**Supplemental Materials**

**Additional Clinical Considerations:**

**1.** **Harm reduction approach** – **Minimize THC and substitute CBD in cannabis use**

Behaviorally, a gradual tapering or replacement method may prove a more feasible transition relative to abstinence, allowing for continued use with reduced psychiatric consequences. Since CBD is nonintoxicating and may have an anxiolytic effect (Kwee et al., 2023), replacing THC-containing products with CBD-dominant or CBD-only products may appeal to some individuals. But this approach carries some caveats. Per recent RCTs, recreational cannabis may lack sufficient CBD to exert an antipsychotic effect (Englund et al., 2022; Lawn et al., 2023), and individual susceptibility to any potential CBD-antipsychotic benefit may vary by frequency of cannabis use (Morgan et al., 2018). Also, low-THC cannabis may not be accepted by all patients. A qualitative study in first-episode cannabis users found that nearly half were uninterested in continuing to use CBD-dominant cannabis because it did not produce a high (Ghelani, 2023). Uncertainty surrounding CBD’s pharmacologic interactions with THC also persists. There have been mixed observations of CBD increasing THC blood levels (Englund et al., 2013; Freeman et al., 2019), and in an RCT, high-dose oral CBD increased oral THC’s intoxication and cognitive impairment, perhaps due to CBD’s inhibition of the enzymes important to oral THC metabolism (Zamarripa et al., 2023). Moreover, despite a degree of regulation in legal cannabis markets, product labels for THC and CBD concentrations may be inaccurate, which may lead to over-intoxication and increased risk for adverse effects. While the safest choice is certainly abstinence, reducing risk by decreasing or eliminating THC in favor of CBD, a compound with potential antipsychotic and/or anxiolytic properties, may be a reasonable harm reduction alternative.

**2.** **Enhancing communication about cannabis use and psychotic symptoms**

Though few studies have finely assessed experiences associated with cannabis consumption in CHR-P individuals, sufficient evidence exists to encourage abstinence or reduced use for those who experience psychotic-like symptoms during their use. Cannabis-induced acute psychotic-like symptoms predicted nearly fivefold greater conversion risk in an observational CHR-P study (McHugh et al., 2017). Though discontinuing cannabis use may not affect an individual’s clinical trajectory, raising awareness of this potential prognostic factor may be crucial in supporting CHR-P individuals in early and preventative intervention.

To facilitate patient communication regarding cannabis use and psychotic-like experiences, practitioners should utilize a collaborative treatment approach, which consistently corresponds to greater improvement in a clients' symptoms and functioning (Hill, 2005; Kraus, Castonguay, Boswell, Nordberg, & Hayes, 2011). A collaborative approach is especially helpful for individuals who are ambivalent or uncertain about changing their behavior, as it can help them explore their motivations, values, and concerns related to change in a supportive and non-judgmental way (Hettema, Steele, & Miller, 2005).

**3.** **Accounting for intersectional identity**

Considering broader socioeconomic and racial health disparities perpetuated in the regulation and use of cannabis products historically, clinicians should bring an intersectional lens to harm reduction conversations. For instance, the frequency of childhood and adolescent traumatic experiences is correlated with both rapid escalation of cannabis use and greater cumulative cannabis use in a retrospective study of first-episode psychosis patients (Pauselli et al., 2018). Youth with marginalized identities in the US are more likely to have experienced trauma (Pumariega, Jo, Beck, & Rahmani, 2022). Taken together, this underscores the importance of thoughtfully considering patients’ multifaceted identities when making sense of their risk factors for psychosis and utilizing a tailored, collaborative approach to harm reduction implementation.

The relationship between individual socioeconomic status (SES) and cannabis use is unclear in CHR-P (Phillips et al., 2002). In the general population, notable predictors of cannabis use initiation and severity include low family SES, substance use within adolescents’ peer networks, residential instability, and parental death before age 15 (Buu et al., 2009; Kosterman, Hawkins, Guo, Catalano, & Abbott, 2000; van den Bree & Pickworth, 2005; Von Sydow, Lieb, Pfister, Höfler, & Wittchen, 2002). Low-SES neighborhoods also tend to have increased police presence, which exacerbates stress for minoritized individuals such as youth of color (Del Toro et al., 2019). For those living in areas where cannabis remains illegal, these additional risks likely impact their cannabis use experience. Practitioners are urged to utilize a nuanced and collaborative lens in considering factors that may exacerbate psychosis risk via the diathesis-stress model (Meehl, 1962).

References

Buu, A., DiPiazza, C., Wang, J., Puttler, L. I., Fitzgerald, H. E., & Zucker, R. A. (2009). Parent, Family, and Neighborhood Effects on the Development of Child Substance Use and Other Psychopathology From Preschool to the Start of Adulthood. *Journal of Studies on Alcohol and Drugs*, *70*(4), 489–498. https://doi.org/10.15288/jsad.2009.70.489

Del Toro, J., Lloyd, T., Buchanan, K. S., Robins, S. J., Bencharit, L. Z., Smiedt, M. G., … Goff, P. A. (2019). The criminogenic and psychological effects of police stops on adolescent black and Latino boys. *Proceedings of the National Academy of Sciences*, *116*(17), 8261–8268. https://doi.org/10.1073/pnas.1808976116

Englund, A., Morrison, P. D., Nottage, J., Hague, D., Kane, F., Bonaccorso, S., … Kapur, S. (2013). Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *Journal of Psychopharmacology*, *27*(1), 19–27. https://doi.org/10.1177/0269881112460109

Englund, A., Oliver, D., Chesney, E., Chester, L., Wilson, J., Sovi, S., … McGuire, P. (2022). Does cannabidiol make cannabis safer? A randomised, double-blind, cross-over trial of cannabis with four different CBD:THC ratios. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*. https://doi.org/10.1038/s41386-022-01478-z

Freeman, A. M., Petrilli, K., Lees, R., Hindocha, C., Mokrysz, C., Curran, H. V., … Freeman, T. P. (2019). How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. *Neuroscience & Biobehavioral Reviews*, *107*, 696–712. https://doi.org/10.1016/j.neubiorev.2019.09.036

Ghelani, A. (2023). Perspectives toward cannabidiol (CBD) among youth in Early Psychosis Intervention programs: A qualitative study. *Early Intervention in Psychiatry*. https://doi.org/10.1111/eip.13428

Hettema, J., Steele, J., & Miller, W. R. (2005). Motivational Interviewing. *Annual Review of Clinical Psychology*, *1*(1), 91–111. https://doi.org/10.1146/annurev.clinpsy.1.102803.143833

Hill, C. E. (2005). Therapist techniques, client involvement, and the therapeutic relationship: Inextricably intertwined in the therapy process. *Psychotherapy: Theory, Research, Practice, Training*, *42*(4), 431–442. https://doi.org/10.1037/0033-3204.42.4.431

Kosterman, R., Hawkins, J. D., Guo, J., Catalano, R. F., & Abbott, R. D. (2000). The dynamics of alcohol and marijuana initiation: Patterns and predictors of first use in adolescence. *American Journal of Public Health*, *90*(3), 360–366. https://doi.org/10.2105/ajph.90.3.360

Kraus, D. R., Castonguay, L., Boswell, J. F., Nordberg, S. S., & Hayes, J. A. (2011). Therapist effectiveness: Implications for accountability and patient care. *Psychotherapy Research*, *21*(3), 267–276. https://doi.org/10.1080/10503307.2011.563249

Kwee, C. M. B., Leen, N. A., Van der Kamp, R. C., Van Lissa, C. J., Cath, D. C., Groenink, L., & Baas, J. M. P. (2023). Anxiolytic effects of endocannabinoid enhancing compounds: A systematic review and meta-analysis. *European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology*, *72*, 79–94. https://doi.org/10.1016/j.euroneuro.2023.04.001

Lawn, W., Trinci, K., Mokrysz, C., Borissova, A., Ofori, S., Petrilli, K., … Curran, H. V. (2023). The acute effects of cannabis with and without cannabidiol in adults and adolescents: A randomised, double‐blind, placebo‐controlled, crossover experiment. *Addiction*, *118*(7), 1282–1294. https://doi.org/10.1111/add.16154

McHugh, M. J., McGorry, P. D., Yung, A. R., Lin, A., Wood, S. J., Hartmann, J. A., & Nelson, B. (2017). Cannabis-induced attenuated psychotic symptoms: Implications for prognosis in young people at ultra-high risk for psychosis. *Psychological Medicine*, *47*(4), 616–626. https://doi.org/10.1017/S0033291716002671

Meehl, P. E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist*, *17*(12), 827–838. https://doi.org/10.1037/h0041029

Morgan, C. J. A., Freeman, T. P., Hindocha, C., Schafer, G., Gardner, C., & Curran, H. V. (2018). Individual and combined effects of acute delta-9-tetrahydrocannabinol and cannabidiol on psychotomimetic symptoms and memory function. *Translational Psychiatry*, *8*(1), 181. https://doi.org/10.1038/s41398-018-0191-x

Pauselli, L., Birnbaum, M. L., Vázquez Jaime, B. P., Paolini, E., Kelley, M. E., Broussard, B., & Compton, M. T. (2018). Demographic and socioenvironmental predictors of premorbid marijuana use among patients with first-episode psychosis. *Schizophrenia Research*, *197*, 544–549. https://doi.org/10.1016/j.schres.2018.01.020

Phillips, L. J., Curry, C., Yung, A. R., Pan Yuen, H., Adlard, S., & Mcgorry, P. D. (2002). Cannabis Use is Not Associated With the Development of Psychosis in an ‘Ultra’ High-Risk Group. *Australian & New Zealand Journal of Psychiatry*, *36*(6), 800–806. https://doi.org/10.1046/j.1440-1614.2002.01089.x

Pumariega, A. J., Jo, Y., Beck, B., & Rahmani, M. (2022). Trauma and US Minority Children and Youth. *Current Psychiatry Reports*, *24*(4), 285–295. https://doi.org/10.1007/s11920-022-01336-1

van den Bree, M. B. M., & Pickworth, W. B. (2005). Risk factors predicting changes in marijuana involvement in teenagers. *Archives of General Psychiatry*, *62*(3), 311–319. https://doi.org/10.1001/archpsyc.62.3.311

Von Sydow, K., Lieb, R., Pfister, H., Höfler, M., & Wittchen, H.-U. (2002). What predicts incident use of cannabis and progression to abuse and dependence? *Drug and Alcohol Dependence*, *68*(1), 49–64. https://doi.org/10.1016/S0376-8716(02)00102-3

Zamarripa, C. A., Spindle, T. R., Surujunarain, R., Weerts, E. M., Bansal, S., Unadkat, J. D., … Vandrey, R. (2023). Assessment of Orally Administered Δ9-Tetrahydrocannabinol When Coadministered With Cannabidiol on Δ9-Tetrahydrocannabinol Pharmacokinetics and Pharmacodynamics in Healthy Adults: A Randomized Clinical Trial. *JAMA Network Open*, *6*(2), e2254752. https://doi.org/10.1001/jamanetworkopen.2022.54752