

recommendations on active ingredient, dose units, or formulations for a specific age group—for example, quinolones in children and xylometazoline 1% formulations for babies.

The proportion of off label prescriptions was highest for 1-2 year olds (68 791 (17.9%, 17.8% to 18.1%) prescriptions) and lowest for 7-11 year olds (40 539 (10.5%, 10.4% to 10.6%) prescriptions).

Of the 181 914 (8.8%) prescriptions for topical treatments of the skin, eye, or ear, 116 060 (63.8%, 63.6% to 64.0%) were off label. The active ingredients of the most commonly prescribed systemic off label drugs are shown in the table.

Off label prescribing was common for cardiovascular drugs (3646; 55.2%, 53.9% to 56.4%), drugs for genitourinary disorders (1869; 48.5%, 46.9% to 50.1%), anti-inflammatory agents (7194; 45.0%, 45.2% to 46.0%), antidepressants (246; 36.6%, 33.0% to 40.4%), and antiepileptics (11; 34.4%, 18.6% to 53.2%), antiepileptic (932; 14.2%, 13.3% to 15.0%), and antipsychotic drugs (54; 10.2%, 7.8% to 13.2%).

Comment

We found that 13.2% of prescriptions for a representative group of children in primary care in Germany were off label. Although we could not detect off label use due to dosage or indication with this database, the proportion of prescriptions that were off label was similar to that in much smaller studies that analysed dosage and diagnoses.^{4 5} Our data show that efforts to

improve the quality of pharmacotherapy in children should not exclude widely marketed and firmly established drugs.

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Contributors: MS, KM, and CG designed the study. PS provided access to Allgemeine Ortskrankenkasse, Baden-Württemberg, and gave information concerning drug prescription patterns in outpatients. HS matched the file with prescription data to another database including the anatomical, therapeutic, and chemical classification of the World Health Organization. BK and HM provided computer based analyses. RB designed the study, coordinated study procedures, determined licence status of prescriptions, analysed the results, and wrote the paper. CG is guarantor.

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Unlicensed and off label drug use by children in the community: cross sectional study

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Studies in various hospital settings showed that many drugs taken by children either are not licensed or are used outside the terms of the product licence.¹⁻³ Information on the extent of paediatric labelling of drugs taken by children in the community is, however, limited and based on small study populations.^{4 5} We studied drugs taken by children in the community, based on the pharmacy records of prescriptions from both general practitioners and outpatient departments. We aimed to determine the number of prescriptions for unlicensed drugs for children in the community and to investigate paediatric labelling of all drugs with a product licence to determine the extent of off label use.

Participants, methods, and results

In the Netherlands people commonly register with one pharmacy, from which they obtain their drugs, including those prescribed as outpatients. Excluded are drugs used during hospital stays and those bought over the counter. We obtained our data on dispensing from the InterAction database, which covers part of the northern Netherlands.

We selected all prescriptions for children aged 0-16 years in 2000. Dutch pharmacies are allowed to

prepare their own formulations and to modify commercial preparations. These pharmacy based preparations are exempt from licensing, and we classified them as unlicensed. For each prescription of a licensed drug (all remaining prescriptions) we examined the official licence information—the summary of product characteristics—in detail. We determined whether the summary mentioned use in children and, if so, the minimum age. When age was unspecified we set it at a minimum of 0 years. If use in children was not mentioned or was advised against without an indication of age, we set the minimum age at 18 years. We considered that a drug with a product licence was used according to the label if the summary of product characteristics stated that it could be used in children, and if the child was of the minimum age for use or older; otherwise we considered the drug was used off label. As information about indications was not available, we were not able to distinguish between different indications in the summary.

We analysed 68 019 prescriptions for 19 283 children aged 0-16 years. General practitioners were responsible for 56 961 (83.7%) of the prescriptions; the remainder came from specialists. Unlicensed drugs amounted to 16.6% (11 288) of the total pre-

Information given in summary of product characteristics of drugs prescribed to children in the community in the Netherlands

Category	Example	No (%) of summaries (n=1421)	No (%) of prescriptions (n=56 731)
Child mentioned with indication of age	Children 2-5 years: 10 mg per day	653 (46.0)	32 180 (56.7)
Child not mentioned	Only "patients" in general mentioned	302 (21.3)	11 688 (20.6)
Child mentioned without indication of age	Children: 0.75 mg/kg in twice daily	280 (19.7)	11 108 (19.6)
Child mentioned but advised against use for all ages	Should not be used in children; safety and efficacy have not been established in children	140 (1.0)	1 328 (2.3)
Child mentioned and age estimated on basis of description	Adults and older children: 10 mg per day	19 (1.3)	219 (0.4)
Child mentioned and age estimated on basis of weight	Children >30 kg: 10 mg per day	13 (0.9)	130 (0.2)
Summary of product characteristics not available		14 (1.0)	78 (0.1)

scriptions and were mainly dermatological and liquid preparations.

The table shows the official labelling of drugs prescribed for children. In 21.3% of the prescriptions for licensed drugs, use in children was not mentioned in the summary, and 19.7% mentioned use in children but without any indication of age. Although the summaries of remaining drugs indicated age, children were often divided into just two age groups.

Overall, 22.7% (15 453) of the prescriptions for children were used off label. Drug groups with the highest percentages of off label use were urologicals or sex hormones (mainly oral contraceptives; 85.9%), ophthalmological and otological drugs (79.4%), dermatological drugs (55.9%), and cardiovascular drugs (48.3%). In the group with the highest number of prescriptions—respiratory drugs—16.1% of all prescriptions were used off label.

Comment

Many licensed drugs used by children in the community are poorly labelled for use in children, resulting in high

percentages of off label use. Therefore labelling for children needs to be improved, with the support of everyone working in pharmacotherapy.

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Unlicensed and off label prescription of drugs to children: population based cohort study

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Drugs are subject to licensing procedures to ensure their quality, efficacy, and safety, but many drugs used to treat children in hospital are either not licensed for use in children ("unlicensed") or are prescribed outside the terms of the product licence ("off label").¹ Little is known about such prescribing in general practice, so we conducted a cohort study in primary care in the Netherlands to investigate the subject.

Methods and results

We retrieved data from the integrated primary care information project, a longitudinal observational database containing information from computer based patient records of 150 general practitioners in the Netherlands. The system complies with European Union guidelines on the use of medical data for medi-

cal research and has been proved valid for pharmacoepidemiological research.²

Within the dynamic population of children (0-16 years) registered in 1998, we conducted a one year population based cohort study. From a source population of 53 702 eligible children, we randomly sampled 25% (n=13 426; 6941 (51.7%) boys), which formed our final study population. During the year 8271 (61.6%) children consulted their general practitioner at least once; the median was one consultation a year. We classified all 17 453 drug prescriptions issued to 6141 (45.7%) children according to the licensing status of the drug,¹ by reference to the official product licence, as provided by the Dutch Medicines Evaluation Board.

Seventy one per cent (12 405) of prescriptions were for drugs licensed for use in children and prescribed in agreement with the product licence. Of the remaining 5048 (28.9%) prescriptions, 2667 (15.3%, 95% confi-

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