The London Exercise And Pregnant smokers (LEAP) trial: a randomised controlled trial of physical activity for smoking cessation in pregnancy with an economic evaluation

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Scientific summary

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Background

Maternal smoking in pregnancy is the main preventable cause of morbidity and death among women and infants. In most high-income countries at least 10% of women smoke during pregnancy and the prevalence is rising in low- and middle-income nations. There is evidence that behavioural support increases the rate at which women can stop smoking but there is no evidence that smoking cessation medication adds to this. The large majority of women who receive behavioural support for cessation during pregnancy do not manage to stop smoking and thus new options that add to the effectiveness of behavioural support are needed.

Physical activity (PA) programmes may add to the effectiveness of behavioural support. There is convincing evidence that PA reduces the intensity of urges to smoke in the general population of smokers, which are the main cause of relapse to smoking. In non-pregnant smokers, the evidence base showing that PA programmes improve cessation rates is mixed, but most trials did not have sufficiently large sample sizes to have a realistic chance of detecting group differences and had other methodological limitations that increase the risk of bias and make the evidence hard to interpret. Moderate-intensity PA (e.g. brisk walking) is recommended during pregnancy and has been shown to reduce cigarette cravings, and pregnant smokers, especially those who are reluctant to use nicotine replacement therapy, are likely to be receptive to such an intervention. We conducted the London Exercise And Pregnant smokers (LEAP) trial to assess the effectiveness and cost-effectiveness of a PA intervention for smoking cessation during pregnancy.

Objectives

The main objective of the study was to investigate whether or not behavioural support for smoking cessation in pregnancy plus a PA intervention is more effective than behavioural support alone in achieving biochemically validated smoking cessation between a quit date and end of pregnancy. A further objective was to assess the cost-effectiveness of the intervention for achieving smoking cessation at the end of pregnancy.

Methods

The LEAP trial was a pragmatic, randomised controlled trial with an accompanying health economic evaluation. Following their first antenatal booking visit, researchers identified pregnant smokers via lists on the computerised patient administration system at 13 hospital trusts. They discussed the study with potential participants by telephone and enrolled women who consented to participate and met the inclusion criteria. We included women who were between 10 and 24 weeks' gestation, who smoked one or more cigarettes daily at trial entry and who had smoked at least five cigarettes daily before pregnancy. Participants set a quit date and researchers offered six weekly sessions of 20 minutes of individual behavioural cessation support. At enrolment, participants were randomly assigned to behavioural support alone or to behavioural support plus a PA intervention that included 14 sessions of supervised exercise on a treadmill combined with nine PA consultations.

Researchers followed up participants at a visit at the end of pregnancy (valid if between 36 weeks' gestation and 10 weeks after the birth) and by telephone at 6 months postnatally. Researchers retrieved birth outcome data from medical records. The primary outcome was self-reported continuous abstinence from smoking between the quit date and end of pregnancy validated by exhaled carbon monoxide and/or salivary cotinine. Temporary, brief smoking lapses of up to five cigarettes in total were permitted following

the quit day. Secondary outcomes included validated abstinence at 4 weeks after the quit date and self-reported abstinence at 6 months postnatally. Self-reports of PA levels were collected at baseline and weeks 1, 4 and 6 after the quit date, at the end of pregnancy and 6 months post partum. To validate self-reported PA levels, a 10% random subsample of participants had their PA objectively measured using an accelerometer (Model GT1M or GT3X; Actigraph, Pensacola, FL, USA). Ratings of withdrawal symptoms, urges to smoke, confidence for quitting smoking and confidence for participating in PA were recorded. Changes in maternal depression were examined between baseline and end of pregnancy and 6 months after the birth. Changes in maternal weight were assessed between baseline and end of pregnancy. Maternal and fetal adverse events (AEs) and birth outcomes were collected from hospital records.

Based on a systematic review it was anticipated that there would be a cessation rate of 15% in the control group, on the basis that 9% of pregnant women who are smokers stop smoking with usual care after their first antenatal visit and an additional 6–7% quit with behavioural support. Based on pilot work, a cessation rate of 23% was anticipated in the treatment group. The aim was to recruit 866 participants, providing 83% power at a 5% significance level to detect an 8% absolute difference in the rate of smoking cessation at the end of pregnancy between the two groups, corresponding to an odds ratio (OR) of 1.69.

Analysis was on an intention-to-treat (ITT) basis; participants with missing outcome data were assumed to be smoking. The proportion of women reporting continuous smoking abstinence at the end of pregnancy was compared between study groups using logistic regression, with adjustment for recruitment centre. Economic analyses assessed the costs of delivering the intervention for each participant in the intervention group compared with the control group and the costs of caring for each woman and her infant during the period between randomisation and the immediate postnatal period.

Results

In total, 789 women were enrolled in the trial. Four women were excluded post randomisation, two because they were enrolled twice in sequential pregnancies and two because they were ineligible at their baseline visit and had been erroneously randomised. Of the 785 women ($n = 392$ in the PA group) included in the ITT analysis, there were 774 singleton births, 10 twin births and one unknown birth as the woman withdrew consent. The follow-up rate for the primary outcome was 88.8% and this was similar for the two study groups.

Adherence

Participants attended a median of four of 14 treatment sessions in the intervention group and three of six in the control group. Women in the intervention group increased their PA levels more than women in the control group. For the PA group compared with the control group, the percentage increase in minutes of moderate- and vigorous-intensity PA was 33%, [95% confidence interval (CI) 14% to 56%] at 1 week, 28% (95% CI 7% to 52%) at 4 weeks and 36% (95% CI 12% to 65%) at 6 weeks ($p < 0.001$). Relative to baseline there was a decrease in self-reported minutes of PA at the end of pregnancy and 6 months after the birth for both groups. According to the accelerometer data there was no significant difference in PA levels between the groups.

Smoking outcomes

There was no significant difference in smoking abstinence rates between the two groups. The rate of validated continuous abstinence at the end of pregnancy was 7.7% in the PA group and 6.4% in the control group (OR for PA group, adjusted for centre only, 1.21, 95% CI 0.70 to 2.10). At 4 weeks the validated abstinence rate was 12.8% in the PA group and 15.5% in the control group (OR, adjusted for centre only, 0.79, 95% CI 0.53 to 1.18). At 6 months postnatally the self-reported abstinence rate was 6.1% in the PA group and 4.1% in the control group (OR, adjusted for centre only, 1.55, 95% CI 0.81 to 2.97).

Psychological outcomes

Between baseline and 1 week post quit, the PA group exhibited a significant increase in ratings of confidence for participating in PA relative to the control group ($p = 0.002$); however, across this period there was no significant difference in change in ratings for individual cigarette withdrawal symptoms or for urge to smoke or confidence for quitting. There was no evidence of any difference in changes in depression between the two study groups.

Birth outcomes

Birth outcomes were similar between treatment groups. The only significant difference was that more caesarean births occurred in the control group than in the PA group (28.7% vs. 21.3%; $p < 0.023$).

Maternal weight gain

There was no evidence for any difference in maternal weight gain between the two study groups.

Adverse events

The rates of AEs and serious adverse events (SAEs) were similar in the two study groups. The number of women or their infants who had at least one AE or SAE was 55.4% in the PA group and 55.7% in the control group.

Economic analyses

The total mean cost (cost of delivering the intervention plus resource use costs) was £35 per participant lower in the PA group than in the control group. This was mainly attributable to increased health-care usage in the control group. However, as shown by the scatterplot, there was substantial uncertainty around this estimate.

Conclusions

Supplementing behavioural support with a PA intervention was no more effective than behavioural support alone in promoting smoking cessation. These findings were observed despite the PA group self-reporting 35–47% greater increases in PA than the control group during the intervention period. There was no evidence that the PA intervention increased AEs or had a harmful effect on birth outcomes and there was some evidence that the PA intervention resulted in fewer caesarean sections. In pregnancy, the PA intervention that we tested is not recommended for smoking cessation but remains indicated for general health benefits.

Recommendations for research

1. It is not recommended to fund further large-scale trials of PA for smoking cessation until much less expensive observational studies have been conducted to provide promising leads, for example to investigate the populations most suitable for such interventions and methods for increasing PA adherence.
2. The reasons for pregnant smokers' low levels of attendance at supervised PA sessions should be investigated, with the aim of using the findings to increase attendance rates. For example, following on from recent work on barriers to PA, further research is needed to explore barriers to attendance and to PA adherence during pregnancy, and to assess whether or not these barriers vary during different stages of pregnancy and vary among women with different comorbidities, including gestational diabetes and obesity.
3. Further methods of increasing PA adherence among pregnant smokers need to be developed and tested. For example, financial incentives have shown some benefit for aiding smoking cessation in this population and they may be used in combination with PA to increase both attendance at exercise sessions and smoking cessation. In addition, interventions are needed that provide regular prompts to remind women to exercise (e.g. text messages or brief telephone calls); such interventions have been successfully piloted with young women but not yet with pregnant women.

4. The reasons why few inactive pregnant smokers were attracted to a PA trial need to be identified and methods are needed to attract these less active pregnant smokers.
5. Studies are needed to establish whether or not the previously reported finding of a short bout of PA reducing cigarette cravings in pregnant smokers is a robust finding. So far, only one study has investigated this issue. If it is a robust finding, interventions need to be developed that can translate this benefit into prevention of smoking relapse.
6. There was no evidence of beneficial effects on maternal weight gain or depression. Studies are needed that focus on women who are at risk of higher maternal weight gain and women who have high levels of depression at baseline.
7. Among pregnant smokers there was no evidence for a PA intervention having an added benefit for smoking cessation beyond that of usual care. However, it is possible that in some circumstances a PA programme alone may be more practical and may aid smoking cessation and this needs to be assessed.
8. There were significantly fewer deliveries by caesarean section in the PA group than in the control group. Further studies are needed to replicate this finding and to explore the underlying mechanisms.

Implications for health care

There was no evidence that offering regular supervised exercise and PA consultations in addition to routine smoking cessation support to women following their first antenatal visit was effective for aiding smoking cessation. Nor was there any evidence for the PA intervention moderating cravings/urges to smoke but it is possible that there are some acute benefits of PA on reducing cravings during pregnancy and the recommendation to use PA to manage cravings acutely remains for all smokers, including those who are pregnant. The PA intervention did not show any benefit for reducing maternal depression and there was no evidence for an effect on maternal weight gain. There was no evidence of increased AEs in the PA group and there was some evidence for a reduced incidence of caesarean sections; therefore, in line with current guidance, PA remains indicated for general health benefits in pregnancy, including among pregnant smokers.

Trial registration

This trial is registered as ISRCTN48600346.

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