The effect of depot medroxyprogesterone acetate on postnatal depression: a randomised controlled trial

Mandisa Singata-Madliki,[1] G Justus Hofmeyr,[2] Theresa A Lawrie[3,4]

For numbered affiliations see end of article.

Correspondence to
Dr Mandisa Singata-Madliki, Effective Care Research Unit, East London Hospital Complex/ University of Fort Hare, Private Bag X9047, East London 5201, South Africa; mandisa.singata@gmail.com

Received 17 August 2015
Revised 8 December 2015
Accepted 14 December 2015
Published Online First 30 March 2016

▶ http://dx.doi.org/10.1136/jfprhc-2016-101529

To cite: Singata-Madliki M, Hofmeyr GJ, Lawrie TA. *J Fam Plann Reprod Health Care* 2016;**42**:171–176.

ABSTRACT

Background Depot medroxyprogesterone acetate (DMPA) is the most commonly used hormonal contraceptive method in South Africa. It is frequently administered in the immediate postnatal period, yet it is unclear whether it affects the risk of postnatal depression (PND).

Aim To determine whether DMPA increases the risk of PND compared with the copper-containing intrauterine device (IUD) when administered after delivery.

Design and setting A single-blind randomised controlled trial conducted at two teaching hospitals in East London, South Africa.

Methods Eligible, consenting women (*N*=242) requiring postnatal contraception were randomised to receive DMPA or an IUD within 48 hours of childbirth and interviewed at 1 and 3 months postpartum. Depression was measured using the Beck Depression Inventory (BDI-II) and the Edinburgh Postnatal Depression Scale (EPDS). Resumption of sexual intercourse, menstrual symptoms and breastfeeding rates were also assessed.

Results One-month EPDS depression scores were statistically significantly higher in the DMPA arm compared with IUD arm (p=0.04). Three-month BDI-II scores were significantly higher in the DMPA arm than in the IUD arm (p=0.002) and, according to the BDI-II but not the EPDS, more women in the DMPA arm had major depression at this time-point (8 vs 2; p=0.05). There were no statistically significant differences in other outcome measures except that fewer women had resumed sexual activity by 1 month postpartum in the DMPA arm (13% vs 26%; p=0.02).

Conclusions The possibility that immediate postnatal DMPA use is associated with depression cannot be excluded. These findings justify further research with longer follow-up.

Clinical trial number PACTR201209000419241.

Key message points

- Contraception provision in the immediate postnatal period is integral to the success of family planning programmes in South Africa.
- Depot medroxyprogesterone acetate (DMPA) is the most commonly used postnatal contraception option in South Africa but uncertainty remains about several potential side effects, including postnatal depression (PND).
- This study was unable to exclude an association between DMPA and PND and more research is needed.

INTRODUCTION

Globally, approximately two-thirds of postnatal women have an unmet need for family planning.[1] Initiation of injectable progestogen contraception (IPC) before 6 weeks postpartum is not recommended by the World Health Organization (WHO) unless other methods are not available or not acceptable, because of unknown long-term effects on the infant.[2] However, in South Africa, where unplanned pregnancy rates are high,[3] the South African Department of Health does not restrict the use of injectable contraceptives in the postnatal period,[4] and these are routinely offered to women before postnatal discharge from health services.[5 6] IPC is thus the most commonly used postnatal contraceptive method and, in one South African study, 91% of new mothers attending a child health clinic had used an injectable contraceptive after delivery.[5]

The postnatal period is critical for mother and infant, and depression during this time has negative effects on mother–infant bonding and child developmental outcomes.[7] Evidence suggests that the prevalence of postnatal depression (PND), and the risk of negative effects of PND on children and women, is higher in low- and middle-income countries (LMICs) than in high-income countries (HICs).[7] Most studies of PND have been conducted in HICs; however, a study conducted in 147 women from a South African peri-urban settlement found the rate of major depression at 2 months postpartum to be 34.7%, three times higher than British samples.[7] In this study, disturbances in mother–infant bonding were strongly linked with maternal depression.[8]

IPC is considered a reliable and safe contraceptive method, with discontinuation mainly attributed to menstrual disturbances,[9] but which may also be linked to depressive symptoms.[10] However, it remains unclear whether the use of IPC in the immediate postnatal period is associated with an increased risk of PND. A retrospective study compared 6-week PND scores of 55 women receiving depot medroxyprogesterone acetate (DMPA) immediately after delivery with 192 women receiving no hormonal contraception and found no statistically significant difference between the groups.[11] Only one randomised controlled trial (RCT) evaluating IPC and PND has ever been conducted. This trial compared the IPC norethisterone enanthate (NET-EN) with placebo and found that NET-EN was associated with an increased risk of PND at 6 weeks postpartum when administered within 48 hours of childbirth.[12] As DMPA is the most commonly used injectable progestogen in South Africa, we designed this RCT to determine whether the use of DMPA in the immediate postnatal period has a similar effect to NET-EN on the risk of PND.

OBJECTIVE

To determine whether DMPA increases the risk of depression compared with the copper-containing intrauterine device (IUD) when administered after delivery.

METHODS

Design and participants

This was a single-blind, RCT conducted at Frere and Cecelia Makiwane Hospitals in East London, Eastern Cape, South Africa. These two teaching hospitals serve a mainly black, Xhosa-speaking, South African population. Trained fieldworkers at the hospitals distributed information leaflets about the trial to attending pregnant women. Those who expressed an interest in participating were referred to research midwives who determined their eligibility. Women were eligible if they were 18–45 years old, willing to use either DMPA or an IUD within 48 hours of childbirth, able to read English or Xhosa, and willing to sign informed consent. Exclusion criteria were major depression, no access to a telephone, and contraindications to using DMPA or an IUD. Research midwives provided eligible women with further information about the trial and invited them to participate; those who were willing to participate signed the study information and consent form.

Procedure

A co-investigator (GJH) not involved in recruitment or outcome assessment prepared a computer-generated random allocation sequence in balanced blocks of variable size in a ratio of 1:1. Allocation cards were packed and sealed in consecutively numbered, opaque envelopes by the data manager of the Effective Care Research Unit, Cecelia Makiwane Hospital. After giving birth, participants were reassessed for eligibility and, if still eligible and within 48 hours of delivery, they were randomly allocated to receive DMPA contraception or an IUD by drawing the next in the series of numbered envelopes. Due to the nature of the interventions, participants were not blinded.

In accordance with the WHO handbook for family planning providers,[13] participants were fully counselled before receiving the allocated contraception method. The hospital family planning providers in consultation with research midwives gave the DMPA injections and inserted the IUDs according to standard protocols. Women receiving DMPA were referred to their local clinic for subsequent 3-monthly DMPA injections; those receiving an IUD were referred to the respective hospital's Women's Health Clinic for a 6-week post-IUD insertion check-up.

An interview schedule was arranged with each participant, who was given copies of the study instruments to be used at the telephone interviews 1 month and 3 months after the intervention. For DMPA users, the timing of these interviews corresponded to high DMPA exposure and low DMPA exposure, as the 3-month interview occurred before the next scheduled injection.[14]

Outcomes and instruments

The primary outcome was depression; secondary outcomes were resumption of sexual intercourse, menstrual flow (none, light, normal, heavy), dysmenorrhoea, and infant feeding method. Two study instruments were used to evaluate depression, namely the Beck Depression Inventory (BDI-II) and the Edinburgh Postnatal Depression Scale (EPDS). The BDI-II has been previously validated, used in the same cultural context, and translated into the local language IsiXhosa.[15] Similarly, the EPDS has been used and validated in South African women.[16] We also administered the Arizona Sexual Experience Scale (ASEX); however, this scale has not been validated in the study population, therefore these data are not presented in this article.

Questionnaires and study instruments were administered at baseline, 1 month and 3 months after randomisation. The baseline questionnaire was completed in a face-to-face interview with research midwives, and the principal investigator, who was not involved with screening or enrolment, performed telephone interviews. At enrolment, participants were requested to keep the contraception method confidential during subsequent telephonic follow-up to ensure that the interviewer remained blinded to the group allocation. During the interviews, instrument questions were read to the participants. In the event that a participant did not understand English, the isiXhosa version of the BDI-II was used, and the interviewer (who was bilingual) translated the EPDS questionnaire.

Statistical methods

Assuming an increase in mean BDI II scores from 6.9 to 11.5 with DMPA,[17] we calculated that we needed a minimum of 73 women in each group (α=0.05; β=90%) using STATA Statistical Software.[18] In anticipation of a possible high loss to follow-up and protocol deviations, we increased the sample size to 242.

We analysed women in the group to which they were allocated (intention-to-treat), including those who did not receive the allocated method. Baseline data were compared to confirm that the randomisation produced well-balanced groups. Depression was analysed as both a categorical and continuous variable. We used standard BDI-II thresholds for any (minor and major) depression and major depression of ≥14 and ≥29, respectively.[19] For the EPDS, we used thresholds of ≥9 and ≥12 for any depression and major depression, respectively, which were shown to correspond to these diagnoses with reasonable sensitivity and specificity in the South African validation study.[16] Categorical outcomes were compared between study groups using the Chi-square (χ^2) test, or Fisher's exact two-tailed test if any cell numbered five or less. For normally distributed continuous data, we used the *t*-test to compare means and standard deviations; for non-parametric data we used the Wilcoxon test to compare medians and interquartile ranges.

Ethics approval and registration

Ethics approval for this trial was obtained from the East London Hospital Complex Ethics Committee and the Faculty of Health Sciences, University of Cape Town, South Africa. This trial was prospectively registered on the Pan African Clinical Trial Registry (http://www.pactr.org) (Registration No. PACTR 201209000419241).

RESULTS

Between 6 December 2012 and 30 March 2013, 242 women were randomised out of a total of 575 women delivering at the two hospitals during this period; 119 and 123 were allocated to the DMPA and IUD arms, respectively (see Figure 1). Eight participants (three in the DMPA arm, five in the IUD arm) were excluded from analysis due to loss to follow-up at both follow-up interviews, giving a total of 234 participants analysed.

Baseline characteristics were comparable between study arms (Table 1), except that, among HIV-positive women (39% of the sample), mean CD4 counts were lower in the IUD arm (p=0.01). More women in the IUD arm were HIV-positive; however, this difference was not statistically significant. Overall, 77% of women reported that their pregnancy had been unplanned.

One-month depression scores were significantly higher with DMPA use compared with IUD use according to EPDS data; 3-month depression scores were higher with DMPA according to BDI-II data. More women in the DMPA arm had severe depression at 1 and 3 months compared with the IUD according to BDI-II scores (borderline statistical significance; Table 2). The two women with BDI scores ≥29 at baseline in the DMPA arm (see Figure 1 for protocol violations) were not among those identified as depressed at 1 and 3 months postpartum.

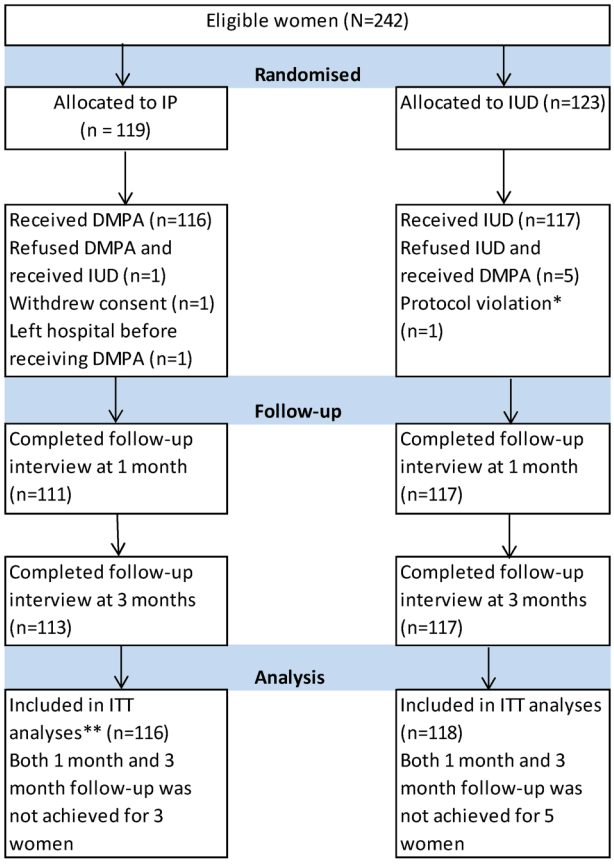

Figure 1 CONSORT diagram showing the flow of participants in the trial. BDI, Beck Depression Inventory; DMPA, depot medroxyprogesterone acetate; ITT, intention-to-treat; IUD, intrauterine device.

Table 1 Demographic and clinical characteristics of depot medroxyprogesterone acetate and intrauterine device groups at baseline

Characteristic	Total (*N*=234)	DMPA (*N*=116)	IUD (*N*=118)	*p*
Age [median (IQR)]	26 (11–23)	26 (10–22)	26.5 (11–22)	
Smoker [*n* (%)]	4 (1.7)	3 (2.5)	1 (0.8)	0.37
Diabetes [*n* (%)]	2 (0.8)	0	2 (1.6)	0.50
Hypertension [*n* (%)]	16 (6.3)	8 (6.7)	8 (6.7)	0.97
HIV-positive [*n* (%)]	91 (39.0)	39 (33.0)	52 (44.0)	0.10
CD4 count [mean (SD)]	385 (177) (*n*=86)	438 (173) (*n*=37)	344 (170) (*n*=49)	0.01*
Previous PID [*n* (%)]	5 (2.1)	2 (1.7)	3 (2.5)	0.98
Unplanned pregnancy [*n* (%)]	181 (77.0)	97 (83.0)	84 (71.0)	0.35
Previous contraception [*n* (%)]				
Injectable	204 (87.0)	100 (86.0)	104 (88.0)	0.66
Pill	20 (8.5)	10 (8.2)	10 (8.2)	0.97
IUD	0	0	0	
Condom use [*n* (%)]	164 (70.0)	78 (67.0)	86 (72.0)	0.35
Married [*n* (%)]	49 (20.0)	21 (18.0)	28 (23.0)	0.33
Employment status [*n* (%)]				
Employed	61 (26.0)	34 (31.0)	27 (22.0)	0.27
Student	37 (15.0)	21 (18.0)	16 (13.0)	0.34
Seeking work	63 (26.0)	28 (24.0)	35 (29.0)	0.34
Education [*n* (%)]				
Primary (minimum)	178 (76.0)	85 (73.0)	93 (78.0)	0.32
Degree or diploma	16 (6.8)	8 (7.0)	8 (7.0)	0.97

*Significant difference $p<0.05$.
DMPA, depot medroxyprogesterone acetate; HIV, human immunodeficiency virus; IUD, intrauterine device; PID, pelvic inflammatory disease; SD, standard deviation.

Some 14/111 (13%) women in the DMPA arm had engaged in sexual intercourse by 1 month postpartum compared with 30/117 (26%) women in the IUD arm ($p=0.02$); however, the difference in this outcome was not statistically significant at 3 months postpartum. There were no statistically significant differences in return of menstruation and reported menstrual flow intensity (normal, light, heavy) at 1 and 3 months postpartum. Fewer women in the DMPA arm reported mild to severe dysmenorrhoea compared with the IUD arm [16/84 (19%) vs 26/91 (29%)]; however, this difference did not reach statistical significance ($p=0.10$). Infant feeding choices were not significantly different between study arms at any of the study time points.

DISCUSSION

To our knowledge, this is the first RCT to evaluate the effect of DMPA on PND. Although the results are highly suggestive of a higher risk of PND with DMPA, the trial findings cannot be regarded as conclusive. Findings at 3 months were statistically significant for BDI-II measurements only, not EPDS measurements. This may be due to the different focus of the instruments, with the EPDS primarily a screening tool adapted to the postnatal period, whereas the BDI-II includes more somatic questions,[18] including loss of interest in sex. Low libido may be independently associated with DMPA,[13 20 21] therefore the relative effect on BDI-II measurements of DMPA versus the IUD may be biased in the direction of the IUD. It might, therefore, have been helpful to confirm instrument measurements of depression with clinical diagnosis.

This is the second RCT to evaluate the effect of IPC use after delivery on PND. Findings of the previous study comparing NET–EN to placebo suggested a significant increase in PND at 5 weeks postpartum.[12] This effect was presumed to have 'worn off' by the 3-month assessment because women in that study received only one injection, and NET-EN has a duration of action of approximately 2 months. Both this and the current trial are limited by the study duration and would have benefited from longer follow-up to determine whether the apparent effect on PND was sustained. Both trials have found overall PND rates (major depression) of 10% or less, lower than suggested by another South African study.[8]

Decreased libido is stated as a potential side effect of IPC in the WHO Handbook[13] and Faculty of Sexual & Reproductive Health clinical guidance,[21] based on limited evidence from observational studies of DMPA use.[22–25] We found that women in the DMPA arm resumed sexual intercourse later than those in the IUD arm, with the rate in the IUD arm comparable to the resumption rate of 29.7% reported in a Nigerian

Table 2 Results of depot medroxyprogesterone acetate versus intrauterine device for primary and secondary outcomes

	Baseline			1-month follow-up			3-month follow-up		
Outcome	**DMPA**	**IUD**	***p***	**DMPA**	**IUD**	***p***	**DMPA**	**IUD**	***p***
Depression	*n=116*	*n=118*		*n=111*	*n=117*		*n=113*	*n=117*	
Categorical data									
EPDS ≥9	62	55	0.36	27	21	0.27	20	17	0.63
EPDS ≥12	35	29	0.41	13	10	0.55	9	10	0.93
BDI-II ≥14	22	17	0.44	34	27	0.25	30	23	0.13
BDI-II ≥29	2	0	0.24	11	7	0.39	8	2	0.05
Continuous data [median (IQR)]									
EPDS	9 (3.0–21.0)	8 (2.0–20.0)	0.20	4 (1.0–18.0)	2 (0–21.0)	0.04*	2 (0.5–19.0)	2 (0–19.0)	0.10
BDI-II	6 (2.5–12.5)	5 (2.0–11.5)	0.10	8 (4.5–19.5)	9 (4.5–14.5)	0.20	9 (4.5–14.5)	5 (2.0–11.5)	0.002*
Sexual activity	*n=116*	*n=118*		*n=111*	*n=117*		*n=113*	*n=117*	
Resumption of sexual intercourse	NA	NA		14	30	0.02†	53 (111)	64 (115)	0.29
Menstruation				*n=110*	*n=117*		*n=110*	*n=115*	
None	NA	NA		64	72	0.70	32	32	0.90
Light flow	NA	NA		26	23	0.50	30	19	0.07
Heavy flow	NA	NA		4	5	0.90	8	14	0.30
Dysmenorrhoea				*n=56*	*n=59*		*n=84*	*n=91*	
Mild to severe pain	NA	NA		9	13	0.50	16	26	0.10
Infant feeding	*n=115*	*n=116*		*n=101*	*n=109*		*n=113*	*n=116*	
Breastmilk only	90	87	0.60	60	67	0.80	47	50	0.90
Formula only	14	14	0.80	24	18	0.20	34	22	0.07
Both	11	15	0.50	17	24	0.40	32	44	1.90

*$p<0.05$ (Wilcoxon test).
†Yates corrected Chi-square (χ^2) test.
BDI, Beck Depression Inventory; DMPA, depot medroxyprogesterone acetate; EPDS, Edinburgh Postnatal Depression Scale; IQR, interquartile range; IUD, intrauterine device; NA, not applicable.

study.[26] By 3 months there was no longer a difference in sexual intercourse resumption rates between our study arms, and it is possible that differences in postnatal bleeding patterns between the two study groups accounted for this finding; however, bleeding patterns *per se* were not assessed in this study.

A limitation of this trial was that it was powered to detect differences in mean depression (BDI-II) scores, not to detect differences in depression rates or secondary outcomes. It is therefore possible that the study failed to demonstrate important differences in these other outcomes (type 2 error). Furthermore, we did not adjust results for a baseline imbalance in CD4 counts between arms, which might have led to bias in favour of the DMPA arm. A further limitation was that we did not include other risk factors for PND in our questionnaire, such as previous PND and poor perinatal outcomes. A larger study of contraceptive options for women in South Africa is planned, which will aim to avoid these shortcomings. This study also plans to evaluate method discontinuation and IUD expulsion rates.

CONCLUSIONS

We were unable to exclude the possibility that immediate postnatal DMPA use is associated with PND. Until further evidence becomes available, women should be counselled about the possibility and, we agree with Hani *et al.*,[5] that decisions regarding timing of initiation need to be weighed against the personal risk of pregnancy and ability to access health care services. These findings justify further research with longer follow-up.

Author affiliations
[1]Deputy Director, Effective Care Research Unit (ECRU), Eastern Cape Department of Health, East London Hospital Complex, Universities of the Witwatersrand and Fort Hare, East London, South Africa
[2]Director, Effective Care Research Unit (ECRU), Eastern Cape Department of Health, East London Hospital Complex, Universities of the Witwatersrand and Fort Hare, East London, South Africa and Professor, Department of Health, Walter Sisulu University and Eastern Cape, East London, South Africa
[3]Research Consultant, Effective Care Research Unit (ECRU), Eastern Cape Department of Health, East London Hospital Complex, Universities of the Witwatersrand and Fort Hare, East London, South Africa

[4]Honorary Research Consultant, Cochrane Office, Education Centre, Royal United Hospital, Bath, UK

Acknowledgements This trial was registered with the University of Cape Town as the PhD thesis of Dr Singata-Madliki. The authors thank the research midwives and fieldworkers of the Effective Care Research Unit of East London Hospital Complex/University of Fort Hare, South Africa for their assistance with participant recruitment, and the women from the Eastern Cape who kindly agreed to take part in this research. Professor Justus Hofmeyr was one of Dr Singata-Madliki's PhD supervisors. Dr Theresa Lawrie assisted with the interpretation of the data and preparation of this manuscript. Professor Doris Khalil also supervised the thesis and her support is gratefully acknowledged.

Funding The Effective Care Research Unit of East London Hospital Complex/University of Fort Hare, South Africa, funded the trial internally. Preparation of this manuscript was supported by a grant from the South African Medical Research Council.

Competing interests None declared.

Ethics approval Faculty of Health Sciences, University of Cape Town, South Africa. Trial registration: Pan African Clinical Trial Registry.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 United States Agency for International Development (USAID) and Maternal and Child Health Integrated Program (MCHIP). Postpartum Family Planning (PPFP) Toolkit. 2015. https://www.k4health.org/toolkits/ppfp [accessed 7 July 2015].
2 World Health Organization (WHO). *Medical Eligibility Criteria for Contraceptive use* (4th edn). Geneva, Switzerland: WHO, 2009.
3 Mshweshwe TN, Mgoli A, Hofmeyr GJ, *et al*. Assessing the prevalence of unwanted pregnancies and barriers to use of preventive measures in East London. Presentation at the *27th Conference on Priorities in Perinatal Care in Southern Africa*. Indaba Hotel, Gauteng, South Africa, 11–14 March 2008.
4 Department of Health, Republic of South Africa. *National Contraception and Fertility Planning Policy and Service Delivery Guidelines*. 2012. http://www.health-e.org.za/wp-content/uploads/2014/05/National-contraception-family-planning-policy.pdf [accessed 7 July 2015].
5 Hani A, Moss M, Cooper D, *et al*. Informed choice – the timing of postpartum contraceptive initiation. *S Afr Med J* 2003;93:862–864.
6 Peltzer K, Chao LW, Dana P. Family planning among HIV positive and negative prevention of mother to child transmission (PMTCT) clients in a resource poor setting in South Africa. *AIDS Behav* 2009;13:973–979.
7 Parsons CE, Young KS, Rochat TJ, *et al*. Postnatal depression and its effects on child development: a review of evidence from low- and middle-income countries. *Brit Med Bull* 2012;101:57–79.
8 Cooper PJ, Tomlinson M, Swartz L, *et al*. Post-partum depression and the mother-infant relationship in a South African peri-urban settlement. *Br J Psychiat* 1999;175:554–558.
9 Draper BH, Morroni C, Hoffman M, *et al*. 2006. Depot medroxyprogesterone versus norethisterone enanthate for long-acting progestogenic contraception. *Cochrane Database Syst Rev* 2006;3:CD005214.
10 Civic D, Scholes D, Ichikawa L, *et al*. Depressive symptoms in users and non-users of depot medroxyprogesterone acetate. *Contraception* 2000;61:385–390.
11 Tsai R, Schaffir J. Effect of depot medroxyprogesterone acetate on postpartum depression. *Contraception* 2010;82:174–177.
12 Lawrie TA, Hofmeyr GJ, De Jager M, *et al*. A double-blind randomised placebo controlled trial of postnatal norethisterone enanthate: the effect on postnatal depression and serum hormones. *Br J Obstet Gynaecol* 1998;105:1082–1090.
13 World Health Organization, United States Agency for International Development, John Hopkins Bloomberg School of Public Health. *Family Planning: A Global Handbook for Providers (2011 Update)*. 2011. http://whqlibdoc.who.int/publications/2011/9780978856373_eng.pdf?ua=1 [accessed 7 July 2015].
14 Westhoff C, Wieland D, Tiezzi L. Depression in users of depo-medroxyprogesterone acetate. *Contraception* 1995;51:351–354.
15 Somhlaba NZ, Wait JW. Stress, coping styles, and spousal bereavement: exploring patterns of grieving among black widowed spouses in rural South Africa. *J Loss Trauma* 2009;14:196–210.
16 Lawrie TA, Hofmeyr GJ, de Jager M, *et al*. Validation of the Edinburgh postnatal depression scale on a cohort of South African women. *S Afr Med J* 1998;88:1340–1344.
17 Gupta N, O'Brien R, Jacobsen LJ, *et al*. Mood changes in adolescents using depot-medroxyprogesterone acetate for contraception: a prospective study. *J Pediatr Adolesc Gynecol* 2001;14:71–76.
18 StataCorp. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP, 2011.
19 Beck AT, Steer RA, Garbin MG J. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clin Psych Review* 1988;8:77–100.
20 Berga SL, Smith YR. Chapter 25: Hormones, mood and affect. In: Fink G, Pfaff D, Levine J (eds), *Handbook of Neuroendocrinology*. San Diego, CA: Academic Press, 551–571.
21 Faculty of Sexual & Reproductive Healthcare Clinical Effectiveness Unit. *Progestogen-only Injectable Contraception*. 2014. http://www.fsrh.org/pdfs/CEUGuidanceProgestogenOnlyInjectables.pdf [accessed 7 July 2015].
22 Ott MA, Shew ML, Ofner S, *et al*. The influence of hormonal contraception and sexual interest among adolescents. *Arch Sex Behav* 2008;37:605–613.
23 Paul C, Skegg DC, Williams S. Depot medroxyprogesterone acetate. Patterns of use and reasons for discontinuation. *Contraception* 1997;56:209–214.
24 Kaunitz AM. Long-acting hormonal contraception: assessing impact on bone density, weight, and mood. *Int J Fertil Womens Med* 1999;44:110–117.
25 Matson SC, Henderson KA, McGrath GJ. Physical findings and symptoms of depot medroxyprogesterone acetate use in adolescent females. *J Ped Adolesc Gynecol* 1997;10:18–23.
26 Ezebialu I, Eke A. Resumption of vaginal intercourse in the early postpartum period: determinants and considerations for child spacing in a Nigerian population. *J Obstet Gynaecol* 2012;32:353–356.