ORIGINAL ARTICLE

Does oral contraceptive use affect maximum force production in women?

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Br J Sports Med 2005;**39**:15–19. doi: 10.1136/bjsm.2003.009886

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Accepted 16 December 2003

Objective: To examine the effects of oral contraceptive use on maximum force production in young women.

Methods: In the study, 21 female subjects (14 pill users and seven eumenorrheic controls) took part. All pill using subjects had been taking a combined, monophasic oral contraceptive pill for at least 6 months. Maximum dynamic and isometric leg strength, maximum isometric strength of the first dorsal interosseus (FDI) muscle, and plasma concentrations of oestradiol and progesterone were measured on days 7 and 14 of pill consumption and day 5 of pill withdrawal. The eumenorrheic group was tested (FDI strength and hormone concentrations) on days 2 and 21 of the menstrual cycle.

Results: There were no significant changes in the concentration of endogenous oestradiol or progesterone or any measure of muscle strength between pill phases ($p<0.05$). The pill group did not significantly differ from the eumenorrheic group ($p<0.05$), despite a significant increase in the concentration of progesterone and oestradiol on day 21 of the menstrual cycle compared with day 2 of the menstrual cycle and pill consumption and withdrawal ($p<0.05$).

Conclusions: These data suggest that oral contraceptive use does not significantly affect muscle strength. Moreover, oral contraceptive users were not stronger or weaker than their eumenorrheic counterparts.

Oral contraceptives are available in single (progesterone only) and combined (oestrogen and progestogen) formulations. The oestrogenic and progestogenic content ranges from 0.02 to 0.5 mg and 0.1 to 1.0 mg, respectively. Phasic oral contraceptives mimic the cyclical variations in endogenous hormones by only providing synthetic ovarian hormones for 21 out of 28 days. The pill acts, via negative feedback, on the hypothalamus and anterior pituitary gland, causing the suppression of follicle stimulating hormone (FSH), lutenising hormone (LH), and gonadotropin releasing hormone (GnRH) secretion. Subsequently, the concentration of endogenous sex hormones (oestradiol and progesterone) is reduced to levels indicative of the menopause. Several researchers have noted that adverse changes in specific muscle strength occur around the onset of menopause in women.[1–7] However, it is difficult to conclude a sex hormone dependent loss in strength using the model of menopause, as it is difficult to control for other age related factors that may affect muscle strength.

Previous research examining the influence of oral contraceptive use on muscle function has been limited, as pill users have been used as a control rather than an experimental group. Sarwar *et al*[8] found that maximum voluntary force of the quadriceps or hand muscles did not change when tested weekly over two cycles in women using oral contraception. All subjects were taking a monophasic combined pill (20–35 μg of ethinyl oestradiol and progestins in different doses). These authors suggested that, as progestin levels can remain elevated for 4–5 days after ingestion, testing at variable times during the withdrawal period may have obscured their results. Similarly, Phillips *et al*[9] found no significant change in maximum voluntary isometric force (MVIF) of the adductor pollicis muscle in subjects taking a non-specified pill. Conversely, Wirth and Lohman[10] found significantly greater handgrip endurance times (made at 50% of maximum voluntary contraction) and force output measurements in eumenorrheic subjects compared with pill users, despite observing no change in maximum voluntary contraction between the two groups. Eight different, non-specified pills were used in this study. However, none of these studies measured the concentration of endogenous oestradiol and progesterone during different phases of pill use; these data are needed to test the relationship between the concentration of reproductive hormones and muscle strength.

Based on the findings of post-menopausal studies, the aim of this study was to investigate whether the low levels of endogenous ovarian hormones induced by oral contraceptive use affects maximum force production in young healthy women by comparing strength measures during pill consumption (day 7 and 14) and withdrawal (day 5). It was hypothesised that maximum force production would increase during pill withdrawal, assuming that endogenous levels of oestradiol and progesterone increase during pill withdrawal as a result of the exogenous hormones being withheld. The concentration of endogenous oestradiol and progesterone was measured to support any such findings. Maximum isometric strength of the first dorsal interosseus (FDI) muscle was also tested in a group of eumenorrheic subjects so that a comparison could be made between cyclical variation (pre-menopausal) and continuous downregulation (post-menopausal) of endogenous reproductive hormone concentration. The present research design (using pill users to mimic post-menopausal hormone status) was designed to limit any potential confounding influence of age on strength assessment.

METHODS

Subjects

From the local university, 21 healthy, sedentary female subjects were recruited. Subjects were considered sedentary if

Abbreviations: C, consumption; EF, early follicular; FDI, first dorsal interosseus; FSH, follicle stimulating hormone; GnRH, gonadotropin releasing hormone; HRT, hormone replacement therapy; LH, lutenising hormone; ML, mid-luteal; MVIF, maximum voluntary isometric force; N, maximum dynamic and isometric force of the quadriceps and hamstring muscles; Nm, maximum voluntary isometric force of the FDI muscle; WD, withdrawal

they were not, or had not been in the last 6 months, involved in a strength/resistance or aerobic training programme. Fourteen subjects had been taking a combined, monophasic oral contraceptive pill (standard strength) for a minimum of 6 months prior to recruitment (table 1). Combined, monophasic pills were used as they contain synthetic oestrogen and progestogen and are taken daily for 21 days, with subsequent courses taken following a 7 day interval. The remaining seven subjects reported normal menstrual cycle function, with mean cycle lengths of 29.01 (1.2) days. Only non-smokers were included in the study.[11] Subjects with any muscular, neurological, or skeletal disorders capable of influencing performance of the hand or leg were excluded. Approval for the experimental protocol was obtained from the institution's human ethics committee and conformed to the Declaration of Helsinki. All subjects provided written consent, having read and understood the details of the experiment.

Experimental design

Subjects were required to abstain from alcohol and caffeine consumption and strenuous physical activity for 24 hours prior to testing to prevent known effects on reproductive hormone concentration and muscle strength.[12–15] All subjects reported to the laboratory in a ''normal'' fed state. In order to control for circadian variation in muscle strength,[16] all testing was undertaken at the same time of day. A 10 ml venous blood sample was obtained prior to any physical testing.

The oral contraceptive users were instructed to consume their pill at 08.00 hours ($\pm$1 hour) for the duration of the study. Prior to experimentation, subjects were familiarised, on two occasions, with the experimental environment and procedures. Following familiarisation, subjects attended the human performance laboratory in the university on three separate occasions over 2 months. Subjects were tested at 09.00 hours ($\pm$1 hour), as peak concentrations of oestradiol and progesterone are observed in the blood 1 h after consumption (Schering Health, Germany), on days 7 (7C) and 14 (14C) of pill consumption and day 5 of pill withdrawal (5WD). The exact timing of consumption and testing was noted in each case, to ensure that only 1 hour had elapsed. These phases were chosen for testing as it takes 7 days of pill consumption to completely downregulate the pituitary hormones (day 14 was used to highlight the non-cyclical nature of pill consumption and confirm down-regulation) and up to 5 days of withdrawal to stabilise progestin levels.[17] Maximum voluntary isometric force of the FDI muscle (Nm) and maximum dynamic and isometric force of the quadriceps and hamstring muscles (N) were assessed as described below.

Following familiarisation, the eumenorrheic subjects were tested on two occasions: days 2 and 21 of the cycle. Day 2 (early follicular (EF) phase) was the day after the onset of menses and day 21 (mid-luteal (ML) phase) was 7 days after ovulation had occurred. The EF and the ML phases of the menstrual cycle were chosen for testing because the concentration of oestradiol is low and high respectively at these times, and oestradiol is the hormone most implicated in strength regulation.[8–10 18] Ovulation was determined using a urinary LH kit (Clearplan, Bedford, UK). In addition, hormonal documentation was used to confirm each phase. Maximum voluntary isometric force of the FDI muscle was also measured. Dynamic leg strength was not measured in this group, as four subjects were involved in another study involving aerobic training (running).

Table 1 Oral contraceptive preparations taken by subjects

Pill type and manufacturer	n	Oestrogen (μg)	Progestogen (μg)
Microgynon (Schering Health, Germany)	7	30	150
Brevinor (Searle, USA)	2	35	500
Ovarnette (Wyeth, Ireland)	1	30	150
Marvalon (Organon, Ireland)	3	30	150
Cilest (Janssen-Cilag, Switzerland)	1	35	250

Hormonal analysis

Ten millilitres of venous blood were drawn from an antecubital vein into a lithium heparin coated tube by a trained phlebotomist. Samples were centrifuged at 70 *g* for 10 minutes at room temperature. Plasma was retained and stored at −70℃ until assayed. Total concentrations of 17-β oestradiol and progesterone were measured using an automated quantitative system (Mini Vidas, BioMerieux, France) and Vidas reagent kits (Vidas Oestradiol and Vidas Progesterone, BioMerieux, France). All samples were analysed using the ELISA technique, an enzyme immunoassay sandwich method with a final fluorescent detection.

Assessment of maximum voluntary isometric force of the first dorsal interosseus muscle

The first dorsal interosseus muscle was chosen for testing for two reasons. Firstly, the FDI muscle is the only muscle that produces abduction of the index finger. Other muscles attached to the finger are active during abduction but, because of their anatomical arrangement, they do not contribute force in this direction. Rutherford and Jones[19] found very similar maximum voluntary and stimulated contraction forces for the FDI muscle, therefore demonstrating that the FDI muscle can be maximally activated and isolated from the action of other hand muscles. Secondly, these and other authors[19 20] have found no difference in force production between dominant and non-dominant hands, suggesting that this muscle is not trainable under normal conditions.

Maximal voluntary isometric force of the FDI muscle was assessed using the techniques previously described by Elliott *et al*.[21] Three submaximal isometric contractions were carried out prior to maximum force assessment. Following a 3 minute rest, three maximum voluntary isometric contractions were performed, the best of which was taken as definitive. A 1 minute rest separated each contraction. Verbal encouragement and visual feedback was offered throughout the testing in order to promote maximum effort. Percutaneous electrical stimulation was used to superimpose electrical impulses onto the FDI muscle during each contraction. Maximum activation was confirmed when the 1 Hz twitch disappeared.

Maximum force assessment of the quadriceps and hamstring muscles

Maximal voluntary isometric force of the quadriceps and hamstring muscles was assessed using the techniques previously described by Elliott *et al*.[22] The knee was flexed at an angle of 90°, using the dominant leg. Two submaximal isometric contractions were carried out prior to MVIF assessment. Following a 3 minute rest, three maximum voluntary isometric contractions were performed. A 1 minute rest separated each contraction. Subjects were tested at 1.04, 2.09, and 4.19 rad/s, as these speeds test absolute to functional strength. Percutaneous electrical stimulation was used to superimpose electrical impulses onto the quadriceps muscles during each maximum voluntary isometric contraction. Two self adhesive surface electrodes (7.6 cm×12.7 cm;

Healthcare, London, UK) delivered 50 Hz twitches at a tolerable current throughout the test. Individual tolerable currents were established prior to MVIF assessment and were defined as the maximum current a subject could sustain without pain or discomfort. The electrodes were positioned on the anterior aspect of the thigh, midway between the superior border of the patella and the anterior superior iliac spine and over the lateral aspect of the thigh, one handbreadth above the patella. Electrical impulses were applied, using a computer driven Digitimer stimulator (Model DS7; Digitimer Ltd, UK), at 250 V with a pulse width of 200 μs duration.

Statistical analysis

SPSS (version 10; SPSS Inc., USA) was used for data analysis. Anderson-Darling normality tests were used to establish if data were normally distributed. The level of significance was taken as $p<0.05$. A repeated measures one way analysis of variance was used to detect significant differences in maximum strength (dynamic and isometric strength of the quadriceps and hamstring muscles and isometric strength of the FDI muscle) and hormone concentration (oestradiol and progesterone) between the 5WD, 7C, and 14C groups. The relationship between force and ovarian hormones was examined using Pearson's correlation coefficient on normally distributed data, and Spearman's rank correlation on non-parametric data. A Mann–Whitney *U* test was used to detect significant differences in MVIF of the FDI muscle and hormone concentration between eumenorrheic and pill subjects.

RESULTS

The mean (SD) for age, height and weight for the pill group was 22 (4) years, 1.5 (0.03) m and 63.3 (1.3) kg. The blood sample analysis showed that there were no significant changes in the concentration of endogenous oestradiol or progesterone between pill consumption and withdrawal (figs 1, 2). The concentration of exogenous oestrogen and progestogen consumed by each subject can be seen in table 1. Repeated measures one way analysis of variance showed no significant differences between groups (5WD, 7C, and 14C), for any of the strength variables measured (table 2). Maximum force production was not affected by oral contraceptive use. Neither hormone (oestradiol and progesterone) significantly correlated with any strength measure (table 3).

The mean (SD) for age, height and weight for the eumenorrheic group was 24 (5) years, 1.5 (0.02) , and 64.1 (1.1) kg. The blood analysis for progesterone showed that all seven eumenorrheic subjects exceeded the 16 nmol/l limit that confirms ovulation.[23] The results for the plasma hormone concentration of oestradiol and progesterone are shown in figs 1 and 2. The concentration of oestradiol and progesterone

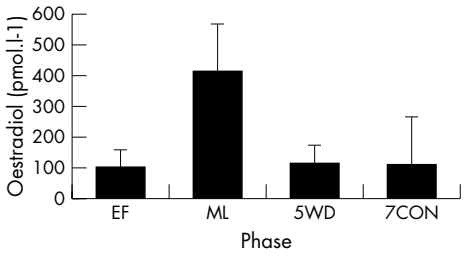

Figure 1 Plasma concentrations of oestradiol during two phases of the menstrual cycle and two phases of pill use. The columns represent the means (SD) of the hormone concentration. The ML phase was significantly different from all other phases ($p<0.05$).

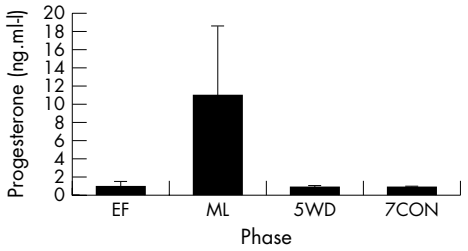

Figure 2 Plasma concentrations of progesterone during two phases of the menstrual cycle and two phases of pill use. The columns represent the means (SD) of the hormone concentration. The ML phase was significantly different from all other phases ($p<0.05$).

Table 2 Maximum dynamic strength of the knee extensor and flexor muscles during pill withdrawal and consumption

Muscle function	Day 5 withdrawal	Day 7 consumption	Day 14 consumption
MVIF of the FDI muscle (N)	34.56 (7.41)	35.18 (7.16)	32.12 (5.80)
Isokinetic extension 1.04 rad/s (Nm)	132.64 (19.15)	139.36 (22.62)	126.43 (32.62)
Isokinetic flexion 1.04 rad/s (Nm)	65.50 (8.14)	72.79 (13.60)	65.07 (16.94)
Isokinetic extension 2.09 rad/s (Nm)	106.86 (18.88)	112.07 (26.20)	108.21 (22.38)
Isokinetic flexion 2.09 rad/s (Nm)	60.29 (8.38)	63.57 (15.96)	64.36 (9.48)
Isokinetic extension 4.19 rad/s (Nm)	81.36 (16.36)	79.79 (19.65)	79.21 (22.33)
Isokinetic flexion 4.19 rad/s (Nm)	55.67 (13.52)	57.36 (13.35)	53.14 (13.56)
Isometric extension (Nm)	139.07 (16.56)	137.64 (20.47)	136.07 (27.00)
Isometric flexion (Nm)	61.07 (16.34)	60.93 (18.00)	56.93 (17.43)

Data are shown as means (SD), n = 14. MVIF, maximum voluntary isometric force; FDI, first dorsal interosseus muscle; ext, knee extension; flex, knee flexion. There were no significant differences between pill consumption and withdrawal for any of the variables.

were significantly higher during the ML than the the EF phase ($p<0.001$ and 0.05 respectively).

There were no significant differences in strength between pill consumption and eumenorrheic subjects ($p = 0.46$ EF and $p = 0.16$ ML) or pill withdrawal and eumenorrheic subjects ($p = 0.41$ EF and $p = 0.05$ ML) (table 4), despite significant differences in the concentration of oestradiol and progesterone between groups (figs 1, 2). The concentration of oestradiol and progesterone was significantly higher (all $p<0.05$) during the ML phase of the menstrual cycle compared with the EF phase of the menstrual cycle and pill consumption (7C) and withdrawal (5WD). Pill users were not stronger or weaker than their eumenorrheic counterparts. There were no significant differences in muscle strength between the EF and ML phases of the menstrual cycle ($p = 0.1$).

DISCUSSION

In the present study, pill administration resulted in the downregulation of endogenous oestradiol and progesterone, to levels indicative of the menopause.[7] Despite seven pill free days, endogenous concentrations of oestradiol and progesterone did not fluctuate. As all subjects experienced menstruation during their seven pill free days, it would appear that

Table 3 Correlation coefficients between the strength parameters and the plasma hormone concentrations of endogenous oestradiol and progesterone

Muscle function	Oestradiol	Progesterone
MVIF of the FDI muscle (N)	−0.290 (0.063)	−0.165 (0.296)
Isokinetic extension 1.04 rad/s (Nm)	−0.038 (0.813)	0.163 (0.304)
Isokinetic flexion 1.04 rad/s (Nm)	−0.312 (0.045)	−0.068 (0.670)
Isokinetic extension 2.09 rad/s (Nm)	−0.089 (0.573)	0.255 (0.103)
Isokinetic flexion 2.09 rad/s (Nm)	−0.084 (0.597)	−0.071 (0.655)
Isokinetic extension 4.19 rad/s (Nm)	−0.009 (0.953)	0.270 (0.083)
Isokinetic flexion 4.19 rad/s (Nm)	0.046 (0.773)	−0.030 (0.851)
Isometric extension (Nm)	−0.305 (0.049)	0.231 (0.141)
Isometric flexion (Nm)	−0.041 (0.795)	−0.209 (0.184)

Data are shown as Pearson and Spearmans correlation coefficients with p values below; n = 42 (14 subjects over three phases). MVIF, maximum voluntary isometric force; FDI, first dorsal interosseus muscle. There were no significant correlations between the strength parameters and the plasma hormone concentration.

Table 4 Comparison of FDI strength (N) between the pill users and eumenorrheic subjects. There were no significant differences in strength between groups

Phase	Mean (SD)
Pill consumption	35.2 (7.2)
Pill withdrawal	34.6 (7.4)
Early follicular	28.2 (4.3)
Mid-luteal	30.9 (7.5)

endogenous levels of oestradiol and progesterone did change, although not significantly ($p>0.05$). Under these conditions, maximum strength of the FDI or thigh muscles did not change significantly. These data suggest that pill use (consumption and withdrawal) does not affect the maximum force generating capacity of young healthy women.

Maximum voluntary isometric force of the FDI muscle was measured during two phases of the menstrual cycle with significantly different concentrations of circulating female reproductive hormones. The results showed no changes in strength across the menstrual cycle. Oral contraceptive users were not stronger or weaker than their eumenorrheic counterparts. This would suggest that the magnitude of downregulation (significant reduction at $p<0.05$) experienced by oral contraceptive users was not sufficient to distinguish them (in terms of maximum isometric force production) from the ''normal'' cyclical population. The eumenorrheic subjects had significantly greater levels of oestradiol and progesterone during the ML phase of the menstrual cycle when compared with all phases of oral contraceptive use. We suggest that future research should also compare the dynamic strength of oral contraceptive users and eumenorrheic women, using an equal sample size (to increase the statistical power of the analysis).

The strength findings from this study indicate that consistently low levels of endogenous sex hormones caused by oral contraceptive use do not affect maximum force production in young healthy women, which has implications for both health and sports performance. Other investigations, using post-menopausal women, have also shown that chronic sex hormone deprivation does not affect muscle strength. Young *et al*[24] found no difference in quadriceps strength in relation to cross sectional area (measured using ultrasound) between young and old women. Similarly, data from the Allied Dunbar National Fitness Survey[25 26] demonstrated that the age related decline in quadriceps and handgrip strength did not accelerate in women during the fifth decade (the average age of menopause in England). On reviewing those studies that have found an accelerated loss in strength coinciding with the menopause,[1–7] the majority have not specified or documented post-menopausal status or the time course associated with changes in strength. Consequently, the length of time over which oestrogen and progesterone are altered and the concentration of these hormones required to elicit changes in strength are unknown. Further research is necessary to confirm a direct relationship between low levels of reproductive hormones and diminished strength. In particular, a significant negative correlation between the concentration of oestrogen and progesterone (or years since menopause) and strength needs to be demonstrated.

Skelton *et al*[7] found that post-menopausal women were significantly weaker than hormone replacement therapy (HRT) users. These authors defined post-menopausal status as having a serum oestradiol level <50 pmol/l. In the present study, the mean oestradiol concentration was 135.59, 156.27, and 128.00 pmol/l in 7C, 14C, and 5WD, respectively. However, neither maximum dynamic or isometric force decreased under these circumstances.

During the menopause, levels of FSH, and to a lesser extent, LH, rise and are secreted in continuous quantities. Post-menopause, FSH and LH levels are increased by 10–15 fold and 3–5 fold respectively, compared with the levels found in the follicular phase of a pre-menopausal woman. As a result of oral contraceptive use, the concentration of LH and FSH declines. However, it is unlikely that the difference in LH and FSH levels between pill use and the menopause is responsible for the reported differences in strength production, as Greeves *et al*[27] found that muscle strength was not influenced by fluctuations in LH and FSH during in vitro fertilisation.

Exogenous, synthetic reproductive hormones (in particular HRT) have been shown to increase strength,[3 5 7] therefore strength might have been expected to increase as a result of oral contraceptive administration and decrease following pill withdrawal. In the present study, pill withdrawal did not affect the concentration of oestradiol and progesterone or any strength measure. Differences in exogenous hormone concentration between pills and HRT may account for the disparity in results between this study and previous research showing increased strength following HRT administration. Conventional pills contain approximately 30 μg and 250 μg of synthetic oestrogen and progesterone, respectively, while HRT pills usually contain 625 μg of exogenous oestrogen and 5–10 mg of exogenous progesterone. The effects of HRT on strength should be viewed with caution, as existing research is inconclusive. HRT has been shown to increase,[3 5 7] maintain,[2] or have no effect[28–31] on a variety of strength measures. We are not aware of any literature at present that suggests that oral contraceptives (as a model of synthetic hormone supplementation) can affect performance in ways other than suppression of endogenous oestradiol and progesterone.

In agreement with this study, Sarwar *et al*[8] showed that maximum strength was unaffected by pill use. These authors tested MVIF of the quadriceps and hand muscles every week over two cycles (including the seven pill free days). All subjects were taking a monophasic combined pill (20–35 μg of ethinyloestradiol and progestins in different doses).

What is already known on this topic

- The exact effects of reproductive hormones on force production in women are unknown.
- Muscle strength has been shown to increase, decrease, or remain unchanged during the menstrual cycle and following the menopause, as a result of hormone replacement therapy and oral contraceptive use.

What this study adds

- The present study is the first to measure levels of endogenous oestradiol and progesterone and directly relate them to muscle strength in oral contraceptive users and eumenorrheic subjects.
- The findings from this study suggest the oestradiol and progesterone do not affect maximum force production in young sedentary women.

Similarly, Phillips *et al*[9] found no cyclical changes in MVIF of the adductor pollicis muscle in subjects using a non-specified pill.

In the present study, a large variation (reflected by the SD values) in hormone concentration was found in both subject groups (pill users and eumenorrheic women). Despite standardising blood collection, the large variation in hormone levels during the menstrual cycle could be due to ultradian patterns (<24 h) of hormone secretion. The variation in the concentration of endogenous oestradiol and progesterone in the pill group is likely to reflect the different pills consumed. Although all pill users ingested a monophasic, standard strength, combined pill, the exogenous oestrogen and progestogen content ranged from 30–35 μg and 150–500 μg respectively. In order to limit this effect, future studies should employ single type pill users only.

In conclusion, the administration or withdrawal of exogenous reproductive hormones caused by oral contraceptive use had no effect on maximum dynamic and isometric strength of the quadriceps and hamstring muscles, or on maximum isometric strength of the FDI muscle. This suggests that oral contraceptive use does not affect the maximum force generating capacity of young women. Moreover, chronic downregulation of endogenous oestrogen and progesterone levels did not distinguish young women from their eumenorrheic counterparts in terms of muscle function, and suggests that the decline in muscle strength seen following the menopause may not be sex hormone dependent. Future research should investigate the effect of oral contraceptive use on other strength and performance based parameters (such as muscle fatigability/endurance trials) and various health measures (such as bone mineral density) so that specific recommendations can be made to the pill user.

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Conflict of interests: none declared

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