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Progestin-only contraception: Injectables and implants

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Progestin-only contraceptive injectables and implants are highly effective, longer-acting contraceptive methods that can be used by most women in most circumstances. Globally, 6% of women using modern contraception use injectables and 1% use implants. Injectables are the predominant contraceptive method used in sub-Saharan Africa, and account for 43% of modern contraceptive methods used. A lower-dose, subcutaneous formulation of the most widely used injectable, depot-medroxyprogesterone acetate, has been developed. Implants have the highest effectiveness of any contraceptive method. Commodity cost, which historically limited implant availability in low-resource countries, was markedly lowered between 2012 and 2013. Changes in menstrual bleeding patterns are extremely common with both methods, and a main cause of discontinuation. Advice from normative bodies differs on progestin-only contraceptive use by breastfeeding women 0–6 weeks postpartum. Whether these methods are associated with HIV acquisition is a controversial issue, with important implications for sub-Saharan Africa, which has a disproportionate burden of both human immunodeficiency virus (HIV) and maternal mortality.
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Introduction

In this chapter, we review salient characteristics, recent research, and particular areas of controversy surrounding progestin-only contraceptive injectables and implants. Progestin-only contraceptive injectables and implants are ideally offered as part of a wide range of contraceptive options. The advantages of these progestin-only contraceptive methods include convenience, high efficacy, and ability to be used by women who cannot use contraception containing oestrogen. We do not provide an exhaustive review of these methods, but highlight areas of interest.

Composition and mechanism of action

Three progestin-only injectables are available: (1) depot medroxyprogesterone acetate (DMPA), 150 mg/ml, provided intramuscularly (DMPA-IM, marketed as Depo-Provera®); (2) depo-subQ provera 104™, 104 mg/0.65 ml, a subcutaneous formulation of DMPA (DMPA-SC) with 30% lower dosage of DMPA; and (3) norethisterone enanthate (NET-EN) 200 mg/ml, provided intramuscularly. DMPA-SC packaged in Uniject™ (a prefilled, sterile, non-reusable subcutaneous injection system) is referred to as Sayana Press®; DMPA-SC in a single-dose, prefilled glass syringe as Sayana® [1]. These three injectable methods prevent pregnancy primarily through ovulation suppression; possible secondary mechanisms include thickening of cervical mucus or endometrial thinning [2]. Combined injectable contraceptives, containing an oestrogen and progestin, are uncommonly used in family planning programmes and not discussed here.

Hormonal implants consist of one or two small (40–44 mm long), thin (2.0–2.5 mm diameter), flexible, non-biodegradable rods [3,4]. Three implants are currently available. The one-rod implant, Implanon® (and its successor Implanon NXT®) contains 68 mg of etonogestrel (ENG) [4]. Implanon NXT® is radiopaque and supplied in a preloaded, single-use, disposable applicator that facilitates correct subdermal insertion; it is otherwise identical to Implanon® [5]. Both two-rod methods, Jadelle® and Sino-implant (II)®, contain 150 mg of levonorgestrel (LNG), 75 mg in each rod [3,6], and are supplied with a single-use disposable trocar [7]. Production of the first-generation implant Norplant®, which contained 216 mg of LNG in six rods, was discontinued in 2008 [8]. Implants continuously release low amounts of progestin, which inhibits ovulation and thickens cervical mucus [3,4].

Contraceptive effectiveness: typical and perfect use

'Typical use' pregnancy rates reflect effectiveness under actual usage patterns, which include inconsistent or incorrect use; 'perfect use' pregnancy rates refer to effectiveness when used precisely according to direction. Data from the USA suggest that 6% of women with typical use and 0.2% with perfect use of DMPA would experience an unintended pregnancy within the first year of use [2,9]. Typical use pregnancy rates may vary by context and population [10]. Several studies report equivalent contraceptive efficacy between DMPA-IM and DMPA-SC [11], and similar pregnancy rates (0.4 per 100 women) for DMPA given at 90-day intervals and NET-EN given at 60-day intervals [12].

Implants are effective within 24 h of insertion [3,4]. They have the highest effectiveness of any contraceptive method, with 0.05% of typical and perfect users expected to experience an unintended pregnancy in the first year of use [9]. Implanon® and Implanon NXT® are labelled effective for 3 years of use [13,14]. Sino-implant (II)® and Jadelle® are labelled effective for 4 and 5 years of use, respectively [3,6,14]. The cumulative pregnancy rate during clinical trials of Jadelle® was 0.3% at 3 years and 1.1% at 5 years [3], comparable to the 5-year pregnancy rate of female sterilisation (1.3%) [15]. Sino-implant (II) first-year pregnancy probabilities are 0.0–0.1%, and cumulative 4-year pregnancy probabilities are 0.9–1.06% [6]. In 11 worldwide studies of Implanon®, no pregnancies occurred with the implant *in situ* [4]. In the first year of typical use, implants are about 120 times more effective than injectables and 180 times more effective than combined contraceptive pills [9].

Effectiveness in overweight or obese women

Progestin-only injectables are not expected to have lower efficacy in overweight or obese women [2,16]; however, data are limited [4,17,18]. In later years of use, implants may have lower efficacy in

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overweight or obese women, as serum concentrations of progestin are inversely related to body weight and decrease with time after insertion [3]. Results of studies are, however, ambiguous, and the quality of evidence is low. Although studies examining Jadelle® and Implanon® observed no trend by body weight [19,20], the World Health Organization (WHO) has recommended that women who weigh 80 kg or more should consider having the LNG implant replaced after 4 completed years because of concerns about reduced effectiveness [14,21].

Eligibility

For most women and most medical conditions, injectables and implants may be used under any circumstances (WHO Medical Eligibility Criteria [MEC] Category 1) or be generally used (MEC Category 2) [14,22]. For most conditions, the MEC categorisation is similar for injectables and implants; differences are mainly among cardiovascular conditions (Category 2 for implants; Category 3 for injectables). Women with known or suspected pregnancy, unexplained vaginal bleeding, history of breast cancer, and presence or history of severe liver disease should generally not use either method (Category 3). The only absolute contraindication (MEC Category 4) is current breast cancer.

Injectables and implants are suitable for women of any age (including adolescents), parity, marital status, or reproductive intention (to delay, space, or limit), or for women who are post-abortal, breast feeding, or living with HIV.

Provision of progestin-only injectables and implants

Injectables and implants may be provided any time during a woman's menstrual cycle if it is reasonably certain she is not pregnant, which can be determined by a pregnancy test or checklist [21,23–25]. A requirement that a woman needs to be menstruating to receive an injectable or an implant is an unjustified barrier to service provision [26]. These methods may be initiated without a pelvic examination, blood or other routine laboratory tests, cervical cancer screening, or a breast examination [14].

DMPA-IM and NET-EN are injected into the upper arm or buttock. DMPA-SC is labelled for the upper thigh or abdomen, although the upper arm is preferred in many countries [27,28], and an injection in this location provides sufficient contraceptive protection for 13 weeks [29]. DMPA-IM and DMPA-SC are administered approximately every 3 months (13 weeks), NET-EN every 2 months (60 days). WHO advises that repeat injections can be given 2 weeks early or up to 2 weeks late for NET-EN and 2 weeks early or up to 4 weeks late for DMPA [25,30].

Return to fertility after a DMPA-IM injection averages between 9 and 10 months (i.e. 6–7 months longer than the expected duration of effect; one study reported a range of 4–31 months) [31,32]. This may be slightly shorter with NET-EN [33]. Time from cessation of injection to return of fertility is not associated with number of years of DMPA use. One study reported a median of 30 weeks to return to ovulation after stopping DMPA-SC [34]. Additional contraceptive protection is not required, although this 'grace period' (for late use) for DMPA may vary by country [24].

Implants are inserted superficially beneath the skin of the upper arm [3,7]. Insertion usually takes 1–2 mins and removal 3–5 mins. A client does not need to commit to implant use for the full length of its labelled use to receive it [14,35]. Complications of insertion or removal are uncommon (less than 2%) [3,4]. Difficulty of removing the implant is directly correlated with deep insertion [3,14]. Return to fertility is prompt; in clinical trials of Implanon®, several pregnancies occurred within 7–14 days after removal [4]. After removal of LNG implants, pregnancy occurs within 6 months in 60% of women, 1 year in 80%, and 2 years in 90% [3]. These rates are similar to those among women who do not use contraception [9]. Routine follow-up visits are not needed [14], but healthcare providers should indicate to the woman that she can return any time, whether for advice, reassurance, treatment of side-effects, or removal. Women should also be instructed to return in the event of a delayed period after several months

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of regular cycles (to rule out pregnancy), severe lower abdominal pain (to rule out ectopic pregnancy), heavy bleeding, or signs of infection at the insertion site. Programmes should provide a written date that the implant needs to be removed or replaced, and have a system of follow up for removals.

Side-effects and other considerations

Thoughtful counselling, including comprehensive information and anticipatory guidance about side-effects, is critical to ensuring informed contraceptive choice and quality service provision [35,36]. Below, we review selected programmatically important side-effects of progestin-only methods; other sources provide information on other potential side-effects (e.g. headache, breast pain, abdominal pain, sexual side-effects, metabolic effects, drug interactions, and mood changes), and potential advantages (e.g. reductions in grand mal seizures or sickle cell crises, reduced pain from endometriosis, and decreased risk of pelvic inflammatory disease) [2].

Changes in menstrual bleeding patterns

Changes in menstrual bleeding patterns (e.g. lighter or heavier bleeding, prolonged or irregular bleeding, or amenorrhoea) are a major cause of hormonal contraceptive discontinuation [2]. Progestin-only methods induce more menstrual irregularity than combined methods [37]. Most women will experience irregular bleeding patterns in the first year of progestin-only contraceptive use, although irregularity reduces over time. [3,38,39] For DMPA-IM and DMPA-SC users, the proportion of women experiencing amenorrhoea increases over time (to 40–50% after 1 year and 80% after 5 years of DMPA use) [2,40–42]; these rates may be lower with NET-EN [12]. Amenorrhoea among LNG implant users is lower than among injectable users, and remains relatively constant over time (about 11%) [40]. Use of ENG implants may be associated with fewer bleeding or spotting episodes and significantly more amenorrhoea (22% in one study) than LNG implant users [4,39]. Despite bleeding irregularities, haemoglobin levels rise with implant use [3], and DMPA and NET-EN may protect against anaemia [14]. A number of practical approaches are available to managing bleeding changes [14,43].

Weight gain

Weight gain is another commonly cited reason for discontinuing (or not initiating) hormonal contraception [44]. In a recent systematic review [45], studies comparing DMPA against combined hormonal contraceptives reported no differences in weight change between methods, but some studies comparing DMPA with a non-hormonal method or no method suggested slightly more weight gain (less than 2 kg) among DMPA users. A prospective study from South Africa reported that adolescent injectable users gained more weight over 4–5 years of use (average of 6.2 kg) than users of the combined oral contraceptive pill, discontinuers, and non-users of contraception (average weight gain 2.3 kg, 2.8 kg, and 2.8 kg, respectively) [46]. Differences in weight gain between DMPA-IM, DMPA-SC, and NET-EN have not been reported [12,42,47]. Two studies comparing Norplant® against non-hormonal intrauterine device users showed increased weight change (0.47–1.10 kg), whereas two studies comparing Norplant to DMPA or Jadelle® found no differences [45]. In trials of Jadelle®, average weight gain over 5 years was 9 pounds, with 20% of women gaining at least 10 pounds in the first year and 50% gaining at least 10 pounds after 5 years [3]. It is unclear how much of this weight gain is attributable to the contraceptive.

Bone mineral density

Both DMPA-IM and DMPA-SC currently carry a US FDA black-box warning [48,49] discouraging use for more than 2 consecutive years as evidence shows that prolonged use reduces bone mineral density (BMD); however, BMD loss generally seems to be temporary and reversible [2]. Although some observational studies suggest DMPA may increase fracture risk [50], currently available randomised data are insufficient to confirm an increase in any clinically relevant outcome (i.e. bone fracture) [51]. Associations observed in some observational studies [50] could be a result of confounding [52]. WHO

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and other groups recommend no restriction of duration of use based on concern about bone health [53,54], and some scientists have called for removal of the FDA black box warning [55]. Data on ENG- and LNG-implants and BMD are mixed, but whether any potential change are clinically significant is unknown [2].

Ectopic pregnancy

Because of their effectiveness at preventing pregnancy, injectables and implants *reduce* the overall risk of ectopic pregnancy. The ectopic pregnancy rate with Jadelle is less than 0.5 per 1000 woman-years [3]. This rate is significantly below the ectopic pregnancy rate for women who do not use contraception (2.7 to 3.0 ectopic pregnancies per 1000 woman-years). Clinicians, however, need to remain alert to the possibility of ectopic pregnancy in women using implants (or injectables) who become pregnant or have lower abdominal pain.

Cancer

Progestin-only contraceptives may reduce the risk of endometrial cancer by up to 80% [56], and are not associated with ovarian cancer [57]. Although most studies suggest no link between progestin-only injectables and breast cancer [2], two recent studies reported transiently increased risks [58,59]. Studies on progestin-only injectables and cervical cancer report mixed findings [59,60]. Few data exist for progestin-only implants and cancer risk, but no increased risk of endometrial or cervical cancer has been observed with ENG implants [61]. Although one small study [62] reported a potential increase in risk of breast cancer among implant users, additional data are needed [62].

Satisfaction, continuation and discontinuation

Injectable contraceptive users report appreciating the ability to use the method without others knowing, freedom from required daily action, and lack of interference with sexual intercourse [14]. Acceptability studies have shown Sayana Press® to be more acceptable than DMPA-IM to women and providers [27,28,63]. Implant users report liking the convenience (no user action required after insertion), high efficacy, long duration of use, and lack of interference with sexual intercourse [14,35,64]. Satisfied users tend to be women who do not experience side-effects or who value the method's positive features enough to tolerate them [64]. User satisfaction, quality of services, and continuation are related [64].

Continuation rates for implants are high, and higher than for injectables, in both high-resource and low-resource countries. A WHO analysis of 60 Demographic and Health Surveys (DHS) between 1990 and 2009 found a probability of discontinuation of injectables of 41% at 12 months, 65% at 24 months, and 74% at 36 months; reasons for discontinuation were mainly related to the method used or to 'side-effects and other health concerns' [65]. Continuation of implants in trials and published studies from a number of countries ranges from 78–96% at 1 year to 50–86% at 3 years [3,4,43,66]. Unacceptable bleeding changes (and their sociocultural implications) are a main factor in discontinuation, as are side-effects [3,43,66]. Early discontinuation of implant use does not necessarily represent a problem; rather, what is to be avoided is discontinuation (of any method) into contraceptive non-use because of service and programme factors (e.g. stockouts of methods, poor counselling or side-effects management) by women who want to avoid unintended pregnancy [67,68].

Service delivery considerations

In addition to being provided by doctors, injectables and implants can be provided safely and effectively by many other cadres of healthcare providers, including clinical officers, nurses, midwives, auxiliary nurses, auxiliary nurse-midwives, and (for injectables) community health workers [69]. Such 'task shifting' or 'task sharing' (i.e. delegation of appropriate tasks to less-specialised health cadres), is critical in addressing shortages of medical professionals and expanding access to contraceptive services for populations in need [69]. Availability of Sayana Press® could help improve clinic injection services

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[27,63,70], encourage countries to permit community health workers to provide injectables, and perhaps facilitate 'home use' (administration at home by a family member or woman herself through self-injection) [1,71].

Implant services can be delivered in static health sites or by mobile outreach (where a mobile team of service providers regularly visits under-served rural and periurban areas) [3,35,72]. Service sites must provide privacy, counselling, good surgical technique, and infection prevention. Access to implant removal as well as insertion must be regularly and reliably available. Implant and injectable (and other family planning) services can be integrated with postpartum visits, postabortion care, and child immunisation sessions. Strong links with community health programmes are important. Ethiopia is training 15,000 rural community health extension workers (the lowest cadre in its health system) to insert ENG implants, with referrals for removal made to providers in higher cadres of the health system [73].

Cost considerations for implants

High-commodity cost has historically limited wider availability of implants [6,35,74,75]; however, the commodity cost of Jadelle® and Implanon®, once as high as around USD $24 per unit [74], has recently been reduced to USD $8.50 per unit (similar to Sino-implant-II's commodity cost of around $8 per unit) owing to donor volume guarantees. Over 40 million implants are to be made available between 2013 and 2018 in low-income countries, as prioritised at the 2012 London FP2020 Summit [76–78]. Once direct and indirect service costs have been factored in, the cost-effectiveness per couple-year of protection (CYP) is now comparable to, or better than, the cost-effectiveness of injectables (and pills), in both low-resource and high-resource countries [75,79,80].

Use and popularity of injectables and implants in family planning programmes

Globally, injectables account for 6% of modern method contraceptive prevalence (MCPR) among women who are married or in union [81]. Injectables account for 43% of MCPR in sub-Saharan Africa, 46% in Southern Africa and 49% in Eastern Africa, and are the most widely used method in those regions. In many low-resource countries, injectables account for one-half or more of modern method use, including Ethiopia, (76%), Indonesia (66%), Madagascar (65%), Malawi (61%), Burundi (59%), Kenya (55%), Uganda (54%), Myanmar (50%), and South Africa (47%) [82]. These disparities partly reflect the difficulty of accessing even longer-acting or permanent methods in low-resource countries [83]. DMPA is the most widely available and commonly used injectable formulation [1].

Implants are registered in over 80 countries [8]. Although global use of implants has been below 1% of MCPR among women who are married or in union, recent evidence suggests that implant use may be rising. About 6 million women were using an ENG implant in 2010 [43]. Marie Stopes International provided 1.7 million implants in 15 sub-Saharan African countries between 2008 to 2012, with provision rising from 80,000 in 2008 to 750,000 in 2012 [72]. Ethiopia procured over 2.4 million implants between 2009 and 2012 compared with 90,000 between 2005 and 2006 [35]. In Zambia, 18 nurse-midwives at high-volume public-sector facilities inserted more than 22,000 implants in 14 months [84]. Seven sub-Saharan African countries (Burkina Faso, Ethiopia, Mali, Rwanda, Uganda, Tanzania, and Zimbabwe) have an implant contraceptive prevalence rate above 2%, with proportionally sizeable increases between their two most recent Demographic and Health Surveys [35]. The implant contraceptive prevalence rate in Rwanda (6.3% among married women) is the highest in Africa and perhaps the world. Implants have become the second most popular method in Ethiopia and Burkina Faso, and the third most popular method in Rwanda.

Use of progestin-only injectables and implants in breastfeeding women 0–6 weeks postpartum

Use of progestin-only methods in breastfeeding women 0–6 weeks postpartum has been controversial owing to concerns about potential adverse neonatal outcomes [85]. Animal data have suggested an effect of progesterone on the developing brain; however, limited data on immediate postpartum DMPA use and neonatal outcomes have not suggested adverse effects, although data on

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long-term effects are limited. The insertion of ENG implants during the immediate postpartum period was not associated with adverse maternal clinical effects, significant maternal metabolic alterations, or decreased infant weight [86]. Recommendations among normative bodies differ considerably. WHO guidance states risks of progestin-only contraceptive use by breastfeeding women 0–6 weeks postpartum outweigh benefits (MEC Category 3) [22]. The US Centers for Disease Control and Prevention assigns MEC Category 2 (benefits outweigh risks) to progestin-only contraceptive use during the first 4 weeks postpartum, and advises that progestin-only contraceptives can be used immediately after birth by breastfeeding women [24]. The UK's Royal College of Obstetricians and Gynecologists advises no restrictions at any time (MEC Category 1) [87]. The Society of Gynaecologists and Obstetricians of Canada advises that progestin-only methods be considered options for postpartum women regardless of breastfeeding status, and may be introduced immediately after delivery [88]. Immediate postpartum provision of implants could offer greatly expanded programme opportunities in low-resource countries [83], as births are increasingly occurring in facilities, and over 90% of postpartum women want to avoid a subsequent pregnancy for at least 2 years [89]. WHO addressed this question during a March 2014 expert meeting to assess newly-available, relevant evidence; recommendations stemming from that meeting are expected to be available later in 2014.

Possible associations with human immunodeficiency virus

The relationship between various hormonal contraceptive methods and human immunodeficiency virus (HIV) has recently been controversial in scientific and lay circles. Several studies have examined whether an association exists between specific methods of hormonal contraception and HIV acquisition in HIV-negative women. Similarly, among women living with HIV, studies have examined whether an association exists between specific methods of hormonal contraception and (1) female-to-male HIV transmission, (2) HIV disease progression, or (3) drug–drug interactions with certain antiretroviral medications.

A recent systematic review [90] clarified that the preponderance of higher-quality epidemiological data suggest no association between oral contraceptive pills and HIV acquisition, but that the body of higher quality epidemiological data on progestin-only injectable contraceptives is mixed and difficult to interpret. Some investigators have reported a 1.5–2.2 times increased risk of HIV acquisition with contraceptive injectables, whereas other investigators have reported no statistically significant association. No study in that systematic review reported a statistically significant association between NET-EN and HIV acquisition, but only three studies were available. Limited or no data were available for contraceptive implants (or patches, rings, and hormonal intrauterine devices). An updated systematic review of this topic including recently published data is currently under consideration for publication.

A second systematic review [91] assessed whether use of a method of hormonal contraception by a woman living with HIV increases risk of female-to-male HIV transmission. Only one study in serodiscordant couples (in which contraceptive use can be measured in the HIV-infected female partner and HIV seroconversion can be measured in the male sexual partner) was available [92]. That study suggested a doubling in risk of female-to-male HIV transmission with use of injectables. No statistically significant association was reported for oral contraceptive pills and female-to-male HIV transmission, but statistical power was limited. Seventeen studies reported mixed results for an association of hormonal contraception with cervicovaginal shedding among women living with HIV, and generally did not report any association with plasma viral load. Thus, the data for the potential for injectables (or oral contraceptive pills) to increase female-to-male transmission are limited, and no data exist on this association for other hormonal contraceptive methods.

A third systematic review [93] assessed whether various hormonal contraceptive methods are associated with accelerated HIV disease progression. Here, the preponderance of evidence suggests that women living with HIV can use oral or injectable contraception without concerns related to HIV disease progression. Data were not available on contraceptive implants and HIV disease progression.

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In 2012, a WHO expert group advised that WHO continue to recommend no restriction on the use of any hormonal contraceptive method for women living with HIV or at high risk of HIV infection, but added a clarification that due to the inconclusive nature of the evidence, women at high risk of HIV using progestin-only injectable contraception should be strongly advised also always to use condoms, male or female, and other HIV preventive measures [94]. Data published between December 15, 2011 and January 15, 2014 were presented at a WHO meeting on Medical Eligibility Criteria for Contraceptive use in March 2014; recommendations related to hormonal contraception and HIV stemming from this meeting are expected to be issued in July 2014.

Considerations are ongoing about how to obtain more definitive evidence. Analytic recommendations for improving the quality of the observational evidence base have been published [95], and discussions are ongoing about whether a randomised-controlled trial is feasible and could provide more definitive data.

In addition, some antiretroviral medications (such as some protease inhibitors, the non-nucleoside reverse transcriptase inhibitors efavirenz and nevirapine, and cobicistat-boosted elvitegravir) may reduce the effectiveness of contraceptive implants (and combined oral contraceptive pills); however, DMPA (as well as the hormonal IUD) is unlikely to lose contraceptive effectiveness when taken with any antiretroviral medication [96].

No contraceptive method, other than male or female condoms, is known to provide any protection against sexually transmitted diseases (STIs), including HIV. All people at high risk of HIV should be provided with access and empowered to use male or female condoms, and they have a right to know about the current scientific uncertainty about a potential, but not definitive, relationship between progestin-only injectable contraceptives and HIV acquisition. Data on implants are too scarce to draw any conclusions.

Highly effective contraception prevents unintended pregnancy, which in turn decreases maternal and infant morbidity and mortality, and recourse to unsafe abortion. Contraceptive use prevents 44% of maternal deaths [97], in addition to numerous non-fatal outcomes related to childbirth, such as fistula. Thus, highly effective contraceptive methods, such as injectable contraception, contribute to saving lives and improving health and well-being. These effects must be balanced, however, against a potential risk of HIV acquisition if such an association is confirmed, and the public health community must grapple with how to balance the risks and benefits of various contraceptive options. A recent modelling study considered the net public health outcome of a reduction in use of injectable contraception in various epidemiological contexts and concluded that, 'unless the true effect size approaches (a more than doubling in risk), it is unlikely that reductions in injectable hormonal contraception could result in a public health benefit, with the possible exception of those countries in southern Africa with the largest HIV epidemics [98].'

Conclusion

Most women may use injectables or implants in most circumstances. Implants have the highest effectiveness of any contraceptive method, with an unintended pregnancy rate of about one in 2000 in the first year of use. A lower-dose, subcutaneous formulation of the most widely used injectable DMPA could hold the promise of improving and expanding injectable services. Low use of contraceptive implants partly reflects the difficulty of accessing long-acting or permanent methods in low-resource countries. Commodity cost of implants has been markedly lowered and their use is rising. Changes in menstrual bleeding patterns with progestin-only contraceptive use are common, and a chief cause of discontinuation. Normative bodies differ on guidance regarding progestin-only contraceptive use in breastfeeding women 0–6 weeks postpartum. Immediate postpartum provision of implants could offer greatly expanded programme opportunities in low-resource countries, as more births are occurring in facilities and over 90% of postpartum women want to avoid a subsequent pregnancy for at least 2 years. The possible association of progestin-only contraceptive with HIV is a controversial issue with important public health and clinical practice implications, especially for sub-Saharan Africa, which carries a disproportionate burden of both HIV and maternal mortality.

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Practice points

- Most women, including adolescents and nulliparous women, may use injectables and implants in most circumstances.
- A woman does not need to be menstruating to receive an injectable or an implant, nor are blood or other laboratory tests prerequisites to use.
- Changes in menstrual bleeding patterns with injectables and implants are common. They are a chief cause of discontinuation, and an important topic for counselling and anticipatory guidance.
- DMPA-SC, a lower-dose, subcutaneous formulation of the most widely used injectable (DMPA-IM), provides equivalent efficacy and is preferred by women and providers.
- Return to fertility after a DMPA-IM injection averages 9–10 months.
- The late reinjection grace period for DMPA is 4 weeks in most countries.
- A woman does not need to commit to using an implant for its full length of labelled use in order to receive it.
- The possible association of injectables and implants with HIV has important counselling and service implications; countries should consider how best to adapt recent WHO guidance to their local epidemiological context.

Research agenda

- Obtain clarity on the relationship between various methods of hormonal contraception with HIV acquisition in women, female-to-male transmission, and drug–drug interactions with antiretroviral therapy.

Conflict of interest

The views and opinions expressed in this paper are those of the authors and not necessarily the views and opinions of the United States Agency for International Development.

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