Hello everybody, and welcome to CDI Management and Post-Acute Care Part 2. My name's Robin Jump, I’m an infectious disease physician at the VA in Cleveland, Ohio and I’m also a member of their faculty at Case Western Reserve University. My academic interests are antimicrobial stewardship in post-acute and long term care and also c.Diff. prevention in that same population. Here are my disclosures. And in Part 2, we’re going to focus on diagnosis and treatment of c.difficile infection as well as infection control and prevention.

So diagnosis and treatment, let’s review diagnostic criteria for c.difficile. C.difficile can be divided into three categories: non-severe, severe, and severe complicated c.difficile. The criteria to diagnose non-severe c.difficile are to have at least three liquid stools per day. A lot of people will say they have diarrhea, but that can mean very different things to different people; sometimes, it means that they’re having more stool than they’re used to having; sometimes it means they’re having loose stool. The criteria for diagnosing diarrhea that’s related to c.Diff is that, the stool must take the form of the container. A second criteria is that they have to have a positive test for c.difficile. These tests vary as to what people are using and where. And this is a particular area of debate in discussion right now among people who think about this a lot. But usually within a healthcare facility or network, there’s just one type of test or one type of testing algorithm. And based on the last five years or so, only one sample of stool is necessary to do that test. In the old days, we used to have to send three stools over three days and that’s no longer the case.

So for people that have non-severe c.difficile, we could definitely consider management outside the hospital, so either in a nursing home or even at home depending on the situation. For people that have severe c.Diff, in addition to the positive test and the three liquid stools, they’ll also have an elevated white blood cell count of greater than 15,000 and they’ll also have an elevated creatinine. The formal criteria say 1.5 times above their baseline, I think the working definition that I use is just, do they have acute kidney injury or some sort? And these are people that are initially managed better in acute care than outside the hospital.

And finally, for severe complicated c.difficile, these are people that are clinically unstable, they may have an ileus, so they’re actually not able to show diarrhea. They’ll have toxic megacolon in some cases, and these are the patients that we’re thinking about a possible ICU transfer, these are people that may require surgery or colectomy. So they need a surgical consult first, and then maybe infectious disease consult afterward. And these people are – the recommendation is to monitor serum lactate and their white blood cell count as their management’s being considered.

So treatment of non-severe c.difficile infections involves, and I forget this all the time and I think a lot of us do, the first thing that we all need to do is to stop the antibiotic that put them at risk for c.difficile in
the first place if it’s still going, and if we can. The recommended treatment based on 2010 guidelines is oral Metronidazole. And if somebody is on Warfarin, then oral Vancomycin should be the first-line treatment and the reason for this is that Metronidazole can increase the effect of the Warfarin and lead to an increased INR.

And I just want to emphasize, what I’m showing you now is based on 2010 guidelines that are published through the Infectious Disease Society of America and Society of Healthcare Epidemiology of America. There are revisions of the guidelines underway and I, like you, I keep waiting for those to come out. So we’ll keep going with the 2010 recommendations that we have at the moment.

One thing I also want to emphasize is that there is no need to do a test of cure. After someone has been [] with c.difficile and once their stools return to normal, they’ll still continue to shed the c.difficile spores for days or weeks, or sometimes even months after their stool has gotten back to a normal or perhaps sometimes a new baseline. If we keep testing those people for c.difficile, we’ll find it and that puts us in the bind of do we keep treating or do we let it go?

So a better approach is to not do a test of cure, to go back clinical criteria to know if someone’s getting better or not, and it’s usually fairly evident that their stools have gotten back to some semblance of normal. It may take even after the c.Diff has been treated effectively, it may take weeks to months, sometimes a year for someone’s tool to return to what it once was. This is unfortunate, and people often need to be counseled through this and sometimes we need to do other medications to help them, and my preferred agent here is fiber; it helps bulk stools up and, therefore can slowdown the transit time.

For people that have recurrent disease, again, we try to stop the inciting antibiotic. For the first recurrence, the treatment of choice is to repeat Metronidazole. For the second recurrence, this is when people go to oral Vancomycin, and that’s after we get past the second recurrence is when we start getting creative, that might be the way to describe it, and we do oral Vancomycin unless people do orals tapers or, as I’m sure that all of you were aware, there is now a whole host of new treatment options that people are exploring and using. One of them is Fidaxomicin, and this is a relatively new antibiotic and is active against c.difficile’s vegetative forms but it seems to spare other members of the gut microbiom.

And the treatment outcomes for primary disease: so, the first infection of c.Diff are equivalent to Vancomycin. But Fidaxomicin has an advantage in that it appears to reduce the risk of recurrent disease. What I’m showing you on the bottom part of the slide here are macrostructures of different antibiotics. So, the antibiotic on the right side of the slide on the top part, the higher one is Penicillin; below that, in the bottom right corner of the slide is Metronidazole; and then that great big thing that takes up the entire middle of the bottom part of the slide is Fidaxomicin. And there are six carbon rings in there and then there’s that huge ring-like structure in the middle and this is how I remember that Fidaxomicin is a member of the class of macrocyclic antibiotics. I think it’s that huge ring that makes it the macrocycle.

One of the disadvantages of Fidaxomicin is, of course, its cost. So on this slide, I’m showing a cost comparison of a 10-day course of Fidaxomicin which in 2013 cost about $3300; oral Vancomycin capsules for a 14-day course is about $2000. What we do at the facility where I work is we take the
Vancomycin that is made to go into somebody’s vein as an IV Vancomycin and compound it into a 100ml of, I think it’s D5W, divide that into eight syringes and then give that to patients and that for a 14-day cost is less than a dollar a dose; we’re looking at $40. And Metronidazole is equally inexpensive at $30 for a 14-day course. So sometimes, this is why people wind up using the less expensive therapy very reasonably so.

We now have a whole host of new treatments that are still being developed and worked out and being made available. And the one that seems to capture all our imagination is Fecal Microbiota Transplant or FMT and this is administration of feces from a healthy donor to someone that’s been suffering with c.difficile. And for those of you that have cared for people with c.Diff, you know that they will do anything to get better including the FMT. And this is an amazing treatment. People have symptom resolution in one to two days, and one of the early clinical trials that looked at this, a 93% cure rate with one or two treatments. And I can think of few things that we do in medicine that are this effective.

And in a small series that looks specifically at older adults that were 80 years and older, eight of ten of them had symptom resolution. So again, it was 80% efficacy among that group. And just to, for full disclosure, that picture on the left is actually just a glass of chocolate milk which you will never look at the same way again.

So we move on from Fresh Fecal Microbiota Transplant to using Frozen Fecal Microbiota Transplant. That’s just chocolate ice cream and this was a study in a randomized non-inferiority study of 232 adults with the average age of about 73 years that had refractory CDI. So, they had recurrent multiple episodes of c.Diff. When someone took frozen poop and thawed it and did a Fecal Microbiota Transplant and found that it worked as well as a fresh transplant. And this opens up a possibility of doing self-donation, it also opens up a possibility of having stool banks so that people can get treatments when they need it as opposed to when they can find a donor and this is a cost-effective and well-tolerated strategy.

So even beyond frozen stool, we’re now moving into an era of Poop Pills and this is now being tried with oral, encapsulated, frozen fecal microbiota. The capsules are stored at -80 degrees Celsius and each treatment is made from a single donor, and the pills themselves are really well encapsulated. They don’t look at all like this chocolate Easter egg on the left hand side of your slide. They are put in several layers of gelatin capsules, that’s in part for aesthetics and it’s also in part to make sure they get through the stomach and into the intestine which is where their effectiveness happens.

On their early trials, it was on 20 patients with ages that range from 7 to 90 years and they took 15 capsules a day for two days, and 14 responded to the first treatment and 4 to a second treatment for a 90% cure rate which is just amazing. This is still a relatively new and somewhat experimental treatment, but it’s working and I think that we’ll see this expand.

And there’s now people that are doing freeze-dried poop pills. And what I wanted to show you in this study is the change in the gut microbiom. So this is a case report of a 46-year old woman with Crohn’s disease who developed refractory c.difficile infection.

Let me walk you through this slide here or the graph on the left. So, the Y axis is a relative abundance and proportions of different species of bacteria; different families of bacteria. The identity isn’t important, what I want you to see is the change in the ratio of the colors. So the first bar here on the left, D is for donor and then the second one is donor frozen, that’s the DF, the third bar that’s mostly
green is the microbiome of the 46-year old woman prior to getting the Fecal Microbiota Transplant. And then at three days, seven days and fourteen days, her microbiome changed dramatically. There’s a huge increase in the purple and a drastic decrease in the green. And she got better. And with the freeze-dried poop pills, we’re now able to actually have people do these treatments at home which means that we’re entering an era that might see a re-envisioning of a slogan from a company that we might all know.

So let’s move on now to infection control and infection, and we’re going to start by talking about nursing-home onset c.difficile. This is a study that was done by my mentor, Curtis Donskey, who looked at the time from admission to a long-term care facility to c.Diff onset. So along the X axis in the bottom are weeks from admission to one of our VA nursing homes, and along the Y axis is the number of patients. And most of our residents developed their c.difficile within five weeks of being admitted to a nursing home and we consider this to be hospital-associated, a Long-term Care Facility onset c. difficile.

The reason why we consider it hospital-associated because they all came from the hospital, and that’s also where they’re exposure to antibiotics happened; that’s where the initial insult to them occurred. And then when they came to the long-term care facility, that may have been where they were exposed to the spores and then became c.difficile. And as you can see by the graph, once people have been in the nursing home for a while, their risk of c.difficile is significantly decreased, and we have far fewer people acquiring c.Diff when they’ve been in the long-term care facility for several weeks.

And this just makes the point that it’s the exposure of c.difficile spores in that early time after transfer to the nursing home that got people sick with this disease and that becomes an argument for infection control as being a principal way to prevent c.difficile infection.

C.difficile spores can be recovered months, truly a months, after it has been left on the surface. C.difficile spores are difficult to kill using routine cleaning agents, so quaternary ammonium compounds which most people are using in hospital and nursing home as cleaners aren’t effective against c.difficile spores. What is effective is 1 to 10 dilution of bleach that has to be made up fresh every 24 hours and unfortunately, that’s fairly corrosive. There are sporicidal agents, and it has to say “sporicidal”, that are available for cleansing within a hospital and long-term care environments. And unfortunately these are expensive and like the bleach, tend to be corrosive, but they certainly are available and should be used to do routine cleansing for people that have recent c.difficile.

The only thing that a lot of us didn’t appreciate is that c.difficile spores are shed onto not only the residents’ environment in nursing home and in acute care, but also under their skin. This petri dish on the left hand side of the slide is a hand print of someone that had just examined a nursing home resident with c.difficile. And the way that this is done is that, we had the person put a glove on, touch the skin of the abdomen of the patient that had recovered from c.difficile and then touch her hand to this petri dish. And those big, fluffy, yellow colonies that you’re seeing are c.Diff. That’s a huge number of c.difficile bacteria that have been picked up after a one to two-second touch of a person’s skin and you can imagine what happens especially for nursing staff and nurses’ aides who are helping people that have c.Diff get bathed or change clothes or use the bathroom. It’s a lot of personal contact and a lot of risk for acquiring c.difficile spores.

One way that we can try to reduce the risk of transmitting c.difficile is to consider extending isolation. This is a graph that shows the time until negative results for c.difficile cultures from a resident’s abdomen or their chest. So it’s time in days along the X axis on the bottom, and the proportion of
people with c.difficile on their skin along the Y axis. So at the time when they had just ended their symptoms of c.difficile, everybody had c.difficile on their skin. But even up to a week later, about half of the patients in the study still have c.difficile on their skin which means that we might need to wait for a week or longer until after someone has gotten better from their c.Diff before we lift contact precautions. It doesn’t mean that they need to stay in their rooms, but it does mean that when healthcare staff are interacting with them and helping them with ADLs and other activities, that we need to wear our gowns and gloves and to use soap and water upon exit from the room.

And this is another study done by Curtis Donskey that looked at asymptomatic carriers and this is an older work which is why we’re using the term CDAD which is C.Difficile Associated Diarrhea. Now, we all say c.difficile infection. And along the X axis, we’ve got patients with c.difficile infection in the first cluster of bars, asymptomatic carriers and noncarriers. And the research team looked for environmental contamination in the rooms of people with this in these three different settings or three different states. And for people that have c.difficile infection, up to 80% had environmental contamination, that’s the solid black bars. But for asymptomatic carriers, that was still 60% and even for noncarriers there’s around 30%. So c.difficile is everywhere.

And for a nursing home resident, while we say that there’s no place like home, it becomes really challenging to clean this because people have all their belongings or personal items and we can’t bleach everything here, which means that cleaning becomes a huge challenge.

So steps that we can take in terms of infection control are to attempt first, to minimize transmission by residents. So if there’s a nursing home resident that we know or we suspect has c.difficile infection, they should, whenever possible, be in a private room. And if that isn’t possible, they could be cohorted with somebody else who may have c.Diff. We have to encourage the residents to do hand hygiene with soap and water. We should talk about sending isolation or contact precautions based on the slide that I showed you just a couple of slides ago.

And also, this is not evidence-based but it makes sense. For people that we know have c.Diff, have them use common equipment like they might use in physical or occupational therapy at the end of the day. And after they’re done, then the people that use – the physical occupational therapist can use bleach or other sporicidal agents to really wipe down the equipment and get it cleaned so it’s fresh and ready to do the following day and they’re not in a rush for time to get the next person in for their appointment. That was a tip I learned from one of my local nursing homes here in Cleveland.

Others steps that we can take for infection control are to minimize transmission by staff. Hand hygiene with soap and water is the best way that we have to reduce the transmission of spores by healthcare workers. C.difficile spores are really sticky on skin, they’re hard to wash off and the soap does an okay job of removing them but it’s still not 100% effective. What does seem to make a difference is the mechanical action of rubbing our hands together while there’s soap on there and then running them under water and basically washing the c.Diff down the drain.

Another way that staff can help reduce the risk of transmission is to make sure that we’re all using single-use and disposable equipment, so glucometers and thermometers should only be used for one person or should be wiped down in between. Whenever possible, dedicated equipment I’m thinking here about blood pressure cuffs and slings, so that one person has their own sling when they’re being
moved around and that can get laundered and then brought back to that person when necessary. And before it goes on to being used for a new person, it should also be laundered.

And then also, mandatory education at least annually for staff. And more often especially for high-turnover staff like nurses’ aides that sometimes have an average work length of like six months in the facility. So with the constant or frequent turnover of staff, it can be hard to maintain kind of an institutional or cultural knowledge of what are good infection control practices, so they may need a refresher as often as every quarter and it can be ten minutes.

Other things that we can do for infection control to minimize transmission by staff is to maintain good contact precaution and this means gowns and gloves. It’s worth reviewing how to put these on and take these off. I’ve seen some very creative uses of gowns and some of them being up over somebody’s chest and going down and doing the full closure on their sleeves with the gloves going over the top and creating that full barrier, I’ve seen people just wear their gown around their waist like it’s an apron. I’ve seen people wear their gowns and not their gloves and some other odd things that you wouldn’t expect. So one thing that we can do is, in addition to educating the staff on how to use the personal protective equipment, is to make sure the equipment is available at the door to the resident’s room and then designate someone every shift whose job it is to go around and replenish supplies. If the gowns and gloves aren’t there, it makes it that much harder to put them on and they have to go get them yourself every time also creates another barrier.

And then finally, supplying the facility and making them available in common areas is to have disinfectant wipes with bleach. There are some wipes that may say they have – they may look like a brand that has bleach in it, but unless it smells like bleach and says it actually contains bleach, it won’t be effective against c.difficile. So, it has to smell like bleach to be effective. And those wipes can be used to clean down common equipment like keyboards or telephones or computers in nursing stations, they can be used to wipe down doorknobs and door handles as well as our stethoscopes, for example, if we’re leaving a room where we think someone might have c.difficile. So they’re good things to have out and available and they don’t violate those regulatory bodies that don’t want us to have liquid around, so bleach wipes are a nice thing to use.

And finally for infection control, we can minimize environmental reservoirs and this means involving and educating the housekeeping staff. I think the housekeeping staff don’t often understand the value of their role in preventing infection by doing good cleaning. They can be encouraged and asked to do daily disinfection of high-touch surfaces. This is where those wipes come in again. And it may be that if there is an increase in the rate of c.difficile at a facility, rather than go to a new cleaning product, the first thing to do is to assess the adequacy of cleaning. And the way that some people do that is through by putting down a dye that glows under UV light or under a blacklight and there are certainly some kits that could be done to do this. There’s also laundry detergent which is a lot less expensive that can be made into a floury and also applied to a surface that will also fluoresce under a blacklight.

And I’m not sure which flavor of Tide it is, but Tide is the one that will fluoresce a little bit and that can be a cost-saving intervention for facilities to assess cleaning. Just a word to the wise though, if you do start assessing efficacy of cleaning using these kind of hidden shopper techniques where you’re putting the spot down and then checking later, once the housekeeping staff catches onto this, they may go out and purchase their own blacklights and also look to see where the dots are so, you have to move those dots sometimes.
And finally, if cleaning isn’t working with the agents that are being used and after lots of education and coaching of the staff then it may be time to clean and disinfect with a sporicidal agent like bleach. And for reasons I mentioned earlier, people don’t often like using that because it could be caustic but it is effective and may be what’s necessary to help bring an outbreak under control.

One of the questions that I’m often asked is about probiotics for primary prevention. There’s a metaanalysis that was done that slightly favors probiotics. One of the concerns I have with probiotics is a lot like saying people are going to Europe. When we say probiotics, we don’t know what the species are, there’s not often control over how those strains may have drifted, we also don’t know how many of them are alive when they’re actually sold and then actually administered, even if they’re kept in the fridge. Longevity of these things isn’t clear. And so, my analogy of probiotics and backpacking in Europe is that, we can say we’re going give a probiotic but we’re not sure what it is. It’s like saying ‘I’m going to Europe and we don’t know if you’re going to Prague or to Portugal or to Paris’. Those are all different things. And probiotics are often proprietary mixtures of bacteria.

And the metaanalysis that slightly favor probiotics was based on trials that were well-controlled clinical trials, not based on kind of everyday use. Finally, there’s also no FDA approved probiotic other than two that we all might consume which is yogurt and something called Kefir which is like a strong liquid yogurt. These are approved and recommended by the Food and Drug Administration. They don’t require a prescription, but we do know what the strain of bacteria is that’s in them and we also know that there’s live bacteria in them. So nursing homes that I talked with have gone to putting a yogurt on somebody’s tray every day and it can be any of the yogurts that says they have live bacteria in them. It doesn’t have to be one of those special yogurts that say they have live bacteria.

Additional steps that we can take for infection prevention across the entire facility are to implement antimicrobial stewardship programs to reduce the risk of exposure to antibiotics and that will reduce the risk of c.difficile. To do surveillance for c.difficile infection. It’s hard to know if rates have changed if you don’t know what the baseline is. So by knowing what the background rate is, if there’s an increase or an outbreak or the appearance of one, then it becomes knowable and steps can be taken. Avoiding tests of cure and also using a laboratory-based alert system so that if somebody has a positive c.difficile, it should be called or faxed or otherwise notified directly to someone at the facility and not kind of stuck on the computer or in a pile of faxes that shows up when they’re back three days later. There needs to be a more active, proactive outreach of the notification and that’s something that can be worked with the laboratory.

Facilities, especially long-term care, may think about doing an early response to potential c.difficile infection, so this means defining criteria which, for most people is going to be at least three liquid stools per day. And in other circumstances especially with someone who either had a history of c.Diff or a recent exposure to antibiotics, doing preemptive contact isolation. It sounds a little mean, but I would rather see someone in isolation for two or three days without than they have that same person who may turn out later to have c.difficile become a source for having c.Diff spores put around the facility and putting a lot of other people at risk. And finally, I think there should be standing orders for nurses to test or to initiate testing for c.difficile once specific criteria are met and that’s a policy that needs to be considered at an individual facility level.
So to wind this up, the take-home messages are that Metronidazole and oral Vancomycin are still the mainstays of treatment, fecal Microbiota Transplant is safe and effective. And as we move to an era where we’re able to do this using freeze-dried capsules, it’s much more palatable for people, and finally, infection control is especially challenging and especially important in post-acute and long-term care settings.

I’d like to end by thanking everyone for listening and I’d also like to thank you for the work that you’re doing on the frontlines to take care of our nursing home residents and our hospitalized patients and to try to reduce the epidemic c.difficile infection. Thank you very much.