Using aspirin to prevent cognitive decline
Is not effective in asymptomatic middle aged to elderly adults

The rationale for using aspirin to prevent mild cognitive impairment and dementia seems compelling. Disorders of cognition affect 10-15% of the general population over 65.1 2 Cerebrovascular disease plays a pivotal role in the development and progression of mild cognitive impairment and dementia.1 2 Aspirin prevents first ever stroke in apparently healthy asymptomatic women,3 and it also prevents first ever and recurrent stroke in high risk populations.3 Thus, by preventing cerebral ischaemia, aspirin would be expected to reduce the burden of cognitive loss to individuals and society. Observational studies have shown an association between the use of aspirin and reduced odds of cognitive impairment,4 5 but randomised controlled trials have been lacking until recently.

In the linked study, Price and colleagues report cognitive outcomes from the aspirin for asymptomatic atherosclerosis (AAA) trial, which randomised 3350 middle aged to elderly volunteers to receive long term enteric coated aspirin 100 mg once daily or placebo.6 Volunteers not already treated with aspirin or warfarin before entry to the study were eligible for inclusion if they were aged 50-75 years; had no history of symptomatic coronary, cerebral, or peripheral artery disease; and had an ankle brachial index of 0.95 or less. Within three months of study entry, participants were assessed for their baseline cognitive ability using the Mill Hill vocabulary scale.

After about five years’ follow-up, participants underwent tests to assess executive function, non-verbal reasoning, memory, mental flexibility, and information processing. All participants were also assessed for anxiety and depression. Outcome measures were a composite score of individual test results (the “general factor” score) and individual test scores. At five years, the groups did not differ significantly in the proportion of participants who scored above the median general factor score or in their individual test scores. An “on-treatment” analysis produced similar results. The effect of aspirin on stroke and other vascular events in the AAA trial is unknown because follow-up for vascular events will not be complete until 2010. However, the women’s health study recently showed no effect of aspirin on cognitive decline in apparently healthy women 45 years or older, although aspirin significantly reduced stroke.8

Why didn’t the benefits of aspirin for preventing stroke previously shown in primary and secondary vascular prevention trials translate into protection against cognitive decline in the AAA trial? Several possible explanations exist. Firstly, cognitive decline was minimal in participants treated with placebo during the AAA trial, which limits the study’s power to detect a benefit of aspirin. Secondly, patients with cognitive impairment might have been over-represented in the patients (almost a third) who withdrew, died, or refused cognitive follow-up, thereby biasing the study results toward the null. Thirdly, the battery of tests used to assess cognitive function might be insensitive to small changes in executive function that may manifest clinically as impairments in instrumental activities of daily living. Finally, an increase in cerebral microbleeds caused by aspirin or progression of coexistent neurodegenerative processes that could not be modified by aspirin could theoretically have masked a reduction in cognitive decline as a result of cerebral ischaemia. Cerebral microbleeds have been linked with executive dysfunction,9 but no convincing evidence exists that aspirin causes microbleeds.

The results of the AAA trial and the women’s health study collectively find no evidence that aspirin effectively prevents cognitive decline in middle aged to elderly patients without established mild cognitive impairment or dementia. The aspirin in reducing events in the elderly (ASPREE) trial is presently evaluating the effect of low dose aspirin on prevention of major adverse vascular and cardiovascular events, dementia, and disability in 18000 elderly patients,10 and it should definitively establish whether aspirin is effective for preventing cognitive dysfunction. Whether the modification of other vascular risk factors might be beneficial for this indication is unresolved. Antihypertensive treatment has shown promise for preventing vascular cognitive decline,11 while randomised trials with statins and glucose lowering drugs have been inconclusive or negative.

What are the implications of the AAA trial results for clinical practice? Clinicians should continue to treat patients at high risk with aspirin to prevent myocardial infarction, stroke, and death from cardiovascular causes. For asymptomatic middle aged to elderly patients, aspirin should be used only if the benefits for preventing major vascular events are expected to outweigh the risk of bleeding, and it cannot be recommended to prevent cognitive decline.

Direct to consumer advertising of prescription drugs

Even attenuated forms such as cross border advertising can cause harm

Are there public health consequences when regulators turn a blind eye to cross border advertising that contravenes national laws? Although Canada prohibits direct to consumer advertising of prescription drugs, no steps are taken to prevent US advertising from reaching the Canadian public. The linked study by Law and colleagues, provides compelling evidence that this does have consequences for public health and of the need for better regulatory oversight.1

Direct to consumer advertising from the United States reaches Canadians via cable television and US magazines sold in Canada. Law and colleagues found that cross border advertising increased prescribing of a minimally effective drug with a poor safety profile,2 which subsequently led to its withdrawal.3

French speaking Canadians, who mainly live in Quebec, watch less US television than their English speaking compatriots and are less exposed to US direct to consumer advertising. Law and colleagues used this difference to examine the effects of US advertising campaigns on prescribing rates. Three drugs met the inclusion criteria of the study on the basis of timing of approval and advertising--tegaserod, etanercept, and mometasone. A clear effect was found for one, tegaserod, a drug for irritable bowel syndrome in women and for chronic constipation.

Direct to consumer advertising had no significant effect on the prescription of etanercept, a biological agent given by infusion to treat rheumatoid arthritis. Etanercept is generally used after failure of initial treatment, and special authorisation is needed for public reimbursement. With a restricted patient population and limited use, the influence of advertising is expected to be attenuated.

Similarly, the lack of observed difference in prescribing of mometasone, a nasal steroid prescribed for allergy in primary care, is not surprising. This drug is fully subsidised in Quebec, not funded at all in Ontario, and is given only to children under 12 in British Columbia and Alberta. Alternatives such as beclometasone are fully subsidised.

Just 40% of the costs of drugs are paid for publicly in Canada.4 However, reimbursement policies can have profound effects on prescribing. British Columbia's restrictive funding of cyclo-oxygenase-2 inhibitors resulted in less than half the prescribing rate seen elsewhere in Canada, with lower rates extending to those without public coverage.5 British Columbians were exposed to more US advertising, but Quebec, with unrestricted funding, had higher rates of use. In the current study, inhaled mometasone was prescribed more often in Quebec throughout the observational period.

Law and colleagues found a 42% increase in prescribing of tegaserod after intensive US advertising campaigns, or an estimated 29 574 extra prescriptions over a two year period (personal communication, 2008). Tegaserod was not covered by public drug plans, but at average costs to large private insurers of $169.44 (£85; €108) for each prescription (B Martinez, personal communication, 2008), this translates to more than $7 5mn (£2.5m).

In a pooled analysis of 29 clinical trials, 13 of 11 614 patients treated with tegaserod had heart attacks, strokes, or serious angina compared with one of 7 031 patients on placebo. Among the extra prescriptions in Canada as a result of direct to consumer advertising, around 29 people, or one in 1023 patients treated, would have experienced serious cardiovascular events over the two years.

Women experienced 88% of the cardiovascular events leading to the withdrawal of tegaserod. In the only analysis of drug safety withdrawals disaggregated by sex, eight of 10 US withdrawals from 1997 to 2001 led to greater harm to women. In four cases this was because of more frequent use by women and in four because of higher risks of cardiac arrhythmias and dose related effects.

Whether direct to consumer advertising leads to disproportionate harm to women is currently under debate in a Canadian court case, in which a media company, Canwest Media, is challenging the ban on direct to consumer advertising as an infringement of its freedom of expression. Health Canada is defending the law on public health grounds. A coalition of unions and non-profit making organisations has obtained standing in court on the government side to introduce two additional concerns—harm to women and effects on employee health benefits.

Central to these concerns is advertising's ability to “expand the boundaries of treatable illness,” shifting the balance of potential benefit to harm as drugs are used for milder problems. Tegaserod is used to treat irritable bowel syndrome, a condition Moynihan and colleagues highlighted as a case study in disease mongering. “What for many people is a mild functional disorder—requiring little more than reassurance about its benign natural course—is currently being reframed as a serious disease attracting a label and a drug.”7 The 2003 television

References

State violence towards sex workers

Police power should be reduced and sex workers’ autonomy and status raised

Stigma affects health in many ways, and this is exemplified in sex workers, who are seen as suitable targets for violence. Studies on transgender sex workers show they are routinely subjected to violence, public humiliation and, and, not infrequently, murder. Male transvestite sex workers are difficult to access and vulnerable in terms of public health and criminal justice policy; both of these facts have implications for the control of sexually transmitted diseases.

The transvestite population is also vulnerable to HIV from silicon implanting and drug misuse, and to multidrug resistant tuberculosis. Few data are available on police violence towards female or transvestite sex workers, but non-governmental organisations in developing countries have reported police harassment or “social cleansing” of transvestite sex workers. Rigorous research is therefore needed to understand the precise context of this multiple vulnerability.

The linked qualitative study by Rhodes and colleagues analysed 31 interviews with 24 female sex workers and seven transvestite male sex workers in two Serbian cities; 15 of these workers, including all of the transvestites, were Roma. Fostering good relationships between researchers and participants is essential for internal validity in qualitative research, especially when studying sensitive topics in vulnerable groups, such as people who practise a stigmatised activity. Rhodes and colleagues ensured integrity by close consultation with local groups and sex workers in Serbia. The interviews show disempowerment of sex workers through the lack of rights in their working environment, which resulted in lack of control over the use of condoms. Police violence was perceived as a greater threat than client violence and was less amenable to risk management. Police violence had three main aspects. The first was deception and coercion, including sex by deception; sex in exchange for freedom from police activity; and sex coerced by violence. The second was the extortion of money from sex workers. The third was discrimination and bullying in rhetorical acts to objectify and dislocate the sex workers from society; this included stigma and punishment, public humiliation and shaming, extreme violence, and contempt—especially of transvestite workers—all of which was perpetrated by racist, sexist, and systematic police brutality.

Rhodes and colleagues’ study adds analytical depth to existing data on the vulnerability of sex workers and adds a further European dimension to the literature. The findings show that discrimination and bullying of sex workers are related to their low social status and they raise theoretical questions about femininity and masculinity. The results also show that cultural complexities are important to understanding vulnerability in public health policy. Future research should examine whether humiliation and shaming by the police is a global enactment of the stigma attached to sex work, or whether the stigma is defined locally.

The implications for policy are that police interventions not only impede harm reduction but can be a danger themselves. Sex workers are at increased risk when the state controls and diminishes them rather than providing services and rights to empower them to control their own health and safety. Policy debates about sex workers often assume that they are exclusively female and that violence towards them is perpetrated only by partners, pimps, or violent men masquerading as clients. Rhodes
and colleagues’ study is therefore highly pertinent to the debate during the ongoing government review of demand for sexual services.

The study is important because public policy is inseparable from global injustice in this era of transnational mobility, and it becomes increasingly important that all aspects of violence and discrimination against sex workers are understood. Rhodes and colleagues raise essential questions for the debate on trafficking of sex workers. Economics is often cited as a reason for the migration of sex workers, who often move to regions where they are paid more. “Client demand” alone is a less sustainable argument to explain migration, but it has gained currency in the recent climate of political panic—bordering on hysteria—about trafficking and substance misuse. This panic resulted in unworkable legal provisions on sex work being put forward by the government, only to be withdrawn in the same parliamentary session.11 Could police violence be a powerful reason for migration? Political panics can lead to increased police power, and Rhodes and colleagues show precisely why that is incompatible with human rights, health, and safety.

New policies are needed to reduce violence in sex work environments.12 The authors present a convincing argument for reducing police power and raising the autonomy and status of sex workers on health grounds. The eradication of violence from the state, which exists not only in explicit physical assault but also in the violation of human rights, can however only be totally removed by the decriminalisation of sex work, promotion of sex workers’ rights, and self organisation of sex workers.


Bariatric surgery
Can reduce weight and improve long term survival, but carries risks

Severe obesity (body mass index ≥40) has been linked to shorter survival, poorer mental and physical health, and substantial healthcare costs. Bariatric procedures, such as gastric bypass and gastric banding, dramatically reduce weight through gastric restriction, malabsorption, changes in neuroendocrine signalling, or a combination of these mechanisms.

One criticism of bariatric surgery has been the paucity of studies comparing its outcomes against non-surgical treatment. However, two recent controlled non-randomised studies found that bariatric surgery improved long term survival.1 The first was a prospective study that matched 2010 patients who had undergone bariatric surgery with 2037 non-surgical controls. After a mean of 10.9 years (with 99.9% follow-up), 6.3% of controls had died compared with 5.0% of surgical patients (hazard ratio 0.76, 95% confidence interval 0.59 to 0.99, number needed to treat 77). The second was a retrospective study of 9949 patients who had gastric bypass surgery and 9628 matched non-surgical controls. After a mean follow-up of 7.1 years, 4.1% of the control group had died compared with 2.7% in the surgery group (0.60, 0.45 to 0.67, 71). In both studies, the rates of death as a result of cardiovascular disease and cancer were significantly lower in surgical patients.1

These studies confirmed the survival benefits reported in two previous studies that were unable to match participants on their baseline weight. Nevertheless, the main limitation of these studies is their lack of randomisation, which can result in surgical cases and controls differing in important ways that were not measured (for example, their health behaviours). The studies were also limited by the lack of an intensive non-surgical intervention for weight loss and risk reduction.

Severe obesity is thought to be a major risk factor for perioperative adverse events. In the above studies, 90 day mortality was 0.25%1 and one year mortality was 0.53%. These findings are consistent with other recent reports, including in-hospital mortality of 0.22% among 51 842 patients undergoing bariatric surgery in the United States, and 30 day mortality of 0.28% in a review of 361 bariatric studies.6 These results confirm that the short term risk of mortality for the average patient having bariatric surgery (age 40, body mass index 47, 80% female) is likely to be low. However, 30 day mortality may be 2.0% or higher in some subgroups of patients—such as those with a body mass index over 50, age over 65, or multiple comorbidities, in addition to beneficiaries of Medicaid and Medicare.8 Other recent studies have established that comorbidities related to obesity, such as type 2 diabetes, resolve or are dramatically improved after bariatric surgery.5 11 The strongest evidence comes from a two year randomised trial that compared gastric banding with a combined medical and behavioural intervention in 60 patients with a body mass index of 30-40 and recently diagnosed type 2 diabetes.6 Resolution of diabetes (fasting plasma glucose <7 mmol/l and glycated haemoglobin <6.2% without oral hypoglycaemic agents or insulin) was achieved in 73% of surgical cases and 13% of controls; the relative risk of resolution of diabetes was 5.5 (95%
Tackling health inequities

WHO calls for global action to ensure health equity within and between countries

Finally, an official report on health inequity has been published that has the honesty and courage to say that “social injustice is killing people on a grand scale.” The report of the World Health Organization’s Commission on Social Determinants of Health synthesizes evidence from a large and disparate range of sources, while recognizing that what constitutes evidence is itself contested and not value free. It presents a wealth of data to show the unquestionable link between economic, social, and bodily wellbeing—within and across countries. In the case of life expectancy, these embodied facts of social inequity can span the equivalent of a lifetime: women born in Botswana can anticipate living an average of 43 years, half that of the 86 years for women in Japan; between the poorest and most affluent parts of Glasgow life expectancy in men ranges from 54 to 82 years.

Many official reports have documented social inequalities in health over the past 170 years, from Chadwick to Sachs. Yet, in contrast to these reports, which subliminally and not so subtly emphasised the detrimental effects of poor health induced by poverty on economic performance, the commission firmly draws the arrow of causality from impoverished environments to ill health, something that is clear to most of the world’s population (if not to some economists).

The ability of this report to make these conclusions rests on its unprecedented broad scope—unlike many other reports that have focused on one country or on groups of countries at similar economic levels, the commission has produced a global picture of economic and social deprivation that makes it impossible not to recognize the importance of economic redistribution, health care, and the direct material consequences of poverty and social inequality across the life course on health.

Once it is acknowledged that poverty, exploitation, oppression, and injustice damage health, the question is clearly what should be done and by whom? The commission offers three overarching recommendations
Firstly, improving the conditions of daily living from before birth to old age will alleviate the health consequences of inequality. Secondly, although the commission accepts that it “was beyond the [ir] remit, and competence . . . to design a new international economic order that balances the needs of social and economic development of the whole global population, health equity, and the urgency of dealing with global warming,” it appropriately identifies the inequitable distribution of power, money, and resources as underlying poor health. Finally, to galvanise action and ensure accountability, it recommends global, national, and local monitoring of health inequities; the assessment of the impact of policies aimed at the alleviation of these inequalities; and the training of all health professionals in the social determinants of health.

Wisely advocating a “both and” rather than a divisive “either or” approach, the commission calls for “bottom-up” and “top-down” action, both within and outside the health sector. Declaring that “health is not a tradable commodity,” it boldly asserts that “certain goods and services such as basic human and societal needs—access to clean water, for example—and health care” must be “made available universally regardless of ability to pay.”

The report’s inclusion of both social and health system policies as social determinants of health follows others’ in moving on from debates that narrowly pit one against the other. Throughout, the report usefully provides diverse concrete examples showing how health equity can be advanced by intersectoral action from grassroots organisations, national and local government, multilateral agencies (including WHO itself), the private sector, and research and teaching institutions. Observing that governments obviously are “not always benign,” the commission underscores the “clear links between a ‘rights’ approach to health and the social determinants approach to health equity.” Highlighting the harmful effects of gender inequity, discrimination, and social exclusion on health (including the health of indigenous populations), it calls for democratic and participatory approaches as the essential glue for integrating multisectoral multiagency activity and making sure this work has an effect. Indeed, as advocated 65 years ago by Morris, the leading health inequalities researcher of the 20th century, the need to include community based, participatory approaches to evaluation and monitoring—often seen to be the domain of “experts”—is as crucial as grassroots involvement. Equally telling, the commission eviscerates the platitudes of bottom-up action from below, and the need to include community based, participatory approaches to evaluation and monitoring—often seen to be the domain of “experts”—as crucial as grassroots involvement.

Equally telling, the commission eviscerates the platitudes of bottom-up action from below, and the need to include community based, participatory approaches to evaluation and monitoring—often seen to be the domain of “experts”—as crucial as grassroots involvement. To return to the question of what is to be done the report clarifies that just as cynicism and inaction are not an option, neither is there one master plan to be dictated from above. Instead, health professionals have clear and plentiful work to do within the many systems in which we work, together with every other sector of society. By placing health equity as a crucial goal and as the standard for accountability, and by recognising that social justice is the foundation of public health, we stand a better chance at rectifying current inequities and playing our part in establishing a more just and sustainable world.