This session is entitled sedative use disorder, key concepts for treatment, I will now pass it over to Dr. Ricardo Restrepo to begin the session .

Thank you all, another meeting with Zoom and we will try to make it useful. It has been a long 1.5 years wearing the mask and distancing, but I hope we keep the optimism and we will learn. That is the objective. Today, it is a very important topic about sedatives. We are going to review how important this topic is. I really hope that you keep the connection that we just made with the alcohol use disorder topic. Because, those two interlink with each other. I do not have any financial disclosures with the presentation. This is the outline. I really hope that we will learn today and remember that my main objective is to cover the things that are going to be in your text. The historical view. The first half of the 20th century pretty much was marred by barbiturates. Even though we know certain stories from different personalities that, unfortunately, died for the combination of barbiturates and alcohol. At the present time, we are part of the generation that started in 1950s, related with benzodiazepine. The first benzodiazepine that came on board was in 1959, it was , after that was the diazepam. The 1960s saw a wave of this, but then we started to see the consequences of the prolonged use of these and we saw withdrawals and we explain more in depth what was happening and right now, with this agenda, we know that the short acting benzos that are very potent , some of them, we can create a sedative use disorder and these days we are trying to allow what is the avenue to follow, what is the best thing to do when we prescribe benzos? As I was telling you, we have three main groups we will cover today. One is called the benzos receptor agonist , we will find there are two main one, benzodiazepine, and the selective non-benzodiazepine hypnotics, which we thought were going to be extremely useful without causing any type of the dependence for disorders. We will figure it out that we need to be cautious. We also are going to discuss the barbiturates and the GHB and others. Always the media, we need to pay attention to the information we get. These days, with the Internet, we need to be more aware than in any other time from where the information is coming from. Take a look at our journals. How they use to promote certain benzodiazepines. I am talking about gender equality. Look who is the center of observation on your left upper corner. And look who is behind the screen. We used to be a mature society. We need to change the language and how we look at who we are in this world. From how and where we get information. Let's review a case. This is basically a case that I am trying to match it with a case we saw initially with the alcohol use disorder. Remember that Mr. RR was a Latino person from Los Angeles, California with a history of alcohol use disorder that initially approached your office because he had insomnia, medical history of hypertension, pancreatitis. Suddenly, a year later, he arrives to an emergency room brought by a friend with confusion. Keep in mind that this is the opening of the case, but suddenly I want to bring you to what we were explaining earlier. Kind of the glutamate, but remember that the benzodiazepine is related with GABAa and the pentameter composed of these GABAa receptors, what is the main rule ? As a big picture, keep in mind that the two As and two Bs, between the A1 and GABAa is the benzodiazepine site , in the GABAa receptor we will find the position for alcohol , barbiturates, but today I am talking about the

GABAa receptor with benzodiazepines. It is known that GABA is estimated to be present in 40% of all synapses in the human brain. It is the main inhibitory neurotransmitter. We saw how alcohol activates the GABA receptor, benzos activates the GABAa receptor . We have two main types GABA,of recently C receptor has been described but I will not talk about it. Today, I want to talk about the GABAa 's inotropic and GABAb, GABAa is where the benzos go . Benzodiazepine increase the number of times the chloride channel opens in the GABAa receptors means the frequency, different barbiturates, that increase the duration of the opening of the chloride channel. These are key elements to keep in mind when we are going more in depth. This is a slide to show you that diazepam needs GABA, benzos need GABA . Look at the memory potential when I combine the benzodiazepine and with the GABA . We are going to review later that limits and blocks affects of benzodiazepine but not barbiturates. Benzodiazepine, to have a mechanism of action, they need the presence of GABA, barbiturates do not require the presence of GABA and that is one of the reasons that the narrow index of the barbiturates is a little bit narrow and we can get more in trouble. We can overdose easier with barbiturates than with benzodiazepines. We already reviewed these. Just to keep in mind that the most important aspects, benzo is the frequency , barbiturates is the duration of the chloride channel. Barbiturates does not need GABA, benzodiazepine needs GABA to interact in that cell and get the influx of chlorine. This is a slide I repeated in the lecture that we were analyzing or reviewing more in depth with alcohol. It is exactly the same mechanisms. Presynaptic calcium channel opens, gets the release of the neurotransmitters, let's say GABA, when I have benzo on board , I will open the channels that I will have the effects of relaxation or kind of feeling relaxed when I take the benzodiazepine. Very interesting, one of the hypothesis that I think is important to note, we need to know why we get a substance use disorder through benzo is this one , put yourself into the interneuron area of the ventral tegmental area. On your left side, if you see that GABA , the neuron, you will see that the alpha-1 GABAa receptor, the one in red, captures the presence of GABA by itself, not talking about GABA with benzo, and GABA by itself with the interneuron attachment it has with dopamine to say, dopamine, modulate the release of dopamine in your system, we don't need to go that fast, I am here to control you. In the same interneuron, in the same alpha-1 GABAa receptor, when I put the benzodiazepine into it, and in the alpha three GABAa receptor in the dopamine neuron, you will see that benzos un-regulates the system , GABA does not have control to recognize the dopamine and I have an avalanche of dopamine release and that is part of the theory of why benzos creates difficulties related with the substance use disorder. An important slide to keep in mind to have a clear understanding from where this is coming from. 80% of your patients with use disorder, they will have other substance use. We will review these in-depth. Pretty much we have two main groups we need to pay attention to. People with alcohol use disorder and opioid use disorder, you always need to ask about the use of benzos . With other substance orders, still ask, but people on methadone programs, you will see a lot of these percentages occurring in that population. People using benzos . Benzodiazepine use is two in women and one in men. As we will see, statistically speaking, what are the age using most benzos these days are the elderly. We will review this more. This has an explanation of why roughly 9 of 10 older adults who use benzos get the prescriptions , they

get it from primary care. We will see what are the specialties that are prescribing more, because they are the front line but important enough. If you are a primary care, you are handling appropriate the benzo use and we hope to generate the questions of avoiding of what happened with the opioids. Look at the percentage of the population in the U.S. with any benzo by sex and age . In your X life you see 18 to 80 and in Ythe column is the benzo use percentage . In general 12% of the women in the United States and 7% of the men, based on this study, are the percentage of people using benzos in our country . More importantly, here we go, in the Y light, you see the annual benzo visits per 1000 population and on the x-axis , you will find the agent by groups. The lighter gray is the new people on benzos and the deeper great is the people who have been on benzos for a long time. Look at the population getting more benzos , it accumulates with age. It is not that age 80 they get more prescriptions, new prescriptions, but they accumulate, because it is the population that has been on benzos for 30 or 40 years, or less, but years of use. Importantly, the benzos rate in the United States has increased almost double. Pay attention because these occur in approximately 14 to 15 years. Very important that we can apply in the context of our clinical work. Again, as I was saying, 95% increased in benzo related visits in 12 years. I don't want to dedicate much time here but I was talking about the specialties prescribing benzos, number of adulatory visits. You find the years. And the different specialties. Look how interesting it is, the use of benzos subscribed by psychiatrist have been stable but increased among other types of physicians, including primary care. What I want to generate with this slide is that we will be aware of what is happening. Why are the specialties that are more incapacity to prescribe benzos the first time and why we are subscribing it and we will continue this growth of assessing this better. We review, the important tool, when we have a person with sedative use disorder, we will match it with another substance use. Because the majority of time we are going to have another primary substance abuse, and then, we will have the sedative use disorder. Important enough, pay attention, alcohol use disorder patients, and their offerings are more likely to experience mood elevation with benzodiazepine. This is interesting because this is related with the aspect and the effects of benzodiazepine in our system, depending on the population. I don't want to be redundant but we know that we will have groups that we need to pay attention to whom we will describe benzodiazepine and why. Those practicing addiction medicine these days always are aware that, when we prescribe opioids, when we have a person drinking, let's avoid treating those patients for anxiety with benzodiazepine as much as you can. Everyone is different. We have different populations. But we need to match these information's with our reality in our practice. As I was telling you, I wanted to show you the primary and secondary benzodiazepine admissions. I know this is old data but it shows you what is happening. It is rare to find that the primary substance abuse will be benzos . You will find many times that other substance use onboard and then the benzo use as the secondary substance use disorder. Very rare to see benzodiazepine as the primary use substance. We have been talking about opioids these days and alcohol these days and the mix with benzodiazepine and the risk that this can cause to our patients. We are aware of the mortality. I don't want to be redundant but look at the studies, the amount of overdose deaths but almost the relation they have with the benzodiazepine. The FDA issued a

drug safety communication about risks with opioid pain or other medications combined with benzos . Important data to keep in mind. I want to stop by here, these are the national drug overdose deaths between 1999 and 2009 involving benzos. On the blue line is all the drug overdoses that involve benzos . The yellow line shows you how the benzo in combination with fentanyl increase since 2014. Look how important the other one that is the lighter gray line, benzos without any other opioids keep the line, a little bit increased but not like when you combine it with synthetic opioids or other drugs. Top five drugs more frequently involved in drug overdose deaths in the United States. 2010, 2017. We will find benzodiazepine. We have the fentanyl and we know that, let's say the stimulant aspect is taken a new wave. This shows us how important it is to keep the attention and the way that we are prescribing these medications, but also in the way that we need to assess our patients and discuss with them the risk and benefits of this type of group of medications. Visits by risk of serious outcomes. Look at the different group pages. As much as we combine benzos with either another substance, in this case opioids or alcohol, the daily visits increase no matter what the age group is. But, of course, as we know, the combination of those three is more serious than the other ones. Pay attention to this data and translate it into your practice. The most frequent pharmaceutical abuse these days, after the opioids, is the benzodiazepines. Alprazolam is the most frequently one used these days. Enzo NASA beans are prescribed at about 70 million, 65 million office-based doctor visits, that is a rate of 27 annual visits per 100 adults. That is an amazing data. It is surprising that that amount of million office-based doctor visits are related with benzodiazepine prescribed. More data related with the increase of prescription of misuse or abuse of benzodiazepines. As I was telling you, take a look at what is coming related with the use of alprazolam. Not far away from the use of painkillers or opioids. We were talking about the prevalence of benzodiazepine use. I was telling you earlier that it is twice the problem in women and it brings utilization with the age. Age has less new prescriptions. But it has more prescriptions accumulated through the course of time. This is another important study done that compares the 1996 and 2013 numbers of adults who feel a benzo prescription, it increased dramatically but specifically from 8.1 million to 13.5 million, an increase by 67%. Important data of prescriptions and overdose mortality as we already reviewed. Here we go. What is the group? I want to understand the essence. What is the group that misused most the benzodiazepine, take a look at the left side. That group of prevalence of benzos use in adults, the one that misused most is the group between 18 and 25. But look, where is the accumulation, as we were seeing, of the prescription, through age, and when you hit 50, it starts to count accumulation from that time, because that group age from 50 to 64, are the ones that these days are getting more and more prescriptions and accumulates benzodiazepine in their system. This is important, we have been talking about a study, six numbers, but around 30 million adults use benzodiazepines in this country. 50 point 2 million adults misuse benzodiazepine. And .5 million adults have sedative use disorder related with this. This helps you to keep the frame and the statistics image with you. Continuing with Mr. RR. He did not get his prescription of alprazolam. He is in front of you, you kind of feel the person angry and you did not prescribe benzos so he went to a psychiatrist to see if he could get a prescription from it for another

doctor. Then Mr. RR reported his heart has been racing and his insomnia has worsened, his friend stated for the past four days he has had difficulty following conversations and focusing on daily tasks. He has been off of alprazolam for seven days and I am sure you have seen this in your practice. When you do the evaluation, looking for stressors, a feeling of depression, he does not have any other type of withdrawal symptoms related with his symptomatology. He denies recent use of alcohol or illicit drugs. What are the factors associated with prescribing benzos? Prescribing can be the beginning of the overuse and then the sedative use disorder. These days we are seeing people treated for pain that are getting more benzos. Take a look at benzodiazepine pattern of use. When you have patients on benzos, some develop substance use disorder, 50% of patients with substance use disorder history will develop a benzodiazepine use disorder. Between 50 and 100 patients prescribed chronic benzo become physically dependent, similar to what we see with other medications, such as opioids for painkillers. Benefits and risks, of course, we need to assess the population, are we using the therapeutical dosage, this is a population over using and running out sooner of the prescription. This is a person that occasionally takes the benzodiazepine. What are the risk factors for sedative use or benzo disorder , if with a longer duration of benzo, more propensity that you will develop the sedative use disorder. Higher benzodiazepine dosage, as we know, lower level of location, great insomnia and current antidepressant use. I am sure that you know these but these are the indications of benzodiazepine. When we describe benzo, as much as we overpass the month, probably we will develop some physical dependence. We need to examine the risk and benefits ratio when we prescribe it. Why we are prescribing it? What is the population that will benefit? Be aware of the mix that sometimes we replace one thing for another one. When the non-benzo family came in board, people thought it was going to be benign to Cprescribe this medication and help people sleep. Take a look at what happened. We know the reality. Important enough, I don't want to be redundant about it. But we know that in our population, the elderly population, that these days is getting more and more benzos, it is an increased risk for falls , hip fractures, sedation, and cognitive impairment. I want to make a parentheses because the cognitive impairment has been related with Alzheimer's disorder. In general, so far, the study is not concluded that benzo creates Alzheimer's disorder. It is not a conclusion so let's not get confused about it. Be aware of the lethality and, based on the metabolism of benzodiazepine in the elderly population, as much accumulation as we have, higher risk for accidents and for all of these situations related. In 2015, the American geriatric Society recommended avoiding benzodiazepine despite consensus recommended and non-risk. Here we go, benzodiazepine prevalence three times in older adults compared to younger adults and roughly 1/4 of long-term benzo use is in patients 65 and older. What are the considerations when we prescribe benzos? Examine the risk benefits, avoid alternate treatment with hypnotic. Try to sit down with the patient and plan the duration of this therapy. Prescribe for brief periods of time. Try to educate the person of why it is important to do random toxicology as part of the treatment. Trying to set up the tone of how you are going to ascribe the benzos. Attempt to educate the person that you are going to attend --tell them about the access you have to the prescription drug monitoring, that the person will know ahead that you are serious when you prescribed this

medication. The equivalent dosage and the elimination of half-life is important because it will help us to make decisions of what benzos we will prescribe . What is important is that we need to take a look at these equivalent dose when we are seeing a person on two or three benzos and we want to do a paper on one of them . We will see later it is a wave or a group of clinicians that we feel much more comfortable switching a person from short acting benzo to long-acting benzo that will help us facilitate the paper. That is not a rule of thumb or written in stone but it is something that can facilitate. You need to keep this equivalent dosage in mind. Important enough, remember that the Ackerman acronym LOT, they are three benzodiazepines that don't need to force your liver to work. They don't force it through the oxidation they jump right away to conjugation and that is primarily the reason that, when we have a person with liver dysfunction, and it is on alcohol withdrawal, we use the Lorazepam because we kind of respect that the liver will not be forced to work much. Keep in mind that these are the three benzos pretty much help when you have a liver dysfunction. These are the types of benzos, the different groups , and I divide them in general, what are the half-lives of them and what are the active metabolites that they have. In general, keep in mind that the big group, when you have diazepam and others, those are long half-life benzos , the intermediate half-lives include the Lorazepam. As we were saying, they don't have active metabolites because they go right away to the conjugation of stage and that helps that the liver will be respected in one way or the other. And then we have a group for short to intermediate half-lives. Those have half-lives around 12 hours or less. The benzos are differentiated by a very important aspect, from a kinetic speaking, metabolism and my publicity. Be aware of the metabolic pathway and onset of action, prize lamb is used more than any other benzos because the action is rapid and the half-life is short. That combination makes attractive it to be overused. I just want to kind of review briefly that, keep in mind these groups, short acting, medium acting, and long-acting benzos, helpful to keep them in mind when you do the paper, when you prescribed them, when you have a plan with your patients. Mr. RR was found tachycardic, hypertensive, a medical workup primarily were within normal limits. Then, you start to see a little bit of differences when you do the mental examination. You saw that Mr. RR was restless , irritable, with twitches in his face and complained about tinnitus. He was subjectively anxious and objectively dysphoric. Then, you said, let me check the mental status examination and suddenly the score was 30 over 30. He had good insight and judgment. He was desperate and he endorsed passive suicidal ideations without a plan. Then, we move along with, what are we going to do with the withdrawal? And what are we going to approach? There are no signs and symptoms of benzodiazepine withdrawal. You will have signs and sometimes the vital signs fluctuate. Unlike acute alcohol withdrawal. We have similarities because benzo and alcohol touches the same receptor, talking about GABAa . When we are in alcohol withdrawal, we will see high blood pressure and high pulse. Sometimes you don't see that with the benzo. This person that we are assessing, Mr. RR, pay attention, he has tinnitus , twitches, related with the use disorder. Management of benzo taper is a challenge, all of us have difficulties, but remember, always find a strategy, taking in consideration what are the possibilities that you have. Are you going to prepare this patient, how you are going to provide the patient, will you use it long acting benzo as opposed to a short acting benzo they are

taking? Are you going to consolidate with one medication for the taper? Individualized the treatment, that is the clear message with all patients. Keeping in consideration that this severity is related with what we already reviewed, the duration of use, the dosage that you use, and the pharmacokinetics. What is the difference between withdrawal, rebound, and recurrence. In the book, it looks like I need to make the difference between recurrence, rebound, and withdrawal, many times you see similarities and sometimes they interlink with each other. What is key is that, when you do a taper , you try to go slow. If withdrawal symptoms show up, and if a recurring symptom shows up, you hold the dosage, try to not go backwards. Try to stick with a plan. If you want to hold a taper for one or two or three weeks, but the person will be ready for the next step, it is better than going back to the original dose. As we were saying, it is so important that we assess, in the case of alprazolam, we see withdrawal within hours and the long acting benzos, the withdrawal can come even a week later after let's say you stop the diazepam. More interestingly, as we know, we are talking about protracted withdrawal these days that we see six months, one year later after the person has stopped the benzos. How will we agree and how we are going to assist our population is the key element. When we prescribed, be aware that when we come over time, 10 days on a benzo, right away we create insomnia when the person that does not have access to a medication. When we hit the month, the physical dependence starts to occur in our system. Of course, the majority of signs, people are telling us, do not prescribe more than one month benzo, the Royal Academy of medicine , that is the advice, but in practice we see patients already, in years they vacate the benzos, we know we are creating a possibility of a substance use disorder and more directly, when a person does not have access to the medication, we will have withdrawal symptoms. The management of benzo withdrawal , when to taper , clear aspects, when you see over-sedation, when you have cognitive impairment in your patients, when you have a combination of hypnotics, plus opioids, plus alcohol, and when you see that the person is overusing or misusing the benzos. Of course, if the patient is agreeable to taper , you can move with those possibilities to taper it down . Different approaches. You can either taper slowly and taper and help the person with other medications such as anticonvulsants as we will discuss in a moment. Primarily, as I was telling you, the rate for dosage of decreasing the systematic discontinuation should be maximum 25% weekly, or biweekly. Average. When you hit the half of the original dose, either because you convert all the benzos that they have taken in , one long acting benzo, and you achieve half of the dose , you hold it and you move by 10% less and less. Be aware that the taper can take months . Not strange for any of us that sometimes you and I, we have patients we are tapering , helping them and they complete one year with us but they're close to finalize the taper in a gentle way . I have been telling you about what is my school of thought, maybe you will agree or disagree, but I encourage you to keep in mind that you can convert to longer acting agents, clonazepam can be helpful when you convert the dosage to this type of long-acting benzo . Taper it gradually and for the symptoms related with the rebound or with the withdrawal, or the aspect that you see the patient is having difficulties with, you have tools. Trazodone, but anticonvulsants, 200 milligrams, some other people use higher dosages. QID Can be helpful in assisting the population. I won't be redundant because we talked about these. When we have a short acting

sedative, the withdrawals will come in 12 to 24 hours and either 24 hours to five days in the duration of the acute withdrawal can last a month. With the long acting benzo, it can take one week to show up withdrawal and the peak will be probably on the 10th day and the duration can be another month. With either short or long acting benzo, you can see protracted withdrawal months later. I will mention a strategy that some of you may be familiar with. I encourage you to do these under the inpatient supervision. Do not do these in the outpatient, the phenobarbital substitution. When to think about doing phenobarbital substitution, when you have people on high dosages and you don't have a clue how much they are taking or that you have a clue, and I saw a person on 60 milligrams of alprazolam, writing to our unit, that is the time to use Dino Barbara Tom as a solution. Pretty much this is the equivalent of the different benzos versus the dose of phenobarbital, when we started, the plan was to give it three times or four times a day and a maximum doses of 500 milligrams. Now, monitor patients for signs of toxicity for phenobarbital, those are sustained horizontal nystagmus. one sign and skip one dosage, two signs, skip two dosages. Maintain the patient on the dose and start to taper slowly once you stabilize. Decrease phenobarbital by 30 milligrams per day . Individualize the case. If you see signs of toxicity or withdrawal, you need to adjust or pay attention to how you will cover the withdrawal. Daily dose is adjusted upward by 50%. Patient is stabilized before continuing withdrawal. This is an important topic. It is another topic of discussion, but interesting to keep it in mind. Talking about pregnancy. Debatable right now if the benzos cost difficulties to the fetal development. Keep in mind that, for now, they crossed the fetal placental barrier and passed into breast milk and create teratogenic effects. We are aware of neonatal withdrawal and the floppy baby syndrome. Talking about Flumazenil . It is not used by many people. It reverses the oxidation and competes right away with the receptor and you can create seizures and acute precipitation with withdrawal which can lead the person to even more difficulties. Remember, the Flumazenil, you given IV, .1 milligrams until you reach one milligram every 30 minutes. And if you leave the patient, be aware that in 60 minutes, if you go back, again, the receptor is taken back by the benzos and the patient will suffer still from an overdose. Be aware that Flumazenil is used by some clinicians but a few of them want to use them because of the adverse effects that I mentioned. Talking about Z drugs. We are approaching the different groups, you are familiar with their names. More importantly, is that the Z-Drugs go to the benzos units, the subunit is related with a hypnotic effect. That is the reason that these medications are promoted as something that helps you sleep. It can create an addictive pattern and we know that. These days, the dosages were decreased to have compared with the standard dose that was originally related. If you check more in depth, women are advised to take half of the dosage, and the elderly population in both genders are also to decrease from the original dose to half. What are the main side effects? Sleep related behavior, eating at night, walking at night those are the things you need to keep in mind. When you have the Z-Drugs, apply the general principle when you prescribe benzos . Talking about barbiturates. The oldest sedative hypnotic. It has a low therapeutical index. You can have an overdose easily from the barbiturates. Interestingly, the same barbiturates induce the --the metabolism of others can be affected. You are familiar with these. For example, the ultrashort meso axonal is what

people do when they do ECT. You are familiar with the short and intermediate barbiturates. Remember, many times these days, we check a person and test positive for barbiturates and the person may be taking a medication that has barbiturates on it and that is the reason we need to match the clinical criteria of why the person tested positive for barbiturates. Also, some people treated with seizure disorder with phenobarbital and test positive for barbiturates. GHB , what an interesting drug to keep in mind. The drug, already is excepted in the medical field for the treatment of narcolepsy to keep the person awake at day. This is the description of GHB by one of her patients . Shared by my colleague. "When I wake up, I feel completely refreshed. In comparison to the other drugs that are supposed to be clean, it really is clean." This is the presentation officially of the GHB to treat narcolepsy. And what it costs is an essential drug like MDMA. It causes relaxation, tranquility, mild euphoria, and temporary amnesia. This is the reason it is a part of the date rape drugs. GHB is a neurotransmitter . It is one of the few medications that goes to the GABAb receptor, benzo goes to the GABAa and GHB goes to the GABAb receptor . The other medication, even though we will not talk about it, it goes to the GABAb receptor . How GABAb works, when I take GHB, I activate primarily the release of dopamine in our system through GHB , that is related with GABA, GABA gives the order and dopamine initially is released with minor dosage. As I keep using GHB , I knock down the dopamine release. And then I get depleted it is regulated by being a scheduled medication. This is the molecular structure of it. The intoxication is pretty much a dose-response curve. Basically, it is a narrow window between one dose and a little one which can create a completely different scenario of the response. That is the reason easily you can get ataxia, loss of coronation, depression. As I was telling you, the overdose is a real danger because it is only, the LD50 is only five times the recreational dose. You need to treat an overdose such as a medical emergency. It is necessary --the withdrawal is rare but severe. You need to treat it like any other sedative use disorder. Possibly with benzo taper . Long-term features, it is possible to recover from GHB . It can create the physiological dependency that we talk about and not an FDA approved medication. As always, with treatment, do not forget that we talk about from the logical aspects. It is so important to learn motivational therapy, cognitive behavioral therapy for all of our patients. Thank you so much, I really appreciate your time, good luck in your practice and good luck in your boards. See you then and all the best. See you next year. Goodbye.

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