Welcome, everyone, this is Marvin Swartz and this initiative, NC ACCEPT, is a joint initiative of the four Departments of Psychiatry to try to encourage cost-effective psychopharmacologic treatment and this is an initiative that is joined by the NC Psychiatric Association and the NC AHEC Program and then reaching out to the various LMEs around the state, CCNCs and CABHAs, and the goal is really to set a climate for better cost-effective prescribing around the state. So, we have residents involved in this in the four departments, as well as faculty at the four departments and then we will also be working with the CABHAS, the CCNCs, particularly the psychiatrists now working with the CCNCs and other stakeholders – and also, primary care departments. Today's presentation is a way to kick this off is by Vaughn McCall who is the Chair at Wake Forest University and an expert on sleep and ECT and we are really pleased to have him and as you see his presentation is on Cost-Effective Options in the Treatment of Insomnia – so, Vaughn, take it away. Please let's just wait at the end for Q & A so Vaughn can get a sense of the timing of the presentation.

Thank you, Marvin, and I'll be giving a full length presentation that's intended to run about 40 minutes and once I begin, I would encourage others to time this to see how long it is because we don't want something that is too long and unwieldy. Before I formally start, let me just lay out the first part that I'm going to present and discuss the rationale for why insomnia should be treated by psychiatrists – the second part talks a little bit about the evaluation of insomnia but the real meat is the last part which talks about treatment options. So, if you listen to this, one thing to keep in mind is the possibility of both a long version that I present and a short version – the short version might include loping off the introductory portions regarding the importance of insomnia and its assessment. So, with that in mind, let me go ahead and launch into this.

For our objectives today, will be to describe the role of insomnia as a risk factor for incident psychiatric illness, to want to make sure participants can discuss the impact of insomnia and the risk of psychiatric illness and the participants should be able to propose a variety of strategies for managing insomnia. Part of what is propelling this discussion is the realization that the use of antipsychotics is growing and in this particular figure, we can see what is particularly interesting is that the light green bars are growing over time, representing an ever increasing proportion of antipsychotic prescriptions that are being given for something other than mood disorders or psychotic disorders. The suspicion is that a portion of this represents antipsychotics being used as surrogate hypnotics. More to the point, within NC – this is NC Medicaid data showing us that 2 psychiatric drugs, Ambilify and Seroquel, occupy the #1 and #2 spots and the largest expenditures for prescription drugs for Medicaid recipients. In specifically looking at Seroquel or quetipine, we can see that while most of the cost and most of the prescriptions appear to be in the larger denomination, remarkably, the significant number of prescriptions and costs associated with smaller denominations ____for example, a 100 mg, 50 mg denominations, which we suspect might be used in part to manage insomnia problems. We are going to be talking about alternatives to that. So, to keep this a little bit interactive, several questions – the first here is, is the most common cause of chronic insomnia psychiatric illness, medical illness or primary insomnia. It's no surprise, given the nature of our talk, the answer is psychiatric illness.

Here we see some data from Dan Buysse from not quite 20 years ago, showing us that looking at the flow of patients through a sleep center, which are admittedly different from say the flow of patients through a primary care practice or psychiatric practice – even within a specialized sleep center, almost half of all the patients who seem to have chronic insomnia had a final diagnosis of psychiatric disorder. This figure pretty much holds true in primary care practices as well. So, presently, it is safe to say that about half of all persons with chronic insomnia, at least adults with chronic insomnia, have it on the basis of a psychiatric disorder and so, it certainly is apropos for psychiatrists to be interested in the topic of insomnia. Another reason for psychiatrists and maybe also primary care doctors, to take interest in this is that it may represent an opportunity for prevention. This has still been a topic that hasn't any details worked out but it certainly looks like, if you do not have a psychiatric disorder today, and your insomnia does not get treated, that within a year's time, there is an increase risk for developing a psychiatric disorder.

Now, I'm going to show you some data on that in just a minute – an important question is, if we treated insomnia more aggressively, could we actually prevent the development of new onset or incident mental disorders. A slight different question with sleep deprivation which is slightly different in concept from insomnia is a risk factor for mania. Looking specifically though at the insomnia data for the next figure – this is again, very ancient data in relative terms, but is it considered a landmark paper showing that if you look at persons with chronic insomnia over a year's period of time, at the end of the year, some of the them will have their insomnia problem resolved; others of course, their insomnia problems will be unresolved, and the question is, is there any difference in overall outcome – the answer is "yes". I'm going to ask us to focus specifically on the light blue bars which are depression and we see that at the end of one year, your chronic insomnia problem is resolved. The likelihood of you developing a new episode of major depression is 0.6% - very, very low really. On the other hand, if you have unmitigated insomnia for one full year, you have a much higher risk, 14%, and if you calculate odds ratio, dividing 14 by 0.6, you are going to get an odds ratio that is pushing 30, which by any standards is very, very high. Another reason why we want to treat insomnia and its relevant psychiatric practice, could we prevent mental disorders and major depression which have the biggest odds ratio by more aggressively treating insomnia.

Now, more commonly in psychiatric practice, you see patients who not only have insomnia but actually already, of course, have a diagnosis of mental disorder and insomnia is simply part of the picture and so, our relevant question is – once the mental disorder begins, do I really still need to pay attention specifically to the insomnia complaint, and we think the answer is "yes" for a couple of reasons – the first is, we know that insomnia is an independent contributor to poor quality of life in depressed patients, even after you control for depressed mood, adhedonia, libidinal loss, appetite problems – all the other symptoms. Insomnia still stands alone, an independent predictor of poor quality of life, and more recently now, it looks like within a group of depressed insomniacs, the intensity of the insomnia complaint is positively proportional to the intensity of suicidal ideation – so, if may be a marker of future suicide risk. Again, that

remains to be worked out, but certainly cross-sectionally, that appears be true and also, going forward over short periods of time, within a clinical trials context, it is also true.

That takes us now to the second question and that is, the most common residual symptom in an otherwise successfully SSRI treated case of depression is sad mood, insomnia, or appetite and by now, of course, you should be able to guess the answer. It has to be "insomnia" – that in fact, is the case. This is, I think, a very interesting paper that came as a result of a Lilly sponsored project back when Lilly had exclusive patent rights over fluoxetine, Prozac, and Lilly was interested in knowing when Prozac worked and the patient was considered to be in remission, what were the most common residual symptoms? So here, remission is described or defined as a HAM-D score of 7 or less and this should not surprise this audience because we've now been living in this new world for many, many years - the most common symptom that was left untouched in otherwise, successfully treated cases of depression with fluoxetine was the sleep complaint. The reason I think this is fascinating when I'm lecturing to trainees who are new to the field and really don't have much history with what they are doing is you will remember very well that up until about 1989, when fluoxetine came out, tricyclics were still the mainstay treatment for depression with insomnia. The first symptom to improve was the insomnia with a tricyclic. And now, in the post modern SSRI world, it looks like the last symptom to improve is the sleep problem. And so, the world has really turned on its head. And so, we're put in the position then of often dealing with the insomnia separately since the SSRIs still don't do such a great job with that and this appears to be the rule and not the exception. This again, is fairly old data, coming from a VA clinic but at that particular clinic they found that fully 60% of patients treated with sertraline and fluoxetine required something extra at bedtime to help them sleep. So, this is not an anomaly situation – this is what we have come to expect. Now, this takes us to the next question.

That is, the complications of residual insomnia after treatment of depression includes metabolic syndrome, low serum cortisol, or increased rates of depressive relapse. And, the answer is increased rates of depressive relapse. Not all the data is absolutely uniform on this point, but there is enough data there to make us worry. So, now just a recap of what we have already seen in the last few minutes – first, if you don't have a mental disorder, having chronic insomnia puts you at risk of getting one. Secondly, if you do have a mental disorder and insomnia compounded together, the insomnia is an independent risk factor for poor quality of life and in proportion to the intensity of suicidal ideation. Third, after a depressive disorder specifically has remitted, if you have residual insomnia, it puts you at risk for relapse. So again, we are trying to make the case here that insomnia is something worse to pay attention to – the question is, well, how do we go about doing that?

So, here, it takes us up to the evaluation of persistent insomnia and _____ psychiatric disorders. There are certainly a lot of reasons this can happen. One is that the initial treatment was incomplete and as a result, this could possibly be iatrogenesis and we know that about 10% of people develop insomnia as a result of being exposed to SSRIs; it can be a concurrent medical disorder, a primary sleep disorder, or the patient may simply have fallen into very poor sleep habits surrounding the time of the mental disorder

and the sleep habits need to be evaluated. And so, let's talk about we might go about that. There are some ancillary tests that are sometimes done – sleep logs or sleep diaries have value, psychometric tests, blood work and polysomnography. We will look at each of these in turn. Sleep logs are the simplest, cheapest and by far and away, the most important supplement to taking a good sleep history. I can't emphasize too much the importance of taking 5 or 10 minutes to nail down the patient's bedtime routine and really all you need to know is: what is the patient's typical time to go to bed; how long does it take them to fall asleep; how many awakenings to they have in the middle of the night; when is their final awakening; and when do they finally get out of bed; and do they go back to bed in the middle of the day or attempt to take naps; and is this the same during the week as compared to weekends. So, you take that sort of sleep habit or sleep behavior history and then you confirm that or supplement that with sleep logs. As you see here, in essence, ask the same sort of questions and this sort of information is at least as powerful if not more powerful than any other sort of ancillary information you may gain and we will show you why that is shortly. Is there a role for laboratory work in the assessment of insomnia – occasionally – it doesn't really produce much. Interestingly, if you were to ask me – what is the single most valuable blood test in the assessment of insomnia, I would say it is serum ferritin and so to the extent that if you ever do see restless leg syndrome in your practice, which is probably not that uncommon quite frankly, we are concerned that maybe 20% or so, or maybe even 25% of patients with restless leg syndrome have low total body iron stores and that can easily be measured with a serum ferritin. That really is one of the few blood tests that is worth doing in those insomniacs that also have the restless leg part as part of the picture. Polysomnography, interestingly, probably has the lowest yield for the greatest cost and for that reason, the Academy of Sleep Medicine says it's not really routinely recommended in the assessment or management of insomnia. There are some occasional situations where it might be justified if the patient has both severe daytime sleepiness along with their insomnia and if there is a high index or suspicion for sleep apnea based upon body ___ or _____ or _____ and finally, refractory insomnia. If you've really done a whale of a job and trying to get at the patient's insomnia complaints and you're not getting any traction, then you can justify a sleep study to see if you are missing something – that should fall fairly far to the bottom of the assessment algorithm.

That now finally takes us to treatment. Earlier, I had talked about the importance of taking good sleep history, maybe supplementing that with sleep logs and that is absolutely essential as a first step if you are going to do anything really useful in terms of non-pharmacologic treatment. There are some common sense things that we, of course, will tell our patients to do, such as: use alcohol, caffeine and tobacco, either not at all or at least in moderation; not exercise too close to bedtime, etc. I want the audience to be aware that there are some specific behavioral and some cognitive therapies that are combined and to no surprise, CBT for insomnia or CBTI, which are remarkably effective. It looks like they are effective both in primary insomnia and there is some early evidence that education in the treatment of insomnia in the context of psychiatric disorders. The next slide will give you just a little taste of the date, at least at it pertains to primary insomnia – this was a JAMA done study by Dr. Charles Morin and Charlie was comparing CBT for insomnia vs pharmacotherapy, PCT, and in this instance,

pharmacotherapy was 30 mg of _____ vs the combined condition of CBT plus _____ or a placebo condition. These patients were treated under these conditions for a number of weeks and what we are seeing here are the pre-post change from the beginning of treatment to the end of treatment and you have both sleep diaries or self-report assessments and polysomnography sleep lab data, too. ____if the patient thinks is going on. There are a lot of variables that we could look at. I have decided to show you ___ time after sleep onset which is basically how much time the patient spends awake in the middle of the night after initially falling asleep. And so, obviously, with placebo, there is not a lot going on – you get a very minor decrement over time and wake time in the middle of the night – you see a powerful effect for cognitive behavior therapy which appears at least equal to if not superior to drug treatment and combined treatments about the same. This is based on the patient's self-report and then the polysmnography basically mirrors that where you see very little happening with placebo but _____ and also _____ both appear to produce good results. I don't have figure to support this next statement but there is now data showing patients who are randomized to the CBT condition, actually enjoy improvement in their sleep that lasts for a month after a formal treatment has been discontinued, presumably because they now have adopted those treatment suggestions as permanent changes in their behavior. Needless to say, once you discontinue the temazepam treatment, that does not happen and the patient tends to regress. And so, I want to show this to you just to demonstrate the importance and relevance of asking questions about sleep habits and giving patients concrete suggestions about how to modify their sleep habits to get a better result. We don't have time today to talk in great detail about cognitive behavior therapy for insomnia but I would like to let you know, it's not that complicated. In my opinion, this is something that does not have to be relegated to our psychology colleagues to manage alone and that psychiatrists certainly and I think, primary care doctors, too, can introduce bits and pieces of CBT in all their insomnia cases.

And finally, we are going to talk a little bit about prescribed pharmacologic treatment. I'm not going to talk at this point about over-the-counter but we can certainly do that during Q&A. And the reason we will focus on the prescribed options is that themselves is a fairly long list as you can see and we are going to work our way through this list over the next several minutes. First, we are going to talk about unlabeled treatment. Certainly there are some benzodiazepine hypnotics that are FDA approved for that purpose including medicines like _____, Halcion, _____, Restoril, Dalmane, _____, etc. Interestingly, we want to focus for a minute now on what is known about the impact of a benzodiazepine at bedtime to facilitate sleep, specifically in patients with psychiatric illness. There is not a lot of data and some of the best data though is for Clonazepam which of course, is not indicated specifically for insomnia but the Clonazepam data as you can see here, generally shows that Clonazepam is beneficial for sleep, at least self-reported sleep, not sleep lab sleep, for a period of about 21 days and these authors were sufficiently excited by this study, they repeated it in a slightly smaller sample of 50. They ran it for 18 weeks instead of 21 days, and they were chagrined to learn that the benefit of Clonazepam on sleep did not seem to last much longer than about 3 weeks. So, this is the longer study and they found that the main benefit of Clonazepam was in the early going and by the middle of therapy, the effects began to merge with the bedtime dose of

placebo. So, some evidence that benzodiazepines can be helpful in managing sleep of psychiatric patients who are also on antidepressants. The data is not as compelling as it might be – but there is still some data. So, pros and cons – some but not all are approved for sleep and they are very inexpensive. Cons – in terms of tolerance and dependence, residual daytime sleepiness, delayed reaction time, putting them at risk for motor vehicle accidents and falls and amnesia and potentially, behavioral disinhibitions. So, then we have a variety of _ drugs, including the first, Zolpidem and again, I'm going to focus not so much on their utility and primary insomnia but what we specifically know about these medications in treating insomnia associated with psychiatric disorders. And, by the way, you've probably noticed that this talk is focusing almost exclusively on major depression and that's because that's where the data is, not to say that insomnia associated with anxiety disorders or schizophrenia is not relevant but we just don't have as much information. So, what do we know about Zolpidem. Here's the study, looking at 190 patients who had depression and insomnia already on SSRIs and after 2-3 weeks of being on SSRIs, if their insomnia was not coming along of its own accord, they were eligible to be randomized to Zolpidem 10 mg of placebo as add-on therapy. Improvement was measured with global well-being as the general measure of quality of life, looking at changes in sleep and overall changes in depression scores. And so, what were the findings? The findings were, first of all, that adding Zolpidem to the mix did indeed, statistically, improve global well-being ___ measure of quality of life. There was some sense that overall depression symptomatology was reduced to a greater extent after 4 weeks and those randomized to Zolpidem at bedtime but the study sadly was not quite powered, it looks like it should have been at 190, but it was not quite powered for this to be statistically significant. There certainly was a hint there that treating insomnia in these depressed insomniacs is gaining something but didn't quite ring the bell. So, pros and cons of immediate relief with Zolpidem - pros are FDA indicated for sleep; it appears to be somewhat useful in its presentation and it's fairly inexpensive, generic Ambein or generic Zolpidem, I have learned from my patients is down to about 10 cents a pill, way down from where it used to be, at more than $3.00 a pill and the cons – presently, immediate release Zolpidem is approved for short-term use and is a controlled substance, with the usual concerns about tolerance and dependence; some concern that it may specifically be associated with hallucinations, visual hallucinations, and cognitive problems.

The next ___ drug I want to talk about is Eszopidone and as a disclosure, I should tell you I was part of this study and will be showing you what has previously been ___ supported investigator on a number of studies. So, with that in mind, let me show you particular data which was larger than the ___ study. Now, we have 545 patients, all depressed insomniacs, all of them were on ____, so you can see the drug assignments down here and the only difference is, some got ___ at bedtime to help with their insomnia and others got placebo. At the end of 8 weeks, looking at Hamilton scores, we see that there is a greater drop in those assigned to the sleeping pill and this is if you take into account all the symptoms of depression including the 3 insomnia items on the Hamilton Scale but remarkably, I think this is probably the most exciting part, if you exclude the 3 insomnia items from the HAM-D17 , you still see a statistical advantage for those assigned to Eszopidone. What this is telling us really, is that above and apart from the

immediate effects on improving sleep, it appears that there is a spill-over effect or maybe a halo effect that by virtue of treating the insomnia, people generally feel better the next day and reporting a lesser degree of daytime depressive symptoms not just nighttime insomnia symptoms which I think very exciting for the field and again, I hope us in the direction of taking insomnia a little more seriously. Of course, there are some cons with Eszopidone. It is approved for sleep and it has a relatively unrestricted label, the cons are again, it is a controlled substance, possible tolerance and dependence but apropos to our discussion, it is very expensive, at least as compared with generic Zolpidem.

Ramelteon - Ramelteon is marketed under the brand name ___ - it is a very different sort of medication. It is different from everything that I have discussed so far in that it is a melatonin 1 receptor ___ and it's pros are – it does seem to have some mild efficacy for sleep onset and it's not a controlled substance; it has no liability for tolerance and dependence – those are all good things; no effects on cognition or balance, but the bad parts are given that so many of our psych patients do complain of middle of the night awakening, this drug appears to have no efficacy for sleep maintenance and like with ___ brand names, brand name Ramelteon, is very expensive. And looking at some of the data on Ramelteon - I'm sorry I do not have any data on Ramelteon.

I'm going to show data on low dose Doxepin. So, these newest kid on the block is brand name drug called ___. ___ is really fascinating at onset. This is a revisitation or ghost from the past, of Doxepin, and I think we are all familiar with the idea from what I have said earlier, that tricyclics do seem to have some sleep promoting properties but in large doses, they are problematic in terms of constipation, dry mouth, etc. So, ___ is now selling ___ and developing these teeny doses, 1, 3 & 6 mg – the doses that are being promoted are basically the 3 & 6 mg and this data seen in primary insomniacs. I don't any studies have been done with this drug, low dose Doxepin, in psychiatric patients. What you are looking at here is sleep efficiency of measuring percent, a little higher sleep efficiency is better and you can see that compared with placebo in the grey line, that the doses of low dose Doxepin were superior and that their best benefit, the best separation, was towards the end of the night. But this is polysomnography, where the data is broken down hour by hour across the night and you can see a statistical significance separating these various doses from placebo is beginning to appear around hour 5 or 6 for the most part. And so, very different – if I were to go back and show you the Ramelteon slide, this drug primarily has efficacy for sleep onset with nothing for middle of the night sleep maintenance. And here, we basically have the reverse for low dose Doxepin where you get your biggest bang for the buck here at the end of the night, with very little happening at the beginning compared with placebos. You really have to be quite clever in how you pick the right one for the right patient. The pros are that low dose Doxepin is FDA approved for sleep; its effective for sleep maintenance problems; it is not a controlled substance – again, a nice thing; open ended duration use. It would be inexpensive as genetic – we'll change that to generic – but the generic is only available in 10 mg capsules. So, we are talking about very cheap 10 mg capsules which really have not been studied yet because the brand patent owner is not interested in studying the generic dosage vs the more expensive brand Silenor at 6 mg and so, we can sit here and obsess

about whether there is really any difference between 6 and 10 mg and I just don't know the answer to that. But, certainly, there is a price difference.

So, we are now going to move in towards a more interesting drug. These are drugs that are not approved for treatment of insomnia. We'll start with ___ which is a focus of the NC ACCEPT group and I apologize if this slide is little bit ugly but what you see on the far left hand side, week by week, are the signs for measurement of the Pittsburgh sleep quality index where a lower score is better, as I recall, and – I had that right – yes, lower scores are better. And so, we are looking at depressed insomniacs, who are on fluoxetine - ___ sounds familiar ___ certain studies are set up that way, with and without low dose ____ added on at bedtime. Low dose ___ which can be 50 or 100 mg I believe and so what you can see is that you go across time, you've got your p values out here week by week that there seems to be an advantage for those depressed insomniacs on ___ who also got low dose ____ at bedtime as opposed to placebo at bedtime. And so, the idea that quetiapine has some inherent sleep benefits does appear to be borne out by some studies like this but like almost every other drug we've seen, there are pros and cons, and I was particularly interested in finding out, well, is low dose quetiapine a free ride; if you only dose 50 or 100 mg, should we be comfortable with the idea that we are really not producing any side effects and when you dig into this a little bit, you will find out that doses as little as 100 mg at bedtime, when added to other stable dose psychotropics, are associated with a modest weight gain. Perhaps not as much as you'd might see with ___ but weight gain nonetheless. Now, and also, if you look at low dose quetiapine 25 or 50 mg ___ for insomnia, a different study, there have been case reports of patients who have developed akathisia and so, I wanted to make sure that we all understood that even at low doses, it is entirely a free ride with ___. And of course, that then gets back to looking at the place that __ falls and the overall cost burden of the Medicaid program and wondering, has it really been deserved and it has the prominence that it is has in terms of prescribing for insomnia. Or, at least, as we think it has for insomnia. But the pros are – there are several studies that do show some sleep benefits for depressed patients. Quetiapine is not a controlled substance – a variety of cons – not FDA indicated, metabolic effects are certainly possible at low doses, akathisia is possible at low doses – you just don't know what it does with cognition and balance, and certainly, it is very expensive approach to treating this problem. How about low dose Trazodone as come near towards the end? Trazodone, despite its prominence, up until about 2002, it was the number one prescribed drug for insomnia in the United States – we just don't know that much about it. All data shows that Trazadone was about as good as Ambien or Zolpidem for the first week that you took it, but it not look as good about the second week – we've got a citation here if you're interested. In non-depressed insomniacs, it appears to be associated with a greater degree of alertness – this is data that has come out of our lab and presently is in press. So, by taking Trazodone at night, sleeping a little bit better, you are actually more alert, not more drowsy the next day. But, Trazodone, too, comes with its own set of problems – I think you are now seeing a theme here – that every drug has pros and cons and so, again, this unpublished data from Wake Forest showing that, on the one hand, multiple sleep latency testing, which is a measure of daytime vigilance, were higher scores and better so that after 7 days of Trazodone, people were actually more alert. It took them longer to fall asleep, more minutes to fall asleep in the middle of the day as

opposed to those insomniacs assigned to placebo. But there did appear to be some costs, including determints to memory, this is called a trigram recall test and this was statistically significant, showing a negative effect for Trazodone on memory, so you are more alert on the one hand but more forgetful on the other hand. So, again, sort of a mixed bag for Trazodone. The pros include: it appears to be somewhat effective for insomnia in some patients; it is not a controlled substance; may actually improve alertness and is very cheap; it is not FDA approved for sleep; looks like it may have adverse memory effects; Priaprism seems to be relatively unlikely at low doses – we don't know a lot about the risk of Priaprism at very low dose.

Now, I think this is the last drug we are going to discuss and that is Mirtazapine at 30 mg dosage. ____ therapy, ___ in depressed insomniacs, ___ we are going to try to get at four symptoms for depression as well as the insomnia with 1 pill. Open trials have looked relatively promising, not only in terms of self-report but here's a study, open study, using Mirtazapine as the end point – the problem, of course, that always occurs with open labeled, the failure of not having placebo control – it's hard to say for sure whether the drug was responsible for these things that you saw. So, pros and cons – Mirtazapine is probably effective for sleep and depressed insomnias; not a controlled substance and inexpensive. Cons – not FDA approved; in terms of weight gain, the possible complication of ___. This is in fact, the last drug – my apologies. This, to me, is one of the more interesting. You know, a lot, I think, the idea that we have about not using a controlled substance in our psychiatric patients, is not simply to produce new substance abuse problems but more to the point, how do you treat insomnia in someone who already has a known substance abuse history – what drugs are effective? I wonder whether Seroquel or Quetiapine is being used to treat insomnia in abstinent alcoholics. Are there any cheaper alternatives? There is some interesting data coming out of the University of Michigan and we will show some of it here – looking at Gabapentin as an alternative. And, we are looking at relatively low dose here, 300 bid vs 600 mg at bedtime in 33 abstinent alcoholics. This was a controlled study and showing that using the Pittsburgh sleep quality index, that low doses of Gabapentin were associated with better sleep quality and near significant improvement of sleep latency and near significant improvements in sleep efficency. Also, equally interesting, is looking at what those bedtime doses of Gabapentin did toward a craving during the daytime. So, we have some visual analog scales of strength for craving and these are 4 different ways of slicing that, showing that those patients who were assigned to Gabapentin were reporting less craving. Now, why is this interesting? It is interesting because there is not wealth of data showing that if you are an alcoholic who is not abstinent and dry, but you have residual insomnia – that residual insomnia is a risk factor for falling into relapse and resuming alcohol use. So, we raise the question – well, if we treat the insomnia in abstinent alcoholics, might we then prevent them from being tempted to resume the use of alcohol, and this sort of data here suggests that maybe it directly impacts craving itself in addition to improving sleep and so, perhaps the most powerful statement in this regard comes from this figure showing that if you look – here we're looking at 1500 mg of Gabapentin vs placebo at bedtime – and 21 abstinent alcoholics over 6 weeks, random blind assignment, and you are looking at number of days until their resumption of first heavy drinking. So, this is a survival curve and you can see those who are assigned to Gabapentin were less likely to

relapse or had a delay into relapse than those who were assigned to placebo. Very, very interesting data and may be Gabapentin is something we should specifically consider when treating our insomnia psychiatric patients who have comorbid alcohol issues.

The pros and cons – looks like Gabapentin may be helpful in treating sleep problems in alcoholics; may curve alcohol cravings; is certainly not a controlled substance; if you have liver problems, excreted unchanged; ___ kidneys and certainly, it is inexpensive. Cons – you know, there really aren't too many cons with Gabapentin unless you take so much of it you get drowsy in the middle of the day, but I think it a pretty safe substance for the most part.

So, taking this now to our summary – I want to get back to taking a sleep history. There is a huge opportunity for helping our insomniac patients out just by asking: when do they go to bed, how long to they stay in bed – once we've gotten in the habit of doing that, I think we'd all be surprised how many of our patients spend upwards of 9 or 10 hours in bed per day and there's just no way they can fill all of that with sleep and that's partly a problem with expectation – they all need to set their expectation with what is reasonable and that goes along with tempering the amount of time they spend in bed. So, we want to help them get reasonable expectations for how much sleep they ought to get; help them modify their sleep habits to get the maximum results; and then, you know, certainly, if we need to give supplemental medications at bedtime, there is a range of inexpensive things that we can do that might help, some of which are controlled substances like Zolpidem, then we have Trazodone, Doxepin, Mirtazapine, ___, and Gabapentin - all are possible alternatives to brand name sleep aids and Gabapentin , and this is my own opinion - I think is emerging as potential favorite treatment for insomnia associated with alcohol.

So, I think that may be the end of my comments – we have some supplemental slides which are not going to get into right now. Why don't we stop there and see how much time that took and take questions.

Swartz: OK – thanks very much, Vaughn – that took about 40 minutes – let me open the lines and see if we have any questions.