



## Secretariat of Pro-Life Activities

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### **Fact Sheet: Greater Access to Contraception Does Not Reduce Abortions**

**1. Contraception is already widely available, and experts have reported that “contraceptive use in the United States is virtually universal among women of reproductive age,”<sup>1</sup> at times when many millions of abortions were performed.**

“Among women at risk of an unintended pregnancy, 89% are using and 11% are not using contraception”; use rises to 91.4% among those who do not intend having any children in the future.<sup>2</sup> “Nearly all (99.1%) sexually experienced women in the United States have used contraception at some time in their lives.”<sup>3</sup> Moreover, “virtually all sexually experienced female teenagers” (99.4%) have used a contraceptive method.<sup>4</sup> During the period when these data were collected, 2002 to 2015, there were almost 16 million abortions in the U.S.

**2. One problem is that with typical use, contraceptives often fail to prevent pregnancy.**

Overall, 10% of women using reversible forms of contraception become pregnant over 12 months of use; failure rates are highest for the condom (13%) and withdrawal (20%). Overall failure rates are higher among teens (11.4%), and among women who already had two or more children (14.6%), are black (15.3%), Hispanic (14%), are cohabiting (14.9%), or are below the federal poverty level (17.3%).<sup>5</sup>

Forty-eight percent of women with unintended pregnancies were using contraception in the month they conceived, and “about half” of pregnancies ended by abortion occur during use of contraceptives.<sup>6</sup> Recent data from the pro-abortion British Pregnancy Advisory Service show that most of the women having abortions at its clinics (51.2%) had been using at least one form of contraception, and a quarter (24.2%) had used methods considered “most effective” (hormonal

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<sup>1</sup> W. Mosher et al., “Use of Contraception and Use of Family Planning Services in the United States: 1982-2002,” Centers for Disease Control and Prevention, *Advance Data from Vital and Health Statistics*, Number 350 (December 10, 2004) at 1; [www.cdc.gov/nchs/data/ad/ad350.pdf](http://www.cdc.gov/nchs/data/ad/ad350.pdf).

<sup>2</sup> J. Jones et al., “Current Contraceptive Use in the United States, 2006-2010, and Changes in Patterns of Use Since 1995,” Centers for Disease Control and Prevention, *National Health Statistics Reports*, Number 60 (October 18, 2012) at 1, 6; <https://www.cdc.gov/nchs/data/nhsr/nhsr060.pdf>.

<sup>3</sup> Id. at 2.

<sup>4</sup> J. Abma et al., “Sexual Activity and Contraceptive Use Among Teenagers in the United States, 2011-2015,” Centers for Disease Control and Prevention, *National Health Statistics Reports*, Number 104 (June 22, 2017) at 7; <https://www.cdc.gov/nchs/data/nhsr/nhsr104.pdf>.

<sup>5</sup> A. Sundaram et al., “Contraceptive Failure in the United States: Estimates from the 2006–2010 National Survey of Family Growth,” 49.1 *Perspectives on Sexual and Reproductive Health* (March 2017) 7-16 at 7, 12 (Table 3); <https://onlinelibrary.wiley.com/doi/pdf/10.1363/psrh.12017>.

<sup>6</sup> Id. at 7, 8-9.

contraception or “long-acting reversible contraceptives” such as implants or the IUD). Says BPAS’s chief executive: “Our data shows women cannot control their fertility through contraception alone, even when they are using some of the most effective methods.” Moreover, the women becoming pregnant while on contraception were more likely to have late-term abortions (after 20 weeks), with higher health risks for women, because the method masked early signs of pregnancy or their contraceptive use led them to believe they could not be pregnant.<sup>7</sup>

Finally, inconsistent or imperfect use of contraceptives increases the likelihood of unintended pregnancy. For example, women taking the daily progestin-only pill are warned that it is much less effective if taken over three hours later than usual.<sup>8</sup> Other factors, including interaction with other drugs, can reduce effectiveness. Simply being overweight can interfere with the effectiveness of the “emergency contraception” pill known as Plan B (levonorgestrel).<sup>9</sup>

### **3. Studies indicate that, instead of reducing abortions, greater access to contraception may lead to higher rates of abortion and unintended pregnancy.**

Studies of contraceptive use, sexual behavior and STD transmission raise a concern about “risk compensation,” that is, the greater likelihood of engaging in potentially risky sexual behavior when one believes risk has been reduced.<sup>10</sup> For example, economics professor David Paton, author of many studies in this area, has found “no evidence” that “the provision of family planning reduces either underage conception or abortion rates.”<sup>11</sup> He sums up the British experience: “It is clear that providing more family planning clinics, far from having the effect of reducing conception rates, has actually led to an increase.... The availability of the morning-after pill seems to be encouraging risky behaviour. It appears that if people have access to family planning advice they think they automatically have a lower risk of pregnancy.”<sup>12</sup>

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<sup>7</sup> Press release, British Pregnancy Advisory Service, “Women cannot control fertility through contraception alone: bpas data shows 1 in 4 women having an abortion were using most effective contraception,” 07 July 2017; <https://www.bpas.org/about-our-charity/press-office/press-releases/women-cannot-control-fertility-through-contraception-alone-bpas-data-shows-1-in-4-women-having-an-abortion-were-using-most-effective-contraception/> (includes links to both studies, on failure rates and on increased resort to late abortion).

<sup>8</sup> U.S. National Library of Medicine, “Progestin-Only Oral Contraceptives,” *MedLine Plus*, at <https://medlineplus.gov/druginfo/meds/a602008.html> (accessed 8/8/19).

<sup>9</sup> A. Edelman et al., “Impact of obesity on the pharmacokinetics of levonorgestrel-based emergency contraception: single and double dosing,” 94 *Contraception* (July 2016) 52-57; [https://www.contraceptionjournal.org/article/S0010-7824\(15\)30184-0/abstract?cc=y](https://www.contraceptionjournal.org/article/S0010-7824(15)30184-0/abstract?cc=y).

<sup>10</sup> See M. Cassell et al., “Risk compensation: the Achilles’ heel of innovations in HIV prevention?,” 332 *British Medical Journal* (11 March 2006) 605-7 and sources cited therein; abstract at <https://www.bmj.com/content/332/7541/605>.

<sup>11</sup> D. Paton, “The Economics of Family Planning and Underage Conceptions,” 21.2 *Journal of Health Economics* (March 2002) 207-25 at 207; abstract at <https://www.sciencedirect.com/science/article/abs/pii/S0167629601001151>. This study found, among other things, that after a British court ruled that parental consent was required for girls under 16 to obtain contraception, there was a steep decline in family planning clinic visits by these girls; but the study found no increase in pregnancies or abortions in this group.

<sup>12</sup> Quoted in K. Ahmed, “Abortions rise in under-age sex crisis,” *The Observer* (London), 17 March 2002; [www.guardian.co.uk/uk/2002/mar/17/medicalscience.socialsciences](http://www.guardian.co.uk/uk/2002/mar/17/medicalscience.socialsciences).

In 2011, researchers reported on contraceptive use and abortions in Spain over a ten-year period, from 1997 to 2007. They found that a 63% increase in use of contraceptives was accompanied by a 108% increase in the rate of elective abortions.<sup>13</sup>

Researchers at Duke University, Yale, and the U.S. Centers for Disease Control concluded in 2012: “Programs that increase access to contraception are found to decrease teen pregnancies in the short run but increase them in the long run.”<sup>14</sup>

A Swedish study found that despite free contraceptive counseling, low-cost condoms and oral contraceptives, and over-the-counter emergency contraception, teen abortion rates rose from 17 per thousand to 22.5 per thousand between 1995 and 2001, and “sexual and reproductive health problems are on the increase among young people.”<sup>15</sup>

In 2017, some U.S. journalists claimed that due to a 2011 policy change that decreased funding for family planning clinics in Texas by two-thirds, “abortion rates have jumped” in the state.<sup>16</sup> This claim arose from an academic study whose conclusions were more modest: It said the cuts “increased teen birth rates by approximately 3.4% over four years,” and offered “suggestive evidence” on a slight increase in abortions, saying this required “further study.”<sup>17</sup> But a 2018 study found that from 2011 to 2014, due to this and other state policy changes, “abortions to Texas residents *fell* 20.5% and births rose 2.6% in counties that no longer had an abortion provider within 50 miles,” and there was “a 1.5% increase in births for counties that no longer had a publicly funded family planning clinic within 25 miles.”<sup>18</sup> The pro-abortion Guttmacher Institute found “a 28% *decline* in the abortion rate in Texas between 2011 and 2014.”<sup>19</sup> Political scientist Michael J. New adds that abortions on minors declined by the same percentage, and “the number of Texas minors who gave birth fell by over 24 percent,” during this period.<sup>20</sup>

<sup>13</sup> J. Dueñas et al., “Trends in the Use of Contraceptive Methods and Voluntary Interruption of Pregnancy in the Spanish Population during 1997-2007,” 83.1 *Contraception* (January 2011) 82-7; abstract at [https://www.contraceptionjournal.org/article/S0010-7824\(10\)00327-6/pdf](https://www.contraceptionjournal.org/article/S0010-7824(10)00327-6/pdf).

<sup>14</sup> P. Arcidiacono et al., “Habit Persistence and Teen Sex: Could Increased Access to Contraception Have Unintended Consequences for Teen Pregnancies?”, 30.2 *Journal of Business & Economic Statistics* (2012) 312-25 at 312; abstract at <https://www.tandfonline.com/doi/full/10.1080/07350015.2011.652052>, full manuscript at <http://public.econ.duke.edu/~psarcidi/teensex.pdf>.

<sup>15</sup> K. Edgardh, “Adolescent Sexual Health in Sweden,” 78 *Sexually Transmitted Infections* (2002) 352-6 at 352; <https://sti.bmj.com/content/sextrans/78/5/352.full.pdf>.

<sup>16</sup> See M. Tuma, “What Happens When Texas Blocks Planned Parenthood? Abortions Rise,” *The Austin Chronicle*, July 12, 2017; <https://www.austinchronicle.com/daily/news/2017-07-12/what-happens-when-texas-blocks-planned-parenthood-abortion-rise/>.

<sup>17</sup> A. Packham, “Family planning funding cuts and teen childbearing,” 55 *Journal of Health Economics* (2017) 169-185 at 168, 180, 183; [https://apackham.github.io/mywebsite/Packham\\_JHE.pdf](https://apackham.github.io/mywebsite/Packham_JHE.pdf).

<sup>18</sup> S. Fischer et al., “The Impacts of Reduced Access to Abortion and Family Planning Services on Abortion, Births, and Contraceptive Purchases,” 167 *Journal of Public Economics* 43-68 (November 2018) at 43 (emphasis added); <https://www.sciencedirect.com/science/article/abs/pii/S0047272718301531>.

<sup>19</sup> Guttmacher Institute, “State Facts About Abortion: Texas” (May 2018) at 1 (emphasis added); <https://www.guttmacher.org/sites/default/files/factsheet/sfaa-tx.pdf>.

<sup>20</sup> M. New, “After Texas Cut Planned Parenthood Funding, Teen Abortions Fell 28% and Teen Births 24%,” *LifeNews*, July 21, 2017; <https://www.lifenews.com/2017/07/21/after-texas-cut-planned-parenthood-funding-teen-abortion-fell-28-and-teen-births-24>.

In 2015, Dr. New analyzed the impact of policies in 28 states requiring health plans to cover contraceptive services. He found that “states with contraception mandates have similar rates of unintended pregnancies as states that do not have contraception mandates.... Additionally, the model indicates that states with contraception mandates actually have higher abortion rates than states without a contraceptive mandate.”<sup>21</sup>

In July 2009, results were published from an expensive three-year program at 54 sites, funded by England's Department of Health to “reduce teenage pregnancy” through, among other things, sex education and advice on access to family planning beginning at ages 13-15. “No evidence was found that the intervention was effective in delaying heterosexual experience or reducing pregnancies.... Some results suggested an adverse effect.” Young women taking part in the program were more likely than those in a comparison group to report that they had become pregnant (16% vs. 6%) and had early heterosexual experience (58% vs. 33%).<sup>22</sup>

#### **4. Programs promoting emergency contraception (EC) do not reduce unintended pregnancies or abortions.**

Twenty-three studies published between 1998 and 2006, analyzed by a research team headed by Dr. James Trussell at Princeton University, measured the effect of increased EC access on EC use, unintended pregnancy, and abortion. “In all but one study, increased access to emergency contraceptive pills was associated with greater use. However, no study found an effect on pregnancy or abortion rates.”<sup>23</sup> Dr. Trussell reaffirmed this finding in 2013, and other studies have reached similar conclusions.<sup>24</sup>

#### **5. Promoting “LARCs” creates problems for medical ethics and women’s health**

Disappointed by the results noted above, contraceptive program advocates have urged greater use of “long-acting reversible contraceptives” (LARCs) such as hormonal implants and intrauterine devices (IUDs). These are effective for years and can only be removed surgically by a medical professional. Supporters applaud them for “eliminating adherence and user dependence from the effectiveness equation,” because their effectiveness is “independent from...

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<sup>21</sup> M. New, “Analyzing the Impact of State Level Contraception Mandates on Public Health Outcomes,” 13.2 *Ave Maria Law Review* (Summer 2015) 345-69 at 363; <https://avemarialaw-law-review.avemarialaw.edu/Content/articles/vXIII.i2.new.final.0809.pdf>.

<sup>22</sup> M. Wiggins et al., “Health Outcomes of Youth Development Programme in England: Prospective Matched Comparison Study,” 339.7713 *British Medical Journal* (18 July 2009) b2534; advance online publication (7 July 2009) at <https://www.bmj.com/content/bmj/339/bmj.b2534.full.pdf>.

<sup>23</sup> E. Raymond et al., “Population Effect of Increased Access to Emergency Contraceptive Pills: A Systematic Review,” 109.1 *Obstetrics & Gynecology* (January 2007) 181-8 at 181; abstract at [https://journals.lww.com/greenjournal/Abstract/2007/01000/Population\\_Effect\\_of\\_Increased\\_Access\\_to\\_Emergency.25.aspx](https://journals.lww.com/greenjournal/Abstract/2007/01000/Population_Effect_of_Increased_Access_to_Emergency.25.aspx).

<sup>24</sup> For documentation see USCCB Secretariat of Pro-Life Activities, “Fact Sheet: Emergency Contraception Fails to Reduce Unintended Pregnancy and Abortion,” June 5, 2014; <http://usccb.org/issues-and-action/human-life-and-dignity/contraception/fact-sheets/upload/contrafactsheet.pdf>.

user motivation” -- that is, they ignore women’s own changing reproductive goals.<sup>25</sup> This approach however, presents problems for medical ethics and for women’s health and free choice.

First, regarding medical ethics and women’s freedom, it is highly unusual for a clinical study to overtly favor a particular outcome or pressure participants towards a certain choice. However, in a demonstration project in St. Louis, often cited as an example of how LARCs can reduce unintended pregnancies and abortions, promoters abandoned the ethical principle of “non-directive counseling,” and instead persuaded low-income women to prefer LARCs over other methods. The study authors expressly state that the primary objective of their study was “to promote the use of long-acting reversible contraceptive (LARC) methods...”. Furthermore, “All participants were read a brief script informing them of the effectiveness and safety of LARC methods...and completed an in-depth...counseling session,” and promoters followed up with them individually afterward to “maximize method continuation.”<sup>26</sup> Even feminists who strongly support contraceptive access have raised concerns about this shift to “directive” counseling toward LARCs, the aggressive promotion of implants and sterilization to low-income women and racial minorities, and the potential for coercive use. For example:

Though few US citizens have been forcibly sterilized in recent years, rates of tubal ligation are enormously stratified by both education level and race...[P]olicy makers and professionals have exhibited more enthusiasm about LARC than contraceptive users themselves...[and] have suggested incentive programs in which poor women receive cash in exchange for having a LARC method inserted and such programs may be in practice already. Evidence also exists that clinicians recommend LARC more to women of color than white women and more to socioeconomically disadvantaged women compared to socioeconomically advantaged.<sup>27</sup>

Campaigns promoting LARCs may also endanger women’s health. For example, in 2016, California saw “a sharp increase in sexually transmitted disease rates, reaching a 20-year high” – and a Planned Parenthood official attributed the higher disease rate among young women to decreased use of condoms as they shift to LARCs for pregnancy prevention.<sup>28</sup> Other studies have also shown a correlation between using LARCs and decreasing use of a barrier method to prevent STDs. For example, “compared to women using oral contraceptives, use of the

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<sup>25</sup> American College of Obstetricians and Gynecologists, “Increasing Access to Contraceptive Implants and Intrauterine Devices to Reduce Unintended Pregnancy,” Committee Opinion Number 642 (October 2015) at 1, 3; <https://www.acog.org/-/media/Committee-Opinions/Committee-on-Gynecologic-Practice/co642.pdf?dmc=1&ts=20190810T2120035995>.

<sup>26</sup> Ironically this was called the “Contraceptive CHOICE” program. J. Peipert et al., “Preventing Unintended Pregnancies by Providing No-Cost Contraception,” 120.6 *Obstetrics and Gynecology* (December 2012) 1291–7; [https://journals.lww.com/greenjournal/Fulltext/2012/12000/Preventing\\_Unintended\\_Pregnancies\\_by\\_Providing.7.aspx](https://journals.lww.com/greenjournal/Fulltext/2012/12000/Preventing_Unintended_Pregnancies_by_Providing.7.aspx). On follow-up to “maximize method continuation” see N. Birgisson et al., “Preventing Unintended Pregnancy: The Contraceptive CHOICE Project in Review,” 24.5 *Journal of Women’s Health* (May 1, 2015) 349-353 at 352; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441000/>.

<sup>27</sup> J. Higgins, “Celebration meets caution: LARC’s boons, potential busts, and the benefits of a reproductive justice approach,” 89 *Contraception* (2014) 239; <https://jennyahiggins.files.wordpress.com/2014/02/higgins-2014-larcs-boons-potential-busts-and-the-benefits-of-an-rj-approach-final.pdf>.

<sup>28</sup> K. Hooks, “Report: California STD rates reach 20-year high,” KXTV (ABC Sacramento), October 30, 2016; <https://www.abc10.com/article/news/local/report-california-std-rates-reach-20-year-high/344232226>.

contraceptive injection or long-acting reversible contraception was associated with lower dual-method [both a contraceptive and a disease prevention] use.”<sup>29</sup> LARCs can have side effects and risks for women that range from irritating (headaches, acne, weight gain) to severe (uterine perforation or pelvic inflammatory disease – a risk associated with IUDs).<sup>30</sup>

Finally, LARCs can prevent a newly formed embryo from imbedding into the mother’s uterus, inducing a very early abortion rather than preventing one. Copper IUDs are particularly known to have this abortifacient effect. Women deserve to be informed about this potential abortifacient effect of LARCs.<sup>31</sup>

Whether this approach necessarily reduces abortions or unintended pregnancies remains to be seen. When the St. Louis project was replicated on a larger scale in Colorado, providing \$23 million for LARCs and training in promoting them at Title X family planning clinics, the project is said to have reduced the teen *birth* rate 6.4% over five years, costing “approximately \$13,531 per teen birth avoided”; but this study did not assess changes in teen sexual activity, pregnancies, abortions, or the effect on adult women. Any effect on pregnancies or abortions would have to be assessed in light of this approach’s real and serious detriments: potential for coercive use, risks to women’s health, undermining of medical ethics, and causing early abortions.

## **6. A decline in teen sexual activity has played a major role in reducing teen (or unwed) pregnancies, births and abortions.**

In 2018, women in the United States had “the lowest number of births in 32 years.” The sharpest decline is among teens aged 15-19, down 8% from the previous year and 60% since 2007.<sup>32</sup> The total number of abortions and the abortion rate (abortions per 1000 women of reproductive age) are also at their lowest levels in many years, especially among teens. And the abortion ratio (abortions per 1000 live births) has declined among teens of all ages, and among women generally.<sup>33</sup> That is, fewer teens and women who do become pregnant are having abortions, which is unlikely to be due to contraception.

<sup>29</sup> D. Eisenberg, “Correlates of Dual-Method Contraceptive Use: An Analysis of the National Survey of Family Growth (2006-2008),” *Infect Dis Obstet Gynecol*. (2012), 1, Published online 2012 Feb 14., <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3296176/>.

<sup>30</sup> For example, see R. Nall, “What are the side effects of an IUD?”, *Medical News Today*, 1 August 2018, at <https://www.medicalnewstoday.com/articles/322655.php>. On the risks of hormonal implants see Nemours Foundation, “About Implantable Contraception,” *KidsHealth*, June 2018; <https://kidshealth.org/en/Parents/about-implantable-bc.html>.

<sup>31</sup> On the methods’ mode of action see USCCB Secretariat of Pro-Life Activities, “Does the HHS Mandate Include Abortifacients?” April 3, 2014; <http://www.usccb.org/issues-and-action/human-life-and-dignity/contraception/upload/Does-the-HHS-Mandate-Include-Abortifacients.pdf>. On hormonal implants see Nemours Foundation, note 30 supra (“The progesterin also thins the lining of the uterus so that if the egg is fertilized, it may be less likely to attach to the wall of the uterus”).

<sup>32</sup> B. Hamilton et al., “Births: Provisional Data for 2018,” National Center for Health Statistics, *NVSS Vital Statistics: Rapid Release*, Report No.007 (May 2019) at 1, 3; <https://www.cdc.gov/nchs/data/vsrr/vsrr-007-508.pdf>.

<sup>33</sup> T. Jatlaoui et al., “Abortion Surveillance – United States, 2015,” Centers for Disease Control and Prevention, 67.13 *Surveillance Summaries* 1-45 (November 23, 2018) at 1, 7-8; <https://www.cdc.gov/mmwr/volumes/67/ss/ss6713a1.htm>.

A major factor in this trend is a significant decline in premature sexual activity among teens. “Having sex went from being the majority experience for high school students (54% of 9<sup>th</sup>-12<sup>th</sup> graders in 1991) to the minority experience (41% in 2015)”;<sup>34</sup> this trend was found in all regions of the U.S. and among both white and black students.<sup>34</sup>

U.S. researchers, using data from the national Youth Risk Behavior Survey regarding 15- to 17-year olds, found that from 1991 to 2001 “53% of the decline in pregnancy rates can be attributed to decreased sexual experience.”<sup>35</sup> A 2015 British study of declining teen pregnancies in England found that the promotion of LARCs had played “a very minor role,” with much of the decline due to higher educational achievement as well as demographic change, such as an increased number of young non-white immigrants “from communities that are at lower risk of very early pregnancy (for example due to relatively high religious observance).”<sup>36</sup>

Uganda's success in combating the epidemic of HIV/AIDS has lessons for reducing unintended pregnancies and abortions among teens and young adults. According to 150 experts in this field, “when targeting young people, for those who have not started sexual activity the first priority should be to encourage abstinence or delay of sexual onset, hence emphasizing risk avoidance as the best way to prevent HIV and other sexually transmitted infections as well as unwanted pregnancy. After sexual debut, returning to abstinence or being mutually faithful with an uninfected partner are the most effective ways of avoiding infection.”<sup>37</sup>

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<sup>34</sup> J. Twenge and H. Park, “The Decline in Adult Activities Among U.S. Adolescents, 1976-2016,” 90.2 *Child Development* (August 2017) 1-17 at 6; abstract at [https://www.researchgate.net/publication/319904508\\_The\\_Decline\\_in\\_Adult\\_Activities\\_Among\\_US\\_Adolescents\\_1976-2016](https://www.researchgate.net/publication/319904508_The_Decline_in_Adult_Activities_Among_US_Adolescents_1976-2016).

<sup>35</sup> J. Santelli et al., “Can Changes in Sexual Behaviors Among High School Students Explain the Decline in Teen Pregnancy Rates in the 1990s?”, 35.2 *Journal of Adolescent Health* (August 2004) 80-90 at 80; abstract at <https://www.sciencedirect.com/science/article/abs/pii/S1054139X0400134X>.

<sup>36</sup> S. Girma and D. Paton, “Is education the best contraception: The case of teenage pregnancy in England?”, 131 *Social Science & Medicine* (April 2015) 1-9 at 1, 2; abstract at <https://www.sciencedirect.com/science/article/abs/pii/S027795361500132X>.

<sup>37</sup> D. Halperin et al., “The time has come for common ground on preventing sexual transmission of HIV,” 364 *The Lancet* (November 27, 2004) 1913-5 at 1913; <https://www.thelancet.com/journals/lancet/article/PIIS0140673604174874/fulltext>. Also see S.J. Genuis and S.K. Genuis, “Primary prevention of sexually transmitted disease: applying the ABC strategy,” 81 *Postgraduate Medical Journal* (2005) 299-301; <http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1743270&blobtype=pdf>.