

- 1 Collaborative Group on Epidemiological Studies of Ovarian Cancer. Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. *Lancet* 2015; **385**: 1835–42.
- 2 Onwude JL. New study does not show that HRT use causes ovarian cancer. *BMJ* 2015; **350**: h840.

A meta-analysis¹ reports an increased risk of ovarian cancer with the use of menopausal hormone therapy. The increase was significant in short-term users, with no difference according to type (oestrogen therapy or combined oestrogen and progestagen therapy) or duration of menopausal hormone therapy.

Several concerns need to be addressed. A major flaw is that the authors claim that the relative risks were adjusted according to body-mass index, age at menopause, and past use of oral contraceptive. However, this information was unavailable in the Danish Sex Hormone Register Study (DaHoRS)² as it is based on data from registers. In the Million Women Study (MWS),³ the risk for present menopausal hormone therapy users among women who had used oral contraceptive for more than 5 years was no longer significant. This is of particular importance since these two studies contributed about 75% of the prospective data. All recently published studies including the MWS⁴ and DaHoRS have reported a greater risk of ovarian cancer with oestrogen therapy than with oestrogen and progestagen therapy, which is contradictory with the present analysis.¹

The authors' statement that women who use menopausal hormone therapy for 5 years at age 50 years have one additional ovarian cancer per 1000 users is misleading and unduly alarming. Since the absolute risk of ovarian cancer is about a tenth of that of breast cancer after menopause,⁵ such a risk level is indefensible. This risk represents in fact a cumulative risk calculated over 15 years by adding up risk per age group. The proper estimated absolute risk would be at

most one in 10 000 per year, which is likely to have no notable public health implications.

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- 1 Collaborative Group on Epidemiological Studies of Ovarian Cancer. Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. *Lancet* 2015; **385**: 1835–42.
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Authors' reply

Users of menopausal hormone therapy are at greater risk of developing ovarian cancer than otherwise similar non-users. Our meta-analyses¹ of virtually all the available epidemiological evidence showed a highly significantly increased risk of ovarian cancer in current users of menopausal hormone therapy; the excess risk declined after hormone use ceased, although a small excess persisted for about a decade after stopping long-duration use.¹ In the few studies of fatal ovarian cancer, findings were typical of those reported for incident disease.^{2,3} Epidemiological studies were eligible for inclusion if

they had information about hormone use in women with ovarian cancer; studies with no cases of the disease were excluded because they are uninformative for the calculation of relative risks.

The two largest prospective studies that contributed information to the meta-analysis were the UK Million Women Study³ and the population-based Danish Sex Hormone Register Study.⁴ Contrary to the claim by Florence Trémollières and colleagues, neither of these studies had reported a significantly greater risk of ovarian cancer with use of oestrogen-only than with oestrogen and progestagen combinations, and the overall results for all studies showed little difference between the effects of the two hormone therapy types. The data from the Million Women Study³ included in the meta-analysis superseded the data from that study reported in 2007, because since then additional cases had accrued with longer follow-up. Adjustment by potential confounding factors, other than age, made little difference to the risk estimates (Article¹ appendix, p 18) and no strong evidence was found that any of the potential risk factors modified the association between ovarian cancer and menopausal hormone use (Article¹ appendix, pp 15–16). Hence the absence of information on every adjustment factor in every study would not materially affect the risk estimates.

The estimated excess incidence of ovarian cancer in women who use menopausal hormone therapy for 5 years starting at age 50 years was one per 1000, based on ovarian cancer incidence rates in England. Had we used incidence rates in other high-income countries where menopausal hormone therapy use is common, the excess would have been much the same; in 2003–05 ovarian cancer incidence from age 50 to 64 years per 1000 women was usually between 4.7 and 6.6 in western Europe, North America, and Australasia⁵—similar to the value

of 5.6 in England that was used to estimate absolute excess risk.

Assuming that the association is causal, each million woman-years of hormone therapy use results in about 20 extra cases of ovarian cancer, of which 12 are fatal. In high-income countries, therefore, where there has been about 600 million women-years of use since 1970 (Article¹ appendix, p 4), menopausal hormone use has caused about 120 000 extra cases of ovarian cancer and about 70 000 extra deaths from the disease.

We declare no competing interests.

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Local implementation of obesity policy

We welcome the *Lancet* Series on obesity and concur with the need for more aggressive policy action and increased accountability. However, an important omission from the series was a discussion of local policy implementation. Failure to implement policy to improve public health, even with the support of government

regulation, is well documented. In the USA, the Healthy, Hunger-Free Kids Act of 2010 recommends that schools ban the sale of all sugar-sweetened beverages, but less than 10% of middle-school and high-school students attend school in districts which ban these drinks. In Australia, less than 40% of schools in all states except for Western Australia comply with mandatory government policies to restrict the sale of unhealthy foods in school canteens,¹ and in Brazil, school canteens frequently sell unhealthy foods that are prohibited.² In the USA and Australia, less than 15% of child-care services serve foods consistent with dietary guidelines,^{3,4} and clinicians do not provide recommended weight management care to patients who are overweight.⁵ Monitoring of policy implementation and systems of accountability are important, and local practitioners need evidence-based strategies to support policy implementation. A report published by the Agency for Healthcare Research and Quality laid bare the nascent state of community implementation research in the field.⁶ Without development of appropriate implementation and supporting policy action, obesity policies will continue not to yield the benefits they were intended to deliver.

We declare no competing interests.

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Preventing childhood obesity starts during pregnancy

Tim Lobstein and colleagues (June 20, p 2510)¹ highlight the global childhood obesity epidemic and the need for preventive strategies. However, greater emphasis on prevention before birth is needed. We have shown that similar fetal growth is observed in mothers at low risk of nutritional, social, and medical constraints,² which justifies using the newly published international newborn standards³ that complement the existing WHO Child Growth Standards. These standards describe how individuals should grow, by contrast with the many current references describing how they have grown at a particular time or place.

The use of local newborn references derived from settings where obesity and diabetes are prevalent normalises babies who are large for their gestational age. Hence, some overweight newborns go unrecognised and the opportunity for early interventions is missed. In England between 2011 and 2012, the recommended national reference placed 54 449 (11%) of 509 332 live singleton babies (born after 33 weeks of gestation) over the 90th percentile by birthweight.⁴ However, the international newborn standard,³ derived from healthy, adequately nourished pregnant populations, identifies an additional 42 988 babies

For the **Healthy, Hunger-Free Kids Act** see <http://www.ncsl.org/research/human-services/healthy-hunger-free-kids-act-of-2010-summary.aspx>



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For the **Lancet Series on obesity** see <http://www.thelancet.com/series/obesity-2015>

For more on **local wellness policies** see http://www.bridgingthegapresearch.org/_asset/hxbby9/WP_2009_monograph.pdf