Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial

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- Editorial: Iron supplementation in pregnancy (*BMJ* 2013;347:f4399)
- Letter: Healthy pregnant women still don't need routine iron supplementation (*BMJ* 2013;347:f4866)
- Research news: Women who have had surgery for obesity have raised risk of preterm babies (*BMJ* 2013;347:f677)

STUDY QUESTION

Does provision of antenatal lifestyle advice to overweight or obese pregnant women effectively improve maternal and infant health outcomes?

SUMMARY ANSWER

For women who are overweight or obese, antenatal lifestyle advice does not reduce the risk of infant birth weight above the 90th centile for gestational age and infant sex or improve maternal pregnancy and birth outcomes.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Overweight and obesity is common during pregnancy, and is associated with maternal and infant complications. Although provision of an antenatal dietary and lifestyle intervention might be effective in limiting gestational weight gain, the effect on clinically relevant outcomes remains to be determined. This study showed that providing an antenatal dietary and lifestyle intervention was not effective at reducing infant birth weight above the 90th centile or improving maternal pregnancy or birth outcomes.

Design

This randomised trial used a central telephone randomisation server, with computer generated schedule, balanced variable blocks, and stratification for parity, BMI category, and hospital to allocate women to lifestyle advice (n=1108) or standard care (n=1104). Women randomised to lifestyle advice participated in a comprehensive dietary and lifestyle intervention during pregnancy delivered by research staff. Women randomised to standard care received pregnancy care according to local guidelines, which did not include such information.

Participants and setting

2212 women with a singleton pregnancy between 10+0 and 20+0 weeks' gestation and body mass index (BMI) >25 were recruited from three public maternity units in South Australia.

Primary outcome

The incidence of infants born large for gestational age (birth weight >90th centile for gestation and sex). Prespecified secondary outcomes included birth weight >4000 g, hypertension, pre-eclampsia, and gestational diabetes. Analyses used intention to treat principles.

Main results and the role of chance

The risk of the infant being large for gestational age was not significantly different in the two groups: 203/1075 (19%) in the lifestyle advice group versus 224/1067 (21%) in the standard care group (adjusted relative risk 0.90, 95% confidence interval 0.77 to 1.07; P=0.24). Infants born to women after lifestyle advice were significantly less likely to weigh above 4000 g (164/1075 (15%) versus 201/1067 (19%); adjusted relative risk 0.82, 0.68 to 0.99; number needed to treat (NNT) 28, 15 to 263; P=0.04).

Harms

We did not identify any increase in the risk of harms.

Bias, confounding, and other reasons for caution

As infant birth weight above 4000 g was a secondary outcome in our trial, it will be important to evaluate this outcome in ongoing randomised trials evaluating the effect of dietary interventions in obese women.

Generalisability to other populations

Our population was predominantly white and of high social disadvantage, with 60% of eligible women declining to participate.

Study funding/potential competing interests

This project was funded by a project grant from the Australian National Health and Medical Research Council (NHMRC) (ID 519240). JMD is supported through a NHMRC Practitioner Fellowship (ID 627005).

Trial registration

Australian and New Zealand Clinical Trials Registry (ACTRN12607000161426).

Outcomes in infants born to mothers with BMI at ≥25 at trial entry by treatment group

Outcome	No (%) of infants		Risk ratio (95% CI)
	Lifestyle advice	Standard care	
Large for gestational age	203 (19)	224 (21)	0.90 (0.77 to 1.07)
Birth weight >4000 g	164 (15)	201 (19)	0.82 (0.68 to 0.99)

Maternal dietary patterns and preterm delivery: results from large prospective cohort study

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- Research news: Women who have had surgery for obesity have raised risk of preterm babies (*BMJ* 2013;347:f677)

STUDY QUESTION

Does an association exist between maternal dietary patterns and risk of preterm delivery?

SUMMARY ANSWER

Women adhering to a "prudent" or a "traditional" dietary pattern (containing a high intake of vegetables, fruit, whole grains, and fish) and drinking water during pregnancy were at lower risk of preterm delivery.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Growing evidence suggests that maternal diet may affect the risk of preterm delivery. Diet matters for the risk of preterm delivery, which may reassure medical practitioners that the current dietary recommendations are sound but also inspire them to pay more attention to dietary counselling.

Participants and setting

We studied 66 000 pregnant women included in the prospective national Norwegian Mother and Child Cohort Study.

Design, size, and duration

Between 2002 and 2008 an extensive self reported food frequency questionnaire was used to prospectively assess maternal diet in mid-pregnancy. Exploratory principal component analysis identified three distinct dietary patterns that we interpreted as "prudent" (for example, vegetables, fruits, oils, water as beverage, whole grain cereals, fibre rich bread), "Western" (salty and sweet snacks, white bread, desserts, processed meat products), and "traditional" (potatoes, fish). Data on gestational age at delivery came from the Medical Birth Registry of Norway. We used a Cox regression model to estimate hazard ratios and 95% confidence intervals for preterm delivery. Models were adjusted for maternal age, pre-pregnancy body mass index, height, parity, total energy intake, maternal education, marital status, smoking, previous preterm delivery, household income, and the other dietary patterns.

Main results and the role of chance

After adjustment for covariates, high scores on the prudent pattern were associated with a significantly reduced hazard ratio of preterm delivery for the highest versus lowest third (0.88, 95% confidence interval 0.80 to 0.97). The prudent pattern was also associated with a significantly lower risk of late and spontaneous preterm delivery. We found no independent association with preterm delivery for the Western pattern. The traditional pattern was associated with a reduced risk of preterm delivery (hazard ratio for highest versus lowest third 0.91, 0.83 to 0.99).

Associations between thirds of dietary pattern scores and preterm delivery in 66 000 pregnant women in Norwegian Mother and Child Cohort Study

Dietary pattern	Preterm delivery—No (%)	Hazard ratio (95% CI)
All	3505 (5.3)	—
"Prudent":		
Third 1	1249 (5.7)	1
Third 2	1141 (5.2)	0.94 (0.86 to 1.02)
Third 3	1115 (5.1)	0.88 (0.80 to 0.97)
P for trend	—	0.006
"Western":		
Third 1	1110 (5.0)	1
Third 2	1166 (5.3)	1.04 (0.95 to 1.13)
Third 3	1229 (5.6)	1.02 (0.92 to 1.13)
P for trend	—	0.695
"Traditional":		
Third 1	1224 (5.6)	1
Third 2	1171 (5.3)	0.98 (0.90 to 1.06)
Third 3	1110 (5.0)	0.91 (0.83 to 0.99)
P for trend	—	0.043

Bias, confounding, and other reasons for caution

The results are observational, and no causal inference is possible. Despite careful consideration of known risk factors and potential confounding factors, residual confounding cannot be ruled out.

Generalisability to other populations

Our findings are likely to be generalisable outside Norway and thus contribute to the general body of research on diet and health. Studies do not show that typical Nordic diets, either in the general population or in pregnant women, contain more "prudent" foods than elsewhere.

Study funding/potential competing interests

This work was supported by the Freemasons Directorate board for Children, the Adlerbertska Foundation, the Hjalmar Svensson Foundation, the Norwegian Research Council, the Jane and Dan Olsson Foundation, the Swedish Medical Society, Swedish government grants, the Norwegian Ministry of Health, the Ministry of Education and Research, and the Norwegian Research Council.

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Associations between palliative chemotherapy and adult cancer patients' end of life care and place of death: prospective cohort study

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Views and reviews: Saying no to chemotherapy (*BMJ* 2013;346:f402)
Research: Survival and risk of adverse events in older patients receiving postoperative adjuvant chemotherapy for resected stages II-IIIA lung cancer (*BMJ* 2011;343:d4013)
Editorial: Chemotherapy in elderly patients with resected stage II-IIIA lung cancer (*BMJ* 2011;343:d4104)
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STUDY QUESTION

Are advanced cancer patients who receive palliative chemotherapy months before death more likely to receive intensive end of life medical care or die in an intensive care unit compared with those who do not receive palliative chemotherapy?

SUMMARY ANSWER

The use of chemotherapy in terminally ill cancer patients in the last months of life is associated with increased risk of undergoing cardiopulmonary resuscitation, mechanical ventilation, or both and of dying in an intensive care unit.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Many patients with metastatic cancer receive chemotherapy in the final months of life, but most are not provided with information on the likely effect on their survival, future care and quality of life, and location of death. Cancer patients, caregivers, and oncologists should have a heightened awareness about the potential risks of continuing palliative chemotherapy near death and should actively engage in advance care planning to ensure that patients' end of life experiences are congruent with their values.

Participants and setting

We studied 386 adult patients with metastatic cancers refractory to at least one chemotherapy regimen, whom physicians in eight outpatient oncology clinics in the United States identified as terminally ill at study enrollment, and who subsequently died.

Design, size, and duration

This was a secondary analysis of a prospective, multi-institution, longitudinal study (Coping with Cancer). We examined associations between receipt of palliative chemotherapy at study enrollment and the intensity of patients' end of life medical care and place of death, using propensity weighting to adjust for differences in patients' demographic, clinical, psychosocial, and institutional characteristics at enrollment. We also examined survival time, late hospice enrollment, and death in patients' preferred place as secondary outcomes.

Main results and the role of chance

Of 386 terminally ill cancer patients, 216 (56%) were receiving palliative chemotherapy at study enrollment, a median of 4.0 months before death. After propensity score weighted adjustment, use of chemotherapy at enrollment was associated with higher rates of cardiopulmonary resuscitation, mechanical ventilation, or both in the last week of life and late referral to a hospice but no difference in survival (hazard ratio 1.11, 95% confidence interval 0.90 to 1.38). Patients receiving palliative chemotherapy were more likely to die in an intensive care unit, compared with those who were not, and less likely to die at home. Patients receiving palliative chemotherapy were also less likely to die in their preferred place, compared with those who were not.

Bias, confounding, and other reasons for caution

We had no information on the timing or nature of patients' decisions about treatment after study enrollment (except for the last week of life), we could not adjust for unobserved confounders, and the analyses were limited to patients who died in 2008. However, the observed associations between palliative chemotherapy and the intensity of patients' end of life care and place of death remained significant in a sensitivity analysis that removed characteristics that often change in response to chemotherapy (such as quality of life and performance status) or disease progression (such as treatment preferences and awareness of terminal illness).

Generalisability to other populations

Studies indicate that the intensity of medical care is increasing over time, which suggests that our findings may be conservative estimates of the current effects.

Associations between chemotherapy at study enrollment and intensity of end of life care, place of death, and attainment of preferred place of death. Values are numbers (percentages) unless stated otherwise

Medical care in last week/place of death	Chemotherapy at enrollment		Adjusted risk difference (95% CI)	P value
	Yes (n=216)	No (n=170)		
Cardiopulmonary resuscitation, ventilation, or both	30 (14)	3 (2)	10.5 (5.0 to15.5)	<0.001
Hospice ≤1 week	113 (54)	61 (37)	13.6 (3.6 to 23.6)	0.008
Died in intensive care unit	24 (11)	4 (2)	6.1 (1.1 to 11.1)	0.02
Died at home	102 (47)	112 (66)	−10.8 (−1.0 to −20.6)	0.03
Death in preferred place	140 (65)	135 (80)	−9.4 (−0.8 to −18.1)	0.03

Study funding/potential competing interests

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Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia

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- Podcast: HPV testing in preventing cervical cancer
- Clinical review: Developing role of HPV in cervical cancer prevention (*BMJ* 2013;347:f478)
- Research: Primary screening for human papillomavirus compared with cytology screening for cervical cancer in European settings (*BMJ* 2012;344:e670)

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STUDY QUESTION

What is the effectiveness of the quadrivalent human papillomavirus (HPV) vaccine against cervical abnormalities up to four years after implementation of the vaccination programme in Queensland, Australia?

SUMMARY ANSWER

The quadrivalent HPV vaccine was 46% effective against high grade cervical abnormalities and 34% effective against any other cervical abnormality in young women who were fully vaccinated at school or up to 27 years of age. Receipt of two vaccine doses provided some, although lesser, protection.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Results from phase III trials have shown 98% efficacy of the quadrivalent vaccine against high grade cervical abnormalities due to the HPV types covered by the vaccine, but less is known about its effectiveness against cervical abnormalities in population settings. The quadrivalent HPV vaccine seemed more effective for preventing high grade than other cervical abnormalities and more effective in younger than older women.

Participants and setting

Women eligible for free HPV vaccination (aged 12-26 in 2007) attending for their first cervical smear test between April 2007 and March 2011 in Queensland, Australia.

Design

We performed a case-control analysis using linked, anonymised data obtained from population registers. High grade cases were women with histologically confirmed high grade cervical abnormalities. Other cases were women with any other abnormality at cytology or histology. Controls were women with normal cytology.

Effectiveness of quadrivalent human papillomavirus vaccine by number of doses at ages 11 to 27 years in 2007

No of vaccine doses	Adjusted odds ratio* (95% CI)	
	Other cases†	High grade cases‡
0	reference	reference
1	0.95 (0.89 to 1.02)	0.95 (0.77 to 1.16)
2	0.79 (0.74 to 0.85)	0.79 (0.64 to 0.98)
3	0.66 (0.62 to 0.70)	0.54 (0.43 to 0.67)

*Adjusted for socioeconomic status, rurality, year of birth, and follow-up time
†Exposure odds ratio (ratio of exposure odds among other cases to exposure odds among controls).
‡Exposure odds ratio (ratio of exposure odds among high grade cases to exposure odds among controls).

Primary outcomes

Exposure odds ratio—the ratio of odds of antecedent vaccination (one, two, or three doses compared with no doses) among cases compared with controls in women whose first ever smear test result defined their status as cases or controls (primary analysis).

Main results

Between April 2007 and March 2011 there were 1062 (1.0%) high grade cases, 10 887 (10.0%) other cases, and 96 404 (89.0%) controls. The adjusted odds ratios for exposure to three doses of HPV vaccine compared with none were 0.54 (95% confidence interval 0.43 to 0.67) for high grade cases and 0.66 (0.62 to 0.70) for other cases compared with controls. This equated to vaccine effectiveness of 46% and 34%, respectively. The adjusted numbers needed to vaccinate to prevent one cervical abnormality at first screening round were 125 (95% confidence interval 97 to 174) and 22 (19 to 25), respectively. The adjusted odds ratios for exposure to two doses were 0.79 (0.64 to 0.98) for high grade cases and 0.79 (0.74 to 0.85) for other cases, equating to vaccine effectiveness of 21%.

Bias, confounding, and other reasons for caution

We used administrative datasets to determine vaccine status and outcome information. It is possible that vaccine status was misclassified in some women owing to inaccuracies in data capture. About one quarter of women aged 19-27 and 12% aged 12-18 recorded on the vaccine register had no record of a first dose but records of subsequent doses. Sensitivity analyses including women with incomplete vaccination data, however, made little difference to effect estimates. The strongest confounder in our analyses was age. We were able to control for a limited number of other covariates; socioeconomic status, rurality, and follow-up time. It is possible that residual confounding by other factors may have occurred (for example, smoking, sexual activity). However, we consider it unlikely that any such confounding would be of sufficient magnitude and in the direction observed to explain these findings.

Generalisability to other populations

Vaccine effectiveness predominantly depends on the extent of previous infection, how common the HPV types targeted by the vaccine are in the population, and the age groups targeted.

Study funding/potential competing interests

This study received no specific funding. For competing interests see bmj.com.