Barriers to Contraceptive Use in Product Labeling and Practice Guidelines

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Many contraceptives are encumbered with potentially unnecessary restrictions on their use. Indeed, fear of side effects, fostered by alarmist labeling, is a leading reason that women do not use contraceptives.

In the United States, hormonal methods currently require a prescription, although research suggests that women can adequately screen themselves for contraindications, manage side effects, and determine an appropriate initiation date, leaving little need for routine direct physician involvement. Sizing, spermicidal use, and length-of-wear limits burden users of cervical barriers and may be unnecessary. Despite recent changes in the labeling of intrauterine devices, clinicians commonly restrict use of this method and in some countries may limit the types of providers authorized to insert them.

Although in some cases additional research is necessary, existing data indicate that evidence-based demedicalization of contraceptive provision could reduce costs and improve access. (*Am J Public Health.* 2006;96:791–799. doi:10.2105/AJPH.2004.040774)

Both in the United States and globally, significant unmet need for contraception remains. Difficulty of use, concerns about side effects or long-term health effects, and barriers to access may deter use of contraceptives.[1–6] New contraceptives under development may be easier to use with fewer side effects. In the interim, however, it may be possible to increase initiation and continuation of use of existing methods by simplifying product labeling and updating practice guidelines.

Two sources provide clinicians and consumers with information and regulations about appropriate contraceptive use: product labeling (the information that the US Food and Drug Administration [FDA] officially permits drug companies to use in their packaging and marketing) and practice guidelines (typically set forth by public sector groups such as the International Planned Parenthood Federation and the World Health Organization [WHO]). Sometimes labeling and practice guidelines are in consonance; however, they often differ. Frequently, product labeling is based on outdated data, potentially misinforming both the public and health care providers. In many cases, this misinformation hinders direct consumer access to contraceptives.

FDA regulations mandate specific requirements on the content and format of labeling for prescription drugs. Regulations are intended to ensure that prescribing physicians and patients are aware of the scientific information and potential risks associated with new drugs, but concerns about product liability litigation may encourage manufacturers to add otherwise unwarranted warnings. The process of determining the prescribing information to include in labeling does not involve objective reviews by researchers or clinical experts. Consumers play no role in the FDA labeling approval process other than taking part in committee hearings (when such hearings are held at all).

The Code of Federal Regulations governs labeling changes and generally requires that a supplement to the New Drug Application or Investigational Device Exemption be submitted to the FDA before labeling changes can be made. However, a manufacturer can add or strengthen warning information without first obtaining FDA approval.[7] Likewise, adverse experience reports, which manufacturers must file to comply with FDA regulations,[8] may lead to stronger labeling changes even when such changes are not strictly warranted by the available evidence.[9–11]

It is difficult, however, to reduce the amount of safety information included or to add indications for use. The latter change generally requires that the manufacturer support the proposed change with at least 2 adequate, well-controlled studies.[12] Yet, as a result of the cost of conducting such clinical studies, there are few incentives for manufacturers to submit the additional paperwork necessary to simplify labeling unless there is a potentially significant increase in market share to be derived from the changes made. In the case of oral contraceptives, manufacturers are generally proscribed from distinguishing products through promotional campaigns or labeling, because oral contraceptives are regulated under class labeling guidelines. Therefore, it is unlikely that a reduction in amount of safety information included will be initiated by manufacturers. As a result, labeling often includes unnecessary and outdated information, much of which was grandfathered in when regulations were established. One study found that overdose management in the labeling of 80% of drugs reviewed involved at least 1 deficiency in terms of advice, and nearly half contained ineffective or harmful information.[13]

All of these factors may result in more alarmist warnings being added to labeling information, with very little pressure to counter this effect. In addition, inaccurate labeling information may lead to overestimation of the dangers associated with a given contraceptive[14] and thus deter eligible women from using what are in fact widely studied, safe, and effective methods. Indeed, research has shown that misinformation included in oral contraceptive labeling leads women to believe that there are medical contraindications to the use of these pills or that they entail health risks so grave as to render their use unsafe.[15] Similarly, a review of studies that evaluated the European Commission guideline descriptors, phrases used to describe the risk of a

given side effect, revealed that people significantly overestimated the likelihood of adverse effects. This resulted in higher ratings of perceived health risks and lower ratings of likelihood of taking the medicine.[16] Perhaps most important, labeling that focuses primarily on liability obfuscates particularly valuable information. Valid concerns regarding legitimate potential complications are overshadowed by a medically unwarranted emphasis on extremely rare complications (e.g., hepatic cancer in the case of oral contraceptives).[17]

The 1951 Durham-Humphrey amendment to the original federal Food, Drug, and Cosmetic Act of 1938 requires that "a drug be made available without a prescription if, by following the labeling, consumers can use it safely and effectively without professional guidance."[18] The Durham-Humphrey amendment suggests that over-the-counter status will result by default once these criteria are achieved, but in reality this legislation is not enforced.

Given that FDA-approved labeling is often out of date or not based on current scientific evidence, physicians often use medications and devices in ways not listed in their labeling, so-called "off-label" use. Off-label use is common, and even the FDA recognizes that advances in medicine often precede changes to labeling.[19] Physicians prescribing a drug or device off label are assumed to be well informed and to base their decision to do so on sound medical evidence.[20] Off-label use is helpful in that it allows physicians to use medications in innovative ways, but the practice transfers liability risk to the provider, and some clinicians may be reluctant to use drugs in this manner. Women without access to clinicians who are knowledgeable about the latest research, particularly women in developing countries, are at a disadvantage because their providers are less likely to be aware of new or less restrictive uses of drugs or devices. As a consequence of the dearth of clinical trials including pregnant women and children, off-label use is extremely common among pediatricians and obstetricians. In 1 study, physicians prescribed medications for an off-label indication to 23% of women attending prenatal clinics.[21]

When physicians prescribe off label, they often look to the other main source of information: expert recommendations or practice guidelines. Clinical guidelines have become increasingly common over the past several years, as more emphasis has been placed on evidence-based medicine and managed care and as research emerges highlighting variations in physician practices.[22] At their best, practice guidelines are systematically developed statements intended to help clinicians make decisions about specific patient circumstances. These guidelines are often developed by experts brought together by professional organizations, such as the Royal College of Obstetricians and Gynaecologists (RCOG) or WHO, and published either by the organization or in peer-reviewed journals.

We reviewed the labeling of the major contraceptives available on the market worldwide, as well as the contraceptive practice guidelines of the leading professional and public sector organizations active in family planning. Our hypothesis was that both labeling and practice guidelines create barriers to access that, if removed, could increase the number of contraceptive users. We identified research priorities to help solidify the evidence supporting simplifying the provision of contraceptives.

METHODS

We reviewed prescribing information (or labeling) for the following contraceptives: combined oral contraceptives (COCs; specifically Ortho-Novum and Modicon tablets), Depo-Provera contraceptive injection, the Ortho Coil Spring and All-Flex diaphragm, and the ParaGard T380A intrauterine copper contraceptive. In addition, we reviewed the most recent practice guidelines from WHO, the International Medical Advisory Panel (IMAP) of the International Planned Parenthood Federation, the Planned Parenthood Federation of America (PPFA), the Maximizing Access and Quality Initiative of the US Agency for International Development, the Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit of RCOG, and the American College of Obstetricians and Gynecologists. Finally, we reviewed the guidelines published in *Contraceptive Technology*.[23]

RESULTS

We identified barriers to use for each contraceptive method, including restrictions on how the product can be dispensed, limitations in the types of providers who can dispense it, and excessive or unproven rules about use and clinician follow-up. Our results are summarized in Table 1.

Hormonal Methods

A number of the practices associated with hormonal methods (i.e., COCs, contraceptive patch, vaginal ring, injectables) could be eliminated to improve access to these methods. The labeling for all hormonal methods recommends a physical examination before provision, although a relatively recent modification allows deferral of this examination until after initiation of use.[17] Regular physician visits are advisable for a number of preventive health procedures such as breast examinations and Papanicolaou tests, but clinicians should not prevent women who decline these services from receiving contraceptives.[24]

At issue is whether, without a clinician visit, women can adequately self-screen for appropriateness of COC use and absorb the relevant information necessary for good compliance and continuation. Very few studies have examined whether women can screen themselves successfully for medical contraindications to COC use. One of the rare studies to tackle this topic was conducted in Mexico, where a prescription for COCs is not required; this study provides some evidence that woman can effectively screen themselves.[25] More definitive studies are necessary to inform the debate about over-the-counter provision in countries where this is not the norm.

Direct clinician counseling on how to use hormonal methods is routine in countries where they are available only by prescription. However, a recent review of studies of contraceptive counseling revealed little evidence demonstrating a benefit to this practice.[26] Even with physician counseling, patient compliance is relatively low. A clinic-based study conducted in the United States showed that 58% of women did not take their pills every day,[27] and similar percentages of women missing pills have been

TABLE 1—Research Needed to Simplify Provision of Contraceptives

Current Practice	Labeling Information	Evidence	Hypothesis	Research Need
		Hormonal methods		
General health screening by clinician before provision of COCs required in United States and many other countries[37–41]	Physical examination should be performed (although it can be deferred until after initiation)[17]	Limited information suggesting women can appropriately self-screen before using COCs[25]	Women can safely self-screen for COC contraindications	Comparison of self-screen with clinician assessment of appropriateness for COC use
Blood pressure screening by a clinician required before provision of COCs in United States and many other countries[37–41]	Physical examination should include special reference to blood pressure[17]	Outside of COC provision, blood pressure self-determination is feasible[42,43]	Women can safely self-screen for hypertension before obtaining COC refills using a blood pressure kiosk	Acceptability/feasibility trial of self-screening with blood pressure kiosk, as well as comparison of accuracy with clinician blood pressure measurement
Risks usually outweigh advantages of COCs during first 6 months of breastfeeding[37,38,41,47]	If possible, nursing mothers should be advised not to use COCs[17]	Studies of effects of COCs on lactation conflicting and of poor quality[48]; women prefer COCs, and some even stop breast-feeding to initiate use[49]	COCs have no significant effect on lactation; continuation and satisfaction are higher with COCs than with progestin-only oral contraceptives during breastfeeding	RCT comparing COCs, progestin-only oral contraceptives, and a placebo among breastfeeding women; outcomes: lactation, efficacy, continuation, satisfaction
Women told to initiate use of COCs at beginning of subsequent menstrual cycle (first day or Sunday)[38,39,47]	First tablet should be taken on the first Sunday after menstruation begins or Day 1 of the menstrual cycle[17]	Quick start (starting on day of clinician visit, regardless of cycle day) of COCs does not worsen side effects and may improve continuation[56,57]	Quick start will reduce pregnancy rates among COC users in developing country settings	RCT of quick start vs menstrual start of COCs in developing country settings; outcomes: efficacy, side effects, satisfaction
Women told to begin use of injectables within first 5 days of menses[51,60]	The first injection of Depo-Provera must be given only during the first 5 days of a normal menstrual period[59]	Quick start of COCs does not worsen side effects and may improve continuation[56,57]	Quick start of injectables will not worsen side effects and will improve continuation	RCT of quick start vs menstrual start of injectable contraceptives in developing country settings; outcomes: efficacy, side effects, satisfaction
Injection requires drawing up medication into syringe (and injection by a clinician in many countries)	. . .	Self-injection with simple prefilled syringes (UniJect) has been demonstrated to be acceptable in small trial of Cyclofem[58]	Use of self-injectable syringes will increase compliance and continuation	Feasibility/acceptability of self-administered UniJect vs clinician injection of contraceptive
Women overdue for injection routinely undergo pregnancy test[60]	If more than 13 weeks since most recent use of Depo-Provera, pregnancy must be ruled out[59]	Data equivocal about whether women are able to self-diagnose pregnancy on symptoms alone[61,62]; home urine pregnancy tests are very accurate[63]	Women can reliably self-assess for pregnancy when overdue for injection using combination of symptoms and home urine testing	Comparison of self-assessment with clinician assessment of pregnancy in women receiving injectable contraceptives
		Barrier methods (diaphragm)		
Diaphragms routinely fit by clinician before dispensing[67–69]	Fitting mandatory[65]	Limited data suggest fitting not necessary[70–72]	Modal-sized diaphragm is as effective as fitted diaphragm	RCT of no fitting vs fitting of diaphragm; outcomes: efficacy, continuation, satisfaction
Spermicide routinely recommended with diaphragm[67–69]	Must be used in conjunction with appropriate spermicide[65]	Limited data suggest spermicide may not affect efficacy of diaphragm[72,78]	Use of spermicide does not affect efficacy of diaphragm	RCT of diaphragm with spermicide vs use without spermicide; outcomes: efficacy, continuation, satisfaction
Continuous use of diaphragm not recommended[67–69]	Continuous wearing of diaphragm for more than 24 hours not recommended[65]	Limited data suggest that continuous usage is safe and effective[78]	Continuous use is safe and effective, as well as more accepted by women	RCT of continuous use vs standard use of diaphragm; outcomes: efficacy, continuation, satisfaction

Continued

TABLE 1—*Continued*

		Intrauterine devices		
Insertion limited to physicians in some countries owing to regulations or lack of training of midlevel providers[79]	Should be placed and removed only by health care professionals who are experienced with these procedures[83]	Nonphysician provision is safe, and complication rates are similar to physician provision[80–82]	Nonphysicians can safely manage IUDs in all settings	Review of nonphysician provision of IUDs and feasibility trial in several countries where such provision not standard
IUDs rarely inserted immediately postpartum	ParaGard has been placed immediately after delivery, although risk of expulsion may be higher than when ParaGard is placed at times unrelated to delivery[83]	Although no RCTs have been conducted, immediate postpartum insertion appears to be safe and effective[85]	Immediate postpartum insertion is safe, effective, and accepted by women	RCT of immediate vs delayed postpartum IUD insertion; outcomes: efficacy and continuation, including expulsion and percentage of women in delayed group who return
IUDs rarely inserted immediately postabortion	ParaGard can be placed immediately after abortion, although immediate placement involves a slightly higher risk of expulsion than placement at other times[83]	Insertion of an IUD immediately after abortion is both safe and practical[84] (only 1 comparative RCT)	Immediate postabortion insertion is effective and accepted by women	RCT of immediate vs delayed postabortion IUD insertion; outcomes: efficacy and continuation, including expulsion and percentage of women in delayed group who return; feasibility/acceptability of immediate IUD insertion
Postinsertion visit is routine[38,41,87–89]	After placement, the patient is examined after her first menses to confirm that ParaGard is still in place[83]	Expulsion is rare (2%–7% of cases), and 80% of expulsions are symptomatic[90]	Routine follow-up is not necessary; women can be taught to recognize expulsion	Observational prospective cohort study of no follow-up after IUD insertion (with education about recognizing expulsion); outcomes: efficacy (i.e., unrecognized expulsion), satisfaction
Nulliparous women often not considered good IUD candidates because of concerns about side effects (cramping, bleeding, expulsion)[91,92]	IUDs are not recommended for women at high risk for sexual infection (reference to parity has been deleted in the most recent revision of the labeling)[83]	For nulliparous women at low risk of STIs, specially designed IUDs are effective and acceptable[94]	IUDs are both effective and acceptable for nulliparous women	RCT of specially designed IUDs for nulliparous women at low risk of STIs; outcomes: side effects, including pelvic inflammatory disease; continuation; satisfaction
Nulliparous women often not considered good IUD candidates because of concerns about subsequent fertility[91,92]	IUDs are not recommended for women at high risk for sexual infection[83]	Subsequent fertility does not appear to be impaired after IUD use[91–93]	IUD use is not associated with subsequent infertility	Case–control study of association between IUD use and subsequent infertility

Note. COC = combined oral contraceptive; RCT = randomized controlled trial; IUD = intrauterine device; STI = sexually transmitted infection.

reported in other settings.[28,29] Poor compliance may be even more common among adolescents, either with or without a doctor's visit.[30]

A study of 6676 European pill users showed that poor compliance was significantly related to lack of an established pill-taking routine, experiencing side effects, and failure to read and understand written materials included with the COC package.[30] This latter result could indicate that current COC labeling is too complex or that women who have already received personal consultations are disinclined to read written materials. Simplified patient instructions for COCs and other contraceptive methods are urgently needed, and studies should address women's comprehension of this material, as was done recently for the proposed over-the-counter labeling of an emergency contraception product.[32] Little research has specifically analyzed the effect of a doctor's consultation on continuation of use. One study from Kuwait revealed similar continuation rates among women who consulted a physician and women who did not.[33] More research is needed to provide an understanding of the effects of over-the-counter provision on compliance, continuation, and overall efficacy.

FDA labeling of hormonal contraceptives emphasizes the importance of blood pressure screening when women undergo their physical examination.[17] Screening for uncontrolled hypertension is important because this condition is a contraindication to COC use; it is also important at follow-up visits given that some women develop hypertension while using COCs.[34–36] All of the practice guidelines we reviewed stressed the importance of women undergoing blood pressure screening before receiving COCs,[37–40] although WHO

recognizes that lack of screening should not be a barrier to dispensing these contraceptives in settings where such measurements are not possible.[41]

A related question arises: in settings where blood pressure measurement is available, must women see a clinician to be screened for hypertension? Research outside of the field of contraception has demonstrated that blood pressure self-determination is feasible.[42,43] Some studies have suggested that blood pressure kiosks in drug and grocery stores are inaccurate[44,45]; however, as this technology improves, women may be able to self-screen for hypertension in settings other than clinicians' offices. There is a need for prospective testing of the accuracy and feasibility of this approach to blood pressure screening both before and during COC use.

Another argument against selling COCs directly to women is that a layperson would not be able to make an informed choice, for example, from among the more than 50 COC brands on the market in the United States. In fact, evidence suggests that there are no significant clinical differences among the various oral contraceptive formulations currently available in terms of progestin.[46] Although the androgenicity of different progestins can be measured in animal models and indirectly via reductions in plasma sex hormone binding globulin, these measurements do not translate into meaningful clinical effects.[46] No COC formulation currently available has clinically important androgenic side effects, and all appear to treat androgenic phenomena such as acne and hirsutism.[46]

Similarly, progestin-induced changes in plasma lipids and lipoproteins do not appear to cause atherosclerosis in animal models and do not translate into an increased risk of myocardial infarction.[46] Balancing estrogenic side effects with breakthrough bleeding remains a valid justification for changing a COC formulation, yet it is unclear that women need to visit a clinician to obtain advice about how to manage minor side effects. Simple advice about managing estrogenic side effects and breakthrough bleeding[40] could be printed on a patient-friendly package insert.

Postpartum use raises another barrier: COC labeling indicates that nursing mothers should not take COCs.[17] In the WHO guidelines, COC use during the first 6 months of breastfeeding falls under classification 3 ("risks usually outweigh advantages").[41] This classification, in accord with the recommendations of IMAP,[37] the Maximizing Access and Quality Initiative,[47] and RCOG,[38] is based on a concern that COCs might diminish the quality and quantity of breast milk; however, the data are not convincing. Studies examining the effects of COCs on lactation have produced conflicting results and have been of poor quality.[48] What is clear is that some women prefer COCs as a form of contraception and even stop breastfeeding to use them.[49] When stopping breastfeeding is not an acceptable alternative, some women may discontinue contraceptive use or use a less effective method, placing themselves at risk of an unintended pregnancy.

Of the practice guidelines we reviewed, only the American College of Obstetricians and Gynecologists,[50] PPFA,[39] and *Contraceptive Technology*[40] guidelines recognized that COCs can be appropriate for well-nourished breast-feeding women after milk flow has been well established. A randomized controlled trial comparing COCs, progestin-only oral contraceptives, and a placebo is needed if there is to be a better understanding of the effects of these medications on lactation and on contraceptive efficacy, continuation, and satisfaction. More liberal use of COCs during breastfeeding would broaden the contraceptive options available to postpartum women.

Labeling also recommends that women commence hormonal contraceptive use at the start of their menstrual cycle,[17] and most of the guidelines we reviewed agree with this recommendation.[38,39,47] If women request these methods at another time of their cycle, they either may be told to return at the time of menses or, in the case of COCs, may be given a package to start with their next menses. But is this practice medically necessary, and does it best serve women's needs? Many women never return for the menstrual visit, and some may not initiate use of their COCs at the appointed time.[27]

According to *Contraceptive Technology*, COC use may be initiated at some time other than the start of the menstrual cycle as long as the woman is certain she is not pregnant and has not had sexual intercourse since her most recent menses.[40] WHO recommendations state that COCs can be started at other times of the cycle (after the first 7 days) if it is reasonably certain that the woman is not pregnant, which, in most cases, means that she has not had intercourse since her most recent menses.[51] Although more liberal than other guidelines, even the WHO recommendations would insist that many women delay initiation of contraception until the subsequent cycle. These guidelines aim to avoid drug exposure during early pregnancy, even though studies have consistently demonstrated that COCs have no teratogenic effects.[52–55]

Several small trials have examined initiation of COC use at the time of a woman's clinician visit regardless of where she is in her cycle, a practice called "quick start."[56,57] Women undergo a sensitive urine pregnancy test before starting the pills and receive emergency contraception if needed.[57] These trials demonstrated that quick start COC initiation does not worsen side effects and may improve rates of continuation. Larger trials are under way with quick start COCs and injectables, and we hope future research will address use of this practice in developing country settings. Research also is urgently needed to provide data about when hormonal contraception may be safely started during the medical abortion process.

In many settings, women are denied direct access to injectable contraceptives because of the requirement that clinicians provide the injection. One small study examined women's self-injection of Cyclofem with the UniJect device, a drug delivery system involving the use of a prefilled syringe and attached needle.[58] A large percentage of women accurately self-injected and wanted to continue to do so. In the case of those who do not prefer self-injection, provision by pharmacy workers may be both feasible and cost-effective. However, more research is needed with other injectable contraceptives to confirm that nonclinician injection is an acceptable alternative to current practices.

Similar to limiting the times at which hormonal methods can be started, the timing of repeat contraceptive injections is an additional

barrier to use. When a woman is overdue for a repeat injection (beyond 13 weeks for Depo-Provera), the labeling states that pregnancy must be ruled out before she can receive her next dose.[59] This requirement is time-consuming, and in some cases the client must pay for a urine pregnancy test. Women who report recent intercourse may be told to abstain or use condoms for 2 weeks and return for a repeat pregnancy test.[60]

The WHO[51] as well as the RCOG[38] guidelines specifically address this issue. According to WHO, the ideal time for reinjection of Depo-Provera is 3 months, whereas the RCOG recommendation is 12 weeks; both allow a period of up to 2 weeks beyond these indicated times during which a woman may be reinjected without further evaluation or additional contraception. If a woman is more than 2 weeks late, the injection may be given if it is reasonably certain that she is not pregnant.[51] It is unlikely that a woman who is late for her injection and has had unprotected intercourse will satisfy 1 of the clinical criteria to exclude pregnancy,[51] and a pregnancy test would be the only way to rule out an existing (but not very early) pregnancy. As with other barriers mentioned here, this practice may end up denying women the opportunity to use a safe and effective form of contraception.

Evidence suggests that women may be accurate in their diagnosis of early pregnancy,[61,62] although self-assessments of pregnancy among users of injectable contraceptives, perhaps through the use of a checklist of symptoms, have not been tested. Home urine pregnancy tests are highly accurate,[63] and women could use these tests outside of clinical settings to replace clinician visits. In the unlikely event that a pregnant woman receives a contraceptive injection, even the Depo-Provera labeling recognizes the minimal risk associated with this exposure.[59]

Cervical Barriers

Use of cervical barriers is burdened by practices that either limit access to the method or make their use more cumbersome. Clinicians and researchers have renewed interest in these female-controlled methods because of their potential to protect against sexually transmitted infections (STIs) as well as pregnancy.[64] If cervical barriers do prevent infection, improving user access will be even more critical. Current requirements[65–69] call for clinician provision of the diaphragm and cervical cap, mostly to fit the devices. Fitting may be justified for the cervical cap, but little evidence supports this requirement for the diaphragm, and limited data suggest that the modal-sized (70 mm) diaphragm is as effective as a fitted one.[70–72] Historical evidence shows that physician fitting was introduced early in the 20th century, nearly 40 years after the immediate precursor of today's diaphragm had been introduced, for reasons entirely unrelated to concerns about diaphragm effectiveness or safety.[73] When the FDA began to regulate medical devices in 1976,[74] the diaphragm's fitting rules were grandfathered into the approved labeling in the absence of empirical evidence.

The labeling of the diaphragm states that the device must be used with spermicide and should not be used for more than 24 hours continuously,[65] but neither of these recommendations are based on evidence, as recognized by IMAP[67] and in *Contraceptive Technology*.[69] Could liberalizing such requirements make the device more attractive to new users without significantly affecting safety or contraceptive efficacy? Several reports have documented women's dissatisfaction with using spermicide, which can be messy and sometimes causes vaginal irritation.[75,76] Recent evidence that nonoxynol-9 may increase HIV transmission among female sex workers provides further motivation to reexamine the use of spermicide with diaphragms.[77] Limited data suggest that diaphragm use without spermicide does not affect efficacy,[72,78] although more research is needed to confirm this finding.

One study examined continuous use of the diaphragm (as opposed to use only around the time of intercourse) and found that this practice was both safe and effective.[78] Continuous diaphragm users had a significantly lower pregnancy rate, as well as fewer side effects. Although this study also needs further confirmation, it appears likely that diaphragm provision and use could be substantially simplified, thereby increasing the popularity of this method.

Intrauterine Devices (IUDs)

Simplifying provision of IUDs by making them available from the most accessible and affordable practitioners, such as midwives and nurses, could greatly increase access to and initiation of this method. Although the labeling for the ParaGard IUD does not specify that a physician must insert the device, training of midlevel providers in the techniques associated with insertion is deficient in many developing countries.[79] When access to physicians is limited by either scarcity or financial barriers, women's contraceptive options narrow. In several settings, studies have shown that nonphysician provision of IUDs is safe, resulting in low complication rates comparable to those associated with physician provision.[80–82] If there is an emphasis on training and quality assurance, IUD insertion by midlevel practitioners could be more cost-effective than physician provision, thereby increasing user access.

The ParaGard labeling was recently updated, and a number of unfounded barriers to access were removed.[83] The labeling was modified to allow insertion in both the postpartum and postabortion periods with a warning that the risk of expulsion may be higher than at other times. Two recent reviews concluded that postabortion and postpartum IUD insertion are both safe and effective.[84,85] Expulsion of the IUD may be more common during these periods, but this possibility needs to be balanced against the convenience of having the device inserted at the time of the accompanying pelvic procedure. In the 1 comparative trial of which we are aware comparing immediate and delayed IUD insertion after abortion, 40% of women randomized to the delayed group did not return for the insertion.[86] Some of these women may have chosen other contraceptive methods, but others may have been dissuaded altogether by the inconvenience.

The practice guidelines we reviewed[47,87,88] followed the WHO medical eligibility criteria for contraceptive use,[41] which generally support postabortion and postpartum IUD insertion. Insertion after first-trimester abortion falls under classification 1 ("use in any circumstance"), and insertion after second-trimester abortion falls under classification 2 ("generally use"), with a caveat about the increased risk of expulsion with later

abortion.[41] Immediate (i.e., less than 48 hours) postpartum insertion of a copper IUD falls under classification 2, also with a caveat about expulsion.[41]

Yet, postabortion and postpartum IUD insertion are not widely practiced. Clinicians are not routinely trained in these procedures, perhaps because of a lack of clear evidence that immediate insertion is better than delayed insertion. As mentioned, only 1 study has directly compared immediate and delayed postabortion insertion, and the IUD brand evaluated is no longer in use. No comparative trials exist on postpartum insertion. Randomized controlled trials that compare immediate and delayed insertion during both periods and show equivalence or superiority of immediate insertion would be useful to motivate governments and family planning programs to promote immediate IUD provision and encourage investment in programs offering training on insertion techniques. In addition, studies are needed to guide clinicians about when IUD insertion is most appropriate after medical abortion.

The ParaGard labeling also specifies that the client should return after her next menses for an examination, primarily to rule out partial or complete expulsion,[83] and this recommendation was upheld in the guidelines we reviewed.[38,41,87–89] Returning to a clinician's office is rarely convenient, and it can be costly in terms of transportation and possible child-care costs as well as lost income. Some women and some providers may be discouraged from using or promoting this highly effective form of contraception because of the required follow-up, and simplifications of the follow-up process may help attract new users. Recent studies have demonstrated that quarterly follow-up visits are not useful,[90] but no research has specifically addressed the utility of the first follow-up visit. Research is necessary to determine whether women can recognize the signs and symptoms of IUD expulsion without the aid of a clinician.

Another barrier to increased use of IUDs is the reluctance to offer this method to nulliparous women, although this is no longer a relative contraindication in the ParaGard labeling.[83] In the WHO recommendations and several other practice guidelines, IUD use among young (less than 20 years) and nulliparous women falls under classification 2 ("generally use").[41,47,87] The PPFA guidelines do not consider nulliparity a contraindication to IUD use provided that the woman is involved in a monogamous relationship and at low risk of acquiring an STI.[89] Hesitation to use the IUD in this population grows out of a fear of infertility after long-term use, especially among young women at risk for STIs, as well as concern that nulliparous women will experience more cramping, bleeding, and spontaneous expulsion with IUDs designed for parous women.[91,92] Evidence that IUD use is not associated with subsequent infertility and is safe in nulliparous women continues to accumulate,[91–93] and labeling and guidelines should keep pace. Evidence associated with new, specially designed IUDs that are smaller in size suggests that these devices can be well tolerated by nulliparous women.[94]

Women at low risk of STIs can be good IUD candidates,[92] yet nulliparous women are often denied access to this highly effective form of contraception. Some argue that the data are not yet strong enough to refute the association between IUD use and infertility and that there is not enough information available about the new IUDs designed for nulliparous women. What would it take for normative bodies to encourage IUD use among women at low risk of STIs? We suspect it would require an additional case–control study (similar to 1 recently published[93]) examining the association between infertility and previous IUD use, as well as additional randomized controlled trials of devices suitable for nulliparous women.

DISCUSSION

Working to make available contraceptives easier to use could be very cost-effective.[95] In a US study, women of reproductive age interviewed at shopping malls reported ease of use as the second most important reason for choosing a contraceptive.[96] If contraceptives were available over the counter, more women might begin using them, or they might switch to a more effective method. In 1 study of women seeking pregnancy tests at public health clinics who reported that their potential pregnancy was undesired, 25% indicated that they would be more likely to use oral contraceptives if they were available over the counter.[1] In a 2004 survey of more than 800 women of reproductive age, the Pharmacy Access Partnership found that most current oral contraceptive, patch, or ring users would probably obtain their hormonal contraceptives directly from a pharmacy if it were an option.[6] Even more interesting is the finding that 41% of women not currently using a contraceptive reported that they would likely begin using one if they could obtain it directly from a pharmacy.

At the moment, few new methods are close to being brought to market. When a hypothetical new product becomes available, some proportion of current contraceptive users *might* switch to the new method, and some proportion of nonusers *might* adopt the method and become new users. Of course, a new method might also fail to attract any new users. For instance, Norplant is now used by fewer than 1% of women of reproductive age in the United States, and it arguably has had little effect on overall contraceptive coverage.[97] Studies, reviews, and advocacy efforts that attempt to improve access to the most commonly used contraceptives could have a larger impact—at a fraction of the cost—than focusing on new contraceptive modalities.

In many developing countries, prescription requirements are seldom enforced, and many women already purchase oral contraceptives essentially over the counter. In these countries, labeling serves as a primary source of (mis)information. In such settings, carefully designed package labeling that accurately and simply describes the risks, side effects, contraindications, benefits, and proper use of a given method could play a large role in improving method choice as well as compliance and acceptability. Practice guidelines must also present the most up-to-date medical evidence, given that clinicians the world over look to these sources for information about best practices, especially in terms of off-label drug and device use.

Unnecessary medical restrictions associated with contraceptive labeling and practice guidelines are costly to women and to society. Labeling with inaccurate or unsubstantiated information might dissuade otherwise suitable and enthusiastic users of a method or foster higher discontinuation rates and elevate unintended

pregnancy rates. If women do not fully understand the risks and benefits associated with use of a particular contraceptive, they are unable to make informed decisions. Evidence-based labeling that eliminates unnecessary barriers could increase contraceptive use and reduce unintended pregnancies. ■

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Contributors

D. Grossman and C. Ellertson originated the review, and all of the authors participated in researching, analyzing, and writing up the findings.

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