Is there a role for abstinence only programmes for HIV prevention in high income countries?

A robust systematic review finds no evidence that such programmes reduce risky sexual behaviours, incidence of sexually transmitted infections, or pregnancy

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RESEARCH, p 248

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The systematic review in this week's *BMJ* by Underhill and colleagues brings valuable insights to a highly contentious issue: whether abstinence only (as opposed to abstinence plus) programmes can stop, delay, or decrease sexual activity and prevent HIV infection.¹ This question is important because 38 million people are currently infected with HIV but, despite 25 years of research, we still have no vaccines to prevent HIV infection. Furthermore, HIV prevention has become a politically charged issue because funds from the US President's Emergency Plan for AIDS Relief (PEPFAR) can be used for abstinence only programmes, but cannot be used for other safer sex strategies, needle exchange, or instructions for using condoms. Is this an effective use of public funds?²

A previous review of abstinence only programmes in the developing world, presented at the 2006 international AIDS meeting,³ found little evidence that they were effective in changing sexual behaviour and preventing HIV infection, either because of weak study designs or the difficulty in measuring outcomes of interest, although these programmes did seem to change knowledge, beliefs, and intentions to delay sex or to use condoms if they had sex, if not actual behaviour.

The systematic review by Underhill and colleagues focuses on the effect of such programmes in the developed world.¹ As the authors point out, in theory such programmes should be more effective in high income populations where people are more likely to be able to decide freely whether and how they have sex. Previous reviews of the effectiveness of abstinence only interventions in high income settings have reported divergent conclusions. However, the current study has more rigorous methodology (including use of a prereviewed Cochrane protocol), it includes published and unpublished studies plus data from many countries, and it focuses on abstinence only and behavioural and biological outcomes related to HIV prevention.

The results of the review make it clear why it has been difficult to show unequivocally that abstinence only programmes are ineffectual in all settings. The authors identified 13 randomised studies that met the inclusion criteria, but a formal meta-analysis could not be performed because of high heterogeneity in both the abstinence programmes and study end

points. The intervention programmes studied varied greatly in their content and length, while control groups varied between no treatment and numerous usual care programmes. The studies' methodological quality was difficult to assess. All trials conducted an analysis of completed cases only instead of the more rigorous intention to treat analysis.

Most sexual behaviour outcomes were limited to vaginal sex, and did not assess oral, anal, or same sex behaviour. All outcomes were self reported. No trial assessed the incidence of HIV—the outcome of real interest. All assessed surrogates including self reported sexually transmitted infections or pregnancy. Furthermore, although Underhill and colleagues searched for studies from all developed countries, all of their included studies enrolled adolescents in the United States, and this limits the generalisability of the review to other populations.

Importantly, however, despite this heterogeneity, the results of the included studies (with more than 15 900 participants) were remarkably consistent. When compared with various control groups, there was little evidence that risky sexual behaviour, incidence of sexually transmitted infections, or pregnancy were reduced in adolescents in abstinence only programmes. Abstinence only programmes did not increase primary abstinence (prevention) or secondary abstinence (decreased incidence and frequency of recent sex).

In contrast to abstinence only programmes, programmes that promote the use of condoms greatly reduce the risk of acquiring HIV,^{4,6} especially when such programmes are culturally tailored behavioural interventions targeting people at highest risk of HIV infection. Therefore, in the United States priority should be given to culturally sensitive, sex specific, behavioural interventions that target black and Hispanic patients in clinics for sexually transmitted infections, men who have sex with men, and adolescents being treated for drug misuse who are at highest risk of acquiring HIV.^{7,8}

In the developing world (especially in African countries), the overwhelming lack of resources initially made abstinence only programmes popular. However, the increasing availability of condoms means that condom use has become a feasible alternative.⁹ While reducing the number of sexual partners may have

been important in the recent reduction of HIV incidence in Uganda and Thailand,¹⁰ the relative contributions of the components of the “ABC” approach of increased abstinence, reducing the numbers of sexual partners (with the “B” standing for “be faithful”), and increased condom use remain unknown.^{11 12}

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Expanding the medical workforce

Is unlikely to be cost effective or produce better outcomes for patients

JOSHUA LOTT/REUTERS

ANALYSIS, p 236

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In a policy marked more by controversy than consensus, medical schools in the United States have joined the United Kingdom in embarking upon the largest expansion in the training of doctors in more than a generation. In this week's *BMJ*, Weiner outlines the rationale for this initiative while questioning the Association of American Medical Colleges' evidence to support such an expansion.¹ Given the differences between the US and other countries within the Organisation for Economic Cooperation and Development, can the US healthcare system provide any generalisable policy lessons?

The question of whether there is or will be a surplus or shortage of doctors is usually answered by projecting today's healthcare system into the future. Using this method the answer is simple—because of population growth and ageing we need more doctors. However, when we consider how to improve the health and well-being of growing populations with limited national funds, a more pertinent question is whether expanding the medical workforce is an evidence based investment.

The most striking feature of the medical workforce is the large difference in per capita supply across countries.¹ Equally important is variation within countries such as the US, where the workforce varies two- to threefold across different hospital referral regions.² These large regional differences can help us investigate whether increasing the number of doctors improves health care. Recent studies on this subject had two main findings.

Firstly, analysis of healthcare markets in the US has shown that doctors do not generally settle where healthcare needs are greater—as measured by patient indicators.² One example is the lack of association between the regional supply of US neonatologists and measures

of perinatal risk (such as birth weight and mother's education), despite the availability of detailed perinatal statistics.³ Such misdistribution of doctors also occurs in countries with more centralised workforce planning, including the UK.⁴

Secondly, epidemiological studies in the US found no association between the number of doctors per person and health outcomes, quality, measures of access, or patient satisfaction.⁵⁻⁷ The exceptions to this finding are that a very low supply of doctors can be harmful, and higher rates of primary care provision are generally associated with higher quality and more efficient healthcare organisations.^{5 8-10} Having more medical specialists per person resulted in higher volumes of medical care and greater costs, with little difference in patient outcomes.^{6 7}

How can a greater supply of doctors have so little affect on the wellbeing of patients? In regions with higher supply, care is disordered—with higher rates of hospital admission, more specialist referrals, and more diagnostic tests and procedures. Where supply is lower, care is more likely to be dominated by tightly integrated doctor-hospital healthcare systems that can prospectively plan staffing and capital investments.

As the total number of doctors grows, their distribution will probably be shaped by the same forces that led to today's pattern of regional variation. From 1979 to 1999, the number of US doctors per person grew by 51%.¹¹ Three out of four new doctors settled in regions that already had a high workforce level. Adding more doctors to systems of care that are already inefficient (higher cost, no better quality) is a poor investment of resources.

Although the benefits of enlarging medical schools are unclear, the economic repercussions are convincing. Training doctors is a long and expensive process. Weiner suggests that the additional US public sector investment would be \$3.5bn (£1.5-2.5bn; €2.2-3.7bn) each year, but this is probably a conservative estimate. Doctors are also the most highly paid members of the healthcare team. In addition to the increase in salaries, the supply of doctors affects regional spending on inpatient care, time in the intensive care unit, diagnostic tests, and procedures.^{6 7}

Most countries assume that increased doctor training rates will improve health care, but evidence indicates that national healthcare funds are better spent on directly improving the delivery of care or promoting evidence based care. The Cochrane Collaboration has identified many examples of effective medical interventions that are incompletely implemented and many instances of ineffective care. Another promising investment is to improve the organisation of care.

Some healthcare systems in the US have already achieved high standards of patient care with a low number of doctors and low costs. The Mayo Clinic in Minnesota is one of many such examples.¹² The result of larger doctor training programmes will probably be disappointing. Implementing what we know can help patients may be a more sound and evidence based investment in our national healthcare systems.

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Hormone replacement therapy comes full circle

Further evidence on the early benefits and late risks does not change advice to menopausal women

RESEARCH, p 239

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The publication of the combined treatment arm of the women's health initiative study in July 2002 led to a dramatic fall in the use of hormone replacement therapy and a revision of the package insert for all hormone therapy preparations. This clinical trial randomised 16 608 women, aged 50-79 years, to 0.625 mg conjugated equine oestrogen and 2.5 mg medroxyprogesterone acetate or placebo.¹ The study was stopped early, at an average follow-up of 5.2 years, because analysis did not find the expected benefit in preventing coronary heart disease. In addition, the global index score—which measures the balance between benefit and harm—showed that the benefits in preventing hip fracture and colorectal cancer were outweighed by the increased risk of breast cancer, stroke, and deep vein thrombosis.

This week's *BMJ* sees the publication of the women's international study of long duration oestrogen after menopause by Vickers and colleagues.² This study was originally powered to detect a 25% reduction in the number of cases of coronary heart disease and aimed to recruit 22 300 women for 10 years' follow-up. The UK Medical Research Council stopped recruitment after the first publication from the women's health initiative, however, and 5692 women, age 50-69 years

Hazard ratios for various outcomes for women 50 to 79 years³

Outcome	Hazard ratio (95% confidence interval)	
	Combined oestrogen and progestogen	Oestrogen only
Stroke (mainly ischaemic)	1.41 (1.07 to 1.85)	1.39 (1.10 to 1.77)
Breast cancer (final results)	1.24 (1.01 to 1.54)	0.77 (0.59 to 1.01)
Deep vein thrombosis	1.95 (1.43 to 2.67)	1.47 (1.06 to 2.06)
Coronary heart disease (final results)	1.24 (1.00 to 1.54)	0.95 (0.70 to 1.16)
Dementia (women ≥65 years)	2.05 (1.21 to 3.48)	1.49 (0.83 to 2.66)
Gall bladder disease and procedure	1.59 (1.20 to 1.97)	1.67 (1.35 to 2.06)
Hip fracture	0.66 (0.45 to 0.98)	0.61 (0.41 to 0.91)
Total fracture	0.76 (0.69 to 0.85)	0.70 (0.63 to 0.79)
Colorectal cancer	0.63 (0.43 to 0.92)	1.08 (0.75 to 1.55)
Total mortality	0.98 (0.82 to 1.18)	1.04 (0.88 to 1.22)

(mean age 63), entered the study. Median follow-up time was 11.9 months. Hormone preparations and doses were similar to those in the women's health initiative, although women who had vaginal bleeding triggered unblinding, and they were offered an increase in the dose of medroxyprogesterone acetate. Women

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who had no uterus and were unwilling to take placebo were randomised to either oestrogen only or combined treatment.

How do the results of this study compare with those from the women's health initiative? Owing to early closure of the study, the number of events was small and only two outcomes reached statistical significance. These were cardiovascular events and venous thromboembolism. All of the 11 cardiovascular events (comprising unstable angina, non-fatal myocardial infarction, or sudden coronary death) occurred in the women taking hormones; nine were using combined therapy. Compared with placebo, hormone use increased the risk of venous thromboembolism, and this risk was higher for those using combined therapy (hazard ratio 7.36; 95% confidence interval 2.20 to 24.60).

The table shows the results from the women's health initiative studies.³ Both these two studies and the study by Vickers and colleagues showed the expected increase in thromboembolism. None, however, found the expected benefit in preventing cardiovascular disease.

As in the women's health initiative trial, most women in the study by Vickers and colleagues were over the age of 65. None of these studies had the power to look at outcomes for younger women, who are the main users of hormones for symptom relief. Ongoing discussion concerns the "timing hypothesis" or "therapeutic window of opportunity." The proposal under debate, which comes from early primate studies, is that oestrogen may be cardioprotective if treatment is started before vasculature has been compromised. Subgroup analyses with small numbers and inadequate power in both women's health initiative hormone trials suggested a non-significant reduction in the risk of coronary heart disease in women aged 50-59 (oestrogen only trial) or in women who reached the menopause less than 10 years earlier (combined trial).⁴ Because these findings were in a similar direction, Roussouw and colleagues did a secondary analysis combining the data from both trials.⁴ They found that women who started taking hormone therapy closer to the menopause tended to have reduced risk of coronary heart disease rather than the increased risk seen in women more distant from the menopause. Again, however, this trend test did not meet the authors' criterion for statistical significance. The risk of stroke was raised regardless of years since menopause. Moreover, women aged 50-59 using combined therapy have a significantly increased risk of deep vein thrombosis.⁵

Roussouw and colleagues have asked the important question, "If early hormone use is cardioprotective, will this benefit continue?" and their comments suggest that the answer is "no." They say, "Age-related progression of atherosclerosis is likely to continue even in the face of hormone therapy. Even if ongoing imaging trials confirm a slowing of early atherosclerosis, it would be unwise to extrapolate such findings to clinical benefit with continued use into old age."⁴

Also, it has been calculated that, even if these were not subgroup analyses and even if the differences

were significant, 1000 women each year would need to use hormone therapy to prevent one cardiovascular event.⁶

A recent surrogate outcome trial has now been published from the women's health initiative group. The coronary artery calcium study looked at the effects of oestrogen on coronary artery calcification in women who were 50-59 years at randomisation in the oestrogen only arm of the original trial.⁷ Women taking oestrogen had a 42% reduction in coronary artery recalcification, supporting the likelihood of a potential cardioprotective effect in younger women. However, the accompanying editorial in the *New England Journal of Medicine*—by a cardiologist—reminds us that the vascular effects of oestrogen are complex: "It is important to emphasize that hormone replacement therapy should not be considered as a strategy to prevent cardiovascular disease and that there are proven therapies for cardiovascular disease that remain underused in women."⁸

So postmenopausal hormone therapy has come full circle.⁹ It was originally used to treat menopausal symptoms, and now the indications for use are again hot flushes, night sweats, and vaginal dryness. It is the best treatment we have at present for these symptoms. Hot flushes and night sweats are mostly self limiting, and current advice recommends short term use with the lowest dose needed for relief of symptoms. Healthy women in early menopause are at a low absolute risk whether they take hormones or not, and they are unlikely to face substantially increased risks when using hormones for a few years.⁹

Long term use of hormone replacement therapy to prevent chronic disease is no longer recommended, because available randomised evidence shows that the negative outcomes outweigh the positive benefits. Menopausal genitourinary symptoms, however, usually last a long time and require ongoing treatment. Current low dose vaginal oestrogen preparations have minimal systemic absorption, and recent position statements support long term use of these preparations as long as distressing symptoms remain.¹⁰

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