MCST 604 Assignment 8.1 – Assess, Ask, Acquire, Appraise, Apply (40 points)

Directions: Review the case posted in Blackboard, then answer the following questions.

To earn full credit for your response to each question, you must:

- Answer the question fully (80% of points)
- Answer the question in your own words (without copying/pasting from resources)
- Communicate clearly and effectively with no spelling or grammatical errors (15% of points)
- Cite sources as appropriate in APA or AMA format. Remember, you should cite all information that is not your own opinion. (5% of points)

Part 1. Assess (6 points)

Assess the situation (EBM Step 1)	
List at least two treatment goals for Ben. For each objective, describe what criteria you will use to determine if the goal has been met. (2 points) *Example: A treatment goal for a patient with chronic pain is to reduce the pain severity to a level acceptable to the patient. Pain severity will be measured using the numeric pain scale.*	**Treatment Goal 1: Reduce anxiety symptoms** Ben's mother rates his anxiety as 8 out of 10 and describes it as "constant and easily triggered." This chronic heightened arousal likely contributes to his difficulty tolerating transitions and unexpected changes. Success would be measured by parent-reported reduction in anxiety severity to a level acceptable to Ben and his family, along with observable decreases in signs of distress during daily activities. **Treatment Goal 2: Increase distress tolerance as measured by decreased frequency of self-harming behaviors and transition-triggered aggression** Ben experiences aggressive outbursts three to four times weekly during transitions, with severe episodes requiring physical intervention every one to two weeks. He engages in daily self-injurious hand-biting during distress. From a neurodiversity-affirming perspective, these behaviors represent distress responses when environmental demands exceed his regulatory capacity, not intrinsic deficits (Doherty et al., 2023). Success would be measured by reduced frequency of outbursts, decreased self-injury, and increased capacity to navigate transitions without crisis.
Identify at least two patient-related factors AND	**Patient-Related Variable 1: Polypharmacy**

two medication-related factors that might affect the decision to recommend medical cannabis for Ben. Why are each of these factors important to consider for this patient? (4 points)	Ben currently takes three psychotropic medications: risperidone, valproic acid, and fluoxetine. This polypharmacy affects the decision to recommend cannabis because adding CBD creates potential for drug interactions, particularly since CBD inhibits some of the same liver enzymes involved in metabolizing his current medications. Any cannabis recommendation would need to include a plan for monitoring and possible dose adjustments to his existing regimen. This factor also matters because Ben's medication burden reflects a treatment approach focused on suppressing behaviors rather than addressing underlying distress. If CBD were to support his anxiety and distress tolerance, it could potentially allow for reducing other medications under supervision. **Patient-Related Variable 2: Other Diseases or Conditions** Ben has co-occurring OCD diagnosed at age two and a history of multiple failed medication trials. Sertraline caused paradoxical hyperactivity, while clonazepam with gabapentin produced sedation without benefit. These conditions and this medication history affect the cannabis recommendation because they suggest Ben does not respond to medications in typical ways. Recent research indicates autistic children demonstrate significant variability in drug metabolism, with genetic overlap between pathways involved in ASD and pathways involved in processing medications (Goodson et al., 2023). Ben's atypical responses likely reflect neurobiological differences requiring an individualized treatment approach. If cannabis were recommended, dosing should begin low with careful titration, anticipating that his response may differ from clinical trial averages. **Medication-Related Variable 1: Mechanism of Action** The endocannabinoid system plays a documented role in sensory processing, modulating the balance of excitation and inhibition in sensory neural circuits (Pretzsch et al., 2019). This is relevant because sensory overwhelm is a core experience for many autistic individuals. Doherty et al. (2023) identify sensory needs as a foundational domain in their Autistic SPACE framework, noting that sensory overload commonly triggers meltdowns and shutdowns. Ben's distress behaviors occur specifically in contexts of unpredictability and sensory demand. CBD modulates endocannabinoid signaling and has demonstrated anxiolytic properties. A 2025 study found autistic adults reported 73% reduction in sensory sensitivity symptoms after cannabis use (Zamarripa et al., 2025). CBD may

	therefore support Ben's capacity to regulate sensory input rather than suppressing his autistic traits. **Medication-Related Variable 2: Pharmacokinetic Properties** CBD is metabolized by liver enzymes and inhibits some of the same enzymes that process Ben's current medications, including risperidone and fluoxetine. These properties matter because drug interactions may take time to manifest, requiring ongoing monitoring rather than single-point assessment. Baseline and periodic liver function testing would be appropriate given the shared hepatic metabolism pathways. Additionally, research suggests autistic children show significant individual variability in how they metabolize medications (Goodson et al., 2023). Given Ben's history of atypical medication responses, an individualized approach with careful titration based on his specific response would be more appropriate than relying on dosing expectations derived from neurotypical populations.

Part 2. Ask (2 points)

Ask (EBM Step 2)	
1. What is your PICO question? (2 points) Make sure all **FOUR** components of PICO are included in your question	In children with Level 3 autism spectrum disorder and co-occurring obsessive-compulsive disorder (P), does cannabidiol-rich cannabis extract (I) compared to placebo (C) reduce anxiety symptoms and increase distress tolerance as measured by decreased frequency of repetitive self-harming behaviors and transition-triggered aggression (O)?

Part 3. Acquire (3 points)

Acquire (EBM Step 3)	
Describe your search strategy: Include your search terms, filters used, years included in the search (2 points)	I searched PubMed using the following terms: ("autism spectrum disorder" OR "ASD") AND ("cannabidiol" OR "CBD") AND ("children" OR "pediatric") AND ("aggression" OR "self-injurious behavior" OR "irritability"). I filtered by article type to prioritize randomized controlled trials. I limited results to the past five years (2021-2026) to capture the most current evidence.
Select an interventional trial	Trauner, D., Umlauf, A., Grelotti, D. J., Fitzgerald, R., Hannawi, A., Marcotte, T. D., Knight, C., Smith, L.,

that has a PICO question that most closely aligns with your PICO question. Write the citation in APA or AMA style (1 points)	Paez, G., Crowhurst, J., Brown, A., Suhandynata, R. T., Lund, K., Menlyadiev, M., & Grant, I. (2025). Cannabidiol (CBD) treatment for severe problem behaviors in boys with autism: A randomized clinical trial. *Journal of Autism and Developmental Disorders*. Advance online publication. https://doi.org/10.1007/s10803-025-06884-y

Part 4. Appraise (15 points)

Appraise (EBM Step 4)	
What is the PICO question of the experimental trial? (1 point)	In boys aged 7-14 with moderate-to-severe autism and persistent aggressive, self-injurious, or repetitive behaviors (P), does orally administered purified cannabidiol at 20 mg/kg/day (I) compared to placebo (C) reduce problem behaviors as measured by the Repetitive Behavior Scale-Revised, Child Behavior Checklist, and Autism Diagnostic Observation Schedule-2 (O)?
What are the results of this experimental trial? (6 points) • Study population (who was studied, n = ? Intervention and comparator • Primary outcome • Study results (Results must include **at least one** quantitative measure of effect (e.g., mean difference, risk ratio, absolute risk reduction) with corresponding statistical significance.) • Reported adverse events	**Study Population:** Fifty-one boys ages 7 to 14 years with moderate-to-severe autism were consented. After baseline assessments and exclusions, 44 were randomized and 39 received at least one dose of study medication, constituting the intent-to-treat analysis population. Thirty participants completed all 20 weeks. Inclusion required confirmed autism diagnosis via ADOS-2, parent report of persistent aggressive, self-injurious, or stereotyped behaviors, and absence of epilepsy or other neurological conditions. The study enrolled only males to reduce variability given documented sex differences in autistic behavioral presentation. **Intervention and Comparator:** The intervention was purified plant-derived CBD (Epidiolex) titrated to 20 mg/kg/day divided into two doses. Placebo was identical in color, consistency, and taste. The crossover design included eight weeks of each treatment separated by a four-week washout period. **Primary Outcomes:** Three primary outcome measures were used: Repetitive Behavior Scale-Revised (RBS-R) Total Score, Child Behavior Checklist (CBCL) Total Score, and Autism Diagnostic Observation Schedule-2 (ADOS-2) comparison scores. **Study Results:** The study did not find CBD to be statistically superior to placebo on primary outcome measures, though a prominent placebo effect was observed across all measures. On the RBS-R, both groups showed significant improvement, with CBD demonstrating a trend toward greater effect than placebo (Cohen's d = -0.44; 95% CI: -0.96 to 0.07; p = 0.095). The effect size for CBD was approximately twice that of placebo, but this difference did not reach statistical significance. The CBCL showed similar improvements in both groups with no significant between-group difference (d = 0.30; 95% CI: -0.23 to 0.83; p = 0.269). Notably, when participants taking behavior-affecting medications were excluded from analysis, CBD treatment showed significant

	improvement on ADOS-2 scores (d = -0.95; 95% CI: -1.71 to -0.18; p = 0.020). Blinded clinician impressions found 68% of participants who completed the study (21 of 31) showed observable behavioral improvements during the CBD phase, including reduced aggression, decreased hyperactivity, and improved communication. The pattern of early withdrawals also suggests a potential treatment effect. Of 10 early withdrawals, 7 were participants who started with CBD, and 4 of those withdrew specifically due to behavioral worsening after the CBD phase ended during washout or placebo. This pattern indicates that some participants may have experienced benefit from CBD that became apparent only when the treatment was discontinued. **Reported Adverse Events:** A total of 118 adverse events were reported across the trial. Fifty-nine occurred during the CBD phase, 49 during placebo, and 10 during the washout period. No serious adverse events were attributed to treatment. The most common adverse events during CBD treatment were diarrhea (n = 5), insomnia (n = 5), elevated liver enzymes (n = 3), increased appetite (n = 3), and irritability (n = 3). During the placebo phase, the most common adverse events were deliberate self-harm (n = 5), insomnia (n = 3), irritability (n = 3), and anxiety (n = 3). The higher rate of self-harm events during placebo is notable and may reflect symptom worsening when not receiving active treatment. No significant changes in weight or electrocardiogram findings occurred. CBD demonstrated an acceptable safety and tolerability profile in this population.
Comment on the internal validity of this study? (How confident are you about the truthfulness of the results of this study based on its methods?) For each bullet point below, describe the methods used AND assess whether they minimized bias or introduced bias into the study. (8 points) • Process of randomization • Process of blinding • Level of care in both	**Process of Randomization** *Methods used:* The study used permuted block randomization with block sizes of 2 and 4. An independent research pharmacist handled assignments using a predetermined protocol, maintaining allocation concealment from investigators. The crossover design allowed each participant to serve as their own control. *Assessment:* This approach effectively minimized selection bias. Baseline characteristics showed similar distributions between groups for age, weight, and medication use, confirming successful randomization. One limitation is that the 4-week washout period may not have fully eliminated CBD carryover effects. If CBD effects persisted into placebo phases for CBD-first participants, this could inflate placebo-phase improvement and reduce the apparent difference between conditions, biasing results toward the null. One participant tested positive for CBD during their

groups of the study (Apart from the experimental intervention, did each study group receive the same level of care?) • Attrition rates at the conclusion of the study	placebo phase, though per-protocol sensitivity analysis showed this did not alter overall results. **Process of Blinding** *Methods used:* The study was double-blind with placebo identical to CBD in appearance, consistency, and taste. All personnel remained blinded until data entry was complete after the final participant finished. *Assessment:* Blinding procedures were rigorous, though certain factors may have compromised the blind. Elevated liver enzymes requiring dose adjustments occurred only during CBD treatment, and diarrhea was more frequent with CBD (5 versus 1 event), potentially signaling active treatment to caregivers. Because primary outcome measures (RBS-R, CBCL) rely on parent report, caregiver expectations could influence ratings. Evidence of this appeared in the blinding assessment, as nearly one-third of completers were incorrectly identified as receiving CBD when they were actually on placebo. This suggests caregivers' perceptions of improvement did not always correspond to actual treatment assignment, meaning reported improvements may partially reflect expectancy rather than true treatment effects. **Level of Care in Both Groups** *Methods used:* The crossover design ensured identical care protocols during both phases. Participants were examined every one to two weeks with consistent monitoring including vital signs, blood draws, physical examinations, ECGs, and standardized behavioral assessments throughout the 20-week study. *Assessment:* These procedures minimized performance bias. Notably, both groups improved significantly on the RBS-R and CBCL, which the authors described as a "prominent placebo effect." While typically framed as a methodological limitation, this may reflect the therapeutic value of consistent, predictable engagement with attentive clinicians. Research emphasizes that predictability and safety are foundational supports that reduce distress for autistic individuals (Doherty et al., 2023). That CBD produced approximately twice the improvement on the RBS-R compared to placebo (d = -0.44), even without reaching statistical significance, suggests CBD may work synergistically with consistent support rather than as a standalone intervention. However, factors outside the study protocol introduced variability. The study was conducted during COVID-19 (2020-2022), with school closures, disrupted therapy services, and masked personnel creating environmental unpredictability in participants' daily lives. These disruptions

	may have differentially affected participants depending on which phase coincided with peak restrictions, increasing behavioral variability and making treatment effects harder to detect. **Attrition Rates** *Methods used:* The study tracked all participants from randomization through completion or withdrawal, documenting reasons for discontinuation. Of 39 participants receiving study medication, 9 withdrew early (23% attrition). Researchers used intent-to-treat analysis including all participants with at least one post-baseline measurement. Five participants were excluded prior to randomization due to inability to tolerate blood draw procedures. *Assessment:* Attrition was asymmetric, with 7 withdrawals from the CBD-first group versus 2 from placebo-first. Critically, 4 of the 7 CBD-first withdrawals occurred because behavior worsened after CBD was discontinued. These families recognized improvement only when it was lost, suggesting these were treatment responders. Their loss from the completer sample likely biased results toward the null, underestimating CBD's true effect. The pre-randomization exclusions due to blood draw intolerance may limit generalizability to children with the most significant sensory sensitivities. **Summary Assessment of Internal Validity** The study demonstrated methodological rigor in randomization, blinding, and consistency of care. The crossover design strengthened validity through within-subject comparisons. However, modest sample size (n=39), asymmetric attrition that likely excluded responders, potential unblinding through side effects, and reliance on parent-report measures susceptible to expectancy effects all temper confidence. Jazz Pharmaceuticals provided the study drug and placebo, representing a potential conflict of interest. Despite these limitations, I have moderate confidence in this study's internal validity. The researchers acknowledged limitations transparently, used intent-to-treat analysis appropriately, and the pattern in outcome measures aligns with what blinded clinicians observed (68% of completers identified as improving on CBD). While not definitive, this evidence points toward CBD as a promising intervention worth pursuing in future research with larger, more diverse samples.

Part 5. Apply (12 points)

Apply your Knowledge (EBM Step 5)

Can the results be applied to your patient? Justify your opinion. (8 points) Consider: • Are the study participants similar to the patient in your care? • Would any differences between your patient and the study participants alter the outcomes reported in the study? • Are the outcomes important to your patient? • Are there any outcomes you would have wanted information on that have not been studied or reported? • Are there any limitations of the study that would affect your decision?	The results of Trauner et al. (2025) can be cautiously applied to Ben, though several patient-specific factors warrant careful consideration. **Participant Similarity** Ben closely matches the study population. He is a 10-year-old male with Level 3 autism and persistent aggressive, self-injurious, and repetitive behaviors. Study participants were boys aged 7 to 14 with moderate-to-severe autism confirmed by ADOS-2, recruited specifically because of severe behavioral challenges requiring constant supervision. Like Ben, many participants were minimally verbal and required substantial daily support. The study's focus on children with the most significant functional limitations makes it directly relevant to Ben's clinical presentation. **Impact of Patient Differences** Several differences may alter Ben's expected response. Most significantly, Ben takes three psychotropic medications within categories the study identified as associated with lower CBD blood levels. Trauner et al. (2025) found that participants using behavior-affecting medications demonstrated lower average CBD concentrations than those on no medications. Ben takes risperidone, fluoxetine, and valproic acid, representing three of the five implicated categories. When participants taking these medications were excluded from analysis, CBD produced significant improvement on ADOS-2 scores ($d = -0.95$, $p = 0.020$). This finding suggests Ben's polypharmacy may reduce therapeutic response at standard doses, potentially requiring higher dosing or medication adjustments to achieve adequate blood levels. Ben's valproic acid use also introduces hepatotoxicity risk. CBD and valproic acid share hepatic metabolism pathways, and their combination has been associated with elevated liver enzymes in up to 30% of patients taking both medications (Wechsler et al., 2024). This interaction would require baseline liver function

	testing and monitoring at one, three, and six months after initiation. Ben's co-occurring OCD was not specifically addressed in the study, though CBD's documented effects on serotonin 5-HT1A receptors suggest potential relevance for anxiety reduction (Pretzsch et al., 2019), which could benefit both his OCD symptoms and anxiety-triggered distress responses. **Importance of Outcomes** The study's primary outcome measures align with Ben's treatment goals, though imperfectly. The RBS-R assesses repetitive and self-injurious behaviors, directly measuring the hand-biting Ben demonstrates daily during distress. The CBCL captures broad behavioral concerns including anxiety and aggression, relevant to his transition-triggered outbursts. However, neither measure specifically evaluates distress tolerance during transitions or captures the late afternoon and evening worsening his mother reports. The prominent improvement observed in both treatment groups reflects something clinically meaningful. Research emphasizes that predictability and safety are foundational supports that reduce distress for autistic individuals (Doherty et al., 2023). The biweekly clinic visits, consistent routines, and attentive engagement from the research team likely provided therapeutic structure independent of pharmacological effects. That CBD produced approximately twice the improvement on the RBS-R compared to placebo (d = -0.44 vs. smaller placebo effect) suggests CBD may work synergistically with consistent supportive care rather than functioning as a standalone intervention. **Outcomes Not Studied** Several outcomes important to Ben were not directly measured. The study did not assess anxiety measures beyond CBCL

	subscales, despite anxiety being Ben's primary concern rated 8/10 by his mother. Transition-specific distress tolerance, the context triggering most of his aggressive episodes, was not evaluated. Quality of life for Ben and his family was not measured, though four families withdrew specifically because their child's behavior worsened after CBD was discontinued, suggesting meaningful functional impact. Long-term outcomes beyond eight weeks remain unknown. **Limitations Affecting Decision** Several study limitations affect clinical decision-making. The modest sample size (n = 39) limited statistical power, and the authors acknowledged a larger study might have demonstrated stronger differentiation between groups. The eight-week treatment duration may have been insufficient for this population. The asymmetric attrition pattern likely biased results toward the null, as four of seven CBD-first withdrawals left specifically because behavior worsened after CBD was stopped. These were likely treatment responders whose data was lost from completer analyses. Jazz Pharmaceuticals provided the study drug, representing a potential conflict of interest, though the company had no role in study design, execution, or analysis. Despite these limitations, I would consider applying these results to Ben because he closely matches the study population, has exhausted multiple traditional medication options with poor tolerance or paradoxical effects, and the safety profile suggests an acceptable risk-benefit ratio for a carefully monitored trial with appropriate hepatic surveillance.
Would the experimental intervention provide greater value to your patient than any of the traditional treatment options? (4 points) Consider: • Based on patient-specific and medication-specific factors that affect your patient, do you think Ben would be a good candidate for medical cannabis? • Describe the benefits and risks of cannabinoid therapy in this patient.	**Candidacy Assessment** Ben would be a reasonable candidate for a carefully supervised trial of pharmaceutical-grade CBD. He has failed multiple traditional medications, with clonazepam and gabapentin discontinued due to sedation without benefit, and sertraline causing paradoxical hyperactivity. His current regimen provides only partial symptom control despite carrying significant side

○ Has your patient tried all traditional treatment and non-pharmacological options before trying this therapy? ○ What benefit does this experimental intervention have over traditional therapy options?	effect burden. His age, severity level, and target symptoms align with the study population and observed clinical improvements. **Benefits and Risks** Potential benefits include reduced aggression, decreased hyperactivity, and improved communication, as observed in 68% of study completers during CBD treatment based on blinded clinician impressions (Trauner et al., 2025). CBD's mechanism through endocannabinoid modulation and serotonin receptor effects may address sensory overwhelm and anxiety in ways Ben's current medications do not target (Pretzsch et al., 2019). Risks include increased hepatotoxicity when CBD is combined with valproic acid, requiring liver function monitoring at baseline and at 1, 3, and 6 months (Wechsler et al., 2024). The study also found that participants taking behavior-affecting medications had lower CBD blood levels (Trauner et al., 2025), suggesting Ben's polypharmacy may reduce CBD effectiveness. Common adverse effects included diarrhea, insomnia, and increased appetite. Given Ben's history of atypical medication responses, this complexity warrants referral to an experienced cannabis clinician. **Traditional Options** Ben has not exhausted all traditional approaches, but the framing of "traditional options" warrants critical examination. Many standard interventions for autistic children operate from a deficit model that pathologizes autistic traits and aims to make autistic individuals appear more neurotypical (Graf-Kurtulus & Gelo, 2025). Applied Behavior Analysis and social skills training, while widely used, have faced significant criticism for prioritizing conformity to societal norms over autistic wellbeing. Research indicates these approaches can promote social camouflaging, which is associated with depression, anxiety, autistic burnout, and feelings of inauthenticity (Graf-Kurtulus & Gelo, 2025). A

	neurodiversity-affirming approach recognizes that attempts to make autistic people appear non-autistic can be deeply harmful (Doherty et al., 2023). Rather than focusing on suppressing Ben's behaviors, interventions should address his underlying distress by adapting his environment to provide predictability, sensory accommodations, and acceptance. **Advantage Over Traditional Therapy** CBD may offer advantages because it addresses the underlying neurobiological mechanisms contributing to Ben's distress rather than attempting to suppress autistic behaviors. CBD modulates endocannabinoid signaling implicated in sensory processing and emotional regulation (Pretzsch et al., 2019). The therapeutic structure in the study produced significant improvement in both groups, reinforcing that predictability and consistent care are themselves therapeutic for autistic individuals (Doherty et al., 2023). Implementation would require coordination with specialists who can integrate pharmacological support with environmental modifications that respect Ben's sensory needs and communication style, treating his distress behaviors as signals that his needs are not being met rather than problems to be eliminated.

References: (2 points)

List full references in APA style for each in-text citation in the answer to the previous question (1 point).	Doherty, M., McCowan, S., & Shaw, S. C. K. (2023). Autistic SPACE: A novel framework for meeting the needs of autistic people in healthcare settings. *British Journal of Hospital Medicine, 84*(3), 1–9. https://doi.org/10.12968/hmed.2023.0006 Goodson, R., Wagner, J., Sandritter, T., & Staggs, V. S. (2023). Pharmacogenetic testing in patients with autism spectrum disorder evaluated in a precision medicine clinic. *Journal of Developmental & Behavioral Pediatrics, 44*(8), e505–e510.

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