Micro-dosing versus standard transfer for methadone-buprenorphine transfers - results from an open-label, non-randomised clinical trial

Chris Tremonti[1,2,9], James Blogg[2,8], Nazila Jamshidi[2,3], Ricky Harjanto[1,4], Nicholas Miles[5], Charlotte Ismay[6], Robert Page[1,7], Llew Mills[3,4,9], Nicholas Buckley[2,3,9], Varan Perananthan[2], Nicholas Lintzeris[3,7,9], Paul Haber[2,3,9]

1 St Vincent's Hospital, Darlinghurst NSW, Australia
2 RPA Hospital, Camperdown NSW, Australia
3 Sydney University, Camperdown NSW, Australia
4 South Western Sydney Local Health District, Liverpool NSW, Australia
5 Northern Sydney Local Health District, St Leonard's NSW, Australia
6 Hunter New England Local Health District, New Lambton NSW, Australia
7 South Eastern Sydney Local Health District, Randwick NSW, Australia
8 Southern NSW Local Health District, Goulburn NSW, Australia
9 NSW Drug and Alcohol Clinical Research and Improvement Network (DACRIN), NSW, Australia

Presenter's email: *chris.tremonti@health.nsw.gov.au*

Introduction: *To compare micro-dosing against standard practice for methadone-buprenorphine transfers.*

Methods: *A non-randomised open-label clinical trial comparing a one-week micro-dosing protocol against standard NSW health guidelines for people wishing to transfer from methadone to buprenorphine. Recruitment occurred across eight sites from NSW. The primary outcome was maintenance on buprenorphine one week post final dose of methadone in the micro-dose arm, and one week post first dose of buprenorphine in the standard transfer arm. Secondary outcomes included retention on buprenorphine at four weeks, rates of precipitated withdrawal, rates of moderate withdrawal defined by COWS, and use of rescue medication to relieve withdrawal symptoms. Logistic regression was used to assess each outcome with demographic differences between the groups included as covariates.*

Results: *There were 101 participants in the micro-dose arm against 16 in standard transfer. There were between-arm differences in mean methadone dose (82mg micro-dose arm against 46mg in standard transfer), methadone trough, time on methadone, alcohol use and benzodiazepine use that were included in the regression analysis. The rate of completed transfer was similar between the two arms – 81% in micro-dose against 80% in standard transfer - with no significant difference in odds (OR=2.22; 95%CI: 0.45,10.91; p=0.327). Higher methadone dose decreased odds of successful transfer by 20% (OR=0.8 per 10mg methadone; 95%CI: 0.7,0.99; p=0.04). Neither treatment arm nor methadone dose was associated with significantly different odds of a participant remaining on buprenorphine at four weeks, odds of precipitated withdrawal (4% in micro-dose versus 6% in standard transfer) or participant experiencing moderate withdrawal. Clonidine use was higher in the micro-dose arm (Estimate=526.26mcg; CI: 267.70,784.81; p<0.001).*

Conclusions: *Similar rates of completed transfer between micro-dose and standard transfer for methadone-buprenorphine transfers. Increasing methadone dose decreased odds of transfer. Rates of precipitated and moderate withdrawal were similar. Clonidine use was higher in micro-dose transfers.*

Implications for Practice: *Micro-dosing is a potential option for patients if they wish to switch from methadone to buprenorphine. The maximum methadone dose for transfers between methadone and buprenorphine is still unknown, but success appears to reduce with increasing dose. Clinicians should plan for expected withdrawal with appropriate rescue medications.*

No pharmaceutical grants were received in the development of this study.