Unidentified Male: We're going to need to move to our last speaker. Varsha Vimalananda who's going to be talking about patient characteristics associated with \_\_\_\_\_ [00:00:10] prescription weight management medications in veterans and VA's MOVE Weight Management Program.

Varsha Vimalananda: Yes, thank you. It's neat for me to be able to talk about weight management medications as a compliment to some of the other approaches that we've heard about today, to prevention and treatment of obesity, diabetes, cardiovascular disease. It's a relatively new thing to be talking about both outside and inside VA's, the research is early, so I'm going to present some results from a preliminary study.

Just to remind you in case you've forgotten, the proality of veterans that receive primary care at the VA are overweight and obese. In 2014 there were nearly 5 million patients in primary care. These categories, the weight categories - underweight, normal weight, overweight, obese. And the sub-categories of obesity. And if you combine overweight and obesity, that's where you get nearly 4 million patients who are overweight or obese. So, almost everybody that we see in the clinic.

We know that obesity produces morbidity and affects how patients feel and function. I don’t need to go through all of these, but just to remind the audience of the burden of the disease. VA and DOD practice guidelines for the treatment of overweight and obesity and many other professional guidelines exist. And they all agree on a couple of things. One is that... Well, I've taken an excerpt of the flow chart out of the VADOD and what I've picked up after diagnosis of obesity and overweight and screening for medications that might be able to be discontinued, is offer a comprehensive lifestyle intervention, set intermediate and long-term weight loss goals, and address barriers.

So, if we follow the flow chart... Has patients met intermediate weight loss goals? Yes? Continue with the current plan. Let's go the other way. Has patient met intermediate weight loss goals? No? Can barriers be further modified? Let's say no. So, we're into the second tier of treatment now. If patient meets appropriate criteria, consider pharmacotherapy and/or bariatric surgery as an adjunct therapy. So, the second tier of treatment for obesity and overweight, after lifestyle change, diet, and exercise, is pharmacotherapy and bariatric surgery.

So, there's significant resources that the VA has allocated to this issue. MOVE, which we've talked about and everybody knows about here. Is offered at every VA facility. Bariatric surgery is at approved centers for patients who have more severe obesity, but for many patients who don’t lose sufficient weight with MOVE and who don’t want or are not candidates for bariatric surgery, there is a big treatment gap here and this is where pharmacotherapy could address this treatment gap. However, we know that in the last two years, fewer than 6,000 overweight or obese VA patients have received a weight management medication.

One of the reasons that pharmacotherapy for weight management has taken its place in treatment guidelines for overweight and obesity is due to some of the evolving science around this issue. I just want to take a minute to address that because I think it helps to strengthen the case for why these medications should be considered. This is the classical model we use to talk about weight regulation. Calories in, calories out. This is consistent with the laws of thermodynamics but is not a very helpful model because usually when we've used this model, we're talking about the brain being in charge of all these things, we're talking about our freewill, volition, and choices that we can make. That is just wrong.

A more accurate model of the pathogenesis and maintenance of obesity looks like this. So, obesity is complex, has multiple causes, and many of the factors that you see in this model are not under the control of patients. They cannot make choices around these and they cannot change them. When I say environmental factors, I am talking about things like policies, neighborhoods. But I'm also talking about things like environmental endocrine disruptors, which patients have no control over. They're a series of factors underneath and \_\_\_\_\_ [00:04:37] which may be modifiable. Physical activity, diet, medications that are sometimes impossible to stop, antipsychotics, antidepressants, insulin. Disrupted circadian rhythm. Poor sleep and stress. All of these interact with individual patient factors, which are not modifiable.

Age, sex, race, genetics, the \_\_\_\_\_ [00:05:00] that we've talked about today and all of these factors converge and impact the neuroendocrine regulation of fat mass. I'm going to take one more basic science slide here and get into that neuroendocrine part because this is where those medications act and this is the reason for using them. So, along the bottom you have these endocrine organs, stomach, tissue, and pancreas. They secrete hormones. Here we have ghrelin, insulin, and leptin. Which act in the hypothalamus primarily on two groups of neurons that increase appetite or inhibit appetite. So, increase food intake or decrease intake, plus/minus. That is the general concept.

So what happens in the setting of obesity is that you get deregulation in these pathways that becomes permanent. The hypothalamus is no longer as sensitive to leptin, for example. Which is an inhibitor of food intake and there's the perpetuation of greater energy intake and weight. So, after weight loss, which as we all know is difficult, weight regain is common. I've mentioned the digestion of the permanent dysfunction, the hypothalamic signaling of the pathways, which leads to a cycle of weight gain. Unfortunately with weight loss, there's also a counter-regulatory increase in appetite as well as food intake. Also unfortunately, when you lose weight, your basal metabolic weight goes down, so there's decreased calorie expenditure per kilogram. So, there are all these things that patients are fighting against.

So, risk factors, not readily altered. Permanent neuro-hormonal changes with weight loss may explain why many patients don’t lose weight or cannot keep weight off, clinically significant weight, with lifestyle change alone. Either in the real-world setting like MOVE, or clinical trials like DPP, Look AHEAD which are highly effective for a relatively small proportion of patients. This provides the rationale for treating obesity with medications, plus behavioral intervention. And the medications I'm going to talk about, should be used long-term because of all of this. They're not the short-term meds, prior to 2010, that you would take for three months and then stop after you've lost some weight. They're intended to be used the way that we would use medications for diabetes or hypertension. They don’t fix the underlying problem. They support the behavioral change by helping to suppress appetite, four of those five act in that way.

So, the point again is that they need to be used long-term. Losing five percent of baseline weight is considered clinically significant. That is not going to get most people down to their prom weight but it is healthy. It has health impacts. And that is also the minimum goal of weight management medications and that's the basis upon which these medications are proved by the FDA. This degree of relatively modest weight lost cuts the risk of diabetes, improves control of diabetes, blood pressure, dyslipodemia, sexual function, quality of life. Decreases the medication burden related to these conditions and decreases mortality in diabetic patients by 25%. So again, I consider this, most people would, a major potential impact.

Five medications approved for long-term weight management. I'll just show them to you here. These are the five. There's one medication still used in the short-term which is Phentermine. These are ones that are just to get you familiar with the names. Orlistat, which is thought of as the fat blocker. Sold at half the strength in Costco under the name of Alli. That was approved in 1999. Again, that's a fat blocker. It doesn’t act the way that the others do. Lorcaserin, which was approved in 2012. Phentermine Topiramate was approved in 2012. Another, bupropion naltrexone, in 2014. And Liraglutide approved in 2014 for obesity. We use it in a lower dose for diabetes. So, those are those medications. They have one year safety data from the drug companies and I mentioned the ethicacy.

So, the next two categories are the weight loss at one year. And so, there's reality in the response to these medications. So, about a percent, half of patients will lose weight at one year with any given one and between eight to 13% discontinue due to adverse events. And more discontinue from the medications than are more effective. So, the aim of our study, which is really a preliminary study to get an idea of the lay of the land, was to identify patient characteristics associated with receipt of these medications, among patients who were already engaged in MOVE. This is a retrospective cohort study using data from the CDW and our analytics sample was patients who initiated MOVE in fiscal years 14 through 16, who met the BMI criteria for weight management medications, which is having a BMI greater than 27 with comorbidities or greater or equal to 30.

We constructed multi-variable logistic regression models and our primary outcome was receipt of any weight management medications because the numbers as you see are pretty small, we decided not to look at all the medications individually. So, those again, are the names of the medications. We included phentromine. We excluded drugs where there was an indication they were being used investigationally or in a research study. And we also identified cases where phentromine and Topiramate were prescribed separately, but within 30 days of one another. So, this is something that people do in clinical practice because the Phentromine Topiramate is a controlled substance, a scheduled narcotic. When clinicians decide to prescribe it, they have to go through... It's actually a brief little training, risk mitigation thing online. Which, people don’t like to do. They just don’t want to deal with it. They try to get around this to prescribe the medications at different approximate doses. We looked for that as well.

We did the same for bupropion naltrexone. This slide is our cohort identification. We started out with 298,704 patients who had one or more visits in fiscal year 2014 to 2016. We restricted that to patients who were initiating MOVE at the beginning of the study period. Meaning that they hadn't been engaged in it for the prior six months. We eliminated, we excluded folks who didn’t have a qualified weight, qualified height, were less than 18, didn’t meet the BMI criteria. We excluded stop codes which didn’t indicate individual or group visits. We got that algorithm from the National Center for Health Promotion and Disease Prevention.

We ended up with a final sample of 153,892 veterans in that two year period. Only 1.2% of those veterans received a medication for weight management. By far, the most common was Orlistat. Out of everyone who received a weight management medication, 58% of people were receiving Orlistat. And the rest were far, far behind. In terms of Phentermine Topiramate, I just mentioned, we looked at those prescriptions separately and about a quarter of those were written as separate drugs, not as the combination drug with the indication. So, mostly use of Orlistat. Which is the oldest of these and also probably the safest because it acts prolifically.

These are some patient characteristics that were positively associated with receipt. Female sex, increasing BMI, history of alcohol abuse, and history of substance abuse. I'm not going to linger in the interest of time but if we want to, we can talk more about these. Additional patient characteristics of obesity related comorbidities are positively associated in addition to diabetes, obstructive sleep apnea, depression, OA, and lower back pain. Some patient characteristics which were negatively associated with weight management med receipt were increasing age and having copays.

We looked at several other factors, which were not associated with receipt at all. Which included race, many comorbidities, also bipolar disorder and anxiety. And the limitations of our study... We may have included some patients who weren't actually eligible for medications in the denominator. We didn’t examine contra indications to specific medications. But the criteria, pretty loose. The broad inclusion criteria, not that many exclusion criteria. Don’t think that was a huge issue but needs to be examined. We may have included patients who declined weight management medications in the denominator. We obviously don’t have data on patient preferences. Although our sense is that it's not... That all the clinicians are offering these meds and all the patients are saying no. We think it's more, the initial problem is at the provider level. And that we may have undercounted the numerator. We didn’t include non VA prescriptions or account for over-the-counter Orlistat. But outside the VA it's almost impossible to get these medications, even in the setting of severe obesity. It's just impossible. You can get them in the VA so we don’t think we missed a lot of prescriptions that were coming.

And again, as in the prior study, we don’t know whether patients actually picked up the medications that were dispensed or adherent to the medications that were prescribed. So, in conclusion, in this preliminary study we find that these medications are under-utilized among patients that are already engaged in behavioral weight management through VA. Just want to remind you, 79% of primary care patients are overweight or obese and among these, 1% of patients is actually getting these medications. There's potentially, a huge place where we could have a big impact on health here.

Several patient characteristics were associated with receipt, including increasing degrees of obesity, history of alcohol or substance abuse, and female sex. Although again, even for a history of alcohol use when the percent was 2.9, that's still really low. And identification of additional patient clinician and organization level predictors of prescribing patterns and qualitative work to understand the reasons for these patterns are needed. We want to know, is the problem at the patient level, do patients not want to take these meds, are providers uncomfortable with them? We know that they are from other literature, survey data. Are the policies in place that make it difficult to prescribe and what's the relative contribution of those? All that is to come.

I think that's it. Oh, there's one more slide. This is the number of patients prescribed to weight management medication in the fiscal year '15 and '16, adjusted for nothing. But this is just by facility. What I want to point out is that about half of the facilities are less than 25 patients who received a prescription. But there is some variation that I think is not simply counted by the prevalence of obesity, the size of the facility. Then we also looked at just number of prescriptions and at 35% of sites. A third, fewer than 10 prescriptions were dispensed in a two year period. Thank you to the following individuals, operational friends. I do think that's it.