et al's reasons for rejecting the three-factor solution was that their third factor comprised heterogeneous items loading for both anxiety (items 7 and 11) and depression (item 14). Our three-factor structure discriminates the original depression factor and two separate constructs of anxiety: 'psychic anxiety' (items 3, 5, 9 and 13) and 'psychomotor agitation' (items 1, 7 and 11). This factor solution captured 48.6% of the variance and was relatively robust; it was not influenced by gender ratio and was also found in two random halves.

Two reasons may account for these discrepancies between our results. First, because of the high proportion of HAD scale non-completers (44%), Mykletun *et al*'s sample may have been biased. Patients with depression are probably not prone to answer such surveys and may therefore be underrepresented. Second, the factor structure of the HAD scale may not be stable across different categories of subjects: those with heterogeneous mental problems and those specifically suffering from major depression.

The HAD scale is not only useful for its initial screening purpose. It also showed potential ability in assessing change in specific symptoms of anxiety ('psychic anxiety' and 'psychomotor agitation' factors of the scale) during antidepressant treatment (Friedman *et al*, 2001). Moreover, recognition and monitoring of psychomotor agitation has several clinical implications: it is a potential side-effect of some antidepressants (Nutt, 1999), it may predict antidepressant response (Flament *et al*, 1999), it may predict adverse outcome and increase the risk of suicide (Schatzberg & DeBattista, 1999).

Declaration of interest

S.F. has formerly been CNS medical adviser for Pfizer France; J-C.S. has received fees from Pfizer France; J.D.G. has received fees from several pharmaceutical companies.

Flament, M. F., Lane, R. M., Zhu, R., *et al* (1999) Predictors of an acute antidepressant response to fluoxetine and sertraline. *International Clinical Psychopharmacology*, **14**, 259–275.

Friedman, S., Samuelian, J. C., Lancrenon, S., *et al* (2001) Three-dimensional structure of the Hospital Anxiety and Depression Scale in a large French primary care population suffering from major depression. *Psychiatry Research*, **104**, 247–257.

Mykletun, A., Stordal, E. & Dahl, A. A. (2001) Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *British Journal of Psychiatry*, **179**, 540–544.

Nutt, D. J. (1999) Care of depressed patients with anxiety symptoms. *Journal of Clinical Psychiatry*, **60** (suppl. 17), S23–S27.

Schatzberg, A. F. & DeBattista, C. (1999) Phenomenology and treatment of agitation. *Journal of Clinical Psychiatry*, **60** (suppl. 15), S17–S20.

S. Friedman, C. Even Clinique des Maladies Mentales et de l'Encéphale (CMME), Centre Hospitalier Sainte-Anne, 1 rue Cabanis, 75674 Paris Cedex 14, France

J.-C. Samuelian CMU de la Timane, Aix Marseille II, France

J. D. Guelfi CMME, Centre Hospitalier Sainte-Anne, Paris, France

Authors' reply: Friedman *et al* raise doubts as to the two-factor structure of the HAD scale reported by us. The size of our sample (n=51 930) allowed us to test our finding in several sub-samples. Using principal-components analysis, the same two-factor solution was also found in all sub-samples reporting somatic and psychiatric problems, as well as in all age- and gender-groups from 20 to 89 years. This indicates that the two-factor structure of the HAD scale is robust and stable. Therefore, eventual minor biases due to response rates cannot account for the discrepancy between Friedman *et al*'s and our findings. Our third factor, which emerged only in sub-samples with low depression scores, always showed a low eigenvalue. Our results are in accordance with the conclusions of a recent literature review on the HAD scale (Bjelland *et al*, 2002) which concludes that a two-factor solution is most commonly found.

Friedman *et al* (2001) have a sample (n=2669) characterised by major depression (DSM–IV), which corresponds to high depression and probably variable anxiety scores on the HAD scale. When performing factor analysis, composition of the sample is essential for the results. If an inclusion criterion restricts the variance and covariance of the variables entered in the factor analysis, this will influence the factor solution found. The results by Friedman *et al* can be interpreted as a consequence of their restriction of their sample to major depression only, as this restricts the covariance between items on the HAD scale. In our sub-sample with *various* mental problems (n=2098) the two-factor solution is robust with high explained variance (82.1%).

Friedman *et al*'s findings are of interest, however, since they answer the question: What is the factor structure of the HAD scale when anxiety appears in major depression? Comparing the fit coefficients between two- and three-factor solutions using confirmatory factor analysis must show the advantage of a three-factor solution. Friedman *et al* seem to presume that the factor structure of anxiety found in major depression is identical to that found for anxiety in the general population.

The advantage of population samples is that selection bias is minimised. In several of our studies based on the unselected HUNT-II population (from the Nord-Trøndelag Health Study) we have found results at variance with those of clinical samples (Engum *et al*, 2002; Wenzel *et al*, 2002). This could also explain the discrepancy between Friedman *et al*'s and our results.

Bjelland, I., Dahl, A. A., Haug, T. T., *et al* (2002) The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *Journal of Psychosomatic Research*, **52**, 69–77.

Engum, A., Bjøro, T., Dahl, A. A., *et al* (2002) An association between depression, anxiety and thyroid function – a clinical fact or an artefact? *Acta Psychiatrica Scandinavica*, in press.

Friedman, S., Samuelian, J.-C., Lancrenon, S., *et al* (2001) Three-dimensional structure of the Hospital Anxiety and Depression Scale in a large French primary care population suffering from major depression. *Psychiatry Research*, **104**, 247–257.

Wenzel, H. G., Haug, T. T., Mykletun, A., *et al* (2002) A population study of anxiety and depression among persons who report whiplash traumas. *Journal of Psychosomatic Research*, in press.

A. A. Dahl, A. Mykletun, E. Stordal
Department of Psychiatry, Aker University Hospital, N-0320 Oslo, Norway

Follow-up of childhood depression: historical factors

The study by Fombonne *et al* (2001), following adolescents with diagnoses of major depressive disorder into adulthood, raises some questions pertaining to the era when they were diagnosed (1970–1983).

First, it was only in the early 1980s that child abuse began to come into the awareness of professionals and, a few years later, the general public. Therefore, it is possible that some of the young people identified with depressive disorders may have had a history of sexual abuse which was not disclosed or enquired about. This raises the question of what would have been the outcome in those young people who had been sexually abused had they made disclosures and had appropriate therapeutic intervention for this. It is well known that

https://doi.org/10.1192/bjp.181.2.166 Published online by Cambridge University Press

childhood sexual abuse is a significant factor in the histories of some adults presenting with depressive syndromes.

Second, this period was also a time when attention-deficit hyperactivity disorder (ADHD) was not recognised and hyperkinetic disorder was only rarely diagnosed. Some of the young people, especially those in the comorbid conduct disorder/major depressive disorder group, may have had undiagnosed and untreated ADHD. Certainly this was long before the use of psychostimulants on a wider basis in the UK and it is possible that some of these young people untreated may have been more vulnerable to development of depressive syndromes because of untreated attentional and other behavioural problems impacting on their self-esteem.

Third, although antidepressants were in use by child and adolescent psychiatrists when the diagnosis was major depressive disorder, they may not always have been used in young people with major depressive disorder with comorbid conduct disorder because of the risks of overdose in such a population. Tricyclic antidepressants were the predominant antidepressants used at that time in this population. With the advent of selective serotonin reuptake inhibitors, child and adolescent psychiatrists probably began prescribing more antidepressants in the comorbid conduct disorder/major depressive group because of the lower risk of serious harm in overdose. This raises the possibility that more effective treatment of these young people might also have an impact on their outcomes in adult life.

Fombonne, E., Wostear, G., Cooper, V., *et al* (2001) The Maudsley long-term follow-up of child and adolescent depression. 1. Psychiatric outcomes in adulthood. *British Journal of Psychiatry*, **179**, 210–217.

J. Hynes, N. McCune Child and Family Clinic, Bocombra Lodge, 2 Old Lurgan Road, Portadown BT63 5SG, UK

Author's reply: The comments of Hynes & McCune raise pertinent questions. As they point out, it is possible that sexual abuse in childhood might have influenced the onset of juvenile depression, and also the likelihood of adult depression recurrence in our sample. In this study, we have collected data on sexual abuse, using both a review of medical charts at the time of Maudsley attendance and from adult interviews based on the Childhood Experience of Care and Abuse (CECA) measure. The effect of sexual abuse in childhood on patterns of adult depression recurrence will be investigated in the next analyses of this data-set, with particular attention given to differential risk processes according to childhood comorbidity.

Regarding comorbid ADHD as a risk factor for adolescent depression, particularly in the depression group with comorbid conduct disorder, we found a significantly increased rate of ADHD in the comorbid group, as we reported (Fombonne *et al*, 2001*a*, Table 2). Yet, it is plausible that the rate of ADHD in this sample was underestimated as many cases were ascertained before ADHD or hyperkinetic disorders were fully recognised as valid diagnostic entities. Nevertheless, our findings suggest that it is possible that ADHD might have been implicated in the development of conduct symptoms in the comorbid group although, because of the small sample size and likely underestimation of ADHD in that group, we cannot test for the specific contribution of (untreated) ADHD in the onset and recurrence of depression.

We had provided explicit data on the use of tricyclic antidepressant drugs during childhood years and found that the rate of prescriptions of these drugs was significantly higher in the non-comorbid group than do the comorbid group (48.4% *v.* 30.2%, $P=0.032$; see Fombonne *et al*, 2001*a*). Most of these prescriptions were for amitriptyline and relied on dosages much lower than those considered appropriate by today's standards. Although the rate of antidepressant use was lower in the comorbid group, antidepressants were nevertheless often prescribed in that group too. Obviously, we could not assess whether or not use of tricyclic medications in that sample influenced long-term outcomes, since our study relied on an observational design. The interesting aspect of these data was to point to the frequent use by practising child psychiatrists of antidepressant drugs (irrespective of their known efficacy) in this sample of youths with depression assessed in the 1970s at a time when child and adolescent depression was largely ignored in professional training and in the literature. Furthermore, the data indirectly validated our diagnostic procedures.

Most of the comments by Hynes & McCune raise questions about the mechanisms underlying recurrence of depression in adulthood following a first episode in childhood or adolescence. The findings of our study (Fombonne *et al*, 2001*a*,*b*) indicated that relapse rates were similar, irrespective of the presence of comorbid conduct disorder in childhood. This result is important in its own right as it refutes previous hypotheses that depression, when occurring in the context of conduct disturbances, reflected mostly local psychosocial circumstances and was not associated with long-term heightened risk of affective disorders in adulthood.

This study was designed to assess mechanisms underlying recurrence of depression in adult life and further reports will address the role of early childhood experiences (such as sexual abuse), life events, family history and individual psychological characteristics on the patterns of adult depressive recurrence. It could well be that, in spite of having similar rates of relapse in adulthood, the mechanisms of depressive recurrence differ for the two groups included in this study, according to childhood comorbidity.

Fombonne, E., Wostear, G., Cooper, V., *et al* (2001*a*) The Maudsley long-term follow-up of child and adolescent depression. 1. Psychiatric outcomes in adulthood. *British Journal of Psychiatry*, **179**, 210–217.

—, —, —, *et al* (2001*b*) The Maudsley long-term follow-up of child and adolescent depression. 2. Suicidality, criminality and social dysfunction in adulthood. *British Journal of Psychiatry*, **179**, 218–223.

E. Fombonne McGill University, Department of Psychiatry, Montreal Children's Hospital, 4018 Ste-Catherine West, Montreal H3Z IP2, Canada

Genetics of Down's syndrome and Alzheimer's disease

In an extremely interesting article which touched upon early-onset dementia I feel that Dr Holmes (2002) failed to mention Down's syndrome as being a particular risk factor for the development of early-onset Alzheimer's disease because of triplication of the amyloid precursor gene. It is well known that almost all adults over the age of 40 years with Down's syndrome display Alzheimer's neuropathology (Mann, 1988) and the prevalence of dementia in people with Down's syndrome is 0–4% under the age of 30 years rising to 29–75% at 60–65 years of age, which falls under the category of early-onset Alzheimer's disease (Zigman

https://doi.org/10.1192/bjp.181.2.166 Published online by Cambridge University Press