women using hormone replacement therapy for up to five years but was not significantly increased in women using it for longer.⁵ Neither of these observations is consistent with a causal relation between sex steroid hormones and cancer, such as that so clearly shown between unopposed oestrogens and endometrial cancer. Price and Little also completely ignore a recent population based case-control study that showed no increase in the risk of breast cancer even when hormone replacement therapy was taken for 20 years and more.⁶

While relying uncritically on the report on use of hormone replacement therapy and breast cancer from the nurses' health study, the authors perfunctorily dismiss the finding from the same cohort of a 50% reduction in the risk of myocardial infarction among women using the therapy. We recognise that epidemiology has provided no easy answer to the question of whether use of hormone replacement therapy has an effect on the risk of breast cancer, but we object to the promulgation of any attitude towards hormone replacement therapy, whether positive or negative, that is based on prejudice and a personal agenda. Making an announcement of a new organisation is no excuse for such abuse of the literature. Sadly, it is all too easy for those with no clinical responsibility for hormone replacement therapy to present a distorted view, to the detriment of women seeking a balanced assessment of the benefits and risks.

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Hormone replacement therapy may not always be right choice to prevent cardiovascular disease

EDITOR,—Hormone replacement therapy in postmenopausal women has been shown to have an overall benefit on mortality.^{1,2} None of the studies, however, were carried out in countries with a low frequency of ischaemic heart disease; nor were trends in mortality taken into account.

We performed a risk-benefit analysis of the effect of hormone replacement therapy on mortality from ischaemic heart disease, breast cancer, stroke, and endometrial cancer in postmenopausal women. Reference mortalities were estimated for successive birth cohorts of Italian women by age range, and a cohort log linear regression model was fitted to corresponding cause specific mortality data.³ Mortalities achievable with mass treatment were estimated by multiplying the reference mortalities by the relative risks derived from the literature.^{1,2,4,5} Italian

Fig 1—Trends in mortality from breast cancer, ischaemic heart disease, and stroke among female birth cohorts in Italy

women were assumed to start taking oral hormone replacement therapy (combined oestrogen and progestin) at age 50 and to continue it for 10 years. No risk or benefit was expected in the first five years of treatment. The benefit for ischaemic heart disease after the start of hormone replacement therapy was assumed to be 0.88 after five years, 0.75 between 10 and 15 years, and 0.88 between 15 and 20 years; the risk for stroke was assumed to be 0.88 between five and 20 years; the risk for breast cancer was assumed to be 1.2 after five years and 1.46 between 15 and 20 years; and no risk or benefit was applied for endometrial cancer.

Oral hormone replacement therapy for 10 years was estimated to produce an overall disadvantage in terms of life expectancy: we estimated that 59 and 62 excess deaths would occur between the ages of 50 and 70 in 100 000 Italian women born in 1940 and 1950, respectively.

This risk-benefit analysis is the first to have been conducted in a country with a low incidence of ischaemic heart disease and that is experiencing a steep decrease in mortality from cardiovascular disease in successive birth cohorts (fig 1). The result suggests that caution is necessary when oral hormone replacement therapy is envisaged as a tool for mass primary prevention of cardiovascular disease in postmenopausal women. This is particularly the case in populations at low risk of ischaemic heart disease, with higher mortality from breast cancer than from ischaemic heart disease before age 60, and with a decreasing trend in mortality from cardiovascular disease, as in other European countries such as France and Spain.

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Modes of administration of morphine in cancer pain

Some doctors lack basic knowledge about prescribing morphine

EDITOR,—The use of morphine is still associated with unfounded fears, even though the modern hospice and palliative care movement has existed for almost 30 years. Hopefully, the explicit guidelines on the use of morphine for cancer pain drawn up by the Expert Working Group of the European Association for Palliative Care will help dispel these fears.¹

Certain concerns are legitimate. A particular worry is the lack of individualisation of both the starting dose of morphine and the continuing dose, especially in patients who have not taken morphine before. Age, frailty, and known or possible renal impairment are often not considered. Twice in recent months we have admitted elderly patients (aged over 80) who had been given an excessive dose of analgesic cover "for the journey"; they had never previously been given morphine. One had been given 10 mg of diamorphine subcutaneously (equivalent to 30 mg of immediate release morphine), while the other had been given 20 mg of immediate release oral morphine. On arrival both patients were heavily sedated, with diminished respiratory drive. Probably a dose of only 2.5 mg of immediate release oral morphine would have sufficed.

Another area for potential mismanagement is when patients are changed from oral morphine to subcutaneous diamorphine given by syringe driver. We recently saw a patient who had been taking a total of 80 mg of controlled release oral morphine daily and had been changed to a syringe driver with 120 mg of diamorphine in 24 hours (equivalent to 360 mg of oral morphine daily). A dose of 25 mg of diamorphine in 24 hours by syringe driver was sufficient.

Doubtless most doctors try to use morphine in a considered manner, but, as is shown above, some have a worrying lack of basic knowledge. Continued reiteration of basic guidelines is essential.

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Formulations of morphine sulphate are easily confused

EDITOR,—The recommendations for the use of morphine in cancer pain produced by the Expert Working Group of the European Association for Palliative Care provide a comprehensive framework that will be of benefit to all health care professionals caring for this group of patients.¹ Prescribing morphine sulphate may, however,

give rise to problems. The current edition of the *British National Formulary* lists several proprietary oral preparations of morphine sulphate, including liquid, sustained release, and non-sustained release preparations, which may result in confusion.

Confusion between sustained release and non-sustained release morphine sulphate tablets and morphine sulphate liquid can result in two different outcomes: high initial peak plasma concentrations of morphine and inadequate duration of analgesia will result if liquid or non-sustained release tablets are given instead of sustained release tablets, while accumulation of morphine and potential toxicity will occur with repeated dosing if a sustained release tablet is given instead of a non-sustained release preparation.

There are two other potential sources of confusion. Firstly, the proprietary name MST has been misinterpreted as being an abbreviation for morphine sulphate rather than a formulation of the drug. Secondly, Oramorph liquid is also available in unit dose vials, which have been reported to have been confused with injectable preparations and given intravenously or intramuscularly in error.²

To minimise such errors in our hospital we aim to ensure that prescriptions for solid oral formulations of morphine sulphate include both the brand name and the approved name—for example, morphine sulphate sustained release (MST) or morphine sulphate (Sevredol). When these items are dispensed by the pharmacy, the containers are labelled with both the proprietary and approved names. As the liquid morphine sulphate preparation listed in our formulary is Oramorph liquid (not in unit dose vials) we have decided not to include Oramorph sustained release tablets, to minimise potential confusion between liquid and tablet formulations.

The guidelines put forward by the expert working group will aid decision making in the prescribing of analgesics. Doctors and pharmacists, however, have an important role in ensuring that the range of products available and the accuracy with which the prescription is written reduce to a minimum the risk of patients receiving the wrong formulation of morphine sulphate.

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1 Expert Working Group of the European Association for Palliative Care. Morphine in cancer pain: modes of administration. *BMJ* 1996;312:823-6. (30 March.)

2 Cousins D, Upton D. Medication errors. Oral solutions can be injected. *Pharmacy in Practice* 1995;5:76-7.

Naming of drugs

Differences between nomenclatures are much greater than editorial suggested

EDITOR,—C F George discusses the difficulties that will result from the European Commission's directive which states that the international non-proprietary name, not the British approved name, must appear on the labels and leaflets of medicinal products from January 1998.¹ George underestimates the problem, however, in asserting that "in total, 41 drugs have a British approved name that is significantly different to their recommended international non-proprietary name." I recently reviewed this issue and compared the official listings of the British approved names and the international non-proprietary names.² If we ignore differences in spelling, such as cyclosporin (whose international non-proprietary name is ciclosporin) and oestradiol (estradiol), the number of important differences between the two nomenclatures is well over 100 (table 1); this figure

Table 1—Main differences between British approved name² and international non-proprietary name⁴ of various drugs

British approved name	International non-proprietary name	British approved name	International non-proprietary name
Acepylline	Acepylline piperazine	Hydroxyurea	Hydroxycarbamide
Acinitrazole	Aminitrozole	Iodipamide	Adipiodone
Acrosoxacin	Rosoxacin	Ipodate	Ipodate
Actinomycin C	Cactinomycin	Ironedatate	Feredatate
Actinomycin D	Dactinomycin	Isobuzole	Glysobuzole
Adrenaline	Epinephrine	Lignocaine	Lidocaine
Aloxidone	Allomethadione	Methadyl acetate	Acetylmethadol
Ametazole	Betazole	Metharbitone	Metharbitol
Amethocaine	Tetracaine	Methimazole	Thiamazole
Amylobarbitone	Amobarbital	Methohexitone	Methohexital
Anoxynaphthionate	Anazolen	Methoin	Mephenytoin
Azetepa	Azetepa	Methotrimprazine	Levomepromazine
Balipramine	Depramine	Methusuximide	Mesuximide
Barbitone	Barbital	Methyl benzoquate	Nequinat
Bendrofluazide	Bendroflumethiazide	Methyl cysteine	Mecysteine
Benzathine penicillin	Benzathine benzylpenicillin	Methylphenobarbitone	Methylphenobarbital
Benzhexol	Trihexyphenidyl	Methypyrone	Methypyrrol
Benztropine	Benzatropine	Mitoxantrone	Mitoxantrone
Bindazac	Bendazac	Mustine	Chlormethine
Bismuth glycolylarsanilate	Glycobarsol	Nealbarbitone	Nealbarbital
Bromodiphenhydramine	Bromazine	Nicoumalone	Acenocoumarol
Buniodyl	Bunamiodyl	Nitrofurazone	Nitrofur
Bupropion	Amfebutamone	Noradrenaline	Norepinephrine
Buthalitone	Buthalital	Norbutrine	Norbutrine
Butoxamine	Butaxamine	Octacosactrin	Tosactide
Carbolonium	Hexcarbarcholine	Oxethazaine	Oxetacaine
Chlophedianol	Clofedanol	Oxentifylline	Pentoxifylline
Chlorbutol	Chlorobutanol	Pentacosactride	Norleusactide
Chlordantoin	Ciodantoin	Pentaerythritol	Pentaerythritol
Chlorfenivphos	Clofenivfos	Pentobarbitone	Pentobarbital
Chlorhexadol	Chloralodol	Pentolinium	Pentolinium
Chlormethiazole	Clomethiazole	Phanquone	Phanquinone
Chlorpheniramine	Chlorpheniramine	Phenobarbitone	Phenobarbital
Colistin sulphomethate	Colistimethate	Phenyl aminosalicylate	Fenamisol
Cyclobarbitone	Cyclobarbitol	Plasmin	Fibrinolysin
Cysteamine	Mercaptamine	Polyoxyl (8,40) stearate	Macrogol ester
Desoxycortone	Desoxycortone	Povidone	Polyvidone
Desferrioxamine	Deferoxamine	Pramoxine	Pramocaine
Diamthazole	Dimazole	Promethoestrol	Methestrol
Diatrizoate	Amidotrizoate	Proquamezine	Aminopromazine
Diazinon	Dimpylate	Quinalbarbitone	Secobarbital
Dichlorphenamide	Diclofenamide	Rolicypram	Rolicyprine
Dicyclomine	Dicycloverine	Secbutobarbitone	Secbutobarbital
Diethylpropion	Amfepramone	Solapson	Solasulfone
Dipenine	Diponium	Stanolone	Androstanolone
Dipyron	Metamizole	Stilboestrol	Diethylstilbestrol
Dothiepin	Dosulepin	Streptonicozid	Streptoniazid
Dyclacaine	Dyclonine	Sulfametopyrazine	Sulfalene
Epithiazide	Epitizide	Sulphaurea	Sulfacarbamide
Ethopropazine	Profenamine	Tetracosactrin	Tetracosactide
Ethybenztropine	Etybenztropine	Tetrahydrozoline	Tetryzoline
Fenchlorphos	Fenclofos	Thiacetazone	Thiacetazone
Fluopromazine	Trifluopromazine	Thialbarbitone	Thialbarbital
Flurandrenolone	Fludrocortide	Thiopentone	Thiopental
Frusamide	Furosemide	Thymoxamine	Moxislyte
Gestronol	Gestonorone	Triacetyloleandomycin	Troleandomycin
Glycalox	Glucalox	Tribavirin	Ribavirin
Halopyramine	Chloropyramine	Trimprazine	Alimemazine
Heptabarbital	Heptabarb	Trimustine	Trichlormethine
Hexachlorophane	Hexachlorophene	Troxidone	Trimethadione
Hexamine	Methenamine	Vinbarbitone	Vinbarbital
Hexobarbitone	Hexobarbital	Vinylbitone	Vinylbital
Hydroxamethocaine	Hydroxytetracaine	Viprynum	Pyrrinium

includes some widely used drugs, such as actinomycin D, bupropion, chlorpheniramine, dipyron, hydroxyurea, nicoumalone, plasmin, povidone, and thiopentone.

The World Health Organisation's international non-proprietary name programme was implemented to overcome this problem of synonyms. In practice, however, it has not achieved this objective, fundamentally because no single official organ is responsible for selecting the valid terms. The World Health Organisation publishes the international non-proprietary names in five languages (Latin, English, French, Spanish, and Russian), but many developed countries have their own nomenclature committees.

In the English speaking world, for example, the United States has its own United States adopted

name.⁵ This may be the same as the international non-proprietary name but different from the British approved name (for example, phenobarbital) or vice versa (povidone), or it may be different from both of these (for example, isoproterenol, whose British and international name is isoprenaline). In extreme cases the same drug has three names, as with aminitrozole, whose British approved name is acinitrazole and United States approved name is nithiamide). In the European Union, which has 11 official languages, the situation is more complex, because several countries have their own list of approved names.

Whatever solution is adopted as a result of the new directive in 1998, clearly none of the member states of the European Union can, in the long term, expect to maintain an official name differ-