Sildenafil for "blue babies". Such unlicensed drug use might be justified as last resort

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Undisclosed payments in research

Patients have the right to know motivations of researchers

Editor—Rao and Sant Cassia discussed the ethics of undisclosed payments to doctors recruiting patients in clinical trials.1 For many years now the greater Glasgow community and primary care local research ethics committee has insisted that reference to doctors’ payment is included in the patient information sheet that goes to all potential participants. I object to the payment being hidden behind such phrases as “your doctor’s research fund will be paid,” which a number of medical research ethics committees allow, and I note that the phrase “for the additional work involved” often appears.

Although the NHS and NHS Scotland are the remit of two different parliaments, cross border acceptance of approval by medical research ethics committees exists. Patients are also likely to see the NHS as a whole and the ethical principles of doctors and other healthcare professionals as not having regional variations. In the interests of equality (as well as informed consent) British guidelines need to be developed on this and other minimum requirements of information to be given to patients. This could include the amount of payment. My quick, non-random survey of my non-medical family and friends shows that the size of the payment and the potential overall income are underestimated.

Other types of personal gain exist for researchers that I also believe potential participants should know about—when the work forms part of the requirements for a degree. Some people who already have a professional qualification and who are using “their” patients in research do not always believe that it is necessary to inform patients that they are registered for a degree for which this research is necessary. Such research may not always reach publication and may be designed as a learning experience rather than a complete piece of research. If patients are to be expected to take part in research for altruistic reasons they have a right to know what reasons motivate the people carrying out the research.

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Guidelines already exist

Editor—I write as a member and former chairman of the ethical issues committee of the Faculty of Pharmaceutical Medicine, a former medical director of the Association of the British Pharmaceutical Industry, and a member of two research ethics committees. Rao and Sant Cassia make several points that disregard the truth about phase IV clinical trials and do not differentiate between phase IV clinical trials and the safety assessment of marketed medicines, both of which are subject to strict guidelines.1 These should be familiar to members of research ethics committees but are clearly unfamiliar to the authors of this paper.

Phase IV clinical trials, soon to be covered by the national legislation that follows the adoption of the European directive on clinical trials, are scientific projects already subject to ethical review. They are conducted in accordance with protocols submitted to medical and local research ethics committees as appropriate, and payments to be made are clearly included in the application for ethical review. Neither they nor safety assessment studies are designed solely to familiarise doctors with new and recently licensed medicines. They may well be required by the licensing authority to be conducted to establish a more robust safety database for a new medicine.

Rao and Sant Cassia seem to be ignorant of what they can already do about the concerns they express. This year’s BMA annual meeting endorsed the need for the suggested fee for clinical research to be widely published so that research ethics committees, among others, can have up to date independent advice on an agreed benchmark for payment to doctors taking part. Every phase IV study sponsored by a pharmaceutical company must be submitted to the appropriate research ethics committee(s), which can turn down an application if the payment is thought to be coercive. Studies into the safety assessment of marketed medicines do not need review by research ethics committees, but a BMA suggested payment exists for these, too. If a third party believes that a study is a marketing exercise masquerading as a research project or a safety assessment study, a complaint can be referred to the Prescription Medicine Code of Practice Authority and the company sanctioned if the complaint is upheld.

I agree that undisclosed payments to doctors recruiting patients in clinical trials would be unethical. However, payments must be disclosed to research ethics committees, which must therefore ensure that disclosure is complete and what is disclosed is acceptable.

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Sildenafil for “blue babies”

Such unlicensed drug use might be justified as last resort

Editor—We were disappointed to hear that a doctor in India has been criticised for treating pulmonary hypertension in three neonates (so called blue babies) with the phosphodiesterase type 5 inhibitor sildenafil (Viagra), a drug not licensed for this purpose.1

Many drugs are widely and appropriately used outside their product licence.2 Such prescribing practice is common in adult medicine, but is particularly prevalent in paediatrics because companies rarely undertake the work necessary to gain a licence for children. The decision to prescribe outwith a drug’s licence should be supported by evidence of safety and potential benefit and, when possible, by a reasonable body of supporting professional opinion.

Of course, controlled clinical trials should be performed when possible to evaluate new treatments for specific indications. But these data are not always available, and then clinicians must make difficult decisions as to whether other information, such as efficacy and safety in other groups of

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patients, justifies unlicensed drug use. Subsequently, case reports should be published, facilitating scientific debate and informing the design of clinical trials.

Evidence is growing that sildenafil acts as a vasodilator in the pulmonary circulation and is effective in lowering pulmonary artery pressure in pulmonary arterial hypertension. The effect has been shown in adults with pulmonary hypertension and healthy volunteers with pulmonary hypertension induced by hypoxia. Intravenous sildenafil also normalised pulmonary artery pressure in an animal model of neonatal pulmonary hypertension.

The evidence currently available is not sufficient generally to recommend the use of sildenafil in neonates with pulmonary hypertension. Assuming, however, that sildenafil was used as a last resort, after standard treatment, we believe that there are sufficient data to support the actions of this doctor. Perhaps the publicity that has arisen about this action will encourage further clinical research into the potential of inhibiting phosphodiesterase type 5 as a treatment for neonatal pulmonary hypertension, which may ultimately result in wider benefit to patients.

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do not allow any checking on the quality of the translation unless you are using a tele-

-133-131.

In an ideal world interpreters would all be university trained and completely reli-

able, but good interpreters in most of the

languages used by refugees are few, most being self taught. So keeping an eye on key

words used, length of delivery, tone of voice, and other markers is crucially important for an adequate and complete interpretation.

Telephone interpreting is also impracti-
cal during examinations. It interrupts the flow and is not conducive to building rapport between doctor and patient. To most patients (and doctors) it seems somewhat artificial.

Since refugees were first assimilated in Glasgow in April 2000 our practice has pro-

vided medical care to refugees. Currently we have about 3200 refugees and asylum seek-

ers registered with us. We arrange about 160-200 appointments weekly with (face to face) interpreters. We now have few (if any) difficulties in accessing interpreting services, maybe because we refused any and all involvement with telephone interpreting services.

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Patient focused approach may help

Enfure—The debate on making the best use of health advocates and interpreters can be broadened by considering the point of view of non-English speaking patients. In Adams’s second scenario, in which a distressed non-English speaker wishes to terminate her pregnancy, the patient may prefer her general practitioner to use a tele-

phone interpreter rather than talk face to face with an interpreter or advocate.

Some non-English speakers take great comfort from the anonymity of a telephone interpreter, particularly in small or closely knit ethnic communities. One of the factors contributing to the patient’s distress in this scenario could be cultural or social pressures from within their community. If the patient is forced to talk to her general practioner with telephone interpreting services.


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Letters

Homosexual related legislation does not reduce suicidal intent in sexual minority groups

Editor—Bagley and D’Augelli contend that suicidal behaviour in bisexual, gay, and lesbian youth is an international problem associated with homophobic legislation.1 Heretofore, no data existed to examine this. I recently found considerable variation in suicidal behaviour by sexual orientation cross culturally.2 I re-examined the data to determine whether variations in suicidal behaviour are associated with national legislative policy related to homosexuality (a) adoption, (b) military service, (c) employment, and (d) marriage or domestic partnership.

A more detailed description of participants and methods can be found elsewhere.1,4 Four English speaking countries were selected from the intercontinental sample to determine whether variations in suicidal behaviour are associated with national legislative policy related to homosexuality. Australia (n=185, 17.3% sexual minority groups), Canada (n=1178, 10.95% sexual minority groups), United Kingdom (n=116, 12.9% sexual minority groups), and United States (n=34 843, 13.41% sexual minority groups). Only countries with 15 or more participants in sexual minority groups were included to detect a proportionate difference of 0.10, assuming a population proportion of M=0.50 (no difference), alpha=0.05, and 70% power. National governments’ positions on issues (a)-(d) above were scored 0 (no position) or 1 (prohibited), and −1 (protected), with a range of 4 to −4.

The scoring was as follows:

- Australia —1: adoption 0, marriage or domestic partnerships 0, employment discrimination 0, military service −1
- Canada −4 (see Canadian Charter of Rights and Freedoms section 15(1), 1982; Human Rights Act 1996; judicial decisions): adoption −1, marriage −1, employment −1, and military service −1
- United Kingdom −2: adoption 0, marriage 0, employment −1, military service −1
- United States 2: adoption 0, marriage 1 (Public Law 104-199), employment 0, military service 1 (Department of Defense directive 1332.14, 28 January 1982).

The table shows suicide ideation and suicide attempts by each sexual orientation in country, with the odds ratio and 95% confidence interval for the risk. The final two columns reflect the Pearson’s correlation and its P value for the relation between the cumulative score for homosexual related legislation (index) and suicidal behaviour cross culturally. The percentage of homosexual suicide attempts were strong and significant but inversely related to the index (r = −0.952, P < 0.05). The index was not significantly associated with other variables of suicidal behaviour.

In contrast to Bagley and D’Augelli’s public policy thesis,5 I tested a social constructivist model that suggests cultural attitudes towards human sexuality mediate the relation between suicidal behaviour and sexual orientation.6 The present study provides empirical evidence to refute the public policy model. Thus, changing cultural attitudes towards human sexuality seems to be a more effective target of intervention for the suicidal behaviour of bisexual, gay, and lesbian youth than direct challenges to public policy related to homosexuality.

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Iron deficiency is neglected in women’s health

Editor—The data by Waalen et al show that 38% of menstruating women living in San Diego are iron deficient using the accepted cut-off point of <20% for transferrin saturation as an indicator of deficiency. These data support our hypothesis that hematological distributions contain a large proportion of iron deficient women.1

By focusing on the mean haemoglobin distribution, Waalen et al lose sight of a fundamental part of our work: why should women have lower reference limits for haemoglobin and serum ferritin concentrations than men?2 Our hypothesis for this was that a significant number of women are iron deficient. Mean values mask anomalies in distribution and are inappropriate to evaluate the issues we have raised. Since women menstruate, men would be expected to have higher mean haemoglobin concentrations because they can attain higher upper limits, so the 10g/l difference found by Waalen et al was not unexpected.

A similar situation occurs in menstruating but not in non-menstruating non-human primates.3 To support their case Waalen et al cite one menstruating non-human primate example—unfortunately this paper included data from infants, adolescents, and female animals half the age of the males, and it is therefore unreliable.4 Data analysis of a sex difference with age is more complex than simply presenting mean values from uncontrolled populations.

Close inspection of the ferritin data in part C of Waalen et al’s study shows a large number of women “falling off” the lower end of the distribution. The haemoglobin difference between the sexes was of the range 15-20 g/l, which represents a significant proportion (30%) of the female distribution having a serum ferritin concentration below the lowest male value. In part B, the transferrin saturation data for 26-55 year old menstruating women show a significant difference in haemoglobin concentration of 15-20 g/l with a transferrin saturation below 20%, the accepted cut-off point for iron deficiency. In postmenopausal women (part D) 29% were affected. Ten percent were classified as normal (haemoglobin concentration >120g/l) but were clearly iron deficient on the basis of having transferrin saturations <10%.

Iron deficiency is a significant and seemingly neglected factor in women’s health. Why should the lower reference level be sex dependent? What compelling evidence is there to support this apparent anomaly? In


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We found similar variability in orthopaedics and cardiology. Referral rates can be reduced in many ways. The aim should be for the right patients to have access to the right level of skill at the right time without necessarily going to a hospital. The means to achieve this include better education, more community-based expertise, mature clinical networks, and better use of technology such as clinical decision support (including referral guidelines) and telemedicine. There is plenty of room for improvement.

Tailored exercise is key to preventing falls

Entoror—The role of exercise in effectively preventing falls has had a mixed press. Profound conclusions have been drawn from research studies with severe limitations, including non-selection of those who had falls, brief intervention periods, and exercise of insufficient intensity to stimulate improvement. Many were alarmed by a trial in which those who had falls fell more often after being encouraged to walk—if the authors had prescribed the balance, gait, and strength exercises used in New Zealand before walking, this unfortunate outcome could have been avoided.1 Today, scepticism about the true impact of exercise still remains among professionals and decision makers in the United Kingdom. The study by Day et al is a welcome addition to the literature countering this alarmist view.1 In the United Kingdom the soon to be published falls management exercise (FaMe) trial by Skelton et al found that in women aged over 65 with a history of falls who participated in prolonged specific group exercise, falls decreased by 60% and injuries due to falls by 75%. Prescribed exercises included those used by Campbell et al, as well as dynamic endurance, balance training, floor exercise, and coping strategies after a fall.2 An accredited training course is now available nationally which covers the specific exercises used (see details below).

To test these study findings outside the research environment we set up a falls and injury prevention exercise service for people who had had falls and were living in the community (average age 81 years) in London in January 2000. Participants showed significant improvement in several known functional risk factors for falls and injuries, in addition to significantly increased scores in the SF36 domains of social contact, mental health, and change in health. Improvement in functional capacity is directly relevant to quality of life. As one participant said: “I can walk upstairs now. I haven’t been able to walk upstairs for four years. I do my exercises every day at home. I know it’s doing me good.”

Primary care trusts and social services departments are under pressure to promote the independence of their older residents. They would do well not to overlook the broad impact of tailored exercise in this area.

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