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**Summary** Factors associated with faster progression to both cannabis use opportunity and dependence are parental drug problems, conduct disorder and weekly tobacco use, all of which have different effect sizes for each transition. A number of factors are uniquely associated with the speed of these transitions.

## Background

- Cannabis commonly used, with lifetime use estimated to exceed 40%<sup>1</sup> in the US and lifetime prevalence of cannabis use in Australian adolescents estimated at 52-66%<sup>2</sup>.
- Opportunity to use is the "exposure" for drug dependence, regardless of whether the individual uses the drug<sup>3</sup>.
- Little is known about factors which correlate with earlier opportunity to use drugs or the overlap of these factors with those associated with faster transition to dependence.
- Exploring this has utility for improving understanding of how dependence develops<sup>4</sup>.

## Aims

Study aims to determine:

- What factors are associated with earlier opportunity to use cannabis or progression from cannabis use opportunity to cannabis dependence.
- Whether factors that are associated with opportunity to use cannabis are associated with more rapid progression to dependence.

## Results

- Factors associated with speed of progression to opportunity and dependence were conduct disorder (opportunity HR 5.57, 95%CI 1.52-20.47; dependence HR 3.46, 95%CI 1.70-7.05), parental drug problems (opportunity HR 7.29, 95%CI 1.74-30.62; dependence HR 4.08, 95%CI 1.99-8.35), weekly tobacco use (opportunity HR 8.57, 95%CI 3.93-18.68; dependence HR 3.58, 95% CI 2.71-4.72), and female gender (opportunity HR 0.69, 95%CI 0.64-0.75; dependence HR 0.43, 95%CI 0.34-0.55).
- Factors uniquely associated with transition to opportunity were frequent childhood religious attendance (HR 0.74, 95%CI 0.68-0.80), parental conflict (HR 1.09, 95%CI 1.00-1.18), parental alcohol problems (HR 1.19, 95%CI 1.08-1.30) and childhood sexual abuse (HR 1.17, 95%CI 1.01-1.34).
- Factors uniquely associated with progression to dependence were depressive episode (HR 1.40, 95%CI 1.09-1.80), tobacco dependence (HR 1.39, 95%CI 1.06 - 1.82), alcohol dependence (HR 2.81, 95%CI 1.62-4.85) and other drug dependence (HR 2.76, 95%CI 1.71-4.47).

## Discussion

- **Key findings:** The profile of speed of transition to cannabis opportunity to use and dependence partially overlaps, with evidence for unique contributions to each transition.
- **Limitations:** Data were based on retrospective self-report, which introduces the possibility of recall bias.
- **Interpretation:** Consideration of multiple stages of drug use from non-use to dependence allows identification of risk factors uniquely associated with specific transitions. The differences and consistencies in risk factors across the stages of drug use provide insight into what may be driving the progression from cannabis use opportunity to the development of dependence.
- **Implications:** The findings have implications for substance use prevention efforts, as both the targeting of intervention as well as the interventions themselves may benefit from being tailored for stages of drug use.

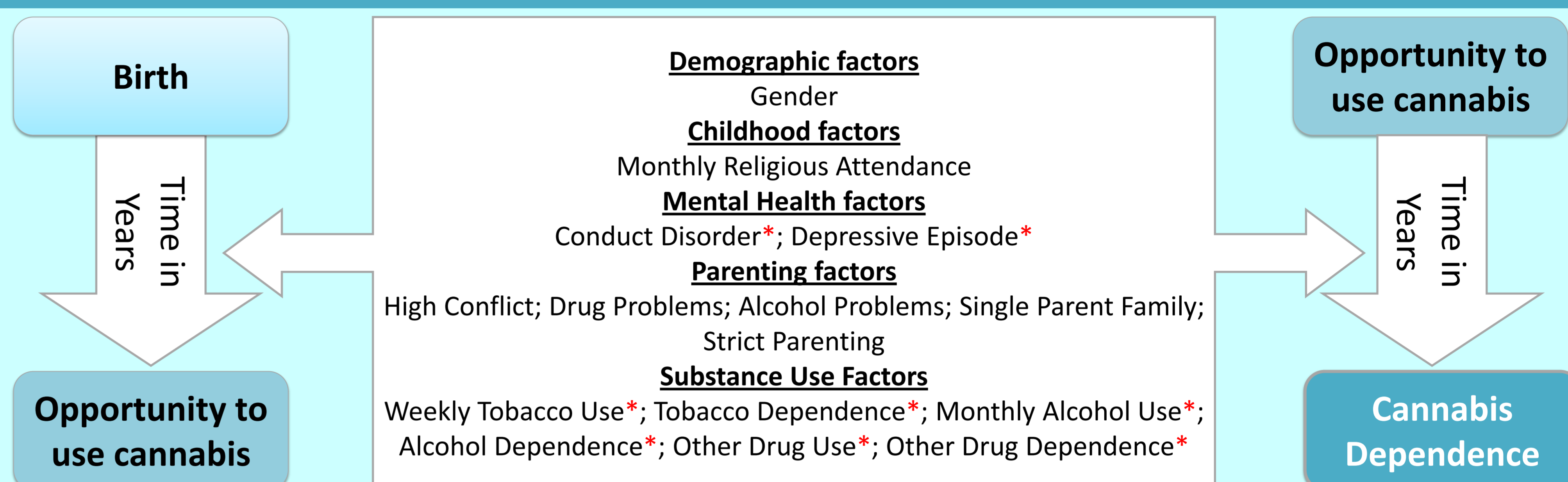


Figure 1. Diagram of the two Cox Proportional Hazard models reported in these results. Factors listed represents a complete list of factors included in the models. Variables marked with \* were modelled as time-varying covariates.

## Methods

- **Sample:** From a cross-sectional telephone interview study of 3824 Australian twins and siblings<sup>5</sup> (mean age at survey=31 SD=3), 3399 participants reported having cannabis use opportunity and 371 reported cannabis dependence.
- **Measures:** Participants were asked if they had been offered or had the opportunity to use cannabis (even if they didn't use it at the time), and how old they were the first time this occurred. Dependence and age of onset assessed in the SSAGA-II<sup>6</sup> using DSM-IV criteria.
- **Analysis:** Cox proportional hazard models were fitted to the data to test the association between (1) opportunity to use cannabis and (2) cannabis dependence and a number of potential associated factors (see Figure 1). Participants were right-censored at age of interview. Variables breaching the proportional hazards assumption had the interaction with analysis time included in the model.

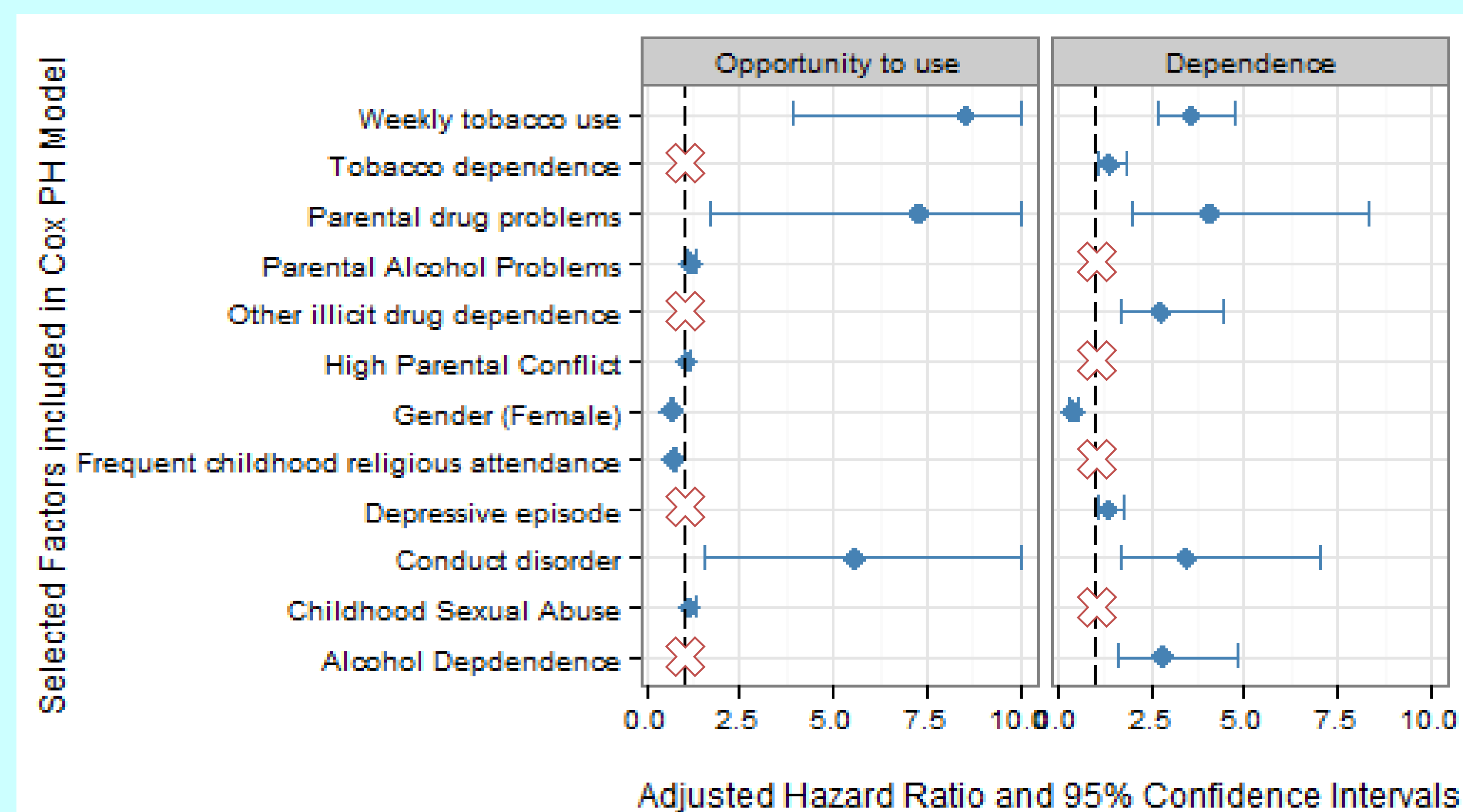


Figure 2. Hazard ratios and 95% confidence intervals for effect of each variable on hazard of cannabis use opportunity, and progression from cannabis use to dependence. All results controlled for the factors listed in Figure 1. Non-significant factors indicated by X. NOTE: Upper 95%CI for conduct disorder (20.47), parental drug problems (30.62) and weekly tobacco use (18.68) in the opportunity to use model were beyond the scale of the chart.

## References

1. Degenhardt, L., Chiu, W.-T., Sampson, N., Kessler, R.C., Anthony, J.C., Angermeyer, M., Bruffaerts, R., de Girolamo, G., Gureje, O., Huang, Y., Karam, A., Kostyuchenko, S., Lepine, J.P., Mora, M.E.M., Neumark, Y., Ormel, J.H., Pinto-Meza, A., Posada-Villa, J., Stein, D.J., Takeshima, T., Wells, J.E., 2008. Toward a Global View of Alcohol, Tobacco, Cannabis, and Cocaine Use: Findings from the WHO World Mental Health Surveys. *PLoS Med* 5, e141.
2. Patton, G.C., Coffey, C., Carlin, J.B., Degenhardt, L., Lynskey, M., Hall, W., 2002. Cannabis use and mental health in young people: cohort study. *BMJ* 325, 1195-1198.
3. Wagner, F.A., Anthony, J.C., 2002. Into the world of illegal drug use: Exposure opportunity and other mechanisms linking the use of alcohol, tobacco, marijuana, and cocaine. *J. Epidemiol.* 918-925.
4. Hines, L.A., Morley, K.I., Mackie, C., Lynskey, M., 2015a. Genetic and Environmental Interplay in Adolescent Substance Use Disorders. *Curr. Addict. Rep.* 2, 122-129.
5. Lynskey, M.T., Agrawal, A., Henders, A., Nelson, E.C., Madden, P.A.F., Martin, N.G., 2012. An Australian Twin Study of Cannabis and Other Illicit Drug Use and Misuse, and Other Psychopathology. *Twin Res. Hum. Genet.* 15, 631-641.
6. Buchholz, K.K., Cadoret, R., Cloninger, C.R., Dinwiddie, S.H., Hesselbrock, V.M., Nurnberger, J., Reich, T., Schmidt, I., Schuckit, M.A., 1994. A New, Semi-Structured Psychiatric Interview for Use in Genetic Linkage Studies: A Report on the Reliability of the SSAGA. *J. Stud. Alcohol Drugs* 55, 149.



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