Specialists challenge claim that fluoxetine plus talk therapy works best for depressed adolescents

Jeanne Lenzer *New York*

A US study of clinically depressed adolescents, showing that a combination of fluoxetine (Prozac) and cognitive behaviour therapy (CBT) works best, has sparked concerns over the interpretation of the data.

The multicentre trial randomised 439 depressed adolescents aged 12-17 years to four arms: fluoxetine alone, CBT alone, CBT plus fluoxetine, or placebo. The results showed that at 12 weeks, 71% of those treated with CBT plus fluoxetine had improved, compared with just over 60% of those taking fluoxetine alone, 43% treated with CBT alone, and 35% taking placebo alone (*JAMA* 2004;292:807-20).

Fluoxetine is the only anti-

depressant in its class to be approved by the US Food and Drug Administration for depression in adolescents.

Dr Thomas Insel, director of the National Institute of Mental Health, which sponsored the \$17m (£9.5m; €14m) research, described it as a "landmark study" because "it's the largest publicly funded study and the only study this size that doesn't have pharmaceutical funding." But six of the 11 authors, including the lead author, John March, have received funding from Eli Lilly, the manufacturer of fluoxetine.

Dr March, from Duke University Medical Center, Durham, North Carolina, said that between 1 in 20 and 1 in 40 US

adolescents developed severe depression. "In some cases it's fatal. Now that we can identify it and treat it, it seems common sense that you ought to provide the resources to [do so]," he said. He stood by the authors' recommendation for mandatory screening and treatment of depressed adolescents and for fluoxetine to "be made widely available, not discouraged."

But the study fails to blind two of the four study arms—those which included CBT alone and CBT plus fluoxetine—which raises questions about the validity of the research, says Dr Michael Wilkes, director of adolescent medicine at the University of California at Davis: "Most methodologists would say combining blinded and unblinded arms is less than ideal. You can't mix apples and oranges and have confidence in the results."

Critics say the authors focused on only one of the study's two primary end point scales—the one with the positive result. The other

primary end point showed that fluoxetine performed no better than placebo.

Harmful behaviour, including suicidal tendencies, was twice as high in adolescents taking fluoxetine (12%) as it was in those receiving placebo (5%).

Concerns about the authors' interpretation of the data have prompted Professor David Antonuccio of the department of psychiatry and behavioural sciences at the University of Nevada School of Medicine to request the raw data under the terms of the Freedom of Information Act.

"The authors' value judgment is that the benefit of a few extra improved patients is worth the cost of a few extra harmed patients," said Professor Antonuccio. "My own risk-benefit analysis leads me to a different conclusion." He suggested that CBT alone, or exercise, should be offered as the first line treatment because of the lower risk of side effects. □

Air conditioned buildings increase risk of sickness

Roger Dobson *Abergavenny*

Women who work in air conditioned offices are more than twice as likely to see an ear, nose, and throat specialist says new research.

The research, based on nearly 1000 women in France, shows that those who worked in buildings with air conditioning systems also had more sickness absence.

"Exposure to [these] systems was a strong and significant risk factor for otorhinolaryngologist attendance and sickness absence," says a report of the research in the *International Journal of Epidemiology* (2004;33:1-4).

The authors say that air conditioning systems are increasingly common in the workplace and that, although they are energy efficient, they have also been implicated in several building related illnesses, including sick building syndrome, whose symptoms can include eye, skin, and upper airway irritation, as

well as headache and fatigue.

"Many studies have considered possible causes and preventive measures for sick building syndrome, yet no attempt has been made to assess the overall health effects and economic impact of air conditioning use in professional buildings. This work is, to our knowledge, the first description of a link between ventilation type and healthcare indicators," wrote the authors, from the French Institute of Health and Medical Research and the Claude Bernard Hospital, Paris.

The researchers investigated the relation between ventilation in the workplace, use of health services, and sickness absence in a nationwide sample of 920 professionally active women aged 49-65 years who had been recruited in France for another study. The results show 15% of the women worked in buildings with air conditioning systems.

The authors then compared the health service use and absence records of the women whose offices were air conditioned with the use and records of those whose offices had natural ventilation.

The women who worked in air conditioned offices were 2.3 times more likely (odds ratio 2.33 (95% confidence interval 1.35 to

4.04)) to consult an otorhinolaryngologist than the women who worked in buildings with natural ventilation, and the likelihood of sickness absence was 1.7 times higher in the women working with air conditioning.

They added, "In temperate areas, characterised by mild winters and cool summers, the

benefits yielded by such systems' energy efficiency and alleged productivity gains might be outweighed by losses resulting from sickness absence and sick building symptom-related discomfort. In more varied climates, these results could stimulate research into ventilation-related health." □

Modern office blocks may look good on the outside, but for workers the inside story can be one of ill health