Hello, and welcome to CDI Management and Post-Acute Care Part 1. My name’s Robin Jump, I’m an infectious disease physician at the VA in Cleveland, Ohio and I’m also at Case Western Reserve University. And my focus of my academic research is on antimicrobial stewardship in older adults, including those in long term care and also on c.Diff. And that’s what we’re going to talk about today. Here are my disclosures.

And let’s move onto a brief overview so we’re going to talk in this Part 1 Session about pathophysiology and risk factors for c.Diff and then we’ll move onto diagnosis and treatment and infection control and prevention in the second part of the talk.

So speaking with pathophysiology, and let me start by showing you on the left-hand side of the screen an actual picture of c.Difficile. This is a gram stain of c.Diff and you can see that they are rods and within each of those rods is a pink portion which is the vegetative part of the bacteria kind of the living and toxin producing part and that purple part is a spore and we’ll come back to that at a later point. The spores tend to hang around for a long time.

Let’s begin by talking about clinical disease. So c.diff in general can be divided into three categories; non-severe, severe and severe complicated. Most people get better from the disease and for a while they will be they’ll be an asymptomatic carrier, they’ll still have the spores that are being shed out of their rectum and onto their skin. And with time those spores go away and that person goes from being an asymptomatic carrier to having no c.Diff., they’re healthy and recovered and all is well in the world.

Some people don’t do well with the disease and will die from it and we have a significant number of deaths each year estimates are from 25,000 to 50,000 deaths annually. And then there’s also an outcome which is most common among elder adults which is recurrent disease, where people get better and seem to get back to normal and then in a few days or a few weeks after stopping medicine for c.Diff the symptoms come back and this can happen again and again. And it’s usually non-severe c.difficile but it’s very burdensome to the individual and the people that take care of them. It really disrupts their lives and they can’t leave the house sometimes. And this is becoming a significant problem for older adults especially.

So let’s talk about how people become sick with c.difficile and this is a picture of an intestine and over on the left-hand side of the slide is a normal microbiome and what I’m trying to show you in there is that it’s a robust and diverse population of bacteria. That’s what the little blue dots and o’s are. And, of course, in the real gut there’s hundreds of different species and millions upon millions of bacteria.

So when someone is exposed to systemic antibiotics, it reduces both the number of bacteria and reduces the species diversity. And under those circumstances, if someone who’s been on antibiotics is
exposed to c. difficile before their gut has been able to recover which can take weeks to months. The c. difficile spores that they ingest can find a place to live within the gut and those spores then can germinate and become vegetative form, those are those little brown clouds there, and those vegetative forms in turn make toxins A and B and those toxins are what make us sick.

There’s many risk factors for c. difficile and as we’ve already mentioned antibiotics is the most important risk factor. And it turns out that even if the individual themselves doesn’t take an antibiotic, the facility antibiotic use will promote c. difficile transmission. This is a four-year retrospective cohort study that examined the patient and ward-level of risk factors among individuals and this is in an acute care hospital. And what they found is that for every ten percent increase in the antibiotics used on a single ward in the facility, the relative risk for the patients on that ward increased by 1.34 and so what happened there is that even if someone didn’t take an antibiotic, they were still at increased risk for getting c. difficile. And the take home message here is that antibiotics put the entire population at risk even those who aren’t getting exposed to them.

And the more that an individual is exposed to antibiotics, that increases their risk of c. difficile infection. There’s a study done of almost half a half million adults that were admitted to 14 hospitals over a two year timeframe and of those less than one percent developed c. difficile infections. So this is about 2600 patients which is still a huge number of patients to look at.

And the investigators of this study looked at the relative risk of getting c. difficile by the rating them by the number of antibiotics to which people were exposed, or the classes of antibiotics. So exposure one class could increase relativeness of getting c. Diff about twofold. And then when someone gets exposed to two classes of antibiotics the relative risk goes up to three to four. And then as we add on more and more antibiotics that risk seems to go up a little bit more.

And this is a pretty common scenario when someone’s in the hospital or in long-term care they’ll start off with an antibiotic for one thing, let’s say, concerns for a urinary tract infection or a pneumonia and if they don’t get better, or if there’s a urine culture that comes back, or there’s a new provider that comes on there’ll be a class switch of antibiotics which means that we’re essentially doubling that person’s risk for c. Diff within just by a medication change. And these are something that -- this is an avoidable factor.

The steps that we can all take to reduce the risk of c. difficile are to cut back on antibiotic use and first and foremost is avoiding antibiotics whenever possible. We need to change the paradigm for antibiotics as being a just in case measure to something that we only use when necessary, only when necessary.

And one way that we can talk about this among ourselves as healthcare providers and to residential patients and to their families is to talk about careful observation. And we’ve been calling this watchful waiting and I’m on a one woman campaign to turn this into a different term which is careful observation.
The idea being when we say watchful waiting we talk about this as we’re just sitting back and kind of waiting around and that’s not the message that we want to convey and, indeed, that’s not what we’re doing. When we’re doing careful observation, when we’re deciding if someone really needs antibiotics we’re doing more frequent vital signs, we’re offering oral hydration, we’re doing support of care and measures and giving them time to show us if they just need a little bit of TLC to feel better or if there is something that needs an antibiotic to treat it.

And if we do careful observation people usually let us know in six hours or twelve hours or twenty four hours if we’ve made the right choice and it’s not a onetime decision. That’s why we keep observing and we keep reliving the decision to wait or not start antibiotics.

When we must use antibiotics three things that we can do are to use shorter courses, to choose narrow spectrum agents, and to also choose agents that have less excretion into the GI tract. So shorter courses, for example, community acquired pneumonia can usually be treated with a five day course of antibiotics. Most common infections that we’re treating especially among older adults should be seven days or fewer.

Another strategy is to choose narrow spectrum agents, for example, when there’s concern for a urinary tract infection we often turn to fluoroquinolones as a first choice but it turns out that Bactrim and Nitrofurantoin which are both narrow spectrum agents are usually equally as effective and they have a less devastating effect on the GI tract and that also hits on the last point, too. Bactrim and Nitrofurantoin are both concentrated into the urine and tend not to undergo all that much GI metabolism and that’s a reasonable strategy to use to try to prevent c.Diff or at least reduce the risk.

Moving on to the next slide. Advanced age is the second most important risk factor for developing c.difficile infection. This became very evident when the epidemic strain emerged around 2004. This is a graph that shows time and years along the X axis on the bottom and along the Y axis is the number of cases per 10,000 people in the population. Looking at the black line that shows everybody in the population; the green line shows people that are aged 65 to 84 and the red line on top is people that are 85 years or older.

So c.difficile was always a disease of older adults and when the epidemic strain came out about 10 years ago older adults were much more affected by this. In this [] is also age related vulnerability. In 2010 greater than 90% of the deaths due to c.difficile infections were in people 65 years or older. And the reasons for this involves the immune senescence that happens with aging and this manifests as a poor antibiotic response to c.difficile. When people have that poor antibody response that correlates with an infection and it also appears to correlate with increased risk of recurrent disease.

And in general, older adults have a less diverse and a less resilient gut microbiome which also makes them more vulnerable. So for advanced age the things that we can do are really not much until we find a fountain of youth we’re stuck with addressing the things that we can address which for the moment is antibiotics.
Other risk factors for *c.*difficile include, not surprisingly, previous hospitalization and being a resident at a long-term care facility. And the reasons for this are antibiotic exposure and also because this is where people with *c.*Diff go which means that people at these institutions are going to be exposed to the *c.*difficile spores. Not surprisingly, underlying disease severity and low albumin also contributes to the risk of *c.*difficile and there’s not much that we can do about those. But we do have the possibility to manage gastric acid suppression.

This turned out to be a pretty significant risk factor for recurrent disease. There’s a study done and published in 2015 in *JAMA Internal Medicine* in which the authors looked at hazard ratios, not ration as it says in my slides, excuse me, for getting recurrent disease so age over 75 years, proton pump inhibitor use which is PPI, antibiotic re-exposure and length of stay all contribute the risk of *c.*difficile infection.

The authors then went on to explore more in depth what were the indications for proton pump inhibitor uses and for over half the patients there was no indication. They were just on it because they’re on it and they didn’t actually have GERD or gastroesophageal reflux disease or any other risk factors that would make them need this.

Some people had an age older than 50 years with two other risk factors that required them to have a proton inhibitor. Some had a history of *c.*difficile and some had GERD with previous 90 days but over half of those folks had no reason for the proton pump inhibitor so this is an opportunity for all of us to question is someone really needs that medicine if we see it on their list.

So steps that we can take to reduce other risk factors; stop PPIs unless they’re truly needed and avoid antibiotic re-exposure whenever possible. And the worst offenders for antibiotics that contribute to the risk of *c.*difficile are Clindamycin, Fluoroquinolones and third and fourth generations of cephalosporins so ceftriaxone, cefepime, ceftobiprole, among others.

So take home messages from Part 1 are that antibiotic exposure is the main risk factor for *c.*difficile infection. Antibiotics disrupt the gut microbiome which is an important and overlooked form of host defense and that proton pump inhibitors appear to increase the risk of recurrence of *c.*difficile infection.

And before we end this segment of the presentation, I’d like to thank you for listening and I also want to thank all of you for the work that you’re doing on the front lines to take care of our patients and our residents and all the work that you’re doing to reduce the risk of *c.*difficile.

Thank you.