

Overview of *Clostridioides difficile* Infection



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Learning Objectives

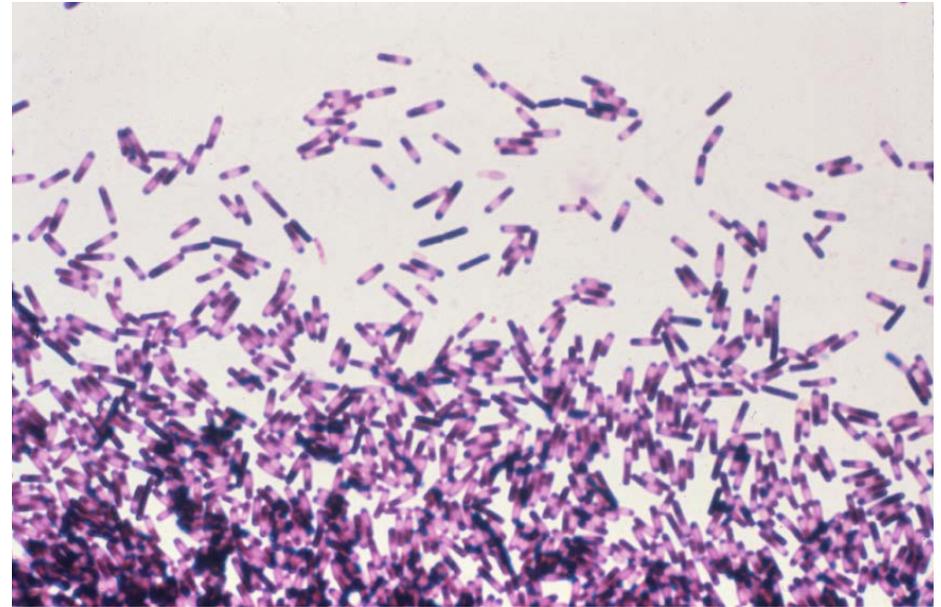
- Outline the impact *Clostridioides difficile* infection (CDI) has on patients
- Demonstrate knowledge of *C. difficile* pathogenesis
- Describe a tiered approach to *C. difficile* infection prevention



The Organism

Clostridioides difficile

- *C. difficile* vegetative cells are anaerobic and die shortly after air exposure
- Spores are difficult to kill
- Toxin production causes disease
- Most common cause of healthcare-associated infections (HAIs) in the US



(Image Source: Jones G, CDC, 1980)



The Infection

- *C. difficile* infection (CDI)
 - Toxins cause symptomatic disease
 - Toxins cause colitis
 - Most common symptom is diarrhea
 - Additional symptoms: cramping, nausea, and fever
 - Range from self-limited diarrheal illness to life-threatening toxic mega-colon and sepsis
- Most cases of CDI occur soon after a new acquisition of toxin producing *C. difficile*

Bristol Stool Chart

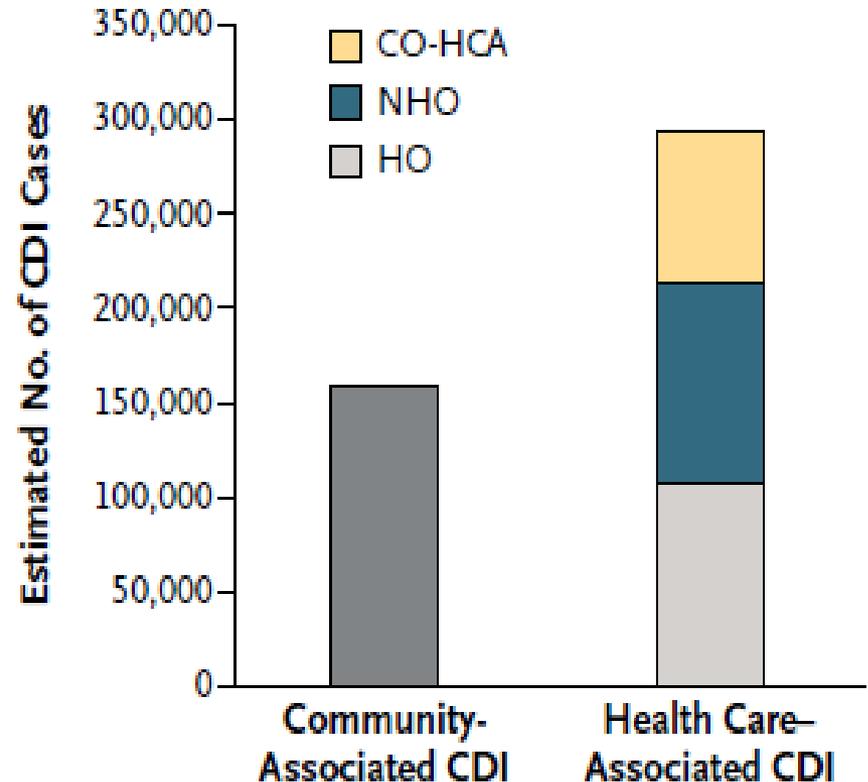
Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

(Caroffa DA, J Clin Microbiol, 2014)



Urgent Threat

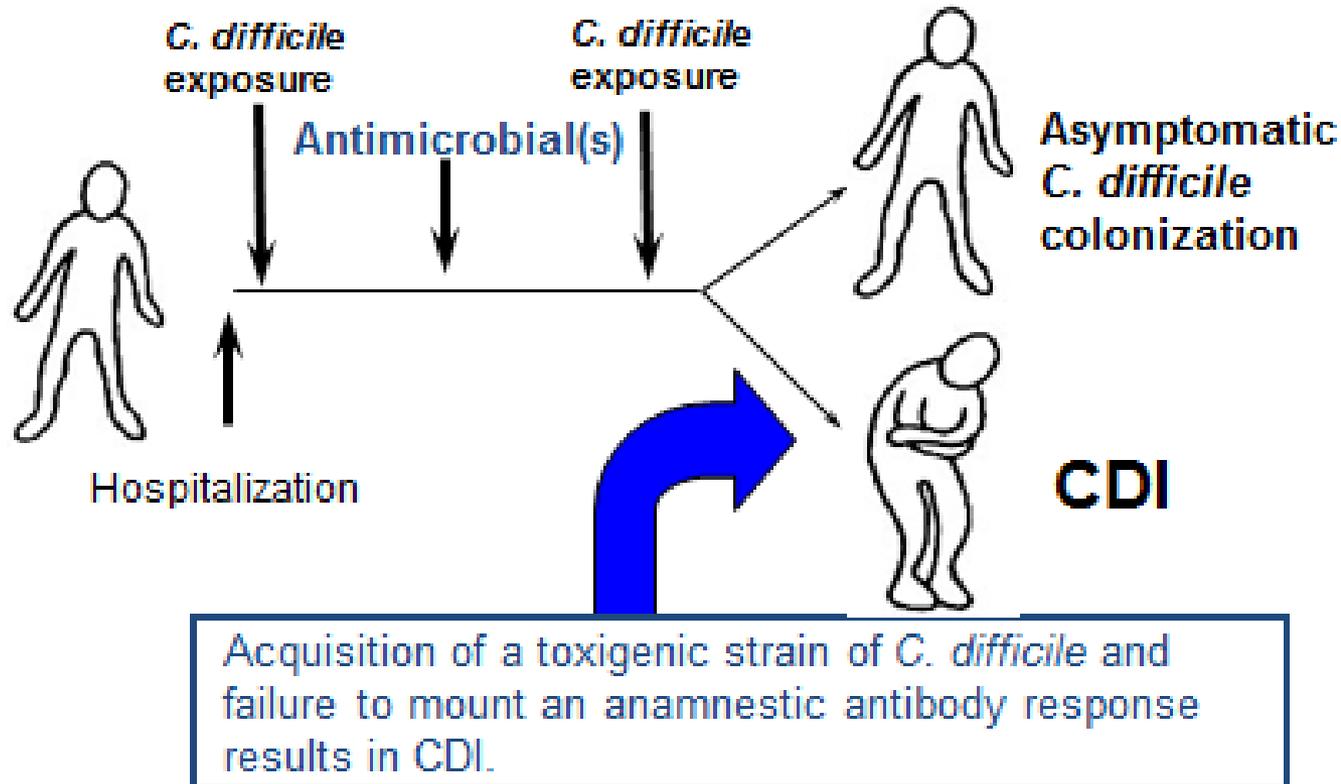
- Over 450,000 initial cases
- Over 29,000 associated deaths
- Recurrent CDI
 - 20% to 30% with at least one recurrence
 - 5% to 10% with multiple (2+)
- Hospital costs: \$5.9 billion



(Lessa FC, *N Engl J Med*, 2015; Kwon JH, *Infect Dis Clin North Am*, 2015)



Pathogenesis Model for CDI



(Johnson S, Gerding DN. Clostridium difficile –associated diarrhea. Clin Infect Dis. 1998; 26(5):1027–1034. - Kyne. NEJM 2000)



Antibiotics and CDI Risk

Very Commonly Related

- Clindamycin
- Ampicillin
- Amoxicillin
- Cephalosporins
- Fluoroquinolones

Less Commonly Related

- Beta-lactam inhibitors
- Macrolides
- Carbapenems
- Tigecycline

Uncommonly Related

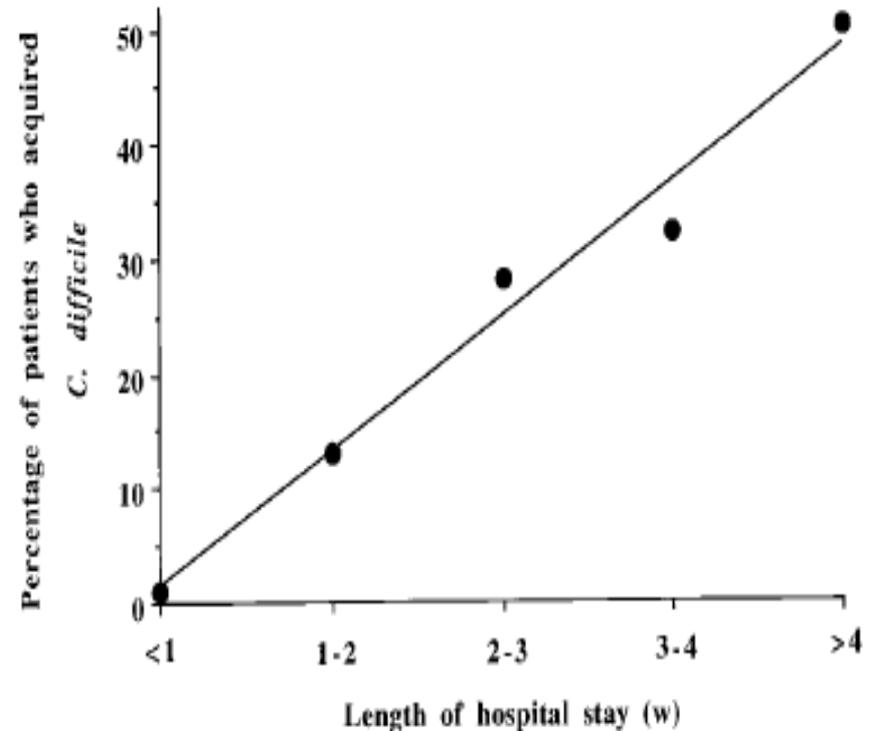
- Aminoglycosides
- Metronidazole
- Rifampin
- Tetracyclines
- Daptomycin
- Sulfonamides
- Trimethoprim

(Bouza E, *Med Clin North Am*, 2006; Loo VG, *N Engl J Med*, 2005)



Acquisition of *C. difficile*

- Healthy adults in community
 - About 3%
 - Stable over time
- Risk of acquiring directly proportional to length of stay
 - 13-50% of all health care patients carry *C. difficile*



(Johnson S, Gerding DN. Clostridium difficile – Associated diarrhea. Clin Infect Dis. 1998; 26: 1027-36.)



Status of CDI Prevention

- Decrease risk of CDI if transmission occurs
 - Antimicrobial stewardship
- Decrease risk of transmission
 - CDI: Contact precautions
 - Gloves/gowns
 - Dedicated patient equipment
 - Environmental decontamination



Tiers of CDI Prevention Practices

TIER 1 Standardize Supplies, Procedures and Processes

(complete all interventions: review and audit compliance with Tier 1 measures prior to moving to Tier 2)

Implement antibiotic stewardship interventions specific to CDI

Conduct early, appropriate CDI testing and alert staff of CDI status

Prevent transmission of CDI through strict glove use and hand hygiene

Initiate Contact Precautions promptly when patients test positive for CDI and maintain for duration of CDI illness

Ensure cleaning and disinfection of equipment and environment

Monitor health care onset-CDI rates and share with staff and leadership

(if CDI rates remain elevated, start with CDI Guide to Patient Safety (GPS) and Target Assessment for Prevention (TAP) Strategy and then proceed with additional interventions)

Perform needs assessment with Guide to Patient Safety (GPS) and TAP Strategy

Tier 2 Enhanced Practices

Initiate Contact Precautions while CDI results are pending (for symptomatic patients) and prolong until discharge after patient becomes asymptomatic

Implement environmental cleaning process tools (audit checklists) and use of an EPA sporicidal agent

Implement hand hygiene with soap and water as preferred method on exit of room with targeted training and monitoring of staff compliance



Tier 1: First Steps to CDI Prevention



- CDI surveillance
- Antibiotic stewardship specific to CDI
 - Avoid unnecessary antibiotics
 - Preference for lower CDI risk antibiotics when appropriate



- Appropriate testing
 - Clinically significant diarrhea without other obvious causes



- Contact Precautions
 - Hand hygiene
 - Gloves use
 - Patient-dedicated equipment



- Good cleaning practices



Tier 2: Enhanced Practices



- CDI rates remain elevated despite Tier 1 interventions



- Define the opportunities for improvement
 - Identify potential barriers to implementation of basic interventions
 - Same rooms versus different rooms
 - Antibiotic use
 - Testing practices
 - Contact precaution compliance
 - Shared equipment



- Intervene based on opportunities found



Summary

- *Clostridioides difficile* is the most common cause of healthcare-associated infections in the United States.
 - CDI is a major cause of morbidity, mortality and costs
- CDI prevention works
 - Antibiotic stewardship
 - Prevent transmission



References

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Speaker Notes



Speaker Notes: Slide 1

Welcome to the first module of the *Clostridioides difficile* infection prevention course. This module, titled “Overview of *Clostridioides difficile* Infection,” will provide background information on the impact *C. difficile* has on patients, the pathogenesis of *C. difficile* infection and *C. difficile* infection prevention. This module will serve to set the stage for subsequent modules in this course.



Speaker Notes: Slide 2

This module was developed by national infection prevention experts devoted to improving patient safety and infection prevention efforts.



Speaker Notes: Slide 3

After completing this module you will be able to

- Outline the impact *Clostridioides difficile* infection has on patients;
- Demonstrate knowledge of *Clostridioides difficile* pathogenesis; and
- Describe a tiered approach to *Clostridioides difficile* infection, or CDI, prevention.



Speaker Notes: Slide 4

Clostridioides difficile, or *C. diff*, is an obligate anaerobe and as a result, the vegetative cells die in 10 to 15 minutes after exposure to ambient air. However, *C. difficile* produces spores. It is the spores that we ingest. This is problematic as bacterial spores are amongst the most difficult to kill biological entities. For *C. difficile* to cause disease, it must produce toxins. Of note, 10 percent to 20 percent of strains do not produce toxins, and these strains are unable to cause *C. difficile* disease. *C. difficile* is now the most common cause of healthcare-associated infections in the US.



Speaker Notes: Slide 5

C. difficile infection is the symptomatic disease that *C. difficile* causes when it produces toxins in the colon. The toxins kill the epithelial lining of the colon and then cause intensive inflammation of the colon, also known as colitis. The most common symptom of CDI is diarrhea, and this is always present except in the rare and unfortunate instances when *C. difficile* infection causes toxic mega-colon and ileus, which results in an absence of bowel movements.



Speaker Notes: Slide 5 Continued

Other common symptoms include abdominal cramping, nausea and fever. *C. difficile* infection can range from a mild, self-limited diarrheal illness, to life-threatening toxic mega-colon and also sepsis. Most cases of *C. difficile* infection occur soon after a new acquisition of toxin producing *C. difficile*, highlighting the importance of preventing *C. difficile* transmission in hospitals.



Speaker Notes: Slide 6

In the 2013 CDC antibiotic resistant threat report, *C. difficile* received the highest threat level, an urgent threat.

Subsequently, the CDC actually found *C. difficile* was worse than originally thought. Based on the CDC Emerging Infections Program-*C. difficile* Infection estimates, there are more than 450,000 initial episodes of *C. difficile* infection per year in the United States, with more than 29,000 associated deaths, numbers that are almost double the estimates used when *C. difficile* was first classified as an urgent threat. Most cases of *C. difficile* infection have onset during or soon after an inpatient healthcare exposure, as demonstrated by the figure.



Speaker Notes: Slide 6 Continued

In addition to the immediate impact *C. difficile* can have on the patient, 20 to 30 percent of patients will develop at least one recurrence of *C. difficile* infection, with 5 to 10 percent of patients developing multiple, recurrent *C. difficile* infection episodes, which comes back again, and again and again. Patients with recurrent *C. difficile* infection suffer from more morbidity, mortality and costs than patients who have a single episode. Lastly, *C. difficile* ends up costing hospitals almost \$6 billion per year in the US.



Speaker Notes: Slide 7

This slide displays our current understanding of CDI pathogenesis. First, *C. difficile* is a ubiquitous organism, meaning it is found everywhere—although disease-causing strains may be more common in some settings, such as healthcare facilities, than others. Antibiotic exposure causing disruptions to patients' microbiota, acquisition of a toxin producing strain of *C. difficile*, and failure to mount an immunological response all play a role in patients developing a full *C. difficile* infection.



Speaker Notes: Slide 7 Continued

Hospitals have a high concentration of people vulnerable to *C. difficile* infection and the potential for *C. difficile* exposure can be higher than in the community. The antimicrobial kills off the good bacteria in our colon that protect us against *C. difficile*, so if we are exposed to *C. difficile* after an antimicrobial exposure, we are much more likely to become colonized.

Fifty to 70 percent of people who acquire *C. difficile* in the healthcare setting remain asymptomatic. The remaining 30 to 50 percent of people fail to mount an antibody response against *C. difficile*, and go on to develop *C. difficile* infection, typically in less than 7 days after *C. difficile* is acquired.



Speaker Notes: Slide 7 Continued

While the majority of patients who develop a primary infection with *C. difficile* will mount an immune response during the course of their symptoms, and then be unlikely to suffer a recurrence, others will not. Overall, 15-25% of patients will go on to suffer a recurrence with CDI. Although there is a commercially available drug to prevent CDI recurrence by boosting immunity (i.e. a monoclonal antibody), there is currently no commercially available test to assess degree of CDI immunity.



Speaker Notes: Slide 8

Some antimicrobials are more strongly associated with *C. difficile* infection than others. Risk of *C. difficile* infection has to do with how effective that antimicrobial is at killing the good bacteria in the colon, and whether *C. difficile* is resistant to that antimicrobial.

The “very commonly related” antimicrobials are those that kill the good bacteria and to which *C. difficile* tends to be resistant. So, *C. difficile* infection can develop while that person is still receiving that antimicrobial.



Speaker Notes: Slide 8 Continued

The “less commonly related” antimicrobials are those that kill the good bacteria, but may also kill *C. difficile*, decreasing the chance of developing *C. difficile* infection while a person is still receiving that antimicrobial. However, once that antimicrobial is discontinued, it can take several months before the protective, good bacteria in the colon return, and during this period, from the time the antimicrobial is stopped to when the good bacteria are replenished, the patient is at high risk for *C. difficile* infection. The uncommonly related antimicrobials tend to be less disruptive to the good bacteria in the colon and also have activity against *C. difficile*.



Speaker Notes: Slide 9

As mentioned previously, *C. difficile* is an ubiquitous organism. It is in the soil, colonizes our pets and livestock and has been cultured from food, water and homes of otherwise healthy people. As a result, we are frequently exposed to *C. difficile* and are periodically colonized. About 3 percent of otherwise healthy adults are colonized with *C. difficile*. When you culture people over time, the 3 % remains constant, but who is colonized changes, consistent with frequent, periodic exposure to *C. difficile*.



Speaker Notes: Slide 9 Continued

However, in healthcare facilities, the risk of acquiring *C. difficile* is directly proportional to the length of stay. Thirteen to 50 percent of people residing in a health care facility are colonized at any one point in time. There are several reasons for this. The first is there is a high proportion of people in health care facilities who receive antimicrobials, so there is a large proportion of people at increased risk for *C. difficile* colonization. Also, people in the hospital have a high acuity of illness, so they are at high risk for developing *C. difficile* infection if they acquire *C. difficile*. Because patients with *C. difficile* infection shed a high number of *C. difficile* spores in stool, they strongly contribute to the spread of *C. difficile* to others.



Speaker Notes: Slide 10

There are two main approaches to preventing *C. difficile* infection in health care facilities.

The first is to decrease a person's risk of developing *C. difficile* infection if they are exposed to *C. difficile*. This is accomplished through antimicrobial stewardship. If a person does not receive an antibiotic that is not indicated, or a lower CDI-risk antibiotic if one is indicated, the potential to develop *C. difficile* infection if *C. difficile* spores are ingested is much lower.

The second approach is to prevent *C. difficile* transmission, or spread. This is accomplished by placing patients with *C. difficile* infection into Contact Precautions and having good environmental cleaning practices.



Speaker Notes: Slide 11

There are two Tiers to *C. difficile* infection prevention. The first Tier includes those interventions best supported by evidence that they are effective at preventing *C. difficile* infection in the hospital setting. These are activities that all acute care hospitals should be doing.

The second Tier is composed of interventions to try if the *C. difficile* infection incidence remains higher than desired despite implementation of Tier 1 interventions. Tier 2 interventions do not have direct data to support them, but there are reasons to believe they can be helpful to prevent *C. difficile* infection when added on to Tier 1 interventions.



Speaker Notes: Slide 11 Continued

To find out more about EPA sporicidal agents:

<https://www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium>



Speaker Notes: Slide 12

The first step to any intervention to prevent disease is to have good surveillance data. These are the data that let you know if there is a problem and are the primary outcome measure to determine the impact of an intervention to prevent that disease. Presumably, all of you are collecting and submitting *C. difficile* infection data to the National Healthcare Safety Network, or NHSN, as this is mandated by the Centers for Medicare and Medicaid Services, or CMS.



Speaker Notes: Slide 12 Continued

Since a key step in the pathogenesis of *C. difficile* infection is exposure to antibiotics, it is probably not surprising that antibiotic stewardship is a Tier 1 intervention. Some research suggests antibiotic stewardship is the most effective *C. difficile* infection prevention measure.

Appropriate testing is important to both detect all *C. difficile* infection cases in a timely fashion and also to minimize the number of false positive tests.



Speaker Notes: Slide 12 Continued

The earlier a patient is diagnosed with *C. difficile* infection, the sooner he or she can be placed into Contact Precautions and prevent *C. difficile* spread to other patients because they can lead to unnecessary patient treatments. False positive tests are problematic because they will falsely increase your *C. difficile* infection incidence, and also divert your prevention resource.

Contact Precautions is used to prevent transmission of *C. difficile* from those with *C. difficile* infection to those susceptible to *C. difficile* infection. Good cleaning practices are important to remove infectious spores from the environment as an adjunct to prevent *C. difficile* transmission.



Speaker Notes: Slide 13

If your *C. difficile* infection incidence remains higher than you desire after implementing Tier 1, the next steps are to re-examine your *C. difficile* surveillance data, and the implementation and barriers to implementation of the Tier 1 interventions.

If gaps remain in the Tier 1 interventions, those should be addressed prior to implementing Tier 2 interventions. The *C. difficile* infection surveillance data will inform you as to which Tier 1 and/or Tier 2 interventions to focus on.



Speaker Notes: Slide 14

In summary, *C. difficile* is the most common cause of healthcare-associated infections in the United States, and it contributes significantly to morbidity, mortality and healthcare costs.

C. difficile infection prevention efforts are effective at reducing *C. difficile* infection incidence.



Speaker Notes: Slide 15

No notes.



Speaker Notes: Slide 16

No notes.

