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Prescribing of unlicensed medicines or licensed medicines for unlicensed applications in child and adolescent psychiatry

AIMS AND METHOD
Child and adolescent mental health services in north-west England (*n*=21) participated in a prospective collection of information regarding all instances of new prescribing of medication over the 6-month period September 1999 to February 2000.

RESULTS
A total of 478 new prescriptions were issued to 411 individuals. Eight prescriptions (2%) were for an unlicensed drug and a further 188 (39%) were of licensed drugs but used in a manner outside of their product licence.

CLINICAL IMPLICATIONS
This level of unlicensed and outside-licence prescribing is similar to levels previously found in studies both within paediatric practice and in adult mental health practice. Anxiety about excessive beyond-licence prescribing by child mental health services is unlikely to be justified.

Effective use of pharmacological treatments is one of the essentials in the child psychiatrist's clinical practice. There is, however, a relative lack of robust research evidence of either efficacy or safety for much of the prescribing of drugs to children and this is reflected in the terms of their product licences. This lack of an age-specific evidence base is of concern to medical and non-medical professionals working with children, parents, the children themselves and politicians (Sutcliffe, 1999; Choonara, 2000). Studies of prescribing patterns within paediatric practice in Europe and within child mental health practice in the US have shown significant levels of prescribing of medication beyond the manufacturer's licence indications for the drug (Conroy *et al*, 2000; Jensen *et al*, 1999). Lowe-Ponsford and Baldwin (2000) reported that 76 out of 200 psychiatrists (of all sub-specialities) in their region had prescribed outside of a drug's product licence within the preceding month. Low numbers did not enable them formally to report differences between the sub-specialities although they do state that most of this prescribing was by adult and old age psychiatrists. Although there have been a number of surveys in the UK of the prescribing practices of child and adolescent psychiatrists, the extent of prescribing unlicensed drugs or prescribing licensed drugs outside of their product licence in treatment of child mental health problems has not previously been systematically studied.

Method

All 21 child and adolescent mental health services (CAMHS) within the Greater Manchester and Lancashire zones of the North Western region of England agreed to participate in a prospective study of all new instances of prescribing occurring during the period 1 September 1999 to 29 February 2000. On each occasion of starting a child or young person on a new medication (or of requesting the general practitioner to do so) the prescribing clinician recorded on a specially designed form (available from authors upon request) the age of the child receiving the medication, the drug prescribed, the maximal dosage reached and the condition being treated. Hospital pharmacists and clinical audit staff were also involved in checking the forms received against their own records in order to ensure the fullest possible ascertainment of cases of new prescribing at each site. Each prescription was then checked against the product licence information in both the *British National Formulary* (*BNF*) (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2000) and the Association of the British Pharmaceutical Industry (ABPI) *Compendium of Datasheets* (ABPI, 1999).

Results

In the 6-month period 478 new prescriptions were initiated to 411 different children. Eight (2%) of these prescriptions were on an unlicensed basis. Each of these

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was for melatonin in severe sleep disturbance, a drug not covered in either the *BNF* or the *ABPI Compendium*, leaving 470 (98%) prescriptions for further analysis regarding possible outside-licence usage. Eighty of these (17% of all prescriptions) were used in an age group outside of the product licence (e.g. methylphenidate in a child under 6 years) and 390 (82% of the 478) in an age group within licence. Of those prescriptions made beyond licence for age, 49 (10% of the 478) were for otherwise licensed indications (e.g. fluoxetine in treatment of depressive disorder in a child under 12 years) and 31 (6% of the 478) were also beyond licence for use in the condition being treated. As product licence dosage limits are highly age (and weight) dependent, these groupings were not broken down further by dosage.

Of the 390 prescriptions made within licensed age limits, 284 (59% of the 478) were for a licensed indication and 106 (22% of the 478) for an indication not covered by the product licence (e.g. risperidone for obsessive–compulsive disorder). Of those beyond licence prescriptions, 84 (18% of the 478) reached a maximal dosage that would have been within dosage limits for a licensed indication, five (1% of the 478) a maximal dosage that would have also been outside dosage limits for any of its licensed indications and in 17 cases (4% of the 478) the maximal dosage was missing. Of those drugs used within age and indication licence limits, the maximal dosages of 2 (0%) were outwith product licence dosage limits, 235 (49% of the 478) were within dosage limits and in 47 (10% of the 478) instances the maximal dosage was missing.

Discussion

Dependent upon the maximal dosages actually prescribed in the 47 cases where full data were missing and the prescription was otherwise within licence, somewhere between 196 (n=478; 41%) and 243 (n=478; 51%) prescriptions were of unlicensed medicines or licensed medicines for unlicensed applications. Although this study was undertaken within a defined geographical area, all the CAMHS within it participated and there is no reason to suppose that practice in north-west England differs markedly from elsewhere within the British Isles. It is also strikingly similar to the 46% found in general paediatric practice across five European centres, albeit that this focused solely upon prescribing for hospital in-patients (Conroy *et al*, 2000).

In some instances good research evidence from an age-specific randomised controlled trial may exist for the use of medication in a manner beyond its product licence (e.g. use of fluoxetine in the treatment of depression in childhood (Emslie *et al*, 1997)) and this apparent contradiction does need careful explanation to children and parents. In many instances, however, the evidence is extrapolated from the results of randomised controlled trials in adults or is founded upon open studies, anecdote and clinical practice. These findings do emphasise the need for better age-specific research evidence of both the safety and the efficacy of psychotropic drugs to underpin delivery of safe and effective treatments to children and adolescents (Choonara, 2000).

Prescribing outwith a product's licence often generates considerable concern in the mind of the prescriber, the employing trust, the child and the family. Lowe-Ponsford and Baldwin (2000) therefore additionally advocate use of their guideline in all cases where any unlicensed or outside-licence prescribing is considered necessary. However, this may be unduly defensive for child psychiatric practice in the light of the policy statement of the Royal College of Paediatrics and Child Health (2000) on the use of unlicensed medicines or licensed medicines for unlicensed applications. This states that "the informed use of some unlicensed medicines or licensed medicines for unlicensed applications is necessary in paediatric practice" and that "in general it is not necessary to take additional steps, beyond those taken when prescribing licensed medicines, to obtain the consents of parents, carers and child patients to prescribe or administer unlicensed medicines or licensed medicines for unlicensed applications".

None the less there is a need for all those prescribing to children (including the general psychiatrist, who may on occasion be called upon for advice in the acute management of a psychiatric emergency in a child (Royal College of Psychiatrists, 2000)) to ensure that their personal development plans include an adequate emphasis upon child psychopharmacology. This needs to be recognised and supported by employing trusts, who will also need to ensure that their risk management and clinical governance strategies do include consideration of issues related to beyond-licence prescribing.

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