Largest review of clinical trials to assess risk of patients using Champix

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Findings from the largest review of clinical trials to date to determine whether patients prescribed the smoking cessation drug Varenicline (brand name Champix in the UK) are at an increased risk of neuropsychiatric events are published online in the *British Medical Journal* (*BMJ*) today. The study was carried out by researchers at the University of Bristol.

The drug, which was first licensed in the UK in 2006, has been shown to be the most clinically effective smoking cessation medicine for reducing nicotine cravings and withdrawal symptoms for short-term abstinence.

However, since its introduction there have been concerns over its neuropsychiatric safety following reports of adverse reactions to spontaneous reporting systems. These were reiterated in October 2014 when the US Food and Drug Administration (FDA) decided to keep the black box warning for Varenicline, the agency's strongest safety warning.

A team of researchers, led by Dr Kyla Thomas at the University of Bristol, carried out the first comprehensive published systematic review and meta-analysis to date on the neuropsychiatric effects associated with Varenicline use. Using results from 39 Varenicline studies the team identified a cohort of 10,761 participants that compared the effects of 5,817 patients who had received the maximum dose of 1mg of the drug twice daily and 4,944 patients who had received a placebo.

The findings showed no evidence of an increased risk of suicidal behavior, depression or death in Varenicline users compared with those in placebo groups. Nor did the results show evidence for a variation in depression and suicidal behaviour by age group, sex, ethnicity, smoking status, or presence or absence of psychiatric illness. The drug was found to be associated with an increased risk of sleep disorders including insomnia and abnormal dreams although these side effects are already well recognised and included in patient information leaflets.

In addition, the results showed a 25 per cent reduction in the risk of anxiety although this is likely to be explained by the positive impact of giving up smoking on mental health. Previous research has shown that smokers who quit have a reduction in depression and anxiety compared with those who continue to smoke.

Dr Kyla Thomas, a National Institute for Health Research (NIHR) Clinical Lecturer in Public Health based at Bristol's School of Social and Community Medicine, said: "This study represents the most comprehensive evaluation of adverse effects associated with Varenicline

use to date and provides reassurance for both users and prescribers of this medicine.

"Smoking related illnesses cost the NHS approximately £5 billion annually. Ongoing fears regarding Varenicline's safety among prescribers and patients may be reflected in the 25 per cent decrease in prescriptions observed between 2011 and 2013. Findings from this study show that the benefits of using Varenicline to give up smoking outweigh the yet unproven risks of suicidal behavior. Therefore, the reduction in prescribing Varenicline should be as much a cause for concern to clinicians, regulatory agencies and policy makers as the unfounded fears regarding the drug's association with suicidal behaviour."

More information: 'Risk of neuropsychiatric adverse events associated with varenicline: systematic review and meta-analysis' by Kyla Thomas et al in the *BMJ*.

Provided by University of Bristol