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# LETTERS

## ANTIPSYCHOTICS AND STROKE RISK

### Effect of antipsychotics on stroke risk remains unproved

The paper by Douglas and Smeeth,<sup>1</sup> does not, as is widely claimed, show that both typical and atypical antipsychotics increase the risk of stroke, especially in patients with dementia.

They find that in patients who have had a stroke and who were prescribed antipsychotics by their general practitioners the stroke is more likely to occur during the time antipsychotics are prescribed than before or after. The method used is wide open to biases of different sorts.<sup>2</sup>

The authors do not consider the possibility that there may be quite direct relations between the clinical situation which leads to the initiation or termination of the prescription of antipsychotics and the stroke. For example, a patient with ongoing deterioration of functioning may have behavioural disturbance and be prescribed an antipsychotic and may then go on to develop what is recognised as a full blown stroke. Likewise, some patients taking antipsychotics will have a stroke and then no longer be prescribed them by their general practitioner because the clinical picture has changed. The most obvious reason for this to occur is that the patient may be in hospital for months, but there are numerous other possible scenarios.

It is extremely alarming that there are widely publicised claims that this paper supports the notion that antipsychotics increase the risk of stroke, whereas the methods used make it impossible to draw such a conclusion.

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Competing interests: None declared.

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## Madness of modern medicine

Douglas and Smeeth's study of the risk of stroke with antipsychotic drugs highlights modern medicine's flawed perspective.<sup>1</sup>

Medicine once served to make patients better, alleviating symptoms and healing



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disease. Now it seems to have degenerated into a risk reducing, patient stratifying, life years adding bioscience disregarding the individual patient's needs. To deny a patient good treatment for disturbing and harassing complaints because of worries about possible side effects is unethical. Nobody would question prescribing morphine for terminal analgesia. Patients at the end of their life with dementia related behavioural problems should be able to expect proper treatment. To withhold this treatment for spurious and debatable reasons is "medicine."

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- 1 Douglas JJ, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. *BMJ* 2008;337:a1227. (28 August.)

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## NEW HIP AND KNEE REPLACEMENTS

### Conclusions from knee and hip registry data miss the point

Your report on a national joint registry data analysis concludes erroneously and misleadingly that unicompartmental knee replacements and hip resurfacings fare worse than total knee and hip replacements.<sup>1</sup> In fact, both do better.<sup>2 3</sup>

The paper reports on the reoperation rate for each procedure but not the extent of reoperation or the severity of symptoms. A day case exchange of bearing of a unicompartmental knee replacement (the smallest reoperation) or conversion to a simple primary total knee replacement is thus bizarrely equated with an amputation (the worst reoperation of total knee replacement). The lower impact of complications after unicompartmental knee replacement has long been established in the

Swedish registry.<sup>4</sup> Total replacement is not more successful, just much harder to revise.

Hip resurfacing is another conservative operation that seems to offer superior function.<sup>3</sup> Failures are being reported more commonly in women, and all devices are required by the Medicines and Healthcare products Regulatory Agency (MHRA) to be sent to the retrieval laboratory in our department. It is too early to say whether failure is another issue of surgeon error, but technologies now can all but eliminate the learning curve in both these demanding operations.<sup>5</sup>

Well performed conservative surgery has great attractions to patients and those who pay for their treatment. Headlines that overinterpret registry data and push people into having big, expensive, and less conservative operations serve only those who stand to gain materially.

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## DEATHS FROM DRUG POISONING

### So much for harm reduction techniques reducing drug deaths

An ageing population of heroin users does not fully explain the five year peak in deaths from drug poisoning in English and Welsh men.<sup>1</sup> The increase is attributable to heroin, methadone, and morphine, and death rates were highest in young adults.<sup>2</sup>

The UK has the highest prevalence of drug misuse in Europe.<sup>3 4</sup> The social laboratory of harm

reduction as practised in the UK does not focus on prevention by creating and implementing drug use prevention activities and increasing drug free recovery facilities. Substitute prescribing protocols and needle exchange facilities have an important role in preventing further harm being incurred by users, but they cannot reduce the mental, physical, spiritual, and social harms caused by continued use or the severity of addiction with continued use.

Methadone maintenance, the flagship of drug treatment in the UK, needle exchange facilities, and drug consumption rooms have all failed to reduce or prevent the increasing use of addictive substances, as well as the associated deaths and bloodborne diseases.<sup>5</sup> The action plan on reducing drug related deaths referred to by the Department of Health spokesperson proposes more of the same. Abstinence is mentioned twice in the eight page plan, but there is no mention of increasing drug free recovery protocols or programmes.

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## HYPERCHOLESTEROLAEMIA

### Should medical science ignore the past?

For their article on hypercholesterolaemia and its management Bhatnagar et al selected reviews only if they included "extensive recent references,"<sup>1</sup> thereby missing important knowledge from the past [full list of references in rapid response].<sup>2</sup> Let me elaborate:

- No association between cholesterol and degree of atherosclerosis has been found in postmortem studies of unselected individuals
- High cholesterol is not a risk factor for women, patients with renal failure, diabetic patients, or old people<sup>3</sup>

- Old people with high cholesterol live longer than those with low cholesterol<sup>3</sup>
- In cohorts of people with familial hypercholesterolaemia, cholesterol is not associated with the incidence or prevalence of cardiovascular disease, and their average life span is similar to other people's
- No randomised, controlled, unifactorial, dietary, cholesterol lowering trial has ever succeeded in lowering coronary or total mortality<sup>4</sup>
- No clinical or angiographic trial has found exposure-response between individual degree of cholesterol lowering and outcome<sup>3</sup>
- More than 20 cohort studies found that patients with coronary heart disease ate the same amount of saturated fat as did healthy controls<sup>4</sup>
- Seven of 10 cohort studies found that patients with stroke ate less saturated fat than did healthy controls
- The concentration of short chain fatty acids in adipose tissue, the most reliable reflection of saturated fat intake, is similar or lower in patients with coronary heart disease compared with healthy individuals in five case-control studies
- The effect of statin treatment is grossly overstated and is not due to cholesterol lowering.<sup>3</sup> Only a small percentage gain benefit—and then only if they are men at high risk—and the benefit is easily outweighed by side effects that are more common and more serious than reported in the statin trials, if reported at all.<sup>5</sup>

Revision of the cholesterol campaign by scientists without links to the food or drug industry seems urgent.

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## Clarifications from adverse drug reactions agency

Struthers's letter on reasons to be cautious about cholesterol lowering drugs may have misled readers in suggesting that the West Midlands Centre for Adverse Drug Reactions

(CADRe) had issued a warning about a potential increased risk of cancer associated with simvastatin and ezetimibe (Vytorin).<sup>1</sup>

We at CADRe have not issued a warning about Vytorin. The posting on our website is one of a series of news items, and we are referring to the work of the US Food and Drug Administration (FDA).<sup>2</sup> We start: "The FDA have issued an early communication about an ongoing safety review concerning a potentially increased risk of cancer associated with simvastatin and ezetimibe . . ."<sup>3</sup> This is clearly a statement about the FDA's analysis, and not our own.

We did not issue a warning "via the FDA": the FDA indicated preliminary information, which it felt was an insufficient basis for a secure judgment, and we reported what it said.

CADRe does not produce the *Adverse Drug Reaction Bulletin*. Although the editorial managers of the journal work in our unit, the journal is published by Wolters Kluwer.

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- FDA. Early communication about an ongoing safety review of ezetimibe/simvastatin (marketed as Vytorin), simvastatin (marketed as Zocor) and ezetimibe (marketed as Zetia) [www.fda.gov/cder/drug/early\\_comm/ezetimibe\\_simvastatin\\_SEAS.htm](http://www.fda.gov/cder/drug/early_comm/ezetimibe_simvastatin_SEAS.htm)

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## HORMONE REPLACEMENT THERAPY

### HRT in premature menopause

Grant's blanket statement,<sup>1</sup> based on the WISDOM study,<sup>2</sup> that "it would be irresponsible to think that any use of hormone replacement therapy (HRT) is justifiable" will confuse those dealing with women with early ovarian failure in their 20s and 30s. National guidelines recommend the use of HRT in this group until the average age of the natural menopause in the early 50s.<sup>3</sup> The results of the WISDOM study, which randomised women with a mean age of 63.8 years, should not be extrapolated to them.

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