stalls, sheds, and coops may become heavily contaminated with fecal flora as well as with *Aspergillus* and other molds that proliferate in hay and other organic matter. Thus, it would be prudent for people with CF to avoid cleaning stalls, pens, or coops and to perform other chores instead.

To date, there are no reports of transmission of potential pathogens from farm animals to people with CF. Nonetheless, farm animals may represent a source of potential pathogens for people with CF. Theoretical concerns include (1) influenza infections; (2) ABPA caused by cleaning stables; (3) MRSA from horses and pigs; and (4) *P. aeruginosa* from horses.<sup>282,291</sup>

In summary, while there are limited data describing zoonotic infections in people with CF, people with CF and their families should follow preventive strategies described in national guidance documents.

### III.D. Acquisition from the Inanimate Environment

#### III.D.1. Nonhealthcare Sources: Soil, Organic Matter, and Water

**Overview.** There has been continuing concern that the natural environment (eg, water and soil) may be a reservoir for CF pathogens, such as *P. aeruginosa*, *Burkholderia* spp., NTM,

and *Aspergillus* spp. *P. aeruginosa* is ubiquitous in rivers, aquatic areas, soil, and plants worldwide. *B. cepacia* complex can be found in rice, wheat, and maize rhizospheres and in human sewage, and *B. gladioli* and *B. cepacia* are well-recognized plant pathogens. Other species, particularly *Burkholderia ambifaria*, exist within the rhizospheres of certain plants, while *B. multivorans* is infrequently recovered from the environment.<sup>292-296</sup> Several investigations since the publication of the 2003 Infection Control Guideline for CF have enhanced our understanding of the potential role played by the natural environment in the acquisition of CF pathogens and possible strain-specific reservoirs.

***Burkholderia* spp.** Implementation of strict IP&C measures has eliminated new acquisition of several epidemic *Burkholderia* strains, including ET12 and SLC6, among people with CF.<sup>154,297</sup> The incidence of infection with the PHDC and the Midwest clone has decreased but has not been eliminated with improved IP&C practices, and individuals with CF have been infected in the absence of apparent contact with others with CF (J.J.L., unpublished observations, October 2013). Strain PHDC has been recovered from agricultural soil in the United States, including onion fields, and from people with CF in diverse locations in the United States and Europe, suggesting that this strain is widely distributed in the natural environment, which serves as a source of ongoing acquisition.<sup>161,298-300</sup> Strains identical to those found in people with CF have also been isolated from onions and onion rot.<sup>301,302</sup> Furthermore, MLST analysis demonstrated that more than 20% of 381 CF isolates of *Burkholderia* were indistinguishable from strains recovered from the natural environment.<sup>301</sup> *B. cepacia* complex isolates with the same nucleotide identity at all 7 MLST loci have been isolated from people with CF and from river water, suggesting another possible environmental reservoir.<sup>302</sup> Finally, *B. cenocepacia* and *Burkholderia vietnamiensis* have been isolated from human sewage in the United Kingdom, but genotyping of these isolates was not performed.<sup>303</sup> In contrast, the Midwest strain of *B. cenocepacia* has not been found in the natural environment in regions where this strain infects people with CF.<sup>157,295</sup>

***P. aeruginosa*.** In the homes of people without CF, *P. aeruginosa* was detected most often from kitchen and bathroom drains but not from soil.<sup>304</sup> Similarly, in the homes of people with CF, *P. aeruginosa* was detected most often from shower drains and bathroom drainpipes.<sup>305,306</sup> While *P. aeruginosa* was recovered from 34% of the homes of newly infected people with CF (6% of samples), only 9 (18%) of 50 paired environmental and patient isolates were the same strain.<sup>306</sup> It remains unclear whether these *P. aeruginosa* strains were transmitted from the individuals with CF to the home environment or vice versa, but it suggests that cleaning and disinfection efforts in the homes of people with CF should focus on bathroom drains. There are insufficient data to determine the optimal frequency of cleaning showerheads. However, showerheads that have smoother surfaces may be less prone toward retaining organisms than those that have more crevices.

In Switzerland, a very low prevalence of *P. aeruginosa* was detected in public outdoor pools, standing water, and running water from the bathroom taps of people with CF.<sup>307</sup> *P. aeruginosa* has been isolated from whirlpool spas and hot tubs, and outbreaks of folliculitis and more serious infections caused by *P. aeruginosa* have been associated with hot tubs and whirlpool bathtubs.<sup>1</sup> In the United States, an observational study of children with newly acquired *P. aeruginosa* did not find that hot tub use was associated with age at *P. aeruginosa* acquisition but did find that swimming pool use in the previous year was protective.<sup>308</sup> These findings may reflect the relatively healthy pulmonary status of the children with CF enrolled in this study.

Natural bodies of fresh water (eg, rivers and lakes) have not been definitely proven to be a source of CF pathogens, but stagnant water should always be avoided due to a heavy burden of potential pathogens that flourish in organic debris. However, after heavy rains fresh bodies of water may be contaminated with sewage overflow, and local/state monitoring should be reviewed before swimming in such water.

In Germany, the *P. aeruginosa* strain designated clone C has been recovered from individuals with CF and from environmental samples from geographically diverse areas.<sup>309</sup> This same strain was subsequently identified from people with CF in the United Kingdom,<sup>173</sup> further suggesting a broad distribution of this particular strain in the natural environment. Other *P. aeruginosa* epidemic strains have not been identified in environmental samples, although genotyping surveys of large numbers of strains recovered from the environment have not been performed.

**Other gram-negative bacteria.** *S. maltophilia* is commonly found in soil and has been identified in well and river water, stream sediment, raw milk, frozen fruit, and sewage.<sup>310,311</sup> Species other than *A. xylosoxidans*, *A. rhulandii*, *Achromobacter piechaudii*, and *Achromobacter denitrificans* are found in soil and rarely cause human infections.<sup>312</sup>

**NTM.** The natural habitat for NTM is soil and water,<sup>313</sup> and the prevalence of NTM in the natural environment has wide geographical variation. Under experimental conditions, high numbers of pathogenic NTM were recovered from aerosols produced by 2 commercial potting soils. When NTM-infected individuals without CF submitted their own potting soils for PFGE analysis, 1 patient-soil pair had indistinguishable strains of *M. avium* and 2 patient-soil pairs had closely related strains of *M. intracellulare*, suggesting that potting soil could be a reservoir for NTM for people with CF who have intense, repeated exposures.<sup>314</sup> Another study isolated *M. avium-intracellulare* from 49% of residential soil samples in Japan and found 6 clinical and corresponding soil isolate pairs with identical genotypes from non-CF case patients with high soil exposure, defined as more than or equal to 2 hours/week, including digging or carrying soils, mowing grass, planting flowers, and exposure to soil dusts when farming or gardening.<sup>315</sup> Thus, although these studies were not conducted in people with CF, they do suggest that it may be prudent to limit exposure to soil.



***Aspergillus spp. and other filamentous fungi.*** The 3 most frequent species of filamentous fungi isolated from people with CF are *A. fumigatus*, *Scedosporium apiosporium*, and *A. terreus*. The natural habitat for *Aspergillus* spp. is soil, where they function as saprophytes growing on organic debris and recycling carbon and nitrogen throughout the environment. As a result, aerosolized conidia are ubiquitous in the environment. Characteristics of *A. fumigatus* that promote successful colonization of the airways include thermotolerance, small and abundant conidia, fast growth rates, and production of toxic metabolites and enzymes that are effective in breaking down complex polysaccharides. *A. terreus* is seldom reported from environmental sources, but in one study of air and surface samples from patient rooms and soil from the park adjacent to the hospital, *A. terreus* was found only in the soil samples; however, there were no common genotypes in patient and soil samples.<sup>105</sup> *S. apiosporium* is found in highly polluted soils and water but is rarely encountered in the environment. In one study of air and surfaces in the homes of 6 people with CF, large concentrations of *S. apiosporium* were isolated from 36 (65%) of 55 potted plants, but no genotyping was reported. In conclusion, the intensity and duration of exposure to these environmental reservoirs of filamentous fungi may increase the risk of acquisition by people with CF. However, without genotyping studies, this link remains unconfirmed.

**Summary.** Although many CF pathogens may be found in the inanimate environment, there are few instances where the same genotypes are found in the natural environment and in isolates from the respiratory secretions of people with CF. Nonetheless, it is prudent to avoid activities that include prolonged and intense exposure to soil, construction, and swimming in pools that are not appropriately chlorinated or swimming in stagnant water.

### III.D.2. Healthcare Sources: Water, Surfaces, Equipment, Air, and Contaminated Products

**Water and other fluids.** Water has been the source of healthcare-associated infections and linked to outbreaks caused by *Legionella*, *Pseudomonas*, *Stenotrophomonas*, *Burkholderia*, and *Achromobacter*.<sup>316</sup> In both inpatient and ambulatory healthcare settings where people with CF receive care, the highest number of positive environmental cultures for *P. aeruginosa* were from the sink drains or showers in patient rooms.<sup>127,317</sup> One study found genetic relatedness in 19 of 21 clinical and environmental strains, but it was uncertain whether *P. aeruginosa* was transmitted from the individuals with CF to the clinical environment or vice versa.<sup>317</sup>

The sources of healthcare-associated infections caused by *S. maltophilia* are poorly understood. In non-CF patients, *S. maltophilia* has been linked to inappropriate use of hand moisturizing lotion, rather than soap, by healthcare personnel<sup>318</sup> and to contamination of faucet aerators in intensive care unit (ICU) sinks.<sup>319</sup> Furthermore, *S. maltophilia* has been

recovered from hospital sink drains, faucets, and potable water.<sup>140,320</sup> In general, genotyping analyses have not shown that isolates obtained from the hospital environmental are the same as those recovered from patients,<sup>141,320</sup> and the majority of non-CF patients infected with *S. maltophilia* had genetically distinct strains.<sup>321</sup> None of 24 *S. maltophilia* isolates recovered from water, taps, and sinks in patient rooms matched the strains recovered from individuals with CF.

Despite these occasional outbreaks related to a water source, routine environmental sampling, including culturing water supplies, is not advised, except for water-quality determinations in hemodialysis settings and other situations where sampling is directed by epidemiologic principles, and results can be applied directly to infection control decisions.<sup>2</sup> Removal, cleaning, and disinfecting of showerheads and tap aerators once a month with an EPA-registered product or a chlorine bleach solution (500–615 ppm [1 : 100 dilution]) has been recommended as part of *Legionella* control measures, but there are insufficient data to support a widespread recommendation and specific time intervals, given the infrequency of outbreaks associated with faucet aerators.<sup>2</sup>

**Healthcare surfaces.** Several studies in healthcare facilities, many of which utilized molecular typing methods, have identified the same pathogens on inanimate surfaces as those recovered from non-CF patients, including VRE, MRSA, *C. difficile*, *Acinetobacter* spp., and norovirus.<sup>322–325</sup> Pathogens shed by patients can contaminate healthcare surfaces at concentrations sufficient for transmission, can survive for extended periods of time, and can be transferred to the hands and clothing of healthcare personnel, leading to further transmission.<sup>5</sup> Surface contamination with VRE resulted from the failure to clean rather than faulty cleaning methods or products, thereby supporting the concept that education about cleaning and compliance monitoring could reduce environmental contamination.<sup>326</sup> As further evidence of the role played by contaminated surfaces in hospital-associated infections, a patient admitted to a room previously occupied by a patient colonized or infected with a pathogen (eg, MRSA, VRE, *C. difficile*, or *Acinetobacter* spp.) has an increased likelihood of developing colonization or infection with that pathogen due to inadequate decontamination of surfaces.<sup>5,327–329</sup>

In healthcare facilities that deliver care to people with CF, contamination of dry environmental surfaces with CF pathogens was low, but contamination of the hands of people with CF was higher.<sup>128</sup> In a Liverpool CF center, contamination of inanimate surfaces was transient and negative after patient discharge and routine cleaning.<sup>127</sup> Similar findings have been noted in other CF clinics.<sup>128,317</sup>

**Healthcare equipment.** Contamination of medical equipment is another potential source of pathogens for people with CF. During simulated examinations, stethoscopes acquired and transferred MRSA and *C. difficile* nearly as often as gloved hands,<sup>330</sup> and RSV has been detected on stethoscopes in non-CF settings.<sup>331</sup> In CF settings, 26 stethoscopes used in a clinic were not found to be contaminated with CF pathogens,<sup>332</sup> and

in a more recent study *P. aeruginosa* and *S. aureus* were rarely recovered from stethoscopes, pulse oximeters, and otoscopes.<sup>128</sup> Nevertheless, there is sufficient evidence to support the importance of cleaning and disinfecting medical equipment after use by one person with CF prior to use by another person with CF, according to hospital protocols.

Numerous outbreaks (and pseudo-outbreaks, ie, no evidence of infection or disease linked to recovery of micro-organism) of *P. aeruginosa*, other gram-negative bacilli, and NTM have been linked to contaminated medical devices. For example, outbreaks of *P. aeruginosa* have been linked to inadequate processing of rigid<sup>333,334</sup> and flexible laryngoscopes,<sup>333</sup> flexible bronchoscopes,<sup>335-337</sup> and defective repro-cessors for bronchoscopes and endoscopes.<sup>338</sup> Similarly, outbreaks and pseudo-outbreaks of NTM have been linked to bronchoscopes,<sup>339</sup> and a hospital hydrotherapy pool contaminated with *M. chelonae* that led to infections in children with CF.<sup>340</sup>

**Air.** Infectious droplets in the air may represent another source of transmission for CF pathogens. *P. aeruginosa* was recovered from the air in hospital rooms 45 minutes to 2 hours after people with CF left,<sup>126,127</sup> and the LES of *P. aeruginosa* was recovered from the corridors of CF clinics as long as 3 hours after individuals had left the area.<sup>127</sup> In the United Kingdom, after individuals with CF performed PFTs or nebulization, the Manchester epidemic strain of *P. aeruginosa* as well as nonepidemic *P. aeruginosa* were recovered from the air.<sup>341</sup> In France, the concentration of *P. aeruginosa* was highest after the person with CF awoke or performed chest physiotherapy.<sup>126</sup> Several CF pathogens (ie, *P. aeruginosa*, MSSA, and MRSA) were recovered from air collected 3 feet from CF subjects in exam rooms; these strains were the same as those infecting the subjects as assessed by PFGE.<sup>128</sup> Similarly, CF pathogens were recovered from the air 6 feet from CF subjects performing PFTs.<sup>125</sup> Factors associated with generating infectious droplets of *P. aeruginosa* are unknown, as exacerbations, sick versus well CF clinic visits, or age were not predictive.<sup>125,128</sup> We emphasize that none of these observational studies were associated with person-to-person transmission, but such data provide evidence of the potential for such transmission and, thus, the importance of implementing strategies to prevent droplet transmission. Furthermore, as previously described the potential for transmission of *M. abscessus* by droplets or droplet nuclei has been suggested,<sup>66,129</sup> but to our knowledge no studies to date have demonstrated the specific route(s) of NTM transmission among people with CF.

**Contaminated products.** *Burkholderia* spp. are the most frequently isolated bacteria in nonsterile and sterile pharmaceutical products that have been recalled.<sup>342,343</sup> Many healthcare-associated outbreaks of *Burkholderia* infections associated with contaminated skin antiseptics, mouthwashes, ultrasound gels, medications, and medical devices have been described.<sup>344-362</sup> Other products that have become contaminated during use include nasal irrigation bottles contaminated with *P. aeruginosa*,<sup>363,364</sup> multiuse albuterol vials contaminated with *B.*

*cepacia*,<sup>348,357</sup> acupuncture devices disinfected with glutaraldehyde contaminated with *M. abscessus*,<sup>365</sup> cosmetic surgical supplies contaminated with mycobacterial spp., and supplies used for liposuction.<sup>366</sup> Outbreaks of *Achromobacter* spp. have been attributed to contaminated disinfectant solutions, dialysis fluids, saline solution, and deionized water.<sup>367</sup> In addition, products used in nonhealthcare settings can become contaminated during manufacturing and can cause extensive outbreaks. These have included alcohol-tattoo ink contaminated with *M. chelonae*<sup>368</sup> and footbaths in nail salons contaminated with NTM spp.<sup>369</sup>

**Summary.** Most potential sources of pathogens that have been identified in the healthcare environment can be eliminated by following facility processes for the cleaning and disinfection of surfaces and equipment. Although there are no published reports of proven acquisition by people with CF from contaminated products, such sources present a potential risk and should be considered during any outbreak investigation in people with CF. The CF care team should receive alerts for contaminated products sent by the Food and Drug Administration's (FDA's) MedWatch and the CDC's Health Alert Network.

### III.D.3. Construction and Renovation

Multiple outbreaks of airborne filamentous fungi, principally due to *Aspergillus* spp., have been reported in hospitals associated with construction, renovation, repair, and demolition.<sup>370-372</sup> While most of the outbreaks were related to construction or renovation, problems with the air supply system have also been implicated. The most common species involved in the outbreaks were *A. fumigatus* and *A. flavus*, although a substantial number involved more than 1 species of *Aspergillus*. Groups at highest risk for nosocomial infection during these outbreaks included persons with hematologic malignancy, solid-organ transplantation, and other immunocompromising conditions (eg, high-dose steroid therapy).

We were unable to find any studies assessing a healthcare source for *Aspergillus* in CF. Furthermore, CF has not been described as a risk factor for acquisition of invasive aspergillosis in nosocomial outbreaks related to construction, renovation, repair, or demolition. Nevertheless, it is prudent to ensure that dust-containment strategies are followed throughout the entire healthcare facility.

## IV. STRATEGIES TO REDUCE TRANSMISSION AND ACQUISITION OF CF PATHOGENS

### IV.A. Overview

Several published experiences have described the effectiveness of stringent IP&C practices and policies for reducing the prevalence of epidemic *B. cepacia* complex,<sup>25</sup> the LES strain,<sup>1,373,374</sup> and other transmissible strains of *P. aeruginosa*.<sup>30,185,375,376</sup> Interventions have included education of healthcare personnel and people with CF and their families about risk factors for

routes of transmission and preventive strategies, emphasizing hand hygiene for people with CF and healthcare personnel, the use of single-patient rooms when people with CF are admitted to the hospital, *Contact Precautions*, avoiding socializing in both healthcare and nonhealthcare settings, improving detection of CF pathogens in microbiology laboratories, decontaminating the healthcare environment, and cohort segregation of patients known to be harboring specific pathogens while in a CF clinic.<sup>1</sup> Most recently, efforts to prevent further transmission of *M. abscessus* subsp. *massiliense* in an adult CF clinic included educating and reinforcing IP&C strategies for CF to the CF care team and individuals with CF, cleaning all clinic and equipment surfaces twice, and the use of a negative pressure room for all NTM-infected individuals.<sup>66,129</sup> In a pediatric CF center experiencing an outbreak of *M. abscessus*, investigators concluded that the PFT laboratory was the most likely source of transmission and changed from performing PFTs in a central laboratory to performing portable spirometry in clinic exam rooms.<sup>230</sup> Notably, several strategies were used to control each outbreak and most likely included enforcing preexisting IP&C practices. Thus, it is impossible to conclude which intervention(s) were most effective. However, similar to other prevention programs in IP&C—such as reducing device-related infections, including central line-associated bloodstream infections and ventilator-associated pneumonia—it is likely that implementation of a bundle of practices is required to reduce transmission of CF pathogens.<sup>377-379</sup>

**The following sections describe the IP&C strategies recommended in this updated guideline. The recommendations are intended for all people with CF, regardless of respiratory tract culture results.** The recommendations should also be followed for people with CF following lung or liver transplantation, as such individuals are immunocompromised, at risk of becoming infected from others with CF, and following transplantation may continue to harbor CF pathogens. The recommendations for healthcare settings are intended for CF clinics and other ambulatory care areas, inpatient settings, diagnostic areas, and all clinical research activities. Successful and consistent implementation of IP&C practices must include the ongoing participation of people with CF and their families and auditing the performance of healthcare personnel. Depending on available resources, a center may choose to implement the recommended IP&C practices in all areas at once or may choose to stage the implementation by setting.

#### IV.B. Education Strategies

**Overview.** To successfully implement the recommendations in this guideline, several stakeholders must be educated, including (1) all healthcare personnel who have contact with people with CF (eg, physicians, nurses, respiratory and physical therapists, radiology and laboratory personnel, social workers, operating room staff members, research coordina-

tors, administrative personnel, and environmental services personnel); (2) all people with CF, from toddlers to adults (individuals may have varied age-appropriate experience, knowledge, and motivation regarding IP&C); and (3) families and friends of people with CF.

Families of older adolescents and adults with CF may struggle to accept the paradigm shift that has taken place for IP&C during the past decade on the basis of new knowledge of transmission of CF pathogens. Families of newly diagnosed individuals are more likely to be receptive to the current recommendations, as they have less prior experience. Therefore, different strategies may be required for educating different groups.

Educators must recognize the needs and levels of understanding of various groups of stakeholders to optimize the effectiveness of educational programs. While the CF Foundation has developed educational tools, individual CF center staff may also create their own tools and include people with CF and their families in the development process. Fortunately, the disciplines of CF and of IP&C have a great deal of experience providing education to other healthcare personnel, patients, and families. Some examples include the myriad educational materials to promote proper hand hygiene, cough etiquette, and respiratory hygiene aimed at preventing the spread of pathogens transmitted by the droplet route; these are available in many languages and literacy levels.<sup>380</sup> Information is also available on the CF Foundation's website (<http://www.cff.org>).

Education should be provided to people with CF and their families on a regular basis using a variety of learning methods, including written, visual, demonstration, and return demonstration. In a survey of people with CF and the parents of children with CF, only 80% reported that they had discussed hand hygiene with their CF care team; fewer were told to perform hand hygiene when entering (39%) and leaving (49%) the CF clinic.<sup>381</sup> This study provides just one example of missed opportunities to improve IP&C education.

The following components of effective education should be incorporated into IP&C education for CF: (1) developing knowledge, skills, and attitudes; (2) identifying and engaging stakeholders; (3) utilizing positive deviance and early adopters as described below; and (4) performing audits and providing feedback.

**Knowledge, skills, and attitudes.** The importance of knowledge, skills, and attitudes in educating individuals to change behavior has been described in the CF community<sup>381,382</sup> as well as for healthcare personnel.<sup>383-387</sup> **Knowledge**, or facts, can be taught using didactic or case-based methods at the bedside or in the clinic. Adults learn best if they perceive the relevance of the information to their personal situation and are provided with the rationale. Adult learning is most effective when flexible and when educational methods encourage networking, critical analysis, and reflection on practice and provide an opportunity for open questioning. In contrast, children will benefit from methods that are age appropriate. Provision of

repeated exposure to educational information is critical to reinforce the principles and allow for questioning. **Skills** are practical tasks that range from very simple procedures to complex techniques applied to varying circumstances. Observations of adult learners and return demonstrations by adult learners are effective methods to assess skill level and competency to perform tasks independently. Children are also eager to demonstrate their mastery of new skills, and their learning can be validated using a show-and-tell strategy. **Attitudes** are the products of individual beliefs and professional and personal life experiences. Focus groups and questionnaires are useful tools for defining the beliefs of the target audience and addressing specific attitudes and beliefs; these techniques have been successful with environmental services workers.<sup>386</sup>

**Stakeholders.** Implementation of the recommendations in this document will likely require many stakeholders to change their practices. Therefore, people with CF, their families, and healthcare personnel must believe that change is necessary. People with CF must believe that change will benefit them. Healthcare personnel must believe that change will benefit their patients and/or themselves in terms of being rewarded for their performance and professionalism. Furthermore, effective education must engage clinical opinion leaders who command the respect of those around them, understand the reasons for change, and can help implement needed change. While senior clinical staff members can serve as role models for needed change, in other settings such individuals may be the most resistant to change. If the latter occurs, focused efforts are needed to engage these individuals and ensure that they understand the importance of the recommended changes in practice and their unique role in modeling these changes. Notably, the lack of positive role modeling among senior clinical staff was cited as a reason for low adherence to hand hygiene practices.<sup>388</sup>

**Positive deviance/early adopters.** Another successful strategy to effect change is the use of positive deviance or early adopters. **Positive deviance** is based on the observation that within every community are individuals or groups whose unique behaviors and strategies enable them to find better solutions to problems than their peers, despite having access to the same resources and facing similar or worse challenges. Positive deviance is an asset-based, problem-solving, community-driven approach that facilitates discovery of successful behaviors and strategies and the development of an action plan to promote their adoption by all concerned.<sup>389</sup> Positive deviance has been used to combat seemingly impossible problems in the community (eg, childhood malnutrition) and in healthcare settings (eg, reduction of MRSA infections and improvement in hand hygiene compliance).<sup>390</sup> Thus, the CF community can be innovative and can include the positive deviance approach to effect change.

**Audits and feedback.** Auditing healthcare personnel adherence to recommended practices (eg, hand hygiene and *Contact Precautions* for patients with MRSA) has become an important part of routine IP&C and/or quality improvement

programs and is required by credentialing organizations, such as The Joint Commission. Feedback may occur at any time and by anyone when a lapse in practice is observed. Trends of audit results should be provided to clinical teams at regular intervals (eg, quarterly, semiannually, or annually). Organizational research has demonstrated that the success of adherence to guidelines is determined by the quality of the feedback.<sup>391</sup> Feedback should be timely, individualized, non-punitive, and customizable and should involve the recipients of the feedback in the planning of the feedback program. Thus, collaboration of the CF care team with IP&C staff to develop an auditing and feedback program is recommended to facilitate implementation of the recommendations in this guideline. The interested reader is referred to a discussion of the theories of feedback interventions.<sup>392</sup>

#### IV.C. Hand Hygiene

Hand hygiene is a component of *Standard Precautions*, which are practices aimed at preventing the transmission of infectious agents. *Standard Precautions* are based on the principle that all blood, body fluids (eg, sputum and saliva), secretions, excretions (eg, urine, stool, and wound drainage but *not* sweat), nonintact skin, and mucous membranes *may* contain transmissible infectious agents. Therefore, containing these potential sources will reduce the risk of transmission of infectious agents. Recommendations for *Standard Precautions* are based on strong evidence from healthcare settings that has been summarized in the CDC/HICPAC 2007 Guideline for Isolation Precautions.<sup>6</sup>

Hand hygiene is the single most important measure to protect people with CF, healthcare personnel, family members, and friends from transmission and acquisition of potential infectious agents and to prevent contamination of the environment. The CDC/HICPAC and the WHO have published comprehensive guidelines for hand hygiene in healthcare settings,<sup>393,394</sup> and the updated SHEA/IDSA Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals, published in 2014, contains information on hand hygiene. Many recommendations in these guidelines can also be applied to nonhealthcare settings, including the home, school, and workplace. Hand hygiene in nonhealthcare settings has reduced respiratory and gastrointestinal tract infections.<sup>395,396</sup> Hand hygiene opportunities for healthcare personnel, people with CF, and families are summarized in Table 7.

Healthcare personnel should perform thorough hand hygiene, as presented in the figures in the 2009 WHO guideline,<sup>394</sup> before and after contact with patients and whenever hands are contaminated with respiratory secretions or other body fluids. Contamination may occur from direct patient care activities, from contact with surfaces or equipment in a patient's environment, and/or following coughing or sneezing by healthcare personnel. Use of an alcohol-based hand rub is the preferred hand hygiene method, as these products have

TABLE 7. Examples of Opportunities for Hand Hygiene by Healthcare Personnel, People with Cystic Fibrosis (CF), and Families

	Healthcare personnel	People with CF	Family members
Entering CF clinic or hospital room	X	X	X
Leaving CF clinic or hospital room	X	X	X
Before or after contact with patient	X	NA	NA
Before and after performing pulmonary function tests	X	X	NA
After obtaining respiratory tract culture	X	X	X
After coughing	X	X	X
Before putting on and after removing gloves	X	NA	NA
When hands are contaminated with respiratory secretions	X	X	X
Before and after cleaning and disinfecting nebulizer equipment	X	X	X
Before donning gloves for performing sterile procedures	X	NA	X <sup>a</sup>
After using restroom	X	X	X

NOTE. X, applicable to this population; NA, not applicable to this population.

<sup>a</sup> If performing activities involving a central venous catheter.

demonstrated greater efficacy in reducing bacterial contamination of hands compared with washing with plain or antimicrobial soap and water.<sup>393</sup> Alcohol-based hand rubs have excellent activity against gram-positive and gram-negative bacteria, including MDROs, NTM, a variety of fungi, and such viruses as rhinovirus, adenovirus, influenza virus, and RSV.<sup>393,394</sup> However, in healthcare settings soap and water are used when hands are visibly dirty, sticky, or contaminated with blood or body fluids. If soap and water are used, antimicrobial soap, such as one containing chlorhexidine gluconate, is preferred when caring for people with CF. Use of commercially available antimicrobial soaps in the home is not recommended, as these products do not provide any additional benefits compared with nonantibacterial soaps.<sup>397</sup>

The hands of healthcare personnel caring for people with CF and the hands of people with CF and their families can become contaminated with CF pathogens due to contact with infectious respiratory secretions. In a study conducted in 7 CF clinics, the hand contamination rate among people with CF ( $n = 100$  participants) was 13.5%, and, in addition, 6.3% of participants without initial detection of CF pathogens contaminated their hands during clinic visits.<sup>128</sup>

Fingernails are of special concern, as the subungual areas of hands harbor high concentrations of bacteria.<sup>398</sup> Compared with healthcare personnel with natural nails, those wearing artificial nails were more likely to harbor gram-negative organisms on their fingertips before and after hand hygiene.<sup>399-401</sup> Artificial nails worn by healthcare personnel have been associated with outbreaks of infectious agents, including *P. aeruginosa*.<sup>402-405</sup> While no specific studies of the role played by artificial nails in the transmission of pathogens in CF have been performed, the clinical experience in ICUs and other healthcare settings can be applied to CF. Thus, healthcare personnel who provide care to people with CF should not wear artificial nails. While studies have not evaluated the risk of artificial nails worn by people with CF or their families, it is prudent to avoid this potential risk factor for acquisition of gram-negative pathogens.

#### IV.D. Personal Protective Equipment (PPE)

PPE are wearable barriers intended to protect healthcare personnel from exposure to or contact with infectious agents. PPE includes gloves, gowns, facemasks, respirators, and eye protection (eg, goggles and face shields). Healthcare personnel can wear PPE alone or in combination, based on the *anticipated* patient interaction and *potential* for exposure to blood or body fluids or for exposure to known or suspected pathogens. PPE is subject to FDA regulations under the device provisions of the federal Food, Drug, and Cosmetic Act.<sup>406</sup> CDC/HICPAC recommendations for standard and transmission-based precautions provide detailed indications for PPE use.<sup>6</sup> A summary of the recommended use of PPE by healthcare personnel, people with CF, and their families is provided in Table 8.

##### IV.D.1. Gowns and Gloves

**Healthcare personnel.** As per CDC recommendations, healthcare personnel wear gowns to protect their skin from contact with blood and body fluids and to prevent soiling or contamination of their clothing. Clothing worn by healthcare personnel can be contaminated with MDROs, including MRSA, VRE, and gram-negative bacilli.<sup>407-410</sup> As per CDC recommendations, healthcare personnel wear gloves for the following reasons: (1) to prevent possible contact with blood or body fluids, mucous membranes, nonintact skin, or other potentially infectious materials; (2) to prevent transmission of pathogens transmitted by the contact route when having direct contact with patients colonized or infected with such pathogens (eg, VRE, MRSA, or RSV); or (3) when handling or touching visibly or potentially contaminated environmental surfaces and patient care equipment.<sup>5</sup> Gloves worn by healthcare personnel reduce the transmission of viral and bacterial pathogens but do not replace hand hygiene—they are worn in addition to the practice of hand hygiene.<sup>411-413</sup>

For *Contact Precautions*, the CDC recommends that healthcare personnel don both gown and gloves **on room entry** for

TABLE 8. Use of Personal Protective Equipment by Healthcare Personnel, People with Cystic Fibrosis (CF), and Families

	Healthcare personnel	People with CF	Family members without CF
Gowns	Wear when caring for all people with CF, per <i>Contact Precautions</i> and per <i>Standard Precautions</i>	Not recommended Perform hand hygiene as described in Table 7	Not recommended routinely Use as defined in local hospital policy when visiting hospitalized patients Perform hand hygiene as described in Table 7
Gloves	Wear when caring for all people with CF, per <i>Contact Precautions</i> and per <i>Standard Precautions</i>	Not recommended Perform hand hygiene as described in Table 7	Not recommended routinely Use as defined in local hospital policy when visiting hospitalized patients Perform hand hygiene as described in Table 7
Masks	Wear surgical (also referred to as isolation or procedure) mask when caring for patients under <i>Droplet Precautions</i> Wear face shield when splashes are likely to occur as per <i>Standard Precautions</i>	Wear surgical (also referred to as isolation or procedure) mask when in common areas in healthcare settings (eg, corridors, waiting areas, radiology) Do not wear when in exam room, in hospital room, or when performing pulmonary function tests	Not recommended in CF clinics Use as defined by local hospital policy when visiting hospitalized patients
Respirator or PAPR <sup>a</sup>	Wear N-95 respirator or PAPR when caring for patients under <i>Airborne Precautions</i>	Not recommended Wear mask as described above	Wear N-95 to enter room for suspected or confirmed tuberculosis according to hospital policy

<sup>a</sup> Powered air-purifying respirators (PAPRs) are recommended for individuals who are unable to tolerate or pass a fit test for an N-95 respirator.

all contacts with the patient and/or environmental surfaces and patient care equipment that could be potentially contaminated.<sup>5</sup> For *Standard Precautions*, an isolation gown is worn only if there is anticipated contact with blood or body fluids. However, application of appropriate *Standard Precautions* may be inconsistent, because healthcare personnel cannot always anticipate potential contact with infectious body fluids and because PPE are not always readily available.<sup>414</sup>

All healthcare personnel should wear gowns and gloves when caring for all people with CF **regardless** of respiratory tract culture results. The rationale for the universal use of gowns and gloves by healthcare personnel caring for people with CF is that direct and indirect contact with respiratory secretions that may contain transmissible pathogens is likely to occur, including through contact with contaminated environmental surfaces and equipment. Additional support for this practice is derived from a study in adult medical and surgical ICUs that demonstrated decreased acquisition of MRSA in units where healthcare personnel wore gowns and gloves for all patient contacts and when entering any patient room.<sup>407</sup>

**People with CF and families/visitors.** There are no data to support a recommendation for people with CF or their families to wear gowns or gloves in healthcare or nonhealthcare settings to prevent the transmission or acquisition of

potential pathogens. However, some high-risk units in hospitals may choose to require visitors to wear gowns and gloves.

#### IV.D.2. Masks, Eye Protection, and Respirators

**Healthcare personnel.** As per the CDC recommendations, facemasks are loose-fitting disposable PPE worn by healthcare personnel when caring for patients with known or suspected infections that require *Droplet Precautions* (eg, influenza, pertussis, or adenovirus infection). Masks, in combination with eye protection, are worn to protect healthcare personnel during procedures and patient care activities likely to generate splashes or sprays of blood, body fluids, or secretions (eg, suctioning, intubation, and operative procedures). These types of masks may be referred to as surgical, procedure, or isolation masks. All facemasks are single use and should be changed whenever damaged, soiled, or damp or if breathing through the mask becomes difficult. While CF pathogens are transmitted patient to patient by the droplet route, such pathogens are not transmitted to healthcare personnel. Thus, healthcare personnel are **not** required to wear a mask routinely when caring for people with CF unless there is an infection with a known or suspected pathogen that requires *Droplet Precautions* or according to *Standard Precautions* as described above.

A respirator is a tight-fitting device worn on the face, covering at least the nose and mouth, to reduce the wearer's risk of inhaling droplet nuclei containing infectious agents. The Occupational Safety and Health Administration sets regulatory standards for respirator use.<sup>415</sup> Healthcare personnel who may have exposure to airborne infectious agents are medically evaluated and fit-tested to wear a disposable respirator, usually one designated N95, which means that while breathing through it the filter removes 95% of airborne particles. Healthcare personnel who cannot wear or be adequately fitted with an N95 respirator may use a PAPR with a disposable hood. Respirators are worn by all healthcare personnel entering the room of a patient under *Airborne Infection Isolation* for pulmonary TB.<sup>4,6</sup> Respirators are also worn when performing an aerosol-generating procedure (eg, open suctioning, emergency intubation, or bronchoscopy) on a patient with known or suspected influenza.<sup>14</sup> Healthcare personnel who will be using an N95 respirator should be fit-tested annually to ensure that the proper size is used.

**People with CF and families/visitors.** Masks prevent ill individuals from spreading infectious respiratory droplets. For people entering healthcare settings, availability of facemasks is an essential component of respiratory hygiene and cough etiquette, particularly during times of seasonal community-onset respiratory infections (eg, influenza).<sup>6</sup> Masks are available in adult and child sizes (designed for ages 5–12 years). As described above (*Section II*), experimental and clinical data have demonstrated the generation of infectious droplets by people with CF; these studies confirm the potential for transmission of CF pathogens to others with CF by the droplet route.<sup>1,120–122,125–127</sup> Thus, to prevent transmission by the droplet route people with CF should routinely don a facemask of appropriate size when entering healthcare settings where they are likely to encounter others with CF. Such settings include the common areas of the CF clinic, when leaving their hospital room, or when leaving the clinic exam room. However, it is possible that very young children, people in respiratory distress, and people exercising may not be able to tolerate a mask. Such individuals should be instructed to practice other components of respiratory hygiene (ie, cough into a tissue, discard the tissue, perform hand hygiene after coughing, etc) and remain at least 6 feet from others with CF.

Respirators are not recommended routinely for patient use, but the CDC recommends that visitors wear respirators when entering the room of a patient under *Airborne Infection Isolation Precautions* with suspected or confirmed pulmonary TB.<sup>4</sup>

#### IV.E. Environmental Cleaning and Disinfection

##### IV.E.1. Overview

Many studies published in the past decade have demonstrated that contaminated environmental surfaces play a role in the

transmission of healthcare-associated pathogens (eg, MRSA, VRE, *C. difficile*, and *P. aeruginosa*) and that improved environmental cleaning and disinfection are effective in reducing the transmission of such pathogens.<sup>322–325,416,417</sup> The importance of the principles of environmental contamination and cleaning and disinfection can be extrapolated to the CF clinic where surface contamination has been studied extensively.<sup>126–128,317</sup> As all people with CF may harbor transmissible pathogens or are at risk of acquiring such pathogens, environmental cleaning and disinfection practices should be implemented when caring for all people with CF.

Four strategies can reduce transmission from contaminated healthcare surfaces and equipment: (1) improve cleaning and disinfection of the rooms of patients known to carry healthcare-associated pathogens after discharge (ie, terminal cleaning); (2) disinfect high-touch surfaces in isolation rooms daily; (3) disinfect portable equipment between patients or use disposable or dedicated equipment in isolation rooms; and (4) expand efforts to improve cleaning and disinfection of all rooms if there is concern that patients harboring MDROs are not identified or are identified after long delays. Automatic disinfection devices (eg, hydrogen peroxide vapor and ultraviolet cleaning) are promising but require additional studies before recommendations for their routine use can be made.<sup>416,418</sup>

Contamination of surfaces most often results from the failure to clean rather than faulty cleaning methods or ineffective products, which supports the importance of education and monitoring adherence.<sup>326</sup> Standardization of cleaning and disinfecting methods, utilizing educational programs, and checklists and audits can all improve effectiveness. Three types of audits after cleaning and disinfecting have been described: (1) direct observation, (2) use of fluorescein powder or ATP detection methods to demonstrate the removal of potentially infectious pathogens, and (3) bacterial cultures of surfaces. Objective measures utilizing fluorescein dye or ATP detection are the most effective and practical to implement.<sup>419,420</sup> Since most IP&C departments are currently engaged in monitoring environmental cleaning, coordination between the CF care team and the IP&C team is advised. Strategies to enhance the effectiveness of environmental cleaning in both ambulatory and inpatient areas are provided in Table 9. Checklists and other tools for cleaning and additional background information are available on the CDC website.<sup>419</sup>

##### IV.E.2. Healthcare Facilities: Respiratory Therapy, Nebulizers, and Diagnostic Equipment

Devices used for respiratory therapy (eg, nebulizers) or for diagnostic evaluation (eg, bronchoscopes and spirometers) are potential reservoirs or vehicles for the transmission of infectious organisms. Routes of transmission may be from a contaminated device to a patient, from a patient to a patient via a contaminated device, or from one body site to the

TABLE 9. Strategies to Enhance the Effectiveness of Environmental Cleaning in Ambulatory and Inpatient Settings for People with Cystic Fibrosis (CF)

Strategies	Elements	Monitoring adherence
Type of programs		
Level 1 (basic)	<ol style="list-style-type: none"> <li>1. IP&amp;C program coordinated with EVS with joint definition of institutional expectations and clearly stated responsibilities</li> <li>2. Structured education of EVS staff that includes techniques of cleaning and disinfection and plans for monitoring</li> <li>3. Routine reporting to IP&amp;C and facility leadership</li> </ol>	<ol style="list-style-type: none"> <li>1. Development of measures for monitoring and identification of individuals to perform auditing and feedback</li> <li>2. Interventions to optimize thoroughness of terminal room cleaning to be a standing agenda item on the IP&amp;C or quality committee agenda</li> <li>3. Documentation of consideration of moving to level 2 program in committee minutes</li> </ol>
Level 2 (advanced)	More comprehensive implementation of above elements	More comprehensive implementation of above elements
Checklists	Develop checklists for cleaning and disinfecting each of the following: <ol style="list-style-type: none"> <li>a. CF clinic exam room after each patient</li> <li>b. PFT machines after each patient</li> <li>c. Common areas of CF clinic daily</li> <li>d. iPads, computers, medical equipment</li> <li>e. Equipment in radiology area or other common procedure areas</li> <li>f. Restrooms</li> <li>g. Inpatient rooms</li> </ol>	Observations ATPase strips Fluorescent marker (eg, Glogerm)
Specialized training	Educate CF clinic staff and EVS staff about IP&C for CF	Appropriate educational level testing to ensure understanding of rationale for recommendations

NOTE. See the Centers for Disease Control and Prevention website for downloadable tools and informational brochures (<http://www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html>). EVS, environmental services; IP&C, infection prevention and control; PFT, pulmonary function test.

respiratory tract of the same patient. Reservoirs of aerosol-producing devices (eg, nebulizers) are subject to overgrowth of bacteria that can be aerosolized during device use. Although a patient's own respiratory flora usually contaminate nebulizers, it is prudent not to introduce those microorganisms into the lower respiratory tract during aerosol treatments. Thus, processes for proper cleaning and sterilization or disinfection of reusable equipment are essential components of a program to prevent infections of people with CF. Evidence-based guidelines for the care of bronchoscopes and other semicritical items have been published, and the latest developments in reprocessing semicritical items were recently reviewed.<sup>421</sup> Hospitals must follow these recommendations.

Several studies of infections that occurred in association with contaminated respiratory therapy and diagnostic equipment have provided important insights into preventing such infections. These include the following: (1) Strict adherence to aseptic technique is important. (2) Proper training of personnel responsible for reprocessing equipment is important, including demonstration of competency initially and then at least annually, as is consistent adherence to reprocessing guidelines.<sup>421</sup> (3) Single-dose medication vials are always pre-

ferred, due to the risk of contamination<sup>349,357,422,423</sup> (if multi-dose medication vials must be used, then the manufacturer's directions for handling, dispensing, and storing must be followed precisely to prevent contamination and the transmission of potential pathogens). (4) Tap water may be used for cleaning nebulizers and other respiratory therapy equipment, but sterile water or water processed by filtration (filter size of less than or equal to 0.2 microns) must be used in the final rinse because tap water and distilled water may be contaminated with CF pathogens.<sup>424</sup> Sterile water or properly filtered water is recommended for filling respiratory therapy equipment reservoirs (eg, humidifiers), and sterile saline is recommended for sinus rinses. (5) Equipment should be cleaned before disinfection or sterilization to ensure that the sterilization process is maximally effective.<sup>7</sup> (6) Air-drying equipment after it has been cleaned and disinfected is an essential step prior to storage because items that remain wet provide favorable conditions for bacterial growth.<sup>1,7</sup>

Bacterial contamination of nebulizers used during hospitalizations has been demonstrated.<sup>320</sup> However, methods of caring for nebulizers in the hospital setting have been widely disparate<sup>424-426</sup> and have included changing nebulizers every



2–7 days; changing mouthpieces after each use; and rinsing them with sterile water, drying them, and then placing them in a plastic bag between uses. In the preparation of recommendations for this guideline, discrepancies in published guidelines were noted.

Furthermore, there are limited data to inform recommendations for care of disposable nebulizers used in the hospital. The care of nebulizers was addressed in a study of 30 people with CF admitted for pulmonary exacerbations who received aerosolized bronchodilator therapy 4 times daily.<sup>427</sup> The nebulizers were not cleaned or disinfected between treatments but were replaced after 24 hours. Cultures of the residual fluid inside the nebulizer cup were obtained before administering successive treatments and prior to discarding the nebulizer after 24 hours of use. None of the 150 nebulizer samples obtained grew CF pathogens. This study did not address the use of disposable nebulizers for longer than 24 hours.

Important principles for the care of **disposable** nebulizers used in the hospital for individuals with CF are as follows: (1) nebulizers are for use in a single patient only; (2) when handling the nebulizer and dispensing the medications, aseptic technique should be followed; (3) nebulizers should be handled away from sinks to prevent contamination; (4) only sterile water should be used for rinsing nebulizers; (5) after each use, residual volume should be rinsed out with sterile water, and masks/mouthpieces should be wiped with an alcohol pad; and (6) nebulizer contamination between uses can be avoided by not placing nebulizers in line with the ventilator circuit, thereby exposing the nebulizer to tubing condensation. The safety of storing moist nebulizers in plastic bags is unknown. Durable, **nondisposable** nebulizers used in the hospital can be processed in a central sterilization area according to the methods described below for home use (**Section IV.E.4**) if they can be returned to the same patient in time for their next treatment.

#### IV.E.3. Nonhealthcare Settings: Nebulizers

Although no published reports have definitively proven that CF pathogens were acquired from contaminated equipment during home therapy, bacterial contamination of home nebulizers of people with CF has been documented in several studies.<sup>428–432</sup> Additionally, cleaning and drying home respiratory therapy equipment between uses was associated with a decreased risk of acquiring *B. cepacia* complex.<sup>1</sup> In a study of experimental contamination of nebulizers, hot water and soap effectively removed most inoculated bacteria.<sup>431</sup> However, these experimental conditions may not mimic true use by people with CF, and, as described above, potential pathogens from environmental sources (eg, tap water) may contaminate equipment inadvertently and thereby cause infection.

Respiratory care equipment used in the home (eg, nondisposable nebulizers) is durable and designed for long-term use. Thus, to prevent infections caused by contaminated respiratory therapy equipment used in the home, equipment

should be cleaned, disinfected, and air-dried after each treatment. (1) Equipment must be cleaned well to remove all organic and inorganic debris before disinfection. After cleaning with dish soap and water, disinfect either by immersion in cold disinfectants or by heat, if permissible by the manufacturer.<sup>7</sup> Dried or baked debris on equipment makes removal more difficult, and the disinfection process becomes less effective or even ineffective.<sup>433,434</sup> (2) Equipment must be disinfected by either heat or cold disinfectant methods, as permissible by the manufacturer. **Heat methods** include immersion in continuously boiling water for 5 minutes; washing in a dishwasher if the equipment is dishwasher safe and the water achieves a temperature greater than 158°F (70°C) for 30 minutes;<sup>7</sup> use of a microwave oven if the equipment is microwave safe and can be placed in a bowl of water in a home microwave oven (2.45 Ghz) for 5 minutes;<sup>435–437</sup> or use of electric steam sterilizer (eg, baby bottle sterilizer).<sup>438</sup> **Cold methods** include soaking in 70%–90% ethyl or isopropyl alcohol for 5 minutes (avoid use near open flames) or in 3% hydrogen peroxide for 30 minutes.<sup>439,440</sup> These preparations will lose activity over time, and the optimal storage time is unknown. Vinegar (acetic acid) is not recommended because it has inadequate activity against some potential CF pathogens (eg, *S. aureus*).<sup>7,441,442</sup> Bleach is no longer recommended because a 0.5% hypochlorite solution did not reduce the number of CF pathogens on home nebulizers.<sup>443</sup> Benzyl ammonium chloride (Control III) is also not recommended for use because it has a narrow spectrum of activity and is slow in action. Additionally, outbreaks have been related to contamination of this agent.<sup>344</sup> (3) Equipment should be rinsed after use of the cold disinfectant with either sterile water or filtered (less than or equal to 0.2 microns) water, as described above. Sterile water can be prepared by boiling tap water and achieving a rolling boil for 5 minutes. Sterile water can become contaminated after use and/or storage, but the frequency of this is unknown. Boiling water immediately before use minimizes this possibility. Distilled water is not recommended for cleaning or rinsing respiratory therapy equipment since contamination with *B. cepacia* complex can occur during the manufacturing process.<sup>355</sup>

#### IV.F. Strategies for CF Clinics

Several epidemiologic studies have provided evidence for potential transmission of CF pathogens in CF clinics, as described above (**Section III.A**). While the risk of transmission in CF clinics cannot be quantified, the health benefits of CF clinics clearly outweigh the risks of acquisition of CF pathogens. The IP&C recommendations for CF clinics are detailed below and in Table 10.

##### IV.F.1. Cohort Segregation versus All-Patient Separation

Many CF centers throughout the world practice cohort segregation, whereby separate clinic sessions are held for people with CF who are infected with the same pathogen. For ex-

ample, there is a separate clinic for people infected with MRSA or a separate clinic for people infected with an epidemic strain of *P. aeruginosa*.<sup>1,161,185,374,375,444-446</sup> While cohort segregation has been associated with a reduced incidence of LES of *P. aeruginosa*<sup>185,373,375,444</sup> and a decrease in the incidence and prevalence of *Burkholderia* spp. in the United States,<sup>44</sup> additional IP&C practices were also implemented at the same time. Concurrent practices included recommending no socialization among people with CF in nonhealthcare settings, alternatives to common waiting rooms, removal of common toys and books, an emphasis on hand hygiene, single-use mouthpieces for PFT equipment, and aggressive eradication protocols for *P. aeruginosa*.<sup>375,444-446</sup> Therefore, it is difficult to conclude which IP&C practices were most important for successfully decreasing transmission.

Furthermore, maintaining cohort segregation is difficult, as people with CF may (1) harbor more than 1 pathogen, (2) need urgent care, or (3) have newly identified pathogens that could change their cohort status. Additionally, respiratory tract cultures do not always accurately detect CF pathogens, and thus all people with CF could harbor potentially transmissible pathogens. Specimens obtained from the upper airway lack sensitivity and specificity for the lower airway.<sup>42</sup> Despite standardized protocols for processing CF specimens, potential pathogens may escape detection due to low organism burden, overgrowth by other species, or misidentification.<sup>1,447</sup> Genotyping studies have also demonstrated the potential for replacement of an initial infecting *Burkholderia* strain with another strain (ie, superinfection) when CF patients have been segregated into groups on the basis of infection status.<sup>159,448</sup>

Many clinicians in centers implementing cohort segregation have noted the cost, stigmatization, and psychosocial stresses associated with this practice and emphasize that cohort segregation should be considered only when there is strong epidemiologic and genotypic evidence for transmission in the CF clinic.<sup>185</sup> Thus, cohort segregation could be implemented on a case-by-case basis if ongoing transmission of a CF pathogen occurs despite implementation of the IP&C recommendations detailed in this guideline.

To date, studies have not compared the impact of cohort segregation versus separation of all patients with CF from each other. Given the lack of definitive support for cohort segregation and the complexity and shortcomings of implementing cohort segregation, recommendations include **separation** of all people with CF, regardless of their respiratory tract culture results, and practicing the IP&C recommendations detailed in this guideline. Additionally, given the adverse clinical impact of many CF pathogens, including MRSA, epidemic strains of *P. aeruginosa*, and *Burkholderia* spp. (**Section III.A**), and the insensitivity of respiratory tract cultures to accurately detect all CF pathogens,<sup>1</sup> maintaining a separate cohort for *Burkholderia*-infected individuals is **not** recommended.

#### IV.F.2. CF Clinic Logistics

As previously described, infectious droplets can travel 6 feet (2 meters; **Section II.C**).<sup>6</sup> Thus, all people with CF (unless they live in the same household) should be separated by at least 6 feet (2 meters) from others with CF to reduce the risk of droplet transmission.<sup>128,447</sup> Strategies to schedule and manage people with CF in clinics must include minimizing waiting time in a common reception area or waiting room. Such strategies could include placement of the individual with CF in an exam room on arrival, use of a pager system if a room is unavailable, a staggered clinic schedule, portable pulmonary function testing, and rotating CF team members into the exam room (Table 9).

#### IV.F.3. Hand Hygiene

People with CF and their accompanying family members should perform hand hygiene on entering and leaving a CF clinic as well as throughout the clinic visit, as contact with respiratory secretions can occur during coughing, sneezing, or contact with contaminated environmental surfaces or equipment. Hand hygiene recommendations for healthcare personnel, people with CF, and their families are described in **Section IV.C** and in Table 7. To promote hand hygiene, all ambulatory areas should have appropriate supplies for hand hygiene, including conveniently placed alcohol-based hand rub in the entryway into the CF clinic, the waiting room, exam rooms, PFT laboratories, and restrooms.<sup>6,393,394</sup> Furthermore, when hand hygiene is not witnessed, people with CF and their families should be empowered to remind healthcare personnel to perform hand hygiene.

#### IV.F.4. Mask Use by People with CF

In the 2003 Infection Control Guideline for CF, the routine use of masks by people with CF was an *unresolved issue* because of a lack of supporting evidence that masks prevented transmission of CF pathogens. In a survey of IP&C practices conducted in CF centers in the United States in 2005, some centers (27/76 [35%]) used masks in the ambulatory setting, but the benefits of this practice had not been studied.<sup>449</sup> However, recent studies have found infectious droplets in the air of CF clinics (**Section III**). This supports the use of masks by people with CF to both contain infectious droplets and prevent acquisition of potential pathogens.<sup>127,128</sup>

Thus, all people with CF should wear a mask of appropriate size in healthcare facilities to reduce droplet transmission and acquisition of CF pathogens. Mask use by people with CF is consistent with CDC recommendations to prevent droplet transmission of pathogens by infected patients and to prevent the acquisition of potential pathogens by susceptible individuals. Masks should be worn throughout the healthcare facility unless the individual with CF is in an exam room or performing PFTs.<sup>6</sup> To facilitate mask use, all CF clinics should provide masks of different sizes on entry into the clinic. Some centers have chosen to implement mask use via respiratory

TABLE 10. Infection Prevention and Control Strategies for Cystic Fibrosis (CF) Clinics to Minimize the Risk of Transmission of Potential Pathogens within 6 Feet (2 Meters)

Specific strategies		Comments
Scheduling	Stagger clinic schedule Place patient in exam room immediately	Assess space available and patient needs
Registration area	Individuals with CF put on masks either on entry into the hospital or on entry into the clinic area Maintain a distance of at least 6 feet (2 meters) between all people with CF Provide hand hygiene supplies Provide tissues and covered receptacles Provide masks of different sizes	Hand hygiene performed by people with CF and families when entering and leaving CF clinic Consider logistics of obtaining mask on entry into the hospital building
Waiting room	Continue strategies used in registration area “No waiting in waiting room” Call patients’ cell phones when exam room available No common toys or computers Instruct patients and families to bring their own toys, books, iPods, iPads, etc	Advise people with CF, if necessary, to wait in another identified location where no others with CF will be present
Common areas	No congregating in hallways, laboratories, radiology, etc	Advise individuals with CF to wear mask in cafeteria, as others with CF may be present
Exam room activities	Obtain heights and weights in exam rooms Provide hand hygiene products in exam room Rotate interdisciplinary staff through exam rooms Encourage people with CF and families to observe staff perform hand hygiene All staff members don gowns and gloves either before or on entry into exam room Disinfect stethoscopes or other equipment that is shared among patients by means of alcohol swabs, per manufacturer’s instructions, or according to local hospital policy People with CF do not need to wear a mask in exam room	People with CF and family members should perform hand hygiene before entering and after leaving the exam room People with CF should perform hand hygiene after coughing or having contact with respiratory tract secretions (eg, after pulmonary function testing or obtaining culture, accidental contamination of hands when coughing) Empower people with CF and families to remind healthcare personnel to perform hand hygiene or use gowns and gloves (can remind verbally or with nonverbal cues)

PFTs	<p>Provide hand hygiene products in PFT labs</p> <p>All staff don gowns and gloves prior to performing PFTs</p> <p>Use one of the following options:</p> <ol style="list-style-type: none"> <li>1. Perform in exam room at start of clinic visit</li> <li>2. Perform in PFT lab, allow 30 minutes to elapse before next CF patient enters lab</li> <li>3. Perform in negative pressure room</li> <li>4. Perform in room with HEPA filters</li> </ol>	<p>Clean surface of PFT machines and other high-touch surfaces (eg, computer keyboard, door handles) after each patient</p> <p>Use disposable mouthpiece for each patient</p> <p>Patients should not touch PFT machines or computers</p>
Restrooms	<p>Keep mask on when entering and using restroom</p> <p>Perform hand hygiene before and after using restroom</p>	<p>Construction of single-person restrooms preferred</p>
Respiratory specimens	<p>Obtain in exam room at start of clinic visit</p>	<p>No additional comments</p>
Clinic cleaning <sup>a</sup>	<p>Exam rooms should be cleaned and disinfected by trained personnel (eg, member of CF team or environmental services) after each patient using a 1-step process and EPA-registered hospital-grade disinfectant/detergent designed for healthcare facilities</p> <p>Schedule daily cleaning by environmental services of exam rooms and common areas, including registration area, waiting room, PFT lab, sinks, and bathrooms in accordance with local hospital policy; include audits of cleaning</p>	<p>Clean and disinfect the following:</p> <ol style="list-style-type: none"> <li>1. Horizontal surfaces (eg, exam tables, chairs, desks)</li> <li>2. Items people with CF may touch (eg, PFT machines, blood pressure cuffs)</li> <li>3. Items healthcare personnel may touch (eg, computer keyboards, sinks)</li> </ol>

NOTE. EPA, Environmental Protection Agency; HEPA, high-efficiency particulate; PFT, pulmonary function test.

<sup>a</sup> See the Centers for Disease Control and Prevention website for downloadable tools and informational brochures (<http://www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html>).

hygiene stations on entry into the facility. Reminders, including signs in ambulatory settings, can instruct individuals with CF to contain their secretions, that is, to wear a mask, cough into a tissue, immediately discard the soiled tissue into a trash receptacle, and perform hand hygiene after contact with respiratory secretions.<sup>6,450</sup>

#### IV.F.5. Gown and Glove Use by Healthcare Personnel

Gowns and gloves should be worn by all healthcare personnel caring for all people with CF in healthcare settings. The use of gowns and gloves by healthcare personnel in CF clinics is consistent with the principles of *Contact Precautions* and *Standard Precautions* (**Section IV.D.1**), as all individuals with CF may harbor potentially transmissible pathogens. By wearing gowns and gloves when caring for people with CF, healthcare personnel protect their clothing and hands from possible contamination due to direct or indirect contact with respiratory secretions and thus avoid serving as vehicles for the transmission of CF pathogens. To facilitate the use of gowns and gloves, all CF clinics must ensure ready availability of gowns and gloves of different sizes in a location convenient to room entry so they can be put on prior to entering the room. They should be removed in the room and discarded in a covered receptacle. Furthermore, people with CF and their families should be empowered to remind healthcare personnel to wear appropriate PPE on entry into their rooms.

#### IV.F.6. Pulmonary Function Testing

PFTs often generate coughing and involve the use of common equipment. Thus, IP&C practices when performing PFTs must be implemented to minimize the transmission of CF pathogens by contact with contaminated equipment and/or by infectious droplets. Hand hygiene should be performed by healthcare personnel and people with CF before and after performing PFTs to prevent hand contamination by potential pathogens. Healthcare personnel performing PFTs should wear gowns and gloves (changing these after each patient) to prevent soiling of clothing and hand contamination with potential pathogens. Droplets can be detected at least 6 feet from people with CF performing PFTs, and these droplets clear the air 30 minutes after performing PFTs.<sup>125</sup> To minimize exposure to infectious droplets, PFTs should be performed using one of the following options: (1) in the exam room at the beginning of the clinic visit, allowing 30 minutes to elapse between CF patients; (2) in a negative pressure room (AIIR); (3) in a PFT laboratory with HEPA filters; or (4) in a PFT laboratory without HEPA filters, allowing 30 minutes to elapse between individuals with CF.

HEPA filters remove 99.97% of particles (more than or equal to 0.3 microns in diameter) from the air that passes through the filter. HEPA filters are used to protect hematopoietic stem cell transplant recipients in a *Protective Environment* from mold infections and can be used to prevent the spread of airborne bacterial and viral infections if air is

recirculated in AIIRs.<sup>6</sup> HEPA filters can be located centrally in the air handler that supplies a specific unit or building or may be located at the point of use within a room. HEPA filters must have a preventive maintenance program of monitoring and replacement in accordance with the manufacturer's recommendations to ensure continued filtration efficiency.<sup>451</sup> HEPA filters with metal frames are recommended rather than those with wood frames, which can get wet and become contaminated with potential pathogens. The effectiveness of a portable HEPA unit depends on (1) room configuration, (2) the amount of furniture and people in the room, (3) placement of the unit, and (4) location of the air supply and exhaust registers.<sup>2</sup> Portable HEPA units should be capable of recirculating all or nearly all of the room air through the HEPA filter and should achieve the equivalent of more than or equal to 12 air exchanges per hour.<sup>452</sup> The facility's engineering department can assist with information regarding air changes.

Ultraviolet germicidal irradiation (UVGI) has been used as an adjunct air-cleaning measure in healthcare settings to reduce transmission of bacterial and viral infections.<sup>2</sup> UVGI can be used within air handling units to disinfect air prior to recirculation or as upper room air irradiation (ie, lamps suspended from the ceiling or mounted on the wall). Implementation of upper room air irradiation requires air mixing between the lower patient care area and the upper room air. There is also concern about the potential for UV light to damage the eyes of people in the rooms. Regular maintenance of UVGI systems is required and includes keeping the bulbs free of dust and replacing old bulbs when needed. Many experts do not recommend UVGI as a substitute for HEPA filtration.<sup>2</sup>

#### IV.F.7. Environmental Practices

In CF clinics, there are numerous opportunities for contamination of environmental surfaces and equipment, such as exam tables, PFT equipment, and high-touch objects (eg, doorknobs). Thus, healthcare personnel in CF clinics and PFT laboratories must ensure that the equipment and horizontal surfaces that people with CF may touch are cleaned and disinfected after each CF patient by using a 1-step process and EPA-registered hospital-grade disinfectant/detergent designed for housekeeping.<sup>1</sup> This includes cleaning and disinfecting common equipment used for individuals with CF (eg, stethoscopes, demonstration equipment for chest physiotherapy, pulse oximeters, and the outside of PFT equipment). The same principles of cleaning, disinfecting, and auditing of cleaning presented in **Section IV.E.2** and the tools presented in Table 10 apply to CF clinics and PFT laboratories. Environmental service personnel trained in the principles of CF IP&C should be available during the hours that people with CF are cared for in the ambulatory clinic to assist the CF care team to ensure appropriate environmental cleaning and disinfection.

Use of common items, such as toys, books, pens, and computers, should be avoided in CF clinics. Instead, patients and families should be encouraged to bring such items with them to the clinic for their own personal use. A recent study addressed the potential of mobile handheld devices (MHDs; eg, iPads) to serve as reservoirs for potential pathogens and created the iPBundle.<sup>453</sup> The iPBundle includes (1) use of a waterproof, nonporous MHD case; (2) disinfection of the MHD as per institutional policies for noncritical items; (3) regular disinfection by setting an alarm on the MHD; and (4) hand hygiene before and after MHD use.

#### IV.F.8. Use of Restrooms

In the 2003 Infection Control Guideline for CF, use of common restrooms in ambulatory settings was an *unresolved issue*.<sup>1</sup> While no studies have shown acquisition of potential CF pathogens from restrooms, these are common areas in ambulatory settings, including CF clinics. Thus, people with CF should wear a mask while using the restroom and should perform hand hygiene before and after using the restroom. Education, providing proper EPA-registered hospital-grade disinfectant/detergent, and signage describing these practices can facilitate adherence to this recommendation. When new clinic areas are designed, single-person-use restrooms are preferred.

#### IV.G. Hospital Room Placement and Transmission-Based Precautions

Single-patient rooms with bathrooms that are not shared with other patients are preferred for all non-CF and CF patients who may harbor MDROs to reduce the risk of transmission.<sup>5,6</sup> For people with CF, it is reasonable for individuals who reside in the same household to share a room. The following types of isolation are relevant when caring for people with CF.

**Contact Precautions** are intended to prevent direct and indirect transmission of infectious agents between patients, prevent transmission from patients to healthcare personnel, and prevent transmission from healthcare personnel to patients. On the basis of the knowledge that we now have about person-to-person transmission of CF pathogens (**Section III.A**) and the possibility of a person with CF harboring an undetected pathogen, *Contact Precautions* are recommended for ALL hospitalized people with CF. When caring for patients under *Contact Precautions*, all healthcare personnel must put on a gown and gloves **on entry** into the room and discard the gown and gloves before exiting the room. Availability of PPE either outside the room or within the room at the point of entry is necessary to ensure adherence to the recommended use. Since bacterial contamination of surfaces and equipment in a patient room can occur, gown and gloves are recommended even if healthcare personnel do not intend to touch the patient. Medical equipment (eg, stethoscopes or blood pressure cuffs) should be dedicated to the patient while under *Contact Precautions*. Cleaning and disinfection of surfaces and

equipment should be performed according to hospital policy. A surgical (procedure or isolation) mask or face shield should be added according to *Standard Precautions* if there is likely to be a splash of respiratory secretions.

**Droplet Precautions** are intended to protect healthcare personnel from becoming infected by pathogens transmitted by the droplet route (eg, influenza virus, adenovirus, *Bordetella pertussis*, or *M. pneumoniae*). When caring for patients under *Droplet Precautions*, all healthcare personnel must wear a surgical (procedure or isolation) mask **on entry** into the patient room. *Droplet Precautions* are recommended only when caring for people with CF with suspected or proven infection with pathogens that could cause disease in healthcare personnel and are spread by the droplet route. People with CF who require *Droplet Precautions* will also be under *Contact Precautions*; therefore, gowns and gloves in addition to a mask will be required on entry into the room.

**Airborne Infection Isolation** is intended to protect healthcare personnel, other patients, and visitors from contracting infections transmitted by **droplet** nuclei (eg, *M. tuberculosis*, varicella-zoster virus, or measles virus). All healthcare personnel entering an AIIR that is housing patients with proven or suspected TB must wear an N95 respirator or a PAPR (**Section IV.D.2**). AIIRs utilize engineering controls to prevent airborne transmission of infectious agents that remain suspended in the air and travel long distances along air currents.<sup>2</sup> AIIRs that have been renovated or constructed since 2001 must have more than or equal to 12 air exchanges per hour, and those renovated or constructed prior to 2001 must have more than or equal to 6 air exchanges per hour. AIIRs must be under negative pressure (eg, the direction of the airflow from the corridor is into the room). Preferably, the air in an AIIR is exhausted to the outside, but it can be recirculated if filtered through a HEPA filter.

People with CF who are positive for AFB for the first time are more likely to have NTM than TB. However, while TB is uncommon in people with CF, it can occur in those who live in geographic locations with TB or with a history of potential risk factors for TB, including exposure to others with TB, foreign birth, or foreign travel to countries with high rates of TB. *Airborne Infection Isolation* is recommended for people with CF until NTM has been confirmed and *M. tuberculosis* has been ruled out. However, in consultation with local IP&C staff, the use of AIIR can be guided by a risk assessment if the person who is AFB positive has **no** risk factors for TB and lives in a geographic location with a very low incidence of TB. Furthermore, if there is evidence within a CF center that NTM are being transmitted by the airborne route, then people infected with NTM should be placed in AIIRs whenever they are hospitalized. People with CF who require *Airborne Infection Isolation* will also be under *Contact Precautions*; therefore, gowns and gloves in addition to an N95 respirator will be required on entry into the room.

#### IV.H. Construction and Renovation

CDC recommendations for preventing infection by filamentous fungi during construction, renovation, remediation, repair, and demolition should be followed in all healthcare facilities.<sup>2</sup> CDC recommendations for preventing nosocomial aspergillosis and managing potential outbreaks of aspergillosis should be followed by institutional IP&C departments.<sup>372,424</sup>

#### IV.I. Nonhealthcare Settings

Applying the IP&C principles developed for healthcare settings in nonhealthcare settings is challenging. The information provided in this section is intended to assist people with CF and their family and friends to make prudent decisions for their activities outside healthcare settings. An IP&C guideline for individuals residing in Ronald McDonald Houses or similar residential facilities is one example of how IP&C in healthcare settings may be adapted to other settings.<sup>454</sup> Families of children with CF can now expect such facilities to be knowledgeable about the importance of separating people with CF from each other and can expect this accommodation. Families should be empowered to request this accommodation if it is not in place.

##### IV.I.1. Camps and Educational Retreats

In historic descriptions of CF camps or educational overnight retreats involving more than 1 person with CF, many opportunities for transmission of CF pathogens existed. Close contact between individuals with CF was difficult to avoid, and activities causing coughing were common. Given the strong evidence of person-to-person spread of CF pathogens in CF camps and educational retreats, people with CF should not participate in these settings with others with CF.<sup>151,455–457</sup> However, people with CF are encouraged to attend camps and retreats with individuals without CF.

##### IV.I.2. Indoor Events

Given the risks of person-to-person spread of CF pathogens within healthcare and nonhealthcare settings, the risk of transmission of CF pathogens between people with CF who attend indoor events at the same time is also present. While the risk of transmission of CF pathogens appears to be greater with epidemic strains of specific pathogens (*Section III*), the risk cannot be quantified for specific microorganisms. Additionally, the risk of transmission is likely to be higher in small enclosed spaces (eg, in a car or small conference room), but the risk associated with specific indoor events cannot be quantified. Furthermore, there are opportunities for individuals with CF to have inadvertent contact within indoor event spaces (eg, in elevators, at vendor booths, in hallways, or in restrooms). Thus, it is recommended that only 1 person with CF attend indoor events and that accommodations for non-face-to-face contact, such as webcasts or teleconferences, be encouraged.

#### IV.I.3. Outdoor Events

Many of the concerns related to the transmission of CF pathogens due to contamination of surfaces or droplet transmission are minimized at outdoor events. However, if more than 1 person with CF attends such an event, they should be separated by at least 6 feet, should avoid congregating in common areas, should avoid participating in common activities (eg, face painting or meals), and should not travel to the event in the same vehicle unless they reside in the same household. Some CF centers offer strategies to avoid inadvertent contact, for example, identifying people with CF to one another by wearing a colored shirt or a large decorative pin or by providing box meals rather than open buffets.

#### IV.I.4. Schools

The risk of transmission of CF pathogens associated with school if more than 1 child with CF attends the same school is unknown. People with CF and their parents or legal guardians are not obligated to disclose the diagnosis of CF or the results of respiratory tract cultures to school personnel. Such information must be maintained as confidential medical information unless the person with CF and/or his or her parent or legal guardian choose to make this information known. However, the student with CF whose diagnosis is disclosed will benefit from the disclosure, as school personnel can then be educated about CF and IP&C principles. This educational process can ensure the implementation of IP&C practices that will benefit *all* students and staff (eg, hand hygiene and respiratory hygiene practices). Thus, provisions for hand hygiene and respiratory hygiene must be available for all students and for school personnel.

**If more than 1 child with CF attends the same school,** disclosure of the diagnosis of CF will allow schools to make recommended accommodations to minimize the risk of transmission of CF pathogens. Students with CF and their families should discuss these recommendations with school leadership to ensure that accommodations can be implemented within a specific school and then work closely with school personnel to determine how best to implement them. The following accommodations can minimize the risk of transmission of CF pathogens: (1) Students with CF should be placed in separate classrooms. If they must use the same classroom at different times, they should not use the same desk or work station. (2) Students with CF should be assigned different restrooms, encouraged to carry their own water bottles, avoid using public water fountains or use different water fountains, and have lockers as far as possible from each other. (3) Students with CF should be scheduled separately for common activities, including lunch, physical education, and recess. (4) Students with CF should be assigned to separate offices to report for routine medications or if they become ill while at school. (5) Students with CF should not be excluded from group activities, such as large assemblies or pep rallies. Such activities are a crucial part of school life, academic

development, and socialization. Students with CF should enter and leave the communal areas using different routes from one another and sit as far apart as possible.

Because each school setting is different, strategies may differ from school to school. Many of the strategies recommended for schools may be applicable to day care centers or university settings as well. Additional strategies for schools can be found at the CF Foundation's website (<http://www.cff.org>).

#### IV.I.5. Prevention of Viral Transmission and Immunizations

Strategies to prevent all people (including those with CF) from acquiring respiratory pathogens include (1) hand hygiene, (2) respiratory hygiene, (3) routine vaccinations, (4) influenza vaccinations, and, when relevant, (5) antiviral chemoprophylaxis for influenza (eg, oseltamivir).<sup>458</sup> Antiviral treatment for influenza should be initiated as early as possible to shorten the duration of symptoms and reduce influenza complications. Antiviral agents are approximately 70%–90% effective in preventing influenza and serve as useful adjuvants to vaccination. People without CF who have acute respiratory illness should avoid close contact with individuals with CF and not share personal items.

**Vaccinations for people with CF.** Vaccines are critically important for people with CF to maintain their health and minimize the risk of morbidity and mortality from vaccine-preventable illness. The ACIP has guidance for age-appropriate vaccination schedules that is updated each year.<sup>115,459,460</sup> Additional updates are published as needed throughout the year. People with CF should receive the same recommended vaccinations as people without CF; many recommended vaccines prevent respiratory tract infections that could exacerbate CF lung disease, including influenza, pertussis, and pneumococcal vaccines.<sup>271</sup> The CF care team should be informed about changes in immunization recommendations. The most recent update affecting people with CF is the expanded use of pneumococcal conjugate vaccine 13 in individuals more than 2 years of age with chronic lung conditions.<sup>461</sup>

Currently, there are no commercially available vaccines for such CF bacterial pathogens as *P. aeruginosa* or *S. aureus*. Trials have not found investigational vaccines to be efficacious.<sup>462–464</sup>

**Vaccinations for family members and close contacts of people with CF.** Vaccination of family members and close contacts of people with CF can help to protect people with CF from vaccine-preventable illnesses. Annual influenza vaccine is recommended for all family members and close contacts of people with CF.<sup>465</sup> This is especially important among the close contacts of infants with CF who may be too young to receive some vaccines, particularly influenza vaccine. The term “cocooning” describes this concept and is advocated for pertussis and influenza.<sup>466</sup> For example, women immunized against influenza during pregnancy had fewer respiratory tract

illnesses in the 6 months after delivery, and their infants had fewer febrile illnesses.<sup>467,468</sup> There are also guidelines for vaccination of people who are immunocompromised that are applicable to individuals with CF who have undergone transplantation and their close contacts.<sup>469</sup>

**Vaccinations for healthcare personnel.** Recent ACIP guidelines have expanded recommendations for healthcare personnel.<sup>459,460</sup> These recommendations are relevant for the CF care team and include immunization or immunity to mumps, measles, rubella, varicella, pertussis, and hepatitis B as well as annual influenza immunization.<sup>465</sup>

#### V. HEALTHCARE PERSONNEL WITH CF

More and more people with CF are living longer, productive adult lives. The following findings reported in the 2012 CFFPR demonstrate the growing need for career counseling for adolescents and young adults: (1) the median predicted survival in 2012 was 41.1 years, nearly 10 years longer than the 31.3 year median survival reported in 2002; (2) 49% of individuals in the CFFPR were 18 years of age or older; and (3) nearly 45% of adults with CF were employed (11.8% were employed part time, and 33.6% were employed full time).<sup>21</sup>

Six studies have reported that 50% of the CF population studied was working and that approximately 50% of those individuals were working in professional occupations, although there was no specific information on healthcare professions.<sup>470</sup> Similarly, a 2003 monograph containing general information on CF in the workplace<sup>471</sup> did not specifically address healthcare professions. Guidelines for adult CF care programs in the United States,<sup>472</sup> for nurses participating in this care transition in Ireland,<sup>473</sup> and a recent study of the health outcomes of adults who transitioned from pediatric to adult care centers<sup>474</sup> did not discuss providing career counseling to individuals with CF who were interested in healthcare professions.

While anecdotal experiences suggest that healthcare professions have attracted individuals with CF, few published data exist to inform decisions on choosing a career in healthcare. In the United Kingdom, a survey of adults with CF conducted in 1994 found that 6.6% of respondents worked in healthcare or closely related professions.<sup>475</sup> Ten CF associations and prominent CF center directors worldwide were surveyed, and none of the 4 countries responding had a written policy for managing healthcare personnel with CF.<sup>476</sup> A French association reported that 19% of adults with CF were working in service fields (eg, education, healthcare, and social care).<sup>476</sup> The relevance of these studies is uncertain; all were conducted prior to the recent era of improved outcomes for adults with CF.

There are no published reports of transmission of infectious agents between healthcare personnel with CF and their patients. Thus, the frequency of such events is likely to be low and goes unrecognized or unreported. Thus, current rec-



ommendations for healthcare personnel with CF must be based on common sense, prudence, and individual health status. An editorial and a review article recommended the following considerations for an individual with CF selecting a healthcare profession: (1) the *infectious risk to healthcare personnel with CF* from healthcare exposures will vary according to the patient population cared for and the healthcare environment; (2) the *infectious risks to patients* from healthcare personnel with CF will vary according to the severity of CF disease, frequency of coughing, types of CF pathogens, and the ability of the individual with CF to follow source-containment recommendations; and (3) individuals with CF should consider the *physical challenges and the ability to perform CF treatments* during and after training when selecting a healthcare profession.<sup>476,477</sup>

The only definite restriction for healthcare personnel with CF is that he or she should not work with patients with CF or other healthcare personnel with CF. With the stricter IP&C practices recommended in this guideline, it will become more challenging for people with CF to work in a healthcare environment where other people with CF receive care. For example, it is not feasible that healthcare personnel with CF could wear a mask routinely in healthcare settings. In contrast, such individuals should wear masks as previously described for all healthcare personnel (*Section IV.D.2*) and when they are in areas frequented by people with CF. Family members of individuals with CF can work in healthcare professions without restrictions.

Adolescents and young adults interested in healthcare professions should seek advice from members of their CF care team to learn about lower-risk options and to receive advice based on their own health status. This type of counseling should be incorporated, when relevant, into programs for transition from pediatric to adult CF care.

Individuals with CF who work in a healthcare profession are encouraged to disclose their diagnosis to their occupational health service to determine the safest work assignment. The occupational health service must comply with Health Insurance Portability and Accountability Act requirements<sup>478</sup> as relevant. The employment laws that govern the protections and procedures for healthcare personnel with CF include the Americans with Disabilities Act and section 504 of the Rehabilitation Act as summarized in the 2003 Infection Control Guideline for CF.<sup>1</sup>

## VI. PSYCHOSOCIAL AND MEDICAL IMPACT OF TRANSMISSION-BASED ISOLATION PRECAUTIONS

Acknowledging the potential psychosocial and medical impact of IP&C recommendations for people with CF, their families, and the CF care team is critical to overcome challenges to implementation and to promote consistent implementation of the recommendations. While few studies have been performed in CF, there are several relevant studies performed in other patient populations.

**Studies among non-CF patients.** Studies have examined the impact of transmission precautions among non-CF patients with MRSA, TB, or SARS-CoV infection or with cancer.<sup>479-482</sup> Patients placed under *Transmission Precautions* may experience increased anxiety, depression, loneliness, and stress as well as anger and hostility.<sup>483,484</sup> Compared with control patients, adult patients isolated for MRSA were more likely to have preventable adverse events (eg, falls, ulcers, or fluid and electrolyte abnormalities), to complain about their care, to have fewer vital signs taken, and to have more days without physician progress notes.<sup>485</sup> Two systematic reviews similarly concluded that patients under *Contact Precautions* had less contact with healthcare personnel; decreased satisfaction with their care; more noninfectious adverse events, including decubitus ulcers and falls; delayed transfer to long-term care facilities; and more symptoms consistent with anxiety and depression.<sup>486,487</sup> Inconsistent use of PPE by healthcare personnel or the time required to put on PPE was confusing and troubling to patients and increased their anxiety.<sup>479</sup>

Others found that patients under *Contact Precautions* were more likely to have symptoms of depression and anxiety at the time of admission but were not at increased risk of developing depression, anxiety, or negative moods **during** hospitalization.<sup>488</sup> Similarly, personal attributes were associated with the development of depression and anxiety rather than the use of isolation precautions.<sup>479</sup>

Not all the psychosocial effects of isolation precautions are negative. Short-term infection prevention measures did not influence patients' level of anxiety, depression, or quality of life, but such patients had a positive attitude toward the precautions used.<sup>484</sup> Some patients felt they had more freedom from ward routines and more control over their own activities. Some liked the privacy and quiet, particularly at night.<sup>479</sup>

**Studies among people with CF.** Parents and children with CF 10 years of age and older were surveyed about their center's segregation policy, whereby children with CF were provided single rooms when hospitalized and had to remain in their room throughout hospitalization.<sup>489</sup> The majority agreed with the policy and understood that it was intended to maintain the children's health. Most parents felt that the health benefits outweighed the negative impacts, including social isolation. Parents worried about boredom, being able to keep their child in the hospital room, and the increased burden of entertaining their child. However, they also expressed relief at not having to worry about cross infection. The primary concerns expressed by the children were boredom and isolation. Factors that influenced the children's opinions were level of maturity, stage of development, and their experiences during previous admission(s). Following the spread of an epidemic clone of *P. aeruginosa*, the majority (85%) of parents and children with CF 12 years of age and older (63%) gave favorable responses for the need for cohort segregation, although negative responses were largely from the adolescent age group.<sup>490</sup>

**Interventions to minimize the impact of isolation precautions.** The CDC recommends that hospitals should anticipate and counteract possible anxiety, depression, perceptions of stigma, reduced contact with healthcare personnel, and other adverse events that may result from isolation precautions.<sup>5,6</sup> Interventions to improve communication and physical facilities can ameliorate the negative effects; patient satisfaction was highest among isolated patients who were kept informed about their care.<sup>491</sup> Providing both written and individualized information with improved communication from staff can increase satisfaction and positive emotions.<sup>492</sup>

Increasing psychological support is also helpful. Investigators emphasize that patients in isolation require frequent contact with other people, including visitors and healthcare personnel, to prevent boredom and loneliness.<sup>492-494</sup> Communication can be enhanced by human touch and humor displayed by healthcare personnel, especially by nurses who generally spend more time at the bedside.

Parents of children with CF emphasized that providing play therapy services, televisions, video games and movies, toys, crayons, and structured daily activities (eg, physiotherapy, school, pet therapy, and exercise) can reduce the impact of isolation.<sup>489,492,494,495</sup> Children suggested that access to the Internet, mobile phones, and interactive resources and being able to leave their rooms would make isolation more tolerable.<sup>489</sup> Physical facilities can also be altered to decrease the impact of isolation. Familiar items from home, such as pictures or personal belongings, can decrease the impact of isolation, as can providing patients with windows that view the ward or the outdoors.<sup>492,494</sup> Possible strategies to minimize the adverse psychosocial impact of isolation precautions are provided in Table 11.

**Online social networking.** Online social networking can provide an opportunity for adults and children with CF to communicate with each other about personal issues and to give and receive valuable peer support outside the healthcare setting.<sup>496</sup> CFfone has been developed to provide an intervention to improve adherence in adolescents with CF via a

web-enabled cell phone that provides CF information and social support.<sup>497</sup> However, CF caregivers should recognize both the power and the potential risks of these tools, should face-to-face meetings result from the communication initiated by online resources.

Thus, while IP&C practices serve to protect people with CF from acquiring or spreading pathogens, awareness of the potential adverse effects of isolation should prompt the CF care team, people with CF, and their families to implement strategies designed to alleviate negative effects. This could improve adherence to IP&C practices and improve the quality of healthcare encounters.

## VII. CHALLENGES TO IMPLEMENTATION OF IP&C RECOMMENDATIONS

**Challenges experienced by healthcare personnel.** Potential challenges to implementation of healthcare guidelines include knowledge, attitude, and practice barriers.<sup>498</sup> Relevant challenges and potential solutions to enhance implementation of the IP&C in CF guideline are displayed in Tables 12<sup>498,499</sup> and 13. Several barriers to implementation of the 2003 Infection Control Guideline for CF were identified among healthcare personnel ( $n = 528$ ). These included lack of awareness of the guidelines (40%), lack of familiarity with the recommendation to discourage socialization among hospitalized people with CF (31%), disagreement with the recommendation to discourage socialization (32%), and lack of confidence (self-efficacy) that the respondent could discourage socialization (48%).<sup>499</sup> Lack of self-efficacy was strongly associated with poor adherence to the recommendation to educate people with CF to perform hand hygiene and to disinfect their nebulizers. Others have similarly reported that recommendations that require counseling and education of patients are associated with a lack of self-efficacy by providers.<sup>498</sup>

Most respondents (84%) caring for individuals with CF believed that implementation of the guideline would improve the health outcomes of their patients.<sup>499</sup> Access to a copy of

TABLE 11. Possible Strategies to Minimize the Adverse Psychosocial Impact of Isolation Precautions among People with Cystic Fibrosis (CF)

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Incorporate people with CF and their families into discussion of daily plan of care
Encourage visits from individuals without CF
Provide additional activities to help children pass the time (eg, art supplies, board and card games)
Provide television, DVDs, and video games
Consider animal-assisted therapy
Enlist visits from child life staff or volunteers
Provide computer and e-mail access
Provide written and individualized information about the need for isolation precautions
Increase psychological support
Bring familiar items from home
Allow to leave room (if feasible) accompanied by a trained staff member at least once daily
Arrange single-patient use of play room with cleaning after individual leaves
Provide daily schedule of medically related interventions
Ensure consistent communication with healthcare personnel

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TABLE 12. Knowledge, Attitudes, and Practice Barriers Related to Implementing the Infection Prevention and Control Guideline in Cystic Fibrosis (CF)

Category, paradigm	Barrier	Potential solutions
<b>Knowledge</b>		
Lack of awareness or familiarity	No knowledge of infection prevention and control guideline or no familiarity with specific recommendations	Easy access to guidelines Review recommendations with CF care team and inpatient staff
Lack of education	No provision of education to healthcare personnel or to people with CF or families	Engage people with CF and their families Develop easy-to-understand, eye-catching educational handouts/brochures Provide education and booster education in age- and language-appropriate form
<b>Attitudes</b>		
Lack of agreement	Disagreement with specific recommendations	Review evidence, provide rationale
Lack of self-efficacy	Not confident can practice specific recommendations	Provide models of best implementation practices and skills workshops Identify successful patient models
Lack of outcome expectancy	Do not believe recommended practice can improve health outcomes	Track center-specific and national trends to link adherence to outcomes and share with staff, patients, and families
Inertia of current practice	Believe recommendations are ineffective or not applicable and reluctant to change familiar practices	Share quality improvement initiatives and successful interventions among CF centers Recruit early adopters, positive deviants
<b>Practices</b>		
Lack of resources	Lack of time, money, personnel, space, supplies, equipment, and/or administrative support Belief that practices are inconvenient, time-consuming, costly	Engage with infection prevention and control teams Provide adequate supplies and equipment at point of care Seek administrative support Use return demonstrations Perform quality improvement initiatives and report outcomes to staff, families and administrators Anticipate and monitor for unintended consequences

NOTE. Modeled after Cabana et al.<sup>498</sup> and Garber et al.<sup>499</sup>

the 2003 Infection Control Guideline for CF was associated with increased agreement with the recommendations and increased self-efficacy. Notably, physicians were more likely to have a copy of the guideline than other members of the CF care team. Interventions to overcome the lack of self-efficacy could include didactic lectures, practical skills workshops and training, and sharing best practices by early adopters of the recommendations (*Section IV.B*).<sup>500</sup>

**Challenges experienced by people with CF and their families.** Potential challenges related to implementation of the 2003 Infection Control Guideline for CF experienced by people with CF and the parents of children with CF were also explored.<sup>381</sup> Among 1,399 respondents, 65% were aware of the guideline. Of those aware, 34% reported that they had never discussed the guideline with their CF care team, and only 30% reported that they had discussed the guideline more

than once. More than 1 discussion with the CF care team was associated with increased knowledge, self-efficacy, and outcome expectancy. This suggests that booster or enhanced education could reduce barriers to implementation of IP&C practices. While 83% knew that germs could be transmitted person to person, only 64% and 59% knew that people with CF should avoid close contact even when *not* coughing or in the CF clinic, respectively. Most respondents were advised to perform hand hygiene (80%), to avoid close contact with others with CF (70%), and to clean their nebulizers (90%). However, fewer were educated about specific practices, such as performing hand hygiene when entering (39%) or leaving (49%) the CF clinic or cleaning their nebulizer after each use (69%). Few respondents believed that their health outcomes could be improved by avoiding close contact during hospitalization (30%) or in the CF clinic (32%). These findings

TABLE 13. Strategies to Enhance Implementation of the Infection Prevention and Control Guideline among Healthcare Personnel, People with Cystic Fibrosis (CF), and Families of People with CF

#### Strategies for Implementing Education Programs

- Use of the language and level of understanding most appropriate to the audience, including different groups of healthcare personnel, people with CF, and their families
- Provide rationale for recommendations to healthcare personnel, people with CF, and their families
- Identify and utilize early adapters/positive deviants among different groups of healthcare personnel, people with CF, and their families
- Involve patients and families in problem solving and developing educational tools
- Provide education that does not require people with CF being together in the same room (eg, webinars, Internet, apps)
- Encourage family members who do not have CF to attend group education sessions
- Distinguish “must dos” from other information provided to guide prudent decision making
- Healthcare personnel, people with CF, and their families can network with other CF centers
- Continually strive to develop innovative methods of education for healthcare personnel, people with CF, and their families and share with others

#### Strategies for Audit and Feedback

- Involve healthcare personnel who will be recipients of feedback in planning the performance feedback program
- Provide audits with immediate feedback and communication of trends in performance to healthcare personnel at regular intervals (eg, quarterly, semiannually, annually)

#### Strategies to Empower People with CF to Advocate for Adherence to Recommended Practices

- Place signage in public areas indicating the importance of promoting patient safety by politely communicating if lapses in IP&C practices are observed
- Provide option for anonymous reporting of lapses

provide insights into specific educational content for individuals with CF and their families. Enhanced educational materials designed specifically for people with CF and their families exist (<http://www.cff.org>) but should be expanded by individual centers as needed.

#### RESEARCH AGENDA

##### SCV *S. AUREUS*

1. The role of SCV *S. aureus* (and SCVs of other species, eg, *P. aeruginosa*) should continue to be studied to provide evidence for the need to standardize the processing of CF specimens to look for this phenotype.

##### TRANSMISSION OF CF PATHOGENS

2. Future studies should continue to address the frequency of shared strains of CF pathogens, including *P. aeruginosa* and NTM. This could potentially be accomplished using reference laboratories, such as have been developed for *B. cepacia* complex.
3. The routes of transmission of *M. abscessus*, including the potential for transmission by droplet nuclei, should be further studied.
4. The role played by specific niches in the natural environment (eg, natural bodies of water or soil) in the transmission of CF pathogens should continue to be studied.

##### DEFINING BEST IP&C PRACTICES

5. Additional studies are needed to describe the implementation and impact of effective IP&C practices in CF cen-

ters without epidemic clones or in CF centers that **reduced** transmission during a recognized outbreak. These should include epidemiologic studies, observational studies, and ethnographic research.

6. Additional studies should be performed to determine the efficacy of cohort segregation based on pathogen status versus all-patient separation.

7. Vaccination rates, particularly for influenza, obtained for people with CF and healthcare personnel could be used as patient safety and quality measures at CF centers.

8. Criteria should be developed to define a person with CF who had previously been culture positive for a specific pathogen and is now culture negative for that pathogen to be free of that pathogen.

##### BARRIERS TO IMPLEMENTATION

9. The CF community is strongly encouraged to engage the IP&C community in discussions to find strategies to implement these recommendations and to overcome barriers to implementation.

10. Additional studies are required to understand the differences between the perceptions of healthcare personnel and people with CF and families regarding outcome expectancy following implementation of IP&C practices.

##### HEALTHCARE PERSONNEL WITH CF

11. In 2003, healthcare personnel with CF were identified as a group that would benefit from further research. Ten years later, that need remains.

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## ACKNOWLEDGMENTS

*Financial support.* The Cystic Fibrosis Foundation provided the publication costs for this document.

*Potential conflicts of interest.* None of the authors have financial support or conflicts of interest to disclose relevant to this guideline.

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The Cystic Fibrosis Foundation is located at 6931 Arlington Road, Bethesda, MD 20804; phone: 1-800-FIGHTCF; website: <http://www.cff.org>.

Presented in part: 26th Annual North American Cystic Fibrosis Conference; Orlando, Florida; October 2012; and 27th Annual North American Cystic Fibrosis Conference; Salt Lake City, Utah; October 2013.

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