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Series: Mild TBI Diagnosis and Management Strategies

Session: Chronic Symptoms After Mild TBI: Early Research Findings from LIMBIC-CENC & Clinical Approach to Optimize Patient Brain Health

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**NOTE:** Due to technical difficulties, a portion of the beginning of this presentation is not available.

Dr. William Walker: …be very inaccurate, reliance on one individual’s assessment can be difficult to replicate. Perhaps it’s accurate, but it’s difficult—it’s not transparent and not necessarily replicable, or generalizable. So we wanted something that was highly standardized, but also accurate. So the algorithm gives us that, and the structured component gives us that tight standardization. But also, we allow for overriding of that through a vetting process that looks at the free-text portion of that interview, and also looks at their medical record information. So to date, about two percent of the automated diagnoses have been overridden because of factors which vary and including someone maybe passing out from heat exhaustion, rather than from a TBI. Or an individual that was sort of under-rating some of the symptoms on the structured portion versus what they told us in the free-text portion.

The battery itself beyond that includes—is most heavy on neurocognitive outcomes, neuropsychological testing, which is our primary outcome measure. We include not only traditional neuropsychological tests, but also the NIH toolbox computerized battery. When we were initially developing the battery under CENC, we had a lot of competing interests and ideas about what we should include in the tests. We had to weigh that against burden. We didn’t want to make it so burdensome that we couldn’t get participants to enroll or stick with the study, so what we settled on is pretty comprehensive, but it is able to be done during one day. It's a pretty full day. Some of our enrollees request that it be broken up into two half-days, and we do that upon request. But it is possible to do it all in one day. We have measures that look at other aspects of chronic traumatic encephalopathy, such as a Parkinson’s motor examination looking at rigidity and tremor, etcetera. Numerous assessments looking at co-factors like PTSD and other confounders like social support and education. We have a number of sensory outcomes, visual systems including computerized eye tracking, smell testing, and hearing testing, including central auditory processing test. The various aspects of assessments include not only symptom measures, but also functional measures, physiologic measures such as EEG and event-related potentials and anatomic structural measures, such as the neuroimaging. So in terms of providing the highest level of evidence of a relationship to outcome, if you can get convergence of these various domains showing relationship to a factor, whether it’s TBI or PTSD or something else, it really gives it the highest level of evidence. So we look at it from all of those angles.

At this point, I’m going to turn back over for another poll question before we move into the next section of the talk.

Moderator: Thanks, Dr. Walker. And thank you Maria, for taking over audio-wise for the first poll. You can go ahead and launch that poll. And the question is: LIMBIC-CENC Multicenter Prospective Longitudinal Study (PLS) eligibility criteria include all of the following, except: Prior military deployment; Combat exposure; Traumatic brain injury; Absence of major neurological disorder other than TBI; and there was an example on the slide that I couldn’t fit on the poll—and none of the above. So we’ll give people a little bit more time to make their choices. We only have about 35 to 40%. And the example for the fourth option was like, spinal cord injury. So absence of major neurological disorder, other than TBI, like spinal cord injury. And it does seem to have leveled off, so we’re going to go ahead and close the poll and share out the results. And Dr. Walker, four percent say prior military deployment. Fourteen percent answered combat exposure. Sixteen percent, traumatic brain injury. Twenty-one percent absence of major neurologic disorder other than TBI. And 46%, by far the largest number, answered none of the above. And now we’re going to close this, hide it, and we’ll be back on your slides.

Dr. William Walker: All right, thank you. So, I’m glad I asked that question. The correct answer is actually C, traumatic brain injury. We do not require traumatic brain injury. So 18 to 19% of our cohort is absent of any lifetime traumatic brain injury, which is a very valuable resource to have in terms of isolating any relationship to TBI. So having a control—a portion of the cohort that’s TBI negative controls for our analysis is a very crucial component that we don’t have to look to some other avenue of pulling in controls to make comparisons with. The other ones are required—having prior military deployment, having combat exposure, and not having a severe neurologic or psychiatric injury.

All right, so I’m moving on to what I was actually asked to talk about today, one of the early manuscripts from this project. So, I’m going to kind of give you the take home from it ahead of time, before I get into some slides giving a little more detail. In this analysis, we compared mild TBI, positive and negative groups. So, we didn’t look at those finer divisions that I mentioned earlier, like the number of TBI or combat or non-combat TBI. This was only unadjusted analyses and it included the first kind of database lock that we had was the first—just under 500 enrollees. So, this represents less than a third of the number of current enrollees, when this data lock was done several years ago.

The main emphasis of the finding is that compared to the controls, the individuals with prior TBI had greater symptoms, had greater perceived life difficulties, and had higher number of comorbidities. By the way, I should mention that in this data set, at that time, we had around 16% controls. As I mentioned, it’s up—the original goal of the study was to have 20%, which our power calculations were based on. We’ve got it up to 18 to 19%, so pretty near what our target is. But at any rate, the TBI-positive group had a lot more symptoms and self-reported problems, as well as higher comorbidities, but the objective measures we did were almost entirely equal.

So, assuming people are interested in a little more details, the next slide is a reminder to me that because this was only the first third of the cohort at the initial CENC project had four enrollment sites. The next four on the list, five through eight, were added during the midst of CENC. So this data comes from Richmond, Houston, Tampa, and San Antonio VAs.

This is just a consort diagram showing that once someone enrolled, very few people did not complete the baseline assessments, but these are the numbers, just a breakdown of the TBI exposed and the TBI negative individuals. So now for the findings, this is some basic characteristics showing that the TBI positive and negative groups are equal in demographics. The only really variable here that came close to being significantly different was the number of combat deployments, which was a median of two in the TBI positive group, versus a median of one in the no-TBI, which certainly makes sense that the more combat deployments you have, the more likely you are to get a TBI. So that I believe is a significant difference, even though statistically, it did not quite reach that 0.05 threshold. Otherwise, the characteristics were identical, as you can see. The TBI-positive ones were a median of 8.2 years since their last TBI. So any findings within this group would certainly be in the chronic stage at this point.

All right, and this is some comorbidities. And the interesting thing is not only you’d expect that there might be a higher level of PTSD and sleep problems in the TBI group, but we also found differences and unexpected comorbidities, or comorbidities that we did not expect to be different, necessarily, including asthma, arthritis, and sleep apnea. Showing that for some reason the TBI group not only has higher symptoms—which I’ll show in a minute—but also has a little different comorbidity profile that may not have any relationship to their TBIs.

Within the symptom measures, this just shows obviously higher symptom levels across the board, really. Widespread symptoms, more problems with hearing, more problems with tinnitus, more problems with dizziness, more problems with headaches, more problems with depression, poorer life satisfaction. So—sorry about that. So really, across the board symptom distress compared to the no-TBI group.

This slide shows some continuous symptom variables including anger, anxiety, emotional and behavioral dyscontrol, the PCL-5 symptom measure of both pain levels and inhibition and daily activities from pain as well. So all significantly higher in the TBI group.

For the more global or functional measures, including social participation, community re-integration, self-reported functional status, and global health status, all worse in the TBI group. One thing just to point out is the differences here in terms of effect size is a little less than in the other symptom measures I just showed. So not quite as robust of difference in these measures, but a difference, nonetheless.

In terms of the performance measures on this slide is the only sub test that showed statistical differences. The caveat is—just real briefly, I’ll explain what each one is for those of you who may not be familiar. The WAIS-IV coding is a neuropsychological test that is a component of a processing speed index. The Trail Making B test is a test of visual perceptual function and executive function. The CDP SOT is a computerized posturography Sensory Condition 2. This computerized posturography test tests six different sensory conditions and two of the conditions showed a statistical difference. The caveat to this is that the effect sizes are very tiny. So if you look, for example, at the Trail Making test, you see an absolute difference of about three points on the T-score. But if you look at the standard deviation, which is over 20 points, the calculated effect size would be roughly 0.15 or less, which is a very small effect size. So doubtful that this is clinically significant, at least at the group level. It’s always possible that you have some—a subset of individuals who do have clinically significant differences. So all of these findings warrant future—a more rigorous look within the larger sample and using adjusted analysis.

Otherwise, the objective tests shown here that we looked at were all exactly the same between groups. And this includes all of the other neuropsych tests we did, all of the sensory systems we looked, at the neuroendocrine labs we looked at, epilepsy rate, and our motor system test, including the other four sensory conditions of the posturography.

Important to point out some limitations. We did not examine mild-TBI subgroups, as I mentioned. This was not adjusted for covariates, and as I pointed out, the groups did differ both in combat exposure level and in the number of comorbidities. We did not look at all of the baseline outcome measures, because some of that data was not an analyzable QA process format that we could easy analyze it at that time. Since then, we have done some of those analyses. This did not include any longitudinal data. We are really expecting that to be in the future, the main way that we’re going to identify problems with late effects, because that allows you to look at within subject changes. When you’re dealing with cross-sectional data, you are strictly only to look at between subject changes. So if there is some sort of deterioration and/or neurodegeneration happening, we would be able to best see that in terms of repeated measures of individuals over time to see different slopes of decline. And I’ve already mentioned that this was a small cohort compared to what’s currently enrolled.

The conclusions, then, very similar to what I mentioned in the lead-in. So there were—among this sample, people with a positive TBI history had greater widespread symptoms and poorer perceived functioning. The actual performance measures, though, were largely the same. There were a few small differences that warrant more future study. And those additional analyses that were mentioned in the limitations, some of them have been completed, others are underway, and there’s many others that are still planned as the cohort enlarges and we get more longitudinal data.

All right, with that, before I move into the clinical translation component of the presentation, I’m going to turn it back over for some poll questions. Thanks.

Moderator: Thanks, Dr. Walker. We’ll launch that poll. And Dr. Walker would like you to answer: These analyses found that compared to TBI negative controls, combat exposed—excuse me for one second—combat exposed SM/Vs with prior mild TBIs have: More PTSD diagnoses and PTSD-type symptoms; More TBI type symptoms; Poorer life satisfaction; Worse self-reported functional status; and all of the above. We have about 50% of your viewing audience having made a decision, so we’re going to leave it open for a little bit longer to give people a chance. It is ramping up quickly. And it looks like it’s just about leveled off, so we’re going to go ahead and close the poll and share out the results. And I will read these off. I just need to make it a little bit bigger on my screen. Thank you for your patience. Three percent answered: More PTSD and PTSD-type symptoms. One percent only answered: More TBI type symptoms. And three percent again: Poorer life satisfaction. Another three percent: Worse self-reported functional status. And a whopping 90% sir, answered: All of the above. And now I will hide this poll, so we’ll be back on your slides. Back to you, Dr. Walker.

Dr. William Walker: Okay, yeah. The right answer was E, so most people got that. I’m glad they are paying attention. The next poll question, if it’s okay, just in the interest of time, because I see—I want to leave enough time. I’ll just kind of give you the answer to this one. Measures that showed minor or no differences—the answer is: All of the above. The performance measures, including cognitive, demographic variables, motor and sensory, were either equal or just showed extremely tiny—a few extremely tiny differences.

So now, kind of the final section, the clinical translation of this information. And so essentially, what this is telling us, patients with mild TBI histories often are distressed, with high symptom levels and poor perceived life functioning, but have little to no objective abnormalities. So to me, the way I interpret that is that we need to approach this condition, this symptom distress, as a syndrome rather than a disease process, per se. So for this type of widespread distress level, a holistic care is really the key providing that. So being empathetic, working with the patients to set common goals to achieve. Providing the all-important education. The literature on mild TBI for acute treatments actually, the only treatment that has been shown to be—well shown to be effective, is actually providing early education on their condition and their prognosis and factors for recovery. Counseling on lifestyle factors is crucial. I’ll get into that in a little bit. There’s mounting research evidence of benefit of physical exercise, not only for concussion recovery, but for brain health, in general, in both disease populations and healthy populations. There’s also an enormous amount of literature on the benefits of physical exercise for lessening risks of later dementia.

So your holistic care needs to include all of those. From the standpoint of specific medical interventions, you may deploy utilizing a symptom-based approach, since this is a condition of symptom distress. So prioritizing the most—what you think might be the worst underlying symptoms, whether it’s headaches or depression or insomnia, and potentially using specific interventions for those problems and also seeking for and addressing the comorbidities, which can be so common, and may be contributing as much or more to the symptom distress as the mild TBI.

Things to avoid. Passive therapies can increase an individual’s reliance on healthcare, while not activating them in terms of making those important changes in their lifestyle that they need to make to get better. So we want the individuals—we want the patients to have a role in getting better. They need to, if they’re going to, they can’t just be treated and then not take the treatment home, in terms of things they do to change their lifestyle to help themselves get better. In general, the medication approach should be very judicious. There’s no cure all global medication that can be used. So if a medication is indicated for a specific symptom, as I mentioned in terms of a symptom-based approach, just be very careful about adding a medication which might have cognitive side effects. One medication that I’ve highlighted here, I think most people are aware of the potential hazards of benzodiazepines in the TBI populations, but many commonly prescribed medicines in this population also have a host of side effects and gabapentin is an example that’s quite pervasively used. Comorbid chronic pain is common in this population. In my experience, your chance of helping their pain is actually less with gabapentin than it is with giving them additional side effects, in terms of fatigue or dizziness. But at any rate, if you do choose to use a medication, just make sure you’re monitoring for side effects and reassessing and stopping it if it’s not providing much benefit. Polypharmacy, in general, should be avoided for the same reasons. Not only that, is you start to get drug/drug interactions on top of it. Although we can’t find objective abnormalities often clinically, is also within this research—we showed we couldn’t. The distress that these patients are having is very real to them. So it shouldn’t be taken for granted or it shouldn’t be messaged to them that what they’re experiencing is not real, even if we don’t know really what the underlying reason is for it, that distress they’re having is very real. And to develop and build your patient’s trust in your care, they need to feel that empathy and that you understand that what they’re going through is distressful. On the other hand, as a provider, we cannot fix this problem. We can’t make it go away. We’ve got to have the patient’s help in the process. So they have got to be an active participant in it.

Some things I always try to hit in my education. So physically activity, not only a structured program but also just increased movement throughout the day. If there’s some specific focal problem, whether it’s spinal pain or a balance problem, you might need to add formal physical therapy on top of the home exercise recommendations you made. Other aspects of education that should be covered are sleep hygiene, stress reduction, nutrition, proper healthy diet, alcohol and tobacco and illicit use, role of—I’ll put aside the role of medications for a second and just mention that all of those bullets, all of those first six bullets get at factors that we know are beneficial not necessarily for TBI recovery, but we know are beneficial for brain health and dementia prevention. So if it’s good for the brain from that aspect, it’s probably important for recovering from a mild traumatic brain injury or multiple mild traumatic brain injuries. In terms of medications, if you do—I talked about the potential hazards of medications, but certainly there is a role for medications. At the very least, even if you’re not going to be advising use of a medication, you should discuss what the option would be for the symptom they’re having and why you might be advising against it. Certainly, if you are advising for that medicine, you should counsel them on the goals, when to take it, including time of day, including if it’s a prn medicine, what target symptoms they should use to determine when that prn would be. What good and what potentially beneficial effects and what potentially bad side effects might result. If you do start a medication, it’s very important on follow up visits, to check about their use of that medication. I found that many times I thought at the end of a visit that the person was on board with trying a medication only to have them come back at the next visit and tell me through the course of the visit, that finally—I sometimes have to pull it out of them—that they aren’t actually taking it. They may have never even started the medication. It may have been that they—at that visit where you prescribed it, they just told you what they thought you wanted to hear, that they would agree to take the medicine. Or they may have done some further research on their own on the internet or talking to people, and decided the risks were greater than the benefits. Related to that, scheduled medicines, I often find out that they aren’t taking them on a daily basis as intended. So it’s important to ask those questions, probe about that. So if you’re using a medication to prevent—a daily medicine to prevent headaches, and they’re taking it when they’re having a headache, but not every day, obviously that was not the goal. But so—and the patients have to feel safe, that they’re able to tell you this information. So they shouldn’t be made to feel threatened or condemned if they’re not following doctor’s orders. So you want them to certainly be safe and honest with reporting their hesitancy to taking medicines and why. And so sometimes when you find out they they’re hesitant about it, you can explain the rationale and maybe why their fears are unfounded. In terms of cognitive and communication compensatory strategies, for any patients who are reporting problems with their thinking abilities, or with communication such as word finding difficulties, the most proven effective treatment is compensatory strategies. And you don’t necessarily have to send someone to a formal cognitive rehabilitation program to deploy those strategies. Some educational materials often do the trick. So if those aren’t enough, if the patient continues to struggle, sometimes patients just aren’t able to implement those for various reasons. Certainly, formal cognitive rehabilitation with speech therapy is a reasonable approach, but regardless, the compensatory strategies should be covered in the education program, in the educational counseling portions of your visits.

Physical exercise. So I think I’m starting to run low on time, so what I would like to do—is here, the next set of slides gets into details on all of these aspects. So I think that I’m going to kind of quickly move through these, so bear with me as I just brisk through these next slides and let you know that the slide set is available, as Robert said, and I’m also happy to email the set of education materials that I use in my clinic to anyone who is interested as well. But these are just basic things that are covered in those education materials. These are dietary recommendations.

Alcohol doesn’t necessarily need to be totally mandated against. There’s some debate about low levels of alcohol quantities being even helpful to your brain. But regardless, we know we don’t want heavy consumption for brain function.

Some sleep hygiene information.

Stress management information, including simple, everyday things, as well as programs such as controlled breathing, yoga, meditation. And seeking a mental health consultation if these more basic measures don’t work, is important.

These are some specific cognitive compensatory strategies that I mentioned.

The key message here in messaging your patient—so the clinician is going to partner and guide the patient. Realistic goals should be stress—that we’re going to try to help lower the symptom distress level and increase functional level, but total cure is really not realistic. There are no magic bullets, and it’s going to take work on the part of the patient to get better.

At that point, I’ll turn it back over for the final poll question and then the wrap up. Thank you.

Moderator: Dr. Walker, we have a number of questions queued up. Would you like to skip this poll as well and just go straight to questions?

Dr. William Walker: Yeah, that’s fine by me. Yep. The answer to this is—the least helpful, a stimulant medication. And I’m happy to go over that with anyone who has any questions about what is—if any, role there is for stimulant medication. But all of those other techniques are helpful. So at that point—

Moderator: Thank you.

Dr. William Walker: Yeah, so I’ll open it up for questions. Thank you.

Moderator: Okay. We may go over by a few minutes, but if we do, audience members if you have to leave right at the top of the hour, please stick around and provide answers to the survey that pops up. And we’ll launch right in. Do you have a clinical opinion or impression concerning treatment?

Dr. William Walker: I think that’s what I just covered. So I’m not sure if we have a more specific—I mean, to me, the cornerstone of treatment is education and counseling. Beyond that, it really depends on what specific high symptom levels there are.

Participant: Bill, I think the questioner was looking at treatment efficacy.

Dr. William Walker: Yeah, well, I think that the most efficacious thing you can do is educate and counsel your patient and get them to begin doing some of those lifestyle changes. Exercising and practicing stress management, eating a healthy diet, those things that I just covered. Like I just said, there’s no magic bullets if we’re talking about this condition as a whole. Now, if you’re talking about some specific symptom disorder, like migraine-type headaches, then I’m happy to answer that as well, but I would need kind of a more specific question.

Moderator: Thank you. What is passive therapy?

Dr. William Walker: I’m sorry, what is what?

Moderator: Passive therapy.

Dr. William Walker: Passive therapy. Thank you for asking that question. So that would be something like acupuncture or taking a medication. So an active therapy is something that the patient is actually expending either physical or mental energy in terms of doing, whether it’s doing a crossword puzzle or going for a brisk walk. So active therapies are patient-engaged therapies versus just having someone passively fix their problem, which again relies—tends to foster dependence and not get the person doing what we think is most beneficial, which is making those necessarily lifestyle changes.

Moderator: Thank you. There’s a question about the absence of African Americans in the sample. I’m not sure if you can comment.

Dr. William Walker: Well, I wouldn’t say there’s an absence. Off the top of my head, I’m not sure what our percentage is, but I can tell you that the site with the largest percentage of African Americans was actually the Richmond site, I believe running somewhere between 30 to 40 percent.

Moderator: Thank you. This next person is asking if the OSU TBI interview is available to the public and is it appropriate to use clinically?

Dr. William Walker: It is available to the public. It’s a—I would say it’s a screening instrument, so I mean it’s not inappropriate to use clinically. It’s more of a research tool. I have on our LIMBIC CENC website, which the actual website is actually posted on this final slide, there’s a knowledge translation center and there’s a clinician packet to take our interview into the clinic. So just go to that website, the knowledge translation section, and you can download the toolkit. It’s an abbreviated clinician-friendly version of what we’re using in the study. So, I would encourage you to do that, if you’re interested in taking that TBI interview into the clinic.

Moderator: Thank you. Can you offer some guidance regarding psychogenic factors, somatoform disorders, and malingering?

Dr. William Walker: Yeah, I’d be happy to. I was going to actually touch on that during one of the slides, because that is a big factor. So unfortunately, as many of you know, if someone has symptom magnification, we never know really what the source of it is, right? Is it conscious malingering, or is it subconscious plea for help? Secondary gain, maybe. We don’t really know what the typology of that symptom magnification is. But I would say that during examination, this is actually one of the few things I can pick up on examination of these patients, because basically, the neurologic exam is going to be normal. So when I find an abnormality on neurologic exam, that I’m thinking—Well, something else is going on. Maybe they had a stroke, right? Or in the case of someone with a functional neurologic disorder, when you test their extraocular movements, they might flitter their eyes around. They might do a lot of excessive blinking. When you test their finger-nose-finger, they may kind of jerk their finger all over the place. So these kind of nonorganic findings. People, when you test their heel-to-toe gait, they may sort of have this increasing non-physiologic sway and loss of balance. So those are the kinds of signs that I pick up on to indicate the individual has what is essentially a functional neurologic disorder in the form of what they think is a post-concussion syndrome. So I think the difference in the approach in those patients is you’re going to need to bring in more mental health resources, potentially get them into formal therapy earlier, and just realize it’s going to be a long, uphill battle. I do have some of those patients who have gradually gotten some better, over time, but rarely do they get back to where they really probably should be. And unfortunately, many times those patients are resistant to even being examined from the angle of mental health. So that can make it much more challenging. But yeah, excellent question. Something that you can pick up on during examination, more so than on history. There are some instruments that can be used to look at nonorganic symptom reporting. We have in our study, one of our questionnaires is the Mild TBI Atypical Symptom Scale. And so if someone’s really elevated on that scale, you can kind of uncover the same thing. Thank you.

Moderator: Thanks, Bill. This person’s asking how to understand the difference between cohorts for allergies, asthma, and sleep apnea.

Dr. William Walker: Yeah, I wish I could. I don’t really know why the TBI patients had more of those, particularly. I would point out that those are not medically documented. Those are self-reported. But yeah, I don’t know. It just goes to show that there’s a lot of—in my mind, from a research standpoint, there potentially is a lot of—when you’re doing observational research, a lot of times we see some association between—let’s say it’s TBI and an outcome, and we just make the assumption that it’s from a TBI without considering that there might be some unmeasured variable that’s different between the individuals. So this just shows, I think to me, the importance of doing—adjusting for other variables in observational study like this. No matter how many you’re going to choose, there may be some that you miss. But yeah, excellent question. I suppose it’s possible that TBI can put you at greater risk for developing those conditions, but that’s something that with longitudinal study, we would be able to show that those individuals would be, over time, accumulating those at a greater rate than the individuals without TBI. So our longitudinal research should ultimately give the answer in terms of these associations that we’re seeing with cross-sectional analyses.

Moderator: Do you find that fatigue is an important contributor that should be intervened on?

Dr. William Walker: Absolutely. I think fatigue can be a red flag for certain things that you would want to potentially investigate for—number one, is sleep. And even if someone is subjectively sleeping well, it’s possible they have sleep apnea, because fatigue is one of the most common symptoms of sleep apnea and can even be seen in someone not reporting other overt symptoms of sleep apnea. But it can also be a sign of neuroendocrine dysfunction, say hypothyroid. So sometimes when I have someone with prominent fatigue, I might do an endocrine screen looking at thyroid or even sometimes growth hormone or cortisol levels. So that’s always something to consider. I think that the other thing that we commonly see is depression. Fatigue is a common symptom with depression. So screening for depression is extra important in those patients. If you’ve ruled out all of those and the individual is sleeping well, that’s when you might want to think about a medication to help and one type of medication, short of using a stimulant, that I sometimes use for cognitive fatigue is amantadine, which shows some efficacy for fatigue in multiple sclerosis patients. I have a handful of patients who we’ve tried that on, and they felt it’s helpful. It’s not a high-yield intervention. A stimulant medication, that would be a potential role, for the right patient, for a stimulant medication as well.

Moderator: Unfortunately, we really only have time for one more question. I’ll give you two and perhaps you can choose the one you have the best answer for. Any sense of how many patients had secondary gain in their backgrounds? And were there any differences noted for those with exposure to repetitive low-level [unintelligible 48:35]?

Dr. William Walker: For the first question, we did not find a difference in the atypical symptom questionnaire between the TBI positive and negative, but I think that that’s certainly going to be a big thing that we’re looking at in the future of research. So hopefully I’ll be able to give you a more definitive answer on that in the future. I’m going to have to kind of defer to low-level blasts as well, because initially that was not a big focus on our study. This has become—when we first proposed CENC. Over time, this has become an increasing recognized potential issue. So we’ve actually added some instruments for that, to get a better measurement of that. Right now, we have a very crude way to measure that. And with that crude way in a smaller sample, we are not seeing differences, but it’s an important thing that we’re looking at and should be able to get some future information on. Not only low-level blasts, but we’ve also rolled out a detailed question on contact sports history, because many of the Veterans and servicemembers also had a history of playing contact sports.

Moderator: Well, thank you Dr. Walker, and thank you, Dr. DePalma, for your work in the VA and for preparing and presenting today. We really do have to wrap it up. So audience members, when you leave, you’ll be met with a short survey. Please do provide answers. We count on those to continue to bring you high-quality Cyberseminars, such as this one. Your questions were recorded, and I’ll make sure that they make it to our host. Dr. DePalma, do you have any closing comments you’d like to make?

Mr. Michael DePalma: Yes, I would just like to thank everybody. There were 270 participants. It’s sort of a world record. And we greatly thank Bill and his sensible clinical approach to the treatment. I’m sure it will be widely applied. And thank you very much for doing this, in these difficult times. Thanks.

Dr. William Walker: My pleasure. Thank you all for joining.

Moderator: Dr. Walker, any closing comments?

Dr. William Walker: No, thank you all for joining. Hopefully, you got something out of it, and it was fun. Thanks.

Moderator: Well, thanks again. With that, I will just wish everyone a good day.

[END OF AUDIO]