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# Marijuana Use in Adolescents and Early-Onset Psychosis CME/CE

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## CLINICAL CONTEXT

The public perception and availability of marijuana have undergone no less than a revolution during the past decade, with nearly 2 dozen states now permitting the use of medical marijuana and that number continually evolving. Colorado and Washington have taken the additional step of decriminalizing the personal use of marijuana. With these major changes comes serious concern regarding the potential impact of marijuana use on young people, with particular attention to its neurocognitive and neuropsychiatric effects. A previous study by Horwood and colleagues, which was published in the August 1, 2010, issue of *Drug and Alcohol Dependence*, combined data from more than 6000 adolescents in Australia and Asia to evaluate the impact of marijuana use on academic performance. Researchers found that the adjusted odds ratio for dropping out of high school among students who used marijuana by age 15 years was 5.6 compared with nonusers. However, weekly marijuana use at ages 16 to 18 years did not significantly affect this outcome. Cannabis use also had detrimental effects on the overall rates of university enrollment and university degree attainment, and this effect appeared to be more profound among young men. Overall, the researchers conclude that marijuana use may promote up to 17% of cases of failure to graduate from high school, attend college, and attain a degree.

Marijuana use poses another potential threat: psychosis. Previous studies have found a link between marijuana use and a higher risk for psychosis. Could the age of marijuana users affect this risk in a manner similar to the risk of dropping out of high school? The current study by Michael T. Compton, MD, and colleagues evaluates this issue. Their results were presented at the American Psychiatric Association (APA) 2014 Annual Meeting.

## STUDY SYNOPSIS AND PERSPECTIVE

Heavy marijuana use between the ages of 15 to 17 years, a period of potentially critical brain development, could result in an earlier age of onset of psychosis in those destined to develop the disorder, new research suggests.

Preliminary data from the Allied Cohort on the Early course of Schizophrenia (ACES) II project, a secondary analysis of ACES, showed that youth who used cannabis when aged 15 to 17 years experienced first-episode psychosis an average of almost 4 years earlier than their counterparts with first-episode psychosis who did not use cannabis.

Any delay in psychosis onset is important because this improves outcomes in the severity of symptoms and functional disability, study investigator Michael T. Compton, MD, chairman, Department of Psychiatry, Lennox Hill Hospital, New York City, and professor of psychiatry, Hofstra University North Shore—LIJ School of Medicine, Hempstead, New York, told delegates attending the APA 2014 Annual Meeting.

Predictors of age of onset of psychosis are male gender and a family history of psychosis, which are not modifiable, said Dr. Compton. "My question has been, does premorbid cannabis use also drive the age of onset?"

The analysis included 247 hospitalized patients who had experienced first-episode psychosis and who were generally treatment naive. Most study participants were single, male, and African American. Approximately 44% had not graduated from high school, and almost 60% had been incarcerated. More than half were living below the poverty line.

In the study cohort, the average age of prodromal symptoms was 19.4 years, age at onset of psychotic symptoms was 21.8 years, and age of hospitalization was 23.1 years.

Researchers asked each patient about marijuana use "in a very detailed way," going back to the first initiation of any use and up to the age of prodromal, psychosis, and first hospitalization, said Dr. Compton. Just fewer than 80% reported ever using marijuana.

The mean age of psychosis onset was 21.07 years in those with cannabis use from ages 15 to 17 years, compared

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with age 23.86 years in those with no cannabis use during that age period ( $P = .0005$ ). For ages 12 to 14 years, the age of psychosis onset was 21.10 years for cannabis users during this period compared with 22.12 for nonusers ( $P = .048$ ).

The relative risk for predicting age of onset of psychosis for cannabis users between ages 15 and 17 years was 1.84 compared with nonusers ( $P = .005$ ).

#### Dose-Dependent Effect?

Researchers also looked at the dose or the average number of marijuana cigarettes smoked per year and found that this was also a predictor of age of onset of psychosis for those using between ages 15 and 17 years. This was not the case with use after age 18 years, noted Dr. Compton.

Dr. Compton acknowledged that it is possible that the people who are likely to have an earlier onset of psychosis are also more likely—for whatever reason, which may be related to personality, social experience, or genetics—to use marijuana.

"That's something my study simply cannot determine definitively," he said. "We've identified what looks like a consistent association, but at the end of the day, it's an association, and there's no way for us to prove that one is causing the other."

#### Critical Period of Development

Teen use of marijuana might be particularly harmful.

"Our best understanding is that those years might be particularly important and impressionable with regard to factors that trigger the onset of a psychotic disorder among people who are destined to have a psychotic disorder," said Dr. Compton.

"There is something about marijuana use in late adolescence, and to some extent in early adolescence, based on our preliminary analysis, that brings forward the age at onset that might otherwise be a couple of years later."

This, he said, is important, because any delay in the onset of a first psychotic episode can improve outcomes.

"Anything we could possibly do that might delay the onset of psychotic disorders will hugely benefit the people who end up with these disorders because the age at onset is in large part what drives the level of social disability in these illnesses.

"If you begin hearing voices in your fourth year of college as opposed to in the tenth grade, you will have accomplished a whole lot more; for example, you would have already graduated from high school, which in and of itself is associated with better physical health, better mental health, and better social outcomes, over the course of the lifespan."

Dr. Compton wants to raise awareness, especially among those at an elevated risk for psychosis, that marijuana use in adolescence may not only increase the risk for schizophrenia, according to previous research, but may also cause an earlier onset among people who are going to get the disorder.

"If we could somehow delay the onset, even if it's just by on average a couple of months or even a couple of weeks — we would give young people a chance to accomplish more social and psychological milestones and therefore have a less severe illness."

#### Marijuana Use Increasing

There are "clues" as to whether a youngster is at risk that clinicians can pick up on, said Dr. Compton. "Let's say a child and adolescent psychiatrist is seeing a 17-year-old with what looks like anxiety symptoms. That 17-year-old is declining in school performance, and he's already at elevated risk because his mother has schizophrenia. In this case, we need in the clinical setting to assess for cannabis use and advise against it."

Is Dr. Compton worried about the impact of marijuana legalization on vulnerable youth?

"My view is that marijuana use is not good for young people, and it's not so much because of my research on psychosis, because psychosis is a rare event. The more important issues in terms of marijuana use in adolescence is that it's associated with poorer school performance, and even academic failure and school dropouts. Not completing education is a huge public health problem."

As well, he added, marijuana use in adolescence is associated with later marijuana addiction.

"Among adolescents, I have not seen evidence of any benefits of using marijuana."

Approximately 4% of the world's population use marijuana. Use is most prevalent among young adult men, those who are single or divorced, and whites.

Marijuana use is on the rise; from late 1990 to 2006, there was a 10% increase in global cannabis consumption, according to Dr. Compton. He added that use appears to be increasing among women.

In high school students, there has been a steady decline in cigarette and alcohol use since approximately 1975, but this is not the case for marijuana, said Dr. Compton. "If anything, the trend has been quite stable, if not increasing, in recent years."

Need for More Research

*Medscape Medical News* asked Jerome Taylor, MD, a resident in psychiatry at Yale University in New Haven, Connecticut, who moderated the APA session on marijuana use and psychosis, to comment on the findings.

Clinicians, said Dr. Taylor, often see the impact of marijuana use on psychotic disorders in their everyday clinical practices.

"The ACES research underscores this link," said Dr. Taylor. "I hope that clinicians will use this data to help patients recognize the risks associated with using marijuana. Explaining the link between marijuana and psychotic disorders is especially important for patients with a family history of schizophrenia and other psychotic disorders."

But despite the growing evidence of the relationship between marijuana and psychosis, further research is needed to determine causality, added Dr. Taylor.

*The study was funded by the National Institute of Mental Health. Dr. Compton and Dr. Taylor have disclosed no relevant financial relationships.*

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STUDY HIGHLIGHTS

- Researchers focused on 247 patients hospitalized for a first episode of psychosis. Most of these patients were treatment naïve.
- The majority of study patients were single, male, and African American. Nearly half had not graduated from high school, and nearly 60% had a history of incarceration. The rate of poverty in the study cohort exceeded 50%.
- The average age of prodromal symptoms of psychosis in the study cohort was 19.4 years. The mean onset of psychiatric symptoms was 21.8 years, and the average age at the time of hospitalization was 23.1 years.
- Researchers conducted a systematic assessment of marijuana use among study participants. The main research question was the association between marijuana use and the age of onset of psychosis. Researchers evaluated this question in terms of any use of marijuana and the quantity of marijuana use.
- Nearly 80% of the study cohort reported ever using marijuana.
- In comparing participants who used cannabis between ages 15 and 17 years vs nonusers during those ages, the respective average ages of onset of psychosis were 21.07 years and 23.86 years, a significant difference. The relative risk for earlier psychosis associated with the use of marijuana between ages 15 and 17 years was 1.84 ( $P < .005$ ).
- There was also a significant difference in the average age of onset of psychosis among marijuana users at ages 12 to 14 years (average age of onset: 21.1 years) compared with nonusers at these ages (average age of onset: 22.12 years).
- Higher numbers of marijuana joints smoked per day were associated with a significant reduction in the age of onset of psychosis among teens who used marijuana between ages 15 and 17 years, but not among users at age 18 years.
- The study researchers also conclude that despite accounting for multiple potential confounders, they cannot prove that smoking marijuana during adolescence directly causes earlier cases of psychosis.

CLINICAL IMPLICATIONS

- A previous study by Horwood and colleagues of more than 6000 adolescents found that marijuana use was associated with worse academic achievement, including a more than fivefold increase in the risk of dropping out of high school among students who used marijuana by age 15 years. Marijuana also affected university enrollment and graduation, particularly among boys.
- The current study by Compton and colleagues, results which were presented at the APA 2014 Annual Meeting, demonstrates that marijuana use during adolescence is associated with an earlier incidence of the first episode of psychosis. Heavier use of marijuana between ages 15 and 17 years appeared to promote psychosis earlier vs more limited exposure to marijuana.

CME TEST

To receive *AMA PRA Category 1 Credit™*, you must receive a minimum score of 75% on the post-test.

You are seeing a 15-year-old boy whose parents recently discovered that he has been smoking marijuana approximately twice per week during the past 4 months. According to the previous study by Horwood and colleagues, what can you tell this patient and his parents regarding the potential effects of marijuana use on his academic potential?

- Only marijuana use at age younger than 13 years promotes worse academic outcomes
- Marijuana use at age 15 years is associated with a higher risk of not completing high school
- Marijuana use at age 15 years is associated with failure to enroll in college but does not harm high school completion rates
- Marijuana use at age 15 years is associated with lack of college completion but does not harm rates of high school completion or college enrollment

According to the results of the current study by Compton and colleagues, what can you tell this family regarding marijuana use and the risk for psychosis?

- Marijuana use during adolescence may promote an earlier incidence of psychosis
- Marijuana use has no significant effect on the incidence of psychosis
- There is no dose-response effect in examining the relationship between marijuana use and psychosis
- Marijuana might cure psychosis

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