STUDY TITLE: Effect of Bright Light Therapy on Depression Symptoms in Adult Inpatients with Cystic Fibrosis (CF) or Chronic Obstructive Pulmonary Disease (COPD)

Final Manuscript, Including Study Protocol and Statistical Analysis Plan

NCT Number: NCT04921332

March 2022

Abstract

Background: Depression is a common comorbidity with chronic illness. Previous studies on depression treatment in these populations have not focused on bright light therapy (BLT) for non-seasonal depression. Patients diagnosed with cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD) can under-report depressive symptoms under the assumption that they are an expected part of the disease process. Symptoms of depression can lead to increased episodes of disease exacerbation and hospitalizations.
Methods: Four adult patients with an existing diagnosis of either CF or COPD were assigned to the intervention of BLT 30 minutes daily for a goal of seven consecutive days. The primary outcome observed was depressive symptom changes recorded by subjective completion of Beck's Depression Inventory II (BDI-II) pre-intervention and post-intervention. The secondary outcome was compliance with daily bright light therapy documented via daily logs by the bedside nurses.
Results: There was not a significant improvement in depressive symptoms pre-intervention versus post-intervention among both populations ($p=0.196$). There was no significant correlation found between number of compliant days with changes in BDI-II scores pre- and post-intervention ($p=0.213$). There were no adverse events to be reported with this trial.
Conclusion: BLT is a well-tolerated intervention for the hospitalized adult CF and COPD population. Larger-scaled studies with a control group may be useful in the future for establishing validity behind this intervention.
Limitations: Limitations include a small sample size, inconsistency with daily compliance, and factors surrounding completion of this study during the COVID-19 pandemic.
ClinicalTrials.gov Identifier: NCT04921332
Keywords: cystic fibrosis; chronic obstructive pulmonary disease; depressive symptoms; chronic illness; affect; bright light therapy

1. Background

Depression in chronic illnesses such as CF and COPD often goes undetected, undiagnosed, and untreated (American Lung Association, 2021b). Many patients suffering from chronic illnesses simply assume that depressive symptoms are just a normal part of the disease process, especially in multifactorial disease such as CF and COPD (American Lung Association, 2021b; Cystic Fibrosis Foundation, 2020). Previous studies have not always observed a chronically ill and frequently hospitalized population. Additionally, most studies have only observed the effects of BLT on seasonal depressive disorders rather than nonseasonal. Focused studies with the CF or chronically ill populations have been limited by small sample sizes.

Complex and chronic respiratory illnesses encompass a variety of diagnoses, including CF and COPD. Quittner et al. (2014) examined the presence of depression and anxiety symptoms among CF patients and their caregivers and found that 29% of adult CF patients had a positive screening on the Center for Epidemiologic Studies Depression Scale (CES-D) ($p<0.001$). Unmanaged depression among patients with CF can result in the individual being less likely to manage his or her treatment plan, exhibit poor lung function, have a lower body mass index, higher health care costs, an increased number of hospitalizations, and an overall decrease in his or her quality of life (Cystic Fibrosis Foundation, 2020). COPD is characterized by long-term disability, early mortality, and currently has no definitive cure (American Lung Association, 2021). Approximately one-third of patients diagnosed with COPD experience symptoms of either anxiety or depression (Griffith et al, 2020). Patients with COPD and major depressive disorder have a 43% increased risk of multiple adverse COPD outcomes, which may include more frequent disease exacerbations, new anxiety or depression events, and increased mortality (Marsh & Guck, 2016).

Treatment with daily BLT is known as a first-line therapy for seasonal depression (Campbell, Miller, & Woesner, 2017). To expand its usage studies investigating the application of BLT in non-seasonal depression found improvement in non-seasonal depressive symptoms when applying BLT to multiple populations which included inpatients with major depressive disorder (MDD) and hospitalized CF patients (Guzel Ozdemir et al. 2015; Kopp et al. 2015; Lam et al. 2016). BLT is overall well-tolerated, affordable, and effective (Yorguner Kupeli et al., 2018). Although BLT can take two weeks or more to reach its maximum effect, symptoms can start to improve within a few days of consistent use (Mayo Clinic Staff, 2017).

The purpose of this project was to apply a daily 30-minute BLT intervention to adult CF or COPD patients hospitalized for acute pulmonary infection or exacerbation to decrease symptoms of depression as measured subjectively by depression inventory scoring. The primary research question being investigated is whether a BLT intervention would be effective in reducing depressive symptoms among hospitalized adult CF and COPD patients.

2. Methods

Ethical Statement

This study was reviewed and approved by the University of Pittsburgh's Internal Review Board. Informed consent was obtained from each participant. Participation in this project was completely voluntary for each individual subject. A nurse caregiver referred eligible patients on the unit to the principal investigator so as to prevent cold-calling. A random identifier was assigned to each participant to maintain confidentiality of recorded data.

2.1 Sample

This study took place on the pulmonary step-down and transplant unit at a 1,600-bed academic medical facility in Southwestern Pennsylvania. Recruitment occurred after the nurse clinician in the pulmonary stepdown unit spoke with the patient and asked if they were comfortable discussing the study with the principal investigator (PI).

Inclusion criteria were adult patients 18 years of age and older with an existing diagnosis of either CF or COPD. The BDI-II survey was administered following a waiver to written consent and only patients with a score of >/= 14 or mild depression symptoms were invited to participate. This minimum score was determined in order to be high enough to allow visible changes in depression symptoms following a seven day intervention. Demographics including diagnosis, education level, ethnicity, and age were recorded for each participant (Table 1).

Exclusion criteria included patients who had pre-existing ophthalmological conditions or photosensitivity due to the use of a bright light; migraines because the bright light could be a trigger; those receiving high dose steroids for transplant rejection due to potential for mood altering qualities; those receiving certain antibiotics that increased light sensitivity; those with bipolar disorder because light therapy may trigger mania; and admissions anticipated to span less than 48 hours because this would not be a long enough span for therapy to produce a visible effect on depressive symptoms. Children were excluded because only adult CF and COPD subjects are admitted to this hospital and unit. This study only consisted of one admission period for the inpatient. If the patient were to be readmitted, potential for bias from previous exposure existed; therefore, re-enrollment was not offered.

The initial target number of patients for this study was 30. With the primary interest being in feasibility and acceptability of this intervention, this study will assist in providing support for a larger-scaled study; therefore, a sample size of 30 is appropriate for these purposes. No power analysis was performed for this study.

.

2.2 Study Design

This was a quasi-experimental, pre- and post- intervention, single group study. No control group was utilized for comparison. A single bright light lamp was assigned to each individual patient throughout the duration of the intervention.

2.3 Intervention

Procedures following consent began with placing a bright light therapy lamp in the participant's room and reviewing verbal instructions on what the subject should anticipate. Verilux HappyLight ® Luxe UV Free LED Therapy Lamp by Verilux was utilized for the purposes of this study. This is a 10,000 lux bright light therapy lamp which is a level of intensity comparable to being outdoors on a sunny but not overly bright day (Sloane, Figueiro, & Cohen, 2008).

Since participants with a history of bipolar mood disorder were excluded from this study, the 15-item "Mood Disorder Questionnaire" was administered manually from a printed paper survey during the pre-screening process to determine history of bipolar disorder symptomatology since this was not able to be determined solely based on medical chart review (Hirschfield, 2006). Basic demographic data including age, disease diagnosis, ethnicity, and education level was manually collected from each participant via a checklist completed by the PI (Table 1). At this time, a random identifying code was assigned to the participant for confidentiality. Bright light therapy began the morning following enrollment. The lamp was placed in a position approximately 16-24 inches from the subject's face by the principal investigator initially. Proper positioning of the lamp was included in bedside nurse education in order to ensure that it was placed correctly before being turned on each morning. A small reference sheet and disposable measuring tape was attached to each lamp to ensure continued proper use and distance from the patient. A preliminary 10-minute session of bright light therapy (BLT) was initiated following consent in order to ensure no acute reactions or sensitivities were experienced from the light. The brightness level was set at 10,000 lux. If the participant experienced sensitivity or adverse effects during this pretest time, which may have included eyestrain, headache, nausea, or irritability, therapy began at 2,500 lux the following day and gradually increased by 2,500 lux per day as tolerated by the patient. The PI was responsible for adjusting this setting in these instances. Color temperature was set to warm white (3,500K), medium white (4,250k), or daylight (5,000k) for the duration of the study depending on the participant's preference during pretesting. The participant was able to request that this be changed during the study when the PI would be present for routine monitoring. The PI also provided contact information to the participant and nursing staff so that she could be reached if needed. These settings were automatically saved when the lamp was turned off making it easy to maintain the same settings for seven days of therapy. The lamp stayed in the subject's room until the seven-day goal was completed or the patient was discharged or transferred. The bedside registered nurse turned on the lamp and set the timer upon entering the room in the morning when the patient would awaken. The automatic timer on the lamp turned off therapy after 30 minutes. The bedside nurse would initial a log documenting the day and time therapy was initiated and whether it was initiated on that day. The PI was responsible for routinely monitoring participants and following up on whether there were disruptions in therapies during each session (this was not the bedside nurse's responsibility). Disruptions may have included the patient self-discontinuing therapy for that day or leaving the

unit for testing, procedures, or hemodialysis. This information was recorded on the compliance log. The completion of this log was included in education regarding BLT provided to the bedside nursing staff by the PI.

The subject was responsible for and educated about how to turn off the lamp in the instance that he or she felt therapy should be disrupted during the 30-minute therapy period. This procedure did not differ on weekends or holidays since this took place in a 24-hour hospital facility. If the participant was discharged prior to completing the repeat Beck Depression Inventory II, he or she would be contacted via phone to verbally administer the inventory as included in the consent form.

When the bright light lamps were not in use, they were properly cleaned with purple top PDI wipes per the unit's infection control representative and stored in a pre-designated locked cabinet on the pulmonary stepdown unit.

2.4 Measurements

Depressive symptoms were obtained subjectively before and after the seven-day allotted intervention period utilizing the 21-item BDI-II scoring system (Beck, 1996). This scoring system considers a total score of 0-13 as minimal, 14-19 as mild depressive symptoms, 20-28 as moderate, and 29-63 as severe. The BDI-II is most often reported to have a Cronbach's Alpha coefficient averaging 0.9 and is shown to be highly reliable with the ability to provide differentiation between depressed versus non-depressed subjects (Wang & Gorenstein, 2013).

Compliance data was measured via a log posted on the participant's room door. This log was completed daily by the assigned bedside nurse and included the data, whether therapy was initiated (Y/N), what time it was initiated, and whether therapy was interrupted (Y/N). Reason for interruption could be added as a comment on the log, but there was no designated area in which to write it. These logs were collected by the principal investigator following completion of the intervention.

2.5 Statistics

Normality of pre- and post-intervention BDI-II scores was tested using the Shapiro-Wilk test. Given data normality, a paired student t-test was used to assess the primary outcome data. The secondary outcome of daily compliance data with the seven-day length intervention was tested utilizing a Chi-Square test. Final data was recorded as standard deviation with a mean with a two-tailed 0.05 significance value.

3. Results

3.1 Patient Characteristics

Four participants were successfully enrolled in this study. Due to potential candidates who met one or more of the exclusion criteria, intensive care unit transfers, and those being transferred to alternative units after becoming COVID-19 positive, only four participants successfully completed the pre- and post- BDI-II scoring.
Twenty additional potential participants were screened and considered for enrollment in this study but met various exclusion criteria. These exclusion criteria included anticipated disposition in less than 48 hours (n=8), pre-existing ophthalmological conditions (n=2), did not meet initial depression inventory score minimum of 14 or greater (n=1), had a history of migraines (n=2), were receiving pulse dose steroids (n=1), and those who expressed general disinterest in participating in the intervention (6) (Table 3). Among these patients, 15 were diagnosed with CF and five were diagnosed with COPD.
Among the four who were successfully enrolled and completed the intervention three were diagnosed with CF and one was diagnosed with COPD. Ages ranged from 36 to 70 years old, with an average of 56.25± 20.25 years. All participants were of Caucasian race. Total admission lengths spanned from 14 to 55 days among participants with the average being 31.25 days.

3.2 Depression Inventory Effects

Changes in individual's BDI-II score were calculated and recorded in Table 2. The Shapiro-Wilk test yielded data normality among the BDI-II pre-intervention and post-intervention scoring; therefore, the paired student t-test via Statistical Package for the Social Sciences (SPSS) V. 26 was utilized to analyze this data (Table 4 & 5). There was not a statistically significant difference found between pre- and post-intervention scoring (p=0.196).

3.3 Therapy Compliance

The goal duration of therapy was seven consecutive days of bright light therapy. Among the final recorded four participants, one completed seven days of consecutive therapy, one completed six days of consecutive therapy, one completed two days of nonconsecutive therapy, and one completed three days of nonconsecutive therapy. Chi square statistical analysis was performed to assess whether significance existed between the days of therapy participated in and change in BDI-II scores from pre- to post-intervention (Table 6). There was no significant association found between days of compliance and the changes in BDI-II scores pre- versus post-intervention (p=0.213).

3.4 Adverse Effects

Potential adverse effects were identified at the beginning of this study that could possibly result from exposure to bright light therapy. These effects included eyestrain, headache, nausea,

irritability or agitation, and breach of confidentiality. There was no occurrence of adverse events to disclose for this project.

4. Discussion

The primary outcome of this study was the mean scoring of the BDI-II pre- and post-intervention had a reduction; however, this reduction was not statistically significant based on the yielded p-value. It is fair to consider whether a seven day intervention period is long enough to produce a change in pre- and post-BDI-II scores. It is also difficult to differentiate internal factors that may have altered the subjective scores for patients. There are many other factors that could impact depressive symptoms aside from bright light therapy especially in a complex and chronically ill patient. A drawback of this intervention is that the trigger of score changes would be virtually impossible to differentiate as bright light therapy or other external or internal factors, such as changes in the participant's prognosis, hospital discharge plan, or personal life. This would also make clinical significance of this intervention difficult to decipher.

The secondary outcome of compliance data was recorded as a "Y" or "N" for each individual day across the seven-day intervention period. Among subjects, there was inconsistency with both the number of days of consecutive treatment. Following statistical evaluation using a chi-square test, there was no association between days of compliance and changes in BDI-II scores pre- and post-intervention.

Depression symptoms continue to be prevalent among the chronically and complex ill population. Such pathology is associated with increased general hospitalization risk, longer length of hospital stays, and an elevated risk of readmission (Prina et al., 2015). The average length of stay among the participants in this study was 31.25 days. The average cost of a general hospital stay per day, not specifically for complex respiratory disease management, is $2,607 (Fay, 2021). Considering this information, reducing depressive symptoms can have not only a subjective impact on depressive symptoms, but also an impact on subject quality of life as well as a financial impact secondary to the additional cost per hospital day caused by increased lengths of hospital stays and readmission rates. Future studies may be useful in examining these factors as secondary outcomes.

5. Limitations

This study had several limitations. According to Doctor Joseph Pilewski, the primary CF physician at UPMC Presbyterian, the recent use of the medication Trikafta ® for CF is reducing the number of hospitalizations among this patient population. This new therapy has recently been FDA approved and has shown in two clinical trials to improve components of pulmonary function (U.S. Food and Drug Administration, 2019). This decreased the potential candidate pool on the inpatient unit. This reduction in candidate availability resulted in the COPD population being included approximately halfway through the data collection period.

The limited availability of nursing staff also impacted this study. Oftentimes, the principal investigator would have difficulty locating the usual caregiver to approach the patient and ask permission to speak with him or her. There was additional difficulty with nursing staff consistently offering bright light therapy to enrolled patients daily. As an attempt to improve the consistency of applying the intervention, education was provided to the staff during monthly staff meetings prior to study initiation and at the halfway point. Despite this additional training, the staff had trouble initiating the intervention due to altered workloads and staffing due to the COVID-19 pandemic.

This study occurred during the COVID-19 pandemic. Some patients were apprehensive about having an extra, unnecessary individual in their room. Many patients were encouraged to avoid hospitalization if possible, during the COVID-19 pandemic. Only one site and one patient care unit were used for recruitment.

It was also challenging for participants to complete the 30-minute bright light therapy sessions due to needing to complete off unit testing and treatment requirements. The patients on this particular unit are still acutely ill and being actively treated while hospitalized. Many are dependent on hemodialysis scheduled early in the mornings, diagnostic procedures, and surgical procedures. This decreased the likelihood that bright light therapy would be completed consistently for those particular days.

This study was not blinded. All participants were aware that they were receiving this intervention. This left opportunity for participant bias on the pre- and post-depression inventory surveys. This also impacted the generalizability of the study given the risk of participant bias, being at a single site, situational factors, and working with specialty populations.

Future studies like this would benefit from a greater length of time for the data collection period, more study team members used during the consent process, and recruitment from multiple sites and units. Future implications for bright light therapy are promising, since this intervention is relatively safe and inexpensive to implement (Mayo Clinic, 2017). Larger scaled studies would be needed prior to implementing bright light therapy in usual care or daily practice.

Author statement

The principal investigator, EO, designed this study, made statistical analysis, performed the study, and drafted the manuscript. Dianxu Ren provided guidance for appropriate statistical test application. All other authors listed commented on the manuscript and provided approval prior to submission of the final draft.

Funding/support

The bright light lamps for this study were personally funded by the principal investigator. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

No conflict of interest declared.

References

American Lung Association. (2021a, March 5). COPD and Emotional Health. https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/living-with-copd/coping-with-emotions

American Lung Association. (2021b, March 5). Learn About COPD. https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/learn-about-copd

Beck, A. (1996). Beck's Depression Inventory II. https://www.kdheks.gov/c-f/integration_toolkits/Beck_Depression_Inventory_II.pdf

Campbell, P. D., Miller, A. M., & Woesner, M. E. (2017). Bright Light Therapy: Seasonal Affective Disorder and Beyond. The Einstein Journal of Biology and Medicine, 32, E13-E25. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6746555/

Cystic Fibrosis Foundation. (2020). Depression. https://www.cff.org/LifeWith-CF/DailyLife/Emotional-Wellness/Depression-and-CF/

Fay, B. (2021, October 12). Hospital and surgery costs – Paying for medical treatment. Debt.org. https://www.debt.org/medical/hospital-surgery-costs/#:%7E:text=Total%20health%20care%20spending%20in,(%243%2C271)%20for%20most%20expensive

Griffith, M. F., Chen, H. P., Bekelman, D. B., Feemster, L. C., Spece, L. J., Donovan, L. M., Au, D. H., & Carey, E. P. (2021). Comorbid anxiety and depression, though Underdiagnosed, are not associated with high rates of low-value care in patients with chronic obstructive pulmonary disease. Annals of the American Thoracic Society, 18(3), 442-451. https://doi.org/10.1513/annalsats.201912-877oc

Özdemir, P. G., Boysan, M., Smolensky, M. H., Selvi, Y., Aydin, A., & Yilmaz, E. (2015). Comparison of Venlafaxine alone versus Venlafaxine plus bright light therapy combination for severe major depressive disorder. The Journal of Clinical Psychiatry, 76(05), e645-e654. https://doi.org/10.4088/jcp.14m09376

Hirschfield, R. (2006). Mood Disorder Questionnaire (MDQ). Mood Disorder Questionnaire. https://www.ohsu.edu/sites/default/files/2019-06/cms-quality-bipolar_disorder_mdq_screener.pdf

Kopp, B. T., Hayes, D., Ghera, P., Patel, A., Kirkby, S., Kowatch, R. A., & Splaingard, M. (2016). Pilot trial of light therapy for depression in hospitalized patients with cystic fibrosis. Journal of Affective Disorders, 189, 164-168. https://doi.org/10.1016/j.jad.2015.08.056

Lam, R. W., Levitt, A. J., Levitan, R. D., Michalak, E. E., Cheung, A. H., Morehouse, R., Ramasubbu, R., Yatham, L. N., & Tam, E. M. (2016). Efficacy of bright light treatment, fluoxetine, and the combination in patients with Nonseasonal major depressive disorder. JAMA Psychiatry, 73(1), 56. https://doi.org/10.1001/jamapsychiatry.2015.2235

Marsh, S., & Guck, T. P. (2016). Anxiety and depression: Easing the burden in COPD patients. Journal of Family Practice, 65(4), 246-256.

Mayo Clinic. (2017, February 8). Light therapy. https://www.mayoclinic.org/tests-procedures/light-therapy/about/pac-20384604#:%7E:text=Light%20therapy%20can%20start%20weeks

Prina, A. M., Cosco, T. D., Dening, T., Beekman, A., Brayne, C., & Huisman, M. (2015). The association between depressive symptoms in the community, non-psychiatric hospital admission and hospital outcomes: A systematic review. Journal of Psychosomatic Research, 78(1), 25–33. https://doi.org/10.1016/j.jpsychores.2014.11.002

Sloane, P. D., Figueiro, M., & Cohen, L. (2008). Light as therapy for sleep disorders and depression in older adults. Clinical Geriatrics, 16(3), 25-31.

Quittner, A. L., Goldbeck, L., Abbott, J., Duff, A., Lambrecht, P., Solé, A., Tibosch, M. M., Bergsten Brucefors, A., Yüksel, H., Catastini, P., Blackwell, L., & Barker, D. (2014). Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: Results of the international depression epidemiological study across nine countries. Thorax, 69(12), 1090-1097. https://doi.org/10.1136/thoraxjnl-2014-205983

U.S. Food and Drug Administration. (2019, October 21). FDA approves new breakthrough therapy for cystic fibrosis. https://www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis

Wang, Y., & Gorenstein, C. (2013). Psychometric properties of the Beck depression Inventory-II: A comprehensive review. Revista Brasileira de Psiquiatria, 35(4), 416-431. https://doi.org/10.1590/1516-4446-2012-1048

Yorguner Kupeli, N., Bulut, N. S., Carkaxhiu Bulut, G., Kurt, E., & Kora, K. (2018). Efficacy of bright light therapy in bipolar depression. Psychiatry Research, 260, 432-438. https://doi.org/10.1016/j.psychres.2017.12.020

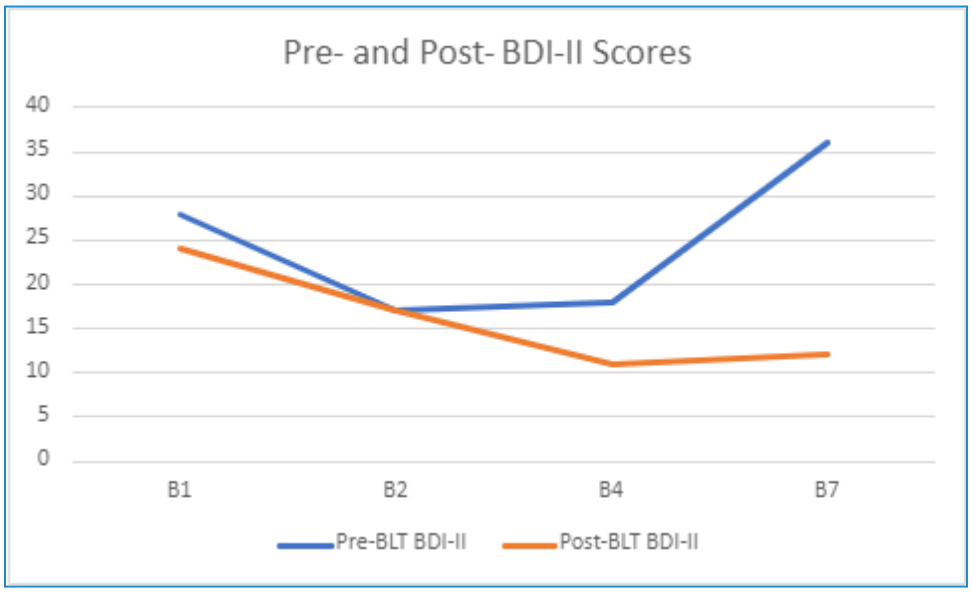
Tables

Table 1. Demographics

Number of participants	4
Diagnosis	
CF (%)	3 (75)
COPD (%)	1 (25)
Ethnicity	
Caucasian (%)	4 (100)

Age (mean in years)	56.25 ± 20.25
Education Level	
High School (%)	2 (50)
College (%)	2 (50)

Table 2. Pre- and Post- BDI-II Scores



*this figure will need color in order to see which color indicates pre- versus post-

Table 3. Reasons for Participant Exclusion

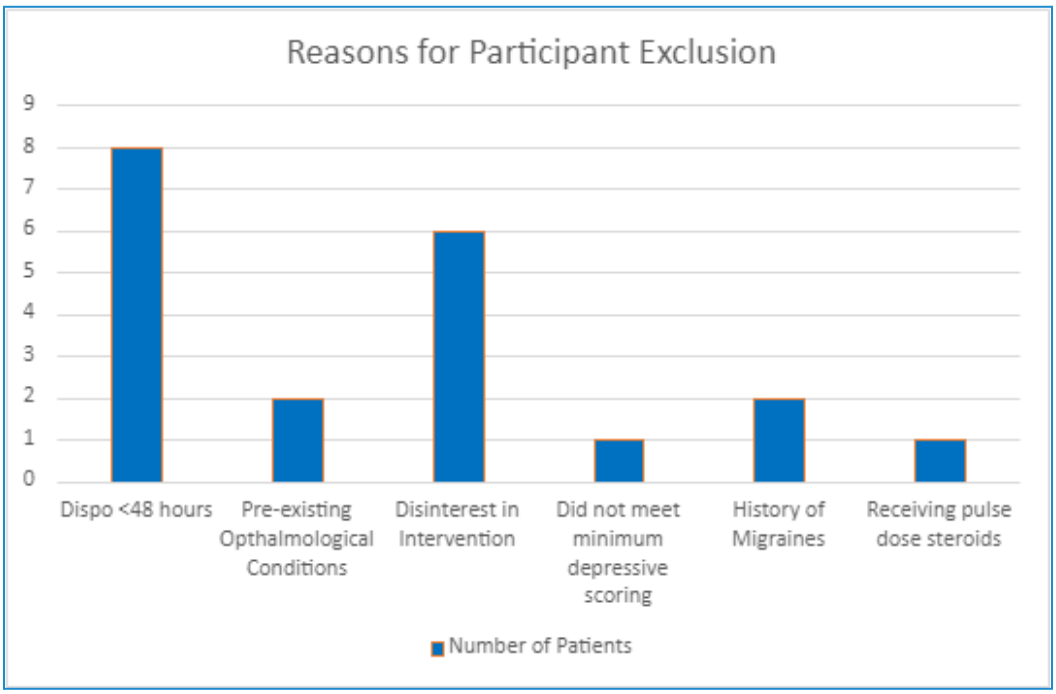


Table 4 & 5. BDI-II Analysis (Primary Outcome)

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-BLT BDI-II	24.75	4	8.995	4.498
	Post-BLT BDI-II	16.00	4	5.944	2.972

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Pre-BLT BDI-II - Post-BLT BDI-II	8.750	10.563	5.282	-8.059	25.559	1.657	3	.196

Table 6. Daily Compliance Analysis (Secondary Outcome)

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	12.000[a]	9	.213
Likelihood Ratio	11.090	9	.270
Linear-by-Linear Association	.998	1	.318
N of Valid Cases	4		

a. 16 cells (100.0%) have expected count less than 5. The minimum expected count is .25.