Title

Cost-effectiveness of emergency contraception options over 1 year

Journal

American Journal of Obstetrics and Gynecology, 218(5)

ISSN

0002-9378

Authors

Bellows, Brandon K
Tak, Casey R
Sanders, Jessica N
et al.

Publication Date

2018-05-01

DOI

10.1016/j.ajog.2018.01.025

Peer reviewed

Title: Cost-effectiveness of emergency contraception options over one year

Authors: Brandon K BELLOWS, PharmD, MS;[1,2] Mr. Casey R TAK, MPH;[1] Jessica N SANDERS, PhD, MSPH;[3] David K TUROK, MD, MPH;[3] Eleanor B SCHWARZ, MD, MS[4]

Affiliations:

1. University of Utah Department of Pharmacotherapy, Salt Lake City, UT, USA
2. SelectHealth, Murray, UT, USA
3. University of Utah Department of Obstetrics and Gynecology, Salt Lake City, UT, USA
4. University of California, Davis, School of Medicine, Sacramento, CA, US

Corresponding Author: Brandon K Bellows; Address: University of Utah Department of Pharmacotherapy, 30 S. 2000 E. Room 4963, Salt Lake City, UT, 84112; Email: brandon.bellows@pharm.utah.edu; Phone: (801) 587-8011 (office); Fax: (801) 587-7923

Conflicts of Interest: BKB has received research funding from Janssen Pharmaceuticals; DKT receives speaking honoraria from Allergan and Medicines360, serves as a consultant for Bioceptive, and serves on advisory boards for Actavis, Bayer, Pharmanest and Teva; and the Department of Obstetrics and Gynecology, University of Utah, receives contraceptive clinical trials research funding from Bayer, Bioceptive, Medicines360, Teva and Veracept.

Role of Funding Source: Support for this project was provided internally.

Previous Presentation: An abstract of this work has been published by the Society of Family Planning: October issue of Contraception. 94(4):432; http://www.societyfp.org/Meetings-and-events/SFP-annual-meeting.aspx

Abstract Word Count: 475

Manuscript Word Count: 2943

Running Title**:** Emergency contraception cost-effectiveness

Condensation: The copper intrauterine device is the most cost-effective emergency contraception option in a population women followed for one year.

2

ABSTRACT

Background:

The copper intrauterine device is the most effective form of emergency contraception and can also provide long-term contraception. The levonorgestrel intrauterine device has also been studied in combination with oral levonorgestrel for women seeking emergency contraception. However, intrauterine devices have higher upfront costs than oral methods, such as ulipristal acetate and levonorgestrel. Healthcare payers and decision makers (e.g., healthcare insurers, government programs) with financial constraints must determine if the increased effectiveness of intrauterine device emergency contraception methods are worth the additional costs.

Objective:

To compare the cost-effectiveness of four emergency contraception strategies, ulipristal acetate, oral levonorgestrel, copper intrauterine device, and oral levonorgestrel plus same-day levonorgestrel intrauterine device, over 1 year from a United States payer perspective.

Study Design:

Costs (2017 United States dollars) and pregnancies were estimated over 1 year using a Markov model of 1000 women seeking emergency contraception. Every 28-day cycle, the model estimated the predicted number of pregnancy outcomes (i.e., live birth, ectopic pregnancy, spontaneous abortion, or induced abortion) resulting from emergency contraception failure and subsequent contraception use. Model inputs were derived from published literature and national sources. An emergency contraception strategy was considered cost-effective if the incremental cost-effectiveness ratio (i.e., the cost to prevent one additional pregnancy) was less than the weighted average cost of pregnancy outcomes in the United States ($5167). The incremental

cost-effectiveness ratios and probability of being the most cost-effective emergency contraception strategy were calculated from 1000 probabilistic model iterations. One-way sensitivity analyses were used to examine uncertainty in the cost of emergency contraception, subsequent contraception, and pregnancy outcomes as well as the model probabilities.

Results:

In 1000 women seeking emergency contraception, the model estimated direct medical costs of $1,228,000 and 137 unintended pregnancies with ulipristal acetate, compared to $1,279,000 and 150 unintended pregnancies with oral levonorgestrel, $1,376,000 and 61 unintended pregnancies with copper intrauterine devices, and $1,558,000 and 63 unintended pregnancies with oral levonorgestrel plus same-day levonorgestrel intrauterine device. The copper intrauterine device was the most cost-effective emergency contraception strategy in the majority (63.9%) of model iterations and, compared to ulipristal acetate, cost $1957 per additional pregnancy prevented. Model estimates were most sensitive to changes in the cost of the copper intrauterine device (with higher copper intrauterine device costs, oral levonorgestrel plus same-day levonorgestrel intrauterine device became the most cost-effective option) and the cost of a live birth (with lower cost births, ulipristal acetate became the most cost-effective option). When the proportion of obese women in the population increased, the copper intrauterine device became even more most cost-effective.

Conclusion:

Over one year, the copper intrauterine device is currently the most cost-effective emergency contraception option. Policy makers and healthcare insurance companies should consider the potential for long-term savings when women seeking EC can promptly obtain whatever

contraceptive best meets their personal preferences and needs; this will require removing barriers and promoting access to IUDs at EC visits.

Keywords: Cost-effectiveness analysis, emergency contraception, incremental cost-effectiveness ratio, intrauterine device

5

INTRODUCTION

Nearly half of all pregnancies in the United States (US) are unintended.[1] Annually, unintended pregnancy costs the US healthcare system approximately $11 billion.[2,3] Among women seeking emergency contraception (EC), oral levonorgestrel (LNG) remains the most commonly used method due to lower upfront costs and over-the-counter (OTC) availability. However, more effective forms of EC are available, including ulipristal acetate (UPA) and the copper T380 (Cu) intrauterine device (IUD).[2,4-6] In addition to being useful for EC, the Cu IUD can provide highly effective long-term contraception for up to 12 years.[2,6-9] While the Cu IUD has been well studied as EC, US women have a strong preference for the LNG IUD, which reduces menstrual bleeding.[10] The LNG IUD has been studied in combination with oral LNG EC for women seeking EC.[8] However, no IUD is currently labeled for use as EC, and women seeking EC are rarely offered the option of an IUD.[2,11]

Healthcare payers and decision makers, such as healthcare insurers and government programs, have been hesitant to allow use of IUDs for EC due in part to higher upfront cost and uncertainty about continued use of IUDs placed as EC.[2,11] Given their financial constraints, healthcare payers and decision makers must determine if the increased effectiveness of IUD EC methods are worth the additional costs.[5,6,8] Building on prior evaluations of contraceptive cost-effectiveness, this study assessed the cost-effectiveness of four EC methods (i.e., oral LNG, UPA, Cu IUD, and oral LNG + LNG IUD) from a US payer perspective over a one-year time horizon.

MATERIALS AND METHODS

Model Description and Analysis

We developed a decision analytic model using TreeAge Pro 2017 (TreeAge software, Williamstown, MA) to examine the cost-effectiveness of EC in a population of women of childbearing age presenting to a clinical setting for EC after an unprotected sexual encounter. We used a 28-day cycle length to represent menstrual cycles and included 13 cycles over the one-year time horizon.

The decision analytic model estimated the costs and number of unintended pregnancies that would occur in 1000 women over one year for each EC strategy. We used the cost and pregnancy outcomes to calculate incremental cost-effectiveness ratios (ICERs), which are interpreted as the incremental cost to prevent one additional pregnancy, for each EC strategy. We also calculated incremental net monetary benefit (INMB), which rearranges the traditional ICER and directly incorporates willingness-to-pay (WTP) values (i.e., how much one is willing to pay to prevent a pregnancy), to determine if the benefits of each strategy outweighed the costs (see online Appendix for detailed description of INMB).[12] We used a weighted average cost of pregnancy outcomes in the US of $5167, which was derived from the Healthcare Cost and Utilization Project (HCUP), as our WTP threshold.[13]

In our model, EC could either be successful in preventing pregnancy or fail (Figure 1). EC failure could result in an ectopic pregnancy, spontaneous abortion, induced abortion, or live birth. The Markov model consisted of health states based on pregnancy outcomes and continuing contraception use: 1) not pregnant and using contraception, 2) not pregnant and not using contraception, 3) ectopic pregnancy, 4) spontaneous abortion, 5) induced abortion, and 6) live birth. After EC, three continuing contraception groups, tiered by effectiveness, were included as separate health states. Highly effective (Tier 1) methods included IUDs and contraceptive

implants. While permanent contraception methods (i.e., sterilization) are also highly effective, our model assumed all women used reversible contraception. Moderately effective (Tier 2) methods included injectable, patch/ring, and oral contraceptives. Methods with the lowest effectiveness (Tier 3) included condoms, diaphragm, sponge, fertility awareness methods, and withdrawal.

Women using an IUD as their EC method could continue using it for contraception. Those using oral EC methods could start using a Tier 1, 2, or 3 contraceptive, or not use any contraception. Each cycle thereafter, women could: 1) continue their current contraception, 2) switch Tiers, or 3) discontinue contraception (see Online Appendix, Tables A1 and A2 for probabilities).

Model Parameters

We derived EC effectiveness, continuing contraception effectiveness, and costs from published literature (Table 1, also see Online Appendix for details of the search strategy and parameter synthesis as well as the probability of continuing contraception).[12] Oral LNG and UPA EC effectiveness estimates, stratified by body mass index (BMI), were derived from a meta-analysis comparing these oral EC methods.[4] We used Centers for Disease Control and Prevention (CDC) epidemiological data to assign proportions for normal (<25 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥30 kg/m^2) BMI for women aged 20-34 years.[14] Cu IUD EC effectiveness estimates were obtained from RCTs and observational studies.[9,15,16] Only one study was found that examined the effectiveness of the oral LNG + LNG IUD as EC.[8]

We employed a US payer perspective for this analysis and thus included only direct medical costs (2017 US$) in the model. Costs were obtained from the HCUP diagnosis-related

groups (DRGs), the Centers for Medicare and Medicaid Services (CMS) Medicare Reimbursement Fee Schedule, Red Book online database average wholesale price (AWP), and published literature (see Online Appendix for details on costs).[13,17,18] The mean EC costs used in the primary analysis were $29 for oral LNG, $43 for UPA, $887 for Cu IUD, and $917 for LNG IUD (Table 1).

Model Assumptions

The model made the following assumptions: 1) pregnancy intentions remained stable over the one-year time horizon; 2) women giving birth would not get pregnant again within one year; 3) women who discontinued contraception would not start again, except possibly after a pregnancy that did not result in a live birth;[19,20] 4) in keeping with a previous cost-effectiveness analysis, women with an ectopic pregnancy were assumed not to be at risk for pregnancy for two menstrual cycles;[21] 5) similarly, after a spontaneous or induced abortion women were assumed not to be at risk for pregnancy for three cycles;[21] 6) effectiveness estimates and probability of discontinuation accounted for contraceptive adherence; 7) side effects of contraception resulted in negligible direct medical costs; and 8) the effectiveness of oral EC decreased as BMI increased.[4]

Analysis

To incorporate the impact of uncertainty in the estimates for probability and cost inputs on model outcomes, we used a probabilistic approach for the primary analysis.[22] The probabilistic approach randomly draws values for each model parameter from predefined distributions to estimate costs and pregnancy outcomes for each EC strategy. The model then repeats this process 1000 times to give 1000 estimates of costs and pregnancy outcomes for each

strategy, which are then used to estimate cost-effectiveness. We used beta distributions for probabilities and gamma distributions for costs. This approach allowed us to describe the uncertainty intervals (UIs) around direct medical cost and pregnancy outcomes as well as determine the probability that an EC strategy was the most cost-effective across a range of WTP thresholds.[22]

We performed several sensitivity and scenario analyses. We performed one-way, deterministic sensitivity analyses, which vary each model parameter over a range of plausible values while holding all other parameters constant, to determine the impact of each parameter on the model (see Online Appendix for details on the one-way sensitivity analyses). Given the wide variation in obesity rates between communities across the US, we performed a separate one-way sensitivity analysis to examine the sensitivity of the model to the proportion of obese women in the population. To estimate the impact of uncertainty around the duration of time of ectopic pregnancies as well as induced and spontaneous abortions, we ran a scenario analysis in which it was assumed women could become pregnant as soon as the next cycle. We also performed a two-way sensitivity analysis examining the impact on cost-effectiveness of simultaneously varying the cost of Cu IUDs and the cost of LNG IUDs. Since much of the benefit of using IUDs for EC is the continuation of effective contraception, we examined how the cost-effectiveness of each strategy changed at the end of each menstrual cycle. As women seeking EC may be more likely to terminate a pregnancy, we also performed a one-way sensitivity analysis examining higher than average rates of induced abortion. Finally, as non-profit clinics eligible for 340B pricing can now obtain LNG IUDs for $50 and are able to acquire other EC options at significantly reduced costs, a *post hoc* scenario analysis using these reduced costs was performed. For this *post hoc* scenario analysis, EC costs were $125 for LNG IUD ($50 IUD cost, $75 insertion fee), $325 for

Cu IUD, and between $0 and $10 for both oral LNG and UPA. All other parameters remained unchanged.

Because this study involved secondary analyses of publicly available, de-identified data, institutional review board approval was not required.

RESULTS

Model Validation

The proportion of women experiencing any pregnancy outcome with each strategy was captured in a microsimulation adaptation of the model and used to internally validate the model against published estimates. The microsimulation adaptation of the model predicted EC failure rates similar to estimates from published literature (see Online Appendix, Table A3). Additionally, the cumulative incidence of pregnancy outcomes during the year after EC use, accounting for contraceptive discontinuation and switching, was predicted for oral LNG and Cu IUD and compared to those reported by Turok et al.[9] Because the model used the EC failure rate from Glassier et al. for oral LNG,[23] the predicted EC failure rate for oral LNG was higher than observed in Turok et al.[9] However, the pregnancy cumulative incidence curves were similar (see Online Appendix, Table A3 and Figure A1). The model predicted one-year pregnancy rates of 7.1% in women choosing Cu IUD and 13.9% in women choosing oral LNG, which are comparable to the published estimates of 6.5% for Cu IUD and 12.2% for oral LNG.[9]

Cost-effectiveness Analysis

In 1000 women seeking emergency contraception, the model estimated direct medical costs would be $1,227,902 with UPA, compared to $1,376,199 with Cu IUD (incremental costs for Cu IUD vs. UPA: $148,297 [95%UI -$611,664 to $659,303]) (Table 2). UPA use was estimated to result in 137 unintended pregnancies, compared to 61 with Cu IUD (incremental pregnancies prevented for Cu IUD vs. UPA: 76 [95%UI 52 to 109]). The resulting ICER for Cu IUD vs. UPA was $1957 per additional pregnancy prevented (Table 2, Figure 2a). At a WTP threshold of $5000, there was a 63.9% probability that Cu IUDs would be cost-effective; at a WTP threshold of $10,000, this probability increased to 84.8% (Figure 2b). Oral LNG was dominated by UPA (i.e., oral LNG cost more and prevented fewer pregnancies than UPA) and oral LNG + LNG IUD was dominated by Cu IUD. Oral LNG alone was not cost-effective at any WTP threshold.

Sensitivity and Scenario Analyses

The one-way sensitivity analyses showed the model estimates were most sensitive to Cu IUD cost, the cost of birth, the cost of induced abortion, the probability of using Tier 3 methods after IUD EC, and the cost of Tier 2 methods (Figure 3). Cu IUD was the most cost-effective strategy even when varying the model parameters over the specified ranges except when: the cost of Cu IUD was at its highest (oral LNG + LNG IUD was then most cost-effective), the cost of a live birth was at its lowest value (UPA was then most cost-effective), or the cost of LNG IUD was at its lowest (oral LNG + LNG IUD was then most cost-effective).

In the one-way sensitivity analysis that varied the proportion of obese women in the model, Cu IUD remained the most cost-effective EC strategy regardless of the proportion obese (see Online Appendix, Figure A2). Additionally, the ICER was similar to the primary analysis when women could become pregnant in the next cycle following an ectopic pregnancy,

spontaneous or induced abortion (Cu IUD vs. UPA ICER $1805). The two-way sensitivity analysis of IUD costs found that Cu IUD remained the most cost-effective EC strategy for most of the ranges of costs examined (see Online Appendix, Figure A3). However, when the cost of a Cu IUD approached $100 more than the cost of an LNG IUD, oral LNG + LNG IUD became more cost-effective.

The time horizon analysis demonstrated that Cu IUDs become cost-effective after approximately 9 months, even when accounting for contraceptive discontinuation and switching (see Online Appendix, Figures A4a and A4b).[12] When examining higher than average rates of induced abortion, Cu IUD remained cost-effective even when up to 75% of the population terminated pregnancies that resulted from contraceptive failure. The *post hoc* scenario analysis using non-profit clinic (340B) pricing for LNG IUD showed oral LNG + LNG IUD to be the most cost-effective strategy (ICER for Cu IUD vs. oral LNG + LNG IUD: $221,428 per additional pregnancy prevented), while UPA and oral LNG were dominated (see Online Appendix, Table A4).[12] These results did not vary significantly when the cost of UPA and oral LNG ranged from $0 to $10.

COMMENT

Our model accurately predicted pregnancy outcomes up to one year after using EC and showed the Cu IUD was the most cost-effective EC option from a US payer perspective over a one-year time horizon. In fact, the Cu IUD remained the most cost-effective EC strategy across a variety of sensitivity and scenario analyses. The initial increased upfront costs of the Cu IUD were only offset by its improved effectiveness in preventing pregnancies after about 9 months.

13

Existing data support the idea that the majority of women who receive IUDs for EC continue use beyond 9 months.[24] In settings with access to 340B pricing, use of a LNG IUD with oral LNG was the most cost-effective option for EC.

While we adhered to current best practices for conducting cost-effectiveness analyses (see Online Appendix, Table A5), there are several considerations to keep in mind while interpreting these results. Although we accounted for EC effectiveness based on variations of BMI, we did not consider differences in pregnancy complications and costs due to obesity, which may be considerable. Because obese women experience higher rates of pregnancy complications and cesarean delivery, the true cost-effectiveness for alternatives to oral LNG may be even greater for obese women than we reported. Also, we performed our analysis from a payer perspective and thus did not include in our analysis indirect and intangible costs to the individual or society that occur with undesired pregnancy.

A potential limitation of our study is that we may have overestimated assumed pregnancy rates for those not using contraception since they were only available for women who self-report "trying to conceive." EC users are trying to avoid conceiving and may have lower rates of pregnancy from single acts of intercourse aided by the use of withdrawal, condoms, or timed intercourse methods. However, EC seekers may also be younger and have higher fecundity than the individuals trying to conceive. Pregnancy rate overestimation may have also occurred by assuming women who discontinued contraception methods would not re-start them for the remainder of the time horizon.

Another potential limitation is that we assumed population estimates of method continuation and 1-year pregnancy rates for oral LNG + LNG IUD were the same for all highly effective reversible contraceptive (Tier 1) methods. While large, rigorously conducted

prospective studies report lower 1-year pregnancy rates for IUD users, they do not account for IUD discontinuation and switching to less effective methods, which may differ between the IUD types.[25] Additionally, continuing contraception effectiveness estimates were pooled into tiers rather than reported for individual types of contraception, which may over- or underestimate the effectiveness of some types of contraception.

Nonetheless, there are a number of strengths to our analysis. We employed multiple one-way sensitivity and scenario analyses to assess for changes in cost or pregnancy outcomes. These analyses suggest that when the cost of the LNG IUD decreases to less than $773, oral LNG + LNG IUD becomes cost-effective. In settings eligible for 340B pricing, oral LNG + LNG IUD is the most cost-effective approach to EC. Given many women's preference for the LNG IUD over the Cu IUD, efforts to reduce the cost of this contraceptive option in all settings is important. Our analysis also incorporated published findings representative of typical EC use and accounted for the initiation of other contraceptive therapies in the year following EC. Finally, as it includes multiple pregnancy outcomes (i.e., spontaneous abortion, induced abortion, ectopic pregnancy, and live birth), the use of $5167 for the WTP is a more realistic estimate of the cost to avoid a pregnancy than the cost of abortion that has been used in prior contraceptive cost-effectiveness analyses.[26] However, our analysis does not include payer costs related to a newborn over the first 3 months of life, which significantly increase the true costs of each live birth, and would increase the WTP to prevent an undesired birth.

Although women can now obtain oral LNG over the counter, many women still go to clinics to obtain EC. When a woman presents for EC, clinicians should recognize her to be at increased risk of unintended pregnancy in the near future, and offer her all available options for EC and continuing contraception. Facilitating use of any IUD as EC will require provider

training, patient education, and removal of economic barriers.[27] Research has shown that every dollar spent on contraceptive services saves more than $5.68 in public expenditures.[28] Oral LNG remains an important EC option due to its wide accessibility and lower upfront cost. However, for women presenting in clinic seeking EC, this analysis supports the cost-effectiveness of EC IUDs. Policy makers and healthcare insurance companies should consider the potential for long-term savings when women seeking EC can promptly obtain whatever contraceptive best meets their personal preferences and needs; this will require removing barriers and promoting access to IUDs at EC visits.

Acknowledgements: The authors wish to thank Natalia Ruiz-Negrón, PharmD, for reviewing and providing comments on the manuscript.

16

REFERENCES

1. Finer LB, Zolna MR. Declines in Unintended Pregnancy in the United States, 2008-2011. *N Engl J Med.* 2016;374(9):843-852.
2. Belden P, Harper CC, Speidel JJ. The copper IUD for emergency contraception, a neglected option. *Contraception.* 2012;85(4):338-339.
3. Trussell J. The cost of unintended pregnancy in the United States. *Contraception.* 2007;75(3):168-170.
4. Glasier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. *Contraception.* 2011;84(4):363-367.
5. Thomas CM, Schmid R, Cameron S. Is it worth paying more for emergency hormonal contraception? The cost-effectiveness of ulipristal acetate versus levonorgestrel 1.5 mg. *The journal of family planning and reproductive health care / Faculty of Family Planning & Reproductive Health Care, Royal College of Obstetricians & Gynaecologists.* 2010;36(4):197-201.
6. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. *Human reproduction (Oxford, England).* 2012;27(7):1994-2000.
7. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. *N Engl J Med.* 2012;366(21):1998-2007.
8. Turok DK, Sanders JN, Thompson IS, Royer PA, Eggebroten J, Gawron LM. Preference for and efficacy of oral levonorgestrel for emergency contraception with concomitant placement of a levonorgestrel IUD: a prospective cohort study. *Contraception.* 2016;93(6):526-532.
9. Turok DK, J.N. S, Royer PA, Thompson I, Eggebroten J. Copper or LNG IUD for Emergency Contraception (COLIEC): Device Choice and Early Pregnancies. *Contraception.* 2014;90:298-351.
10. Peipert JF, Zhao Q, Allsworth JE, et al. Continuation and satisfaction of reversible contraception. *Obstetrics and gynecology.* 2011;117(5):1105-1113.
11. Hughes D, McGuire A. The cost-effectiveness of family planning service provision. *Journal of public health medicine.* 1996;18(2):189-196.
12. Hoover KW, Tao G, Kent CK. Trends in the diagnosis and treatment of ectopic pregnancy in the United States. *Obstetrics and gynecology.* 2010;115(3):495-502.
13. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). 2013; http://hcupnet.ahrq.gov/. Accessed February 19, 2016.
14. National Center for Health Statistics. *Health, United States, 2014: With Special Feature on Adults Aged 55-64*. Hyattsville (MD)2015.
15. Cheng L, Gulmezoglu AM, Oel CJ, Piaggio G, Ezcurra E, Look PF. Interventions for emergency contraception. *The Cochrane database of systematic reviews.* 2004(3):Cd001324.
16. Wu S, Godfrey EM, Wojdyla D, et al. Copper T380A intrauterine device for emergency contraception: a prospective, multicentre, cohort clinical trial. *BJOG : an international journal of obstetrics and gynaecology.* 2010;117(10):1205-1210.

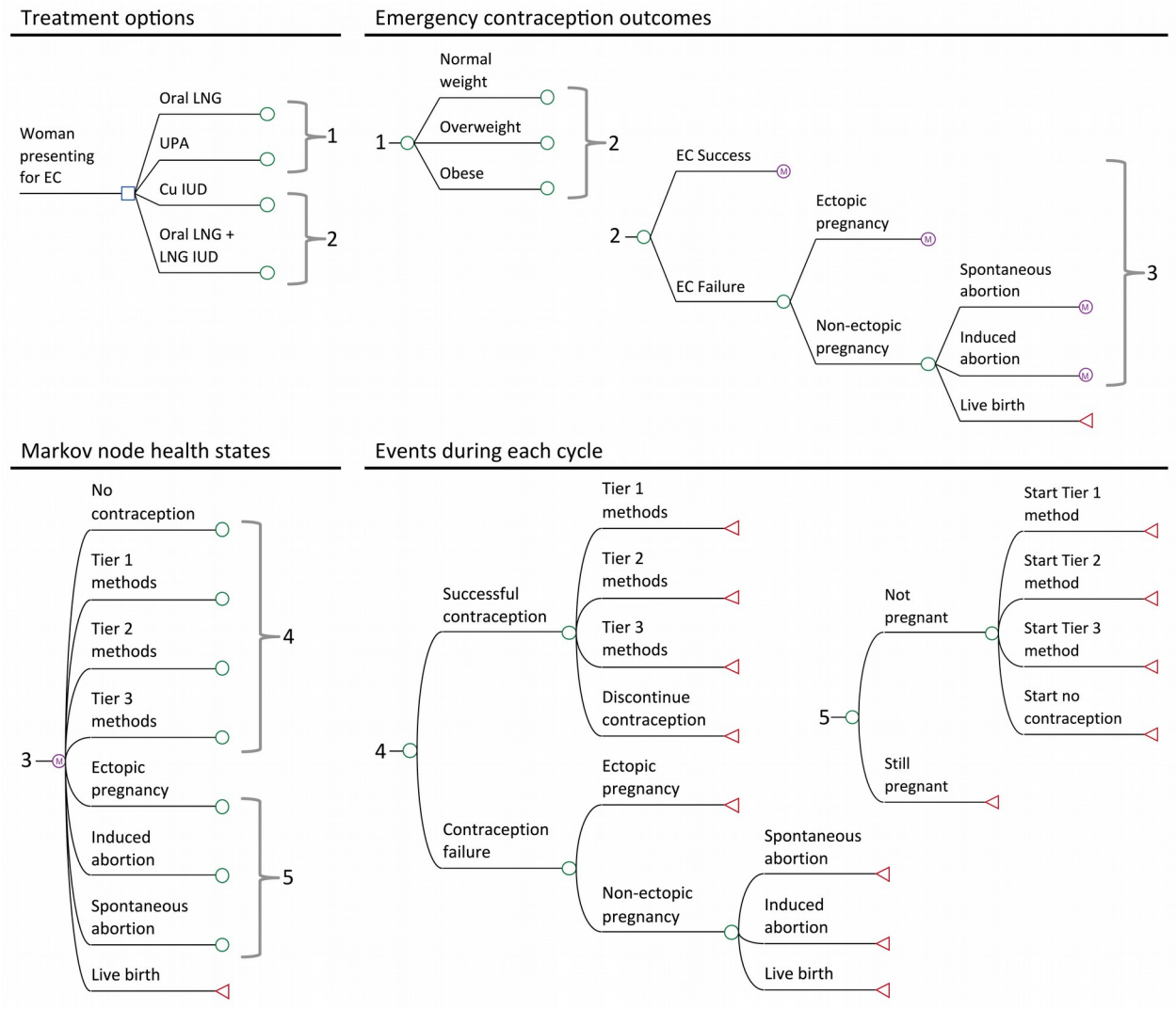
35417. Centers for Medicare and Medicaid Services. Medicare Physician Fee Schedule, CPT
355 Code Book and Medicare Outpatient Prospective Payment System. 2016. Accessed
356 February 19, 2016.
35718. Truven Health Analytics: Micromedex Solutions. RED BOOK Online Search. 2016.
358 Accessed February 19, 2016, 2016.
35919. Steinberg JR, Tschann JM, Henderson JT, Drey EA, Steinauer JE, Harper CC.
360 Psychological distress and post-abortion contraceptive method effectiveness level chosen
361 at an urban clinic. *Contraception.* 2013;88(6):717-724.
36220. White K, Potter JE, Hopkins K, Grossman D. Variation in postpartum contraceptive
363 method use: results from the Pregnancy Risk Assessment Monitoring System (PRAMS).
364 *Contraception.* 2014;89(1):57-62.
36521. Trussell J, Hassan F, Henry N, Pocoski J, Law A, Filonenko A. Cost-effectiveness
366 analysis of levonorgestrel-releasing intrauterine system (LNG-IUS) 13.5 mg in
367 contraception. *Contraception.* 2014;89(5):451-459.
36822. Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats TG. *Cost-effectiveness in*
369 *health and medicine.* Second ed: Oxford University Press; 2017.
37023. Glasier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy
371 despite using emergency contraception? Data from randomized trials of ulipristal acetate
372 and levonorgestrel. *Contraception.* 2011;84(4):363-367.
37324. Sanders JN, Turok DK, Royer PA, Thompson IS, Gawron LM, Storck KE. One-year
374 continuation of copper or levonorgestrel intrauterine devices initiated at the time of
375 emergency contraception. *Contraception.* 2017;96(2):99-105.
37625. Heinemann K, Reed S, Moehner S, Minh TD. Comparative contraceptive effectiveness of
377 levonorgestrel-releasing and copper intrauterine devices: the European Active
378 Surveillance Study for Intrauterine Devices. *Contraception.* 2015;91(4):280-283.
37926. Trussell J, Lalla AM, Doan QV, Reyes E, Pinto L, Gricar J. Cost effectiveness of
380 contraceptives in the United States. *Contraception.* 2009;79(1):5-14.
38127. Harper CC, Blum M, de Bocanegra HT, et al. Challenges in translating evidence to
382 practice: the provision of intrauterine contraception. *Obstetrics and gynecology.*
383 2008;111(6):1359-1369.
38428. Sonfield A, Kost K, Gold RB, Finer LB. The public costs of births resulting from
385 unintended pregnancies: national and state-level estimates. *Perspectives on sexual and*
386 *reproductive health.* 2011;43(2):94-102.
38729. National Center for Health Statistics. *Health, United States, 2014: With Special Feature*
388 *on Adults Aged 55-64.* Hyattsville (MD); 2015.
38930. Reeves MF, Zhao Q, Secura GM, Peipert JF. Risk of Unintended Pregnancy Based on
390 Intended Compared to Actual Contraceptive Use. *American journal of obstetrics and*
391 *gynecology.* 2016.
39231. Kost K, Singh S, Vaughan B, Trussell J, Bankole A. Estimates of contraceptive failure
393 from the 2002 National Survey of Family Growth. *Contraception.* 2008;77(1):10-21.
39432. Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. Ectopic pregnancy and emergency
395 contraceptive pills: a systematic review. *Obstetrics and gynecology.* 2010;115(6):1263-
396 1266.
39733. Westrom L, Bengtsson LP, Mardh PA. Incidence, trends, and risks of ectopic pregnancy
398 in a population of women. *British medical journal (Clinical research ed).*
399 1981;282(6257):15-18.

40034. Backman T, Huhtala S, Blom T, Luoto R, Rauramo I, Koskenvuo M. Length of use and
401 symptoms associated with premature removal of the levonorgestrel intrauterine system: a
402 nation-wide study of 17,360 users. *BJOG : an international journal of obstetrics and*
403 *gynaecology.* 2000;107(3):335-339.
40435. Backman T, Rauramo I, Huhtala S, Koskenvuo M. Pregnancy during the use of
405 levonorgestrel intrauterine system. *American journal of obstetrics and gynecology.*
406 2004;190(1):50-54.
40736. Furlong LA. Ectopic pregnancy risk when contraception fails. A review. *The Journal of*
408 *reproductive medicine.* 2002;47(11):881-885.
40937. Finer LB, Zolna MR. Shifts in intended and unintended pregnancies in the United States,
410 2001-2008. *American journal of public health.* 2014;104 Suppl 1:S43-48.
41138. Sonfield A, Kost K. *Public costs from unintended pregnancies and the role of public*
412 *insurance programs in paying for pregnancy-related care: National and state estimates*
413 *for 2010.* New York (NY): Guttmacher Institute;2015.
41439. Optum EncoderPro. https://www.encoderpro.com/epro. Accessed February 19, 2016.
41540. Jones RK, Kooistra K. Abortion incidence and access to services in the United States,
416 2008. *Perspectives on sexual and reproductive health.* 2011;43(1):41-50.
41741. Pazol K, Creanga AA, Jamieson DJ. Abortion Surveillance - United States, 2012.
418 *Morbidity and mortality weekly report Surveillance summaries (Washington, DC : 2002).*
419 2015;64(10):1-40.

420

TABLES & FIGURE LEGENDS

Figure 1: Detailed decision analytic model structure



Acronyms/abbreviations: Cu – copper, EC – emergency contraception, IUD – intrauterine device, LNG – levonorgestrel, OTC – over-the-counter, Prob – probability, UPA – ulipristal acetate.

Notes: The blue square represents the decision node, or the point at which a treatment is chosen. The green circles represent chance nodes after which a probability is assigned to each event. The purple "M" circles represent Markov nodes after which women transition between health states each menstrual cycle. The red triangles represent terminal nodes, which, in the Markov node, indicate the state to which women will transition in the next cycle. Women

accrue costs and effectiveness throughout the time horizon based on the health states and events that occur during each cycle. The model assumed that women who discontinued contraception would not use contraception for the remainder of the time horizon. However, if they experienced a pregnancy outcome, they may have started contraception. The ectopic pregnancy, induced abortion, and spontaneous abortion health states were tunnel states where patients spent two to three menstrual cycles before being forced into a non-pregnant health state. Patients who became pregnant and went on to have a live birth were assumed to not get pregnant again during the time horizon. Tier 1 methods include IUDs and implants; Tier 2 methods include injection, pill, patch, ring; and Tier 3 includes barrier methods.

21

439***Table 1: Cost-effectiveness model input parameters***

Variable	Mean	Low	High	Source
BMI Distribution				
Normal (<25 kg/m^2)	0.448	0.403	0.493	[29]
Overweight (25-29.9 kg/m^2)	0.252	0.205	0.299	[29]
Obese (≥30 kg/m^2)	0.300	0.275	0.326	[29]
Probability of EC failure				
Oral LNG				
Normal	0.013	0.008	0.022	[23]
Overweight	0.025	0.014	0.048	[23]
Obese	0.058	0.036	0.097	[23]
UPA				
Normal	0.011	0.007	0.019	[23]
Overweight	0.011	0.005	0.029	[23]
Obese	0.026	0.014	0.059	[23]
Cu IUD	0.001	0.0004	0.003	[9,15,16]
LNG IUD + Oral LNG	0.002	0.0007	0.013	[9]
Probability of continuing contraception failure (per cycle)				
Tier 1 methods	0.001	0.001	0.003	[9,30]
Tier 2 methods	0.004	0.003	0.007	[9,30]
Tier 3 methods	0.012	0.009	0.016	[9,31]
No method	0.020	0.008	0.077	[9,21]
Contraception failure pregnancy outcomes				
EC – probability of ectopic pregnancy				
Oral LNG	0.010	0.004	0.031	[32]
UPA	0.006	0.003	0.019	[32]
Cu IUD	0.029	0.021	0.043	[33]
LNG IUD + Oral LNG	0.516	0.403	0.641	[34,35]

Variable	Mean	Low	High	Source
Continuing contraception – probability of ectopic pregnancy				
Tier 1 contraceptives	0.192	0.147	0.252	36
Tier 2 contraceptives	0.026	0.010	0.100	36
Tier 3 contraceptives	0.010	0.003	0.062	26
No contraceptive*	0.010	0.003	0.062	Assumption
*Non-ectopic pregnancy probabilities***				
Live birth	0.422	0.393	0.452	Assumption
Spontaneous abortion	0.168	0.148	0.192	26
Induced abortion	0.400	0.372	0.430	37
Contraception method selected continuing contraception				
Oral LNG and UPA EC				
Tier 1 methods	0.063	0.041	0.103	9
Tier 2 methods	0.320	0.268	0.382	9
Tier 3 methods	0.557	0.498	0.619	9
No method	0.059	0.038	0.098	9
Cu IUD and LNG IUD EC				
Tier 1 methods	0.800	0.739	0.854	9
Tier 2 methods	0.072	0.045	0.123	9
Tier 3 methods	0.117	0.080	0.175	9
No method	0.011	0.004	0.044	9
Post-ectopic pregnancy/abortion contraception method selected				
Tier 1 methods	0.293	0.288	0.297	19,20
Tier 2 methods	0.439	0.434	0.444	19,20
Tier 3 methods***	0.218	0.214	0.222	19,20,Assumption
No method***	0.050	0.048	0.053	19,20,Assumption
Costs (2017 US$)				
EC methods				

23

Variable	Mean	Low	High	Source
Oral LNG	$29	$22	$36	[18]
UPA	$43	$30	$51	[18]
Cu IUD	$887	$627	$1045	[18]
LNG IUD	$917	$665	$1109	[18]
IUD insertion	$74	$56	$93	[17]
Continuing contraception methods				
Tier 1 methods	$899	$737	$1061	[18]
Tier 2 methods	$58	$42	$73	[18]
IUD removal	$97	$72	$121	[17]
Pregnancy outcomes				
Live birth	$10,858	$2181	$13,936	[13,38,39]
Spontaneous abortion	$1366	$330	$3538	[17,38]
Induced abortion	$705	$607	$6694	[40,41]
Ectopic pregnancy	$7590	$5692	$9488	[13]

Acronyms/abbreviations: Cu – copper, EC – emergency contraception, IUD – intrauterine device, LNG – levonorgestrel, UPA – ulipristal acetate, US$ – US dollars.

Notes: Tier 1 methods include IUDs and implants; Tier 2 methods include injection, pill, patch, ring; and Tier 3 includes barrier methods.

*No contraception ectopic pregnancy outcomes assumed to be the same as Tier 3 methods.

**Other pregnancy outcomes were assumed to be the same as the Tier 3 pregnancy outcome distribution. Pregnancies not resulting in an ectopic pregnancy, spontaneous abortion, or induced abortion were assumed to result in a live birth. As ectopic pregnancies vary between methods, ectopic pregnancy was included as a separate branch and the remaining pregnancy outcomes used a Dirichlet distribution to ensure they always summed to 1.

***The probability of no contraception after pregnancy was assumed. Women not using Tier 1, Tier 2, or no methods were assumed to be using Tier 3 methods.

24

Table 2: Costs, pregnancies, and incremental cost-effectiveness ratio of emergency contraception methods in 1000 women over one year

Emergency Contraception	Mean Cost (2017 US$)	Inc. Cost (2017 US$) (95% UI)	Mean Pregnancies	Inc. Pregnancies Prevented (95% UI)	ICER* (2017 US$)	Probability Cost-effective**
UPA	$1,227,902	-	137.2	-	-	25.2%
Oral LNG	$1,278,877	$50,975 (-$22,788; $208,392)	150.0	-12.8 (-29.7; 1.1)	Dominated by UPA	1.5%
Cu IUD	$1,376,199	$148,297 (-$611,664; $659,303)	61.4	75.8 (52.3; 108.8)	$1957	63.9%
Oral LNG + LNG IUD	$1,557,610	$181,412 (-$137,314; $542,283)	62.7	-1.3 (-7.1; 1.3)	Dominated by Cu IUD	9.4%

Acronyms/abbreviations: Cu – copper, ICER – incremental cost-effectiveness ratio, Inc. – incremental, IUD – intrauterine device, LNG – levonorgestrel, UPA – ulipristal acetate, US$ – United States dollars, 95% UI – 95% uncertainty interval (i.e., 2.5th to 97.5th percentile).

Notes: Incremental costs, incremental pregnancies prevented, and incremental cost-effectiveness ratio are in reference to the next least costly, non-dominated option. An option is dominated if it costs more and is less effective than another option. For example, Cu IUD incremental costs are in reference to UPA as Oral LNG was dominated by UPA.

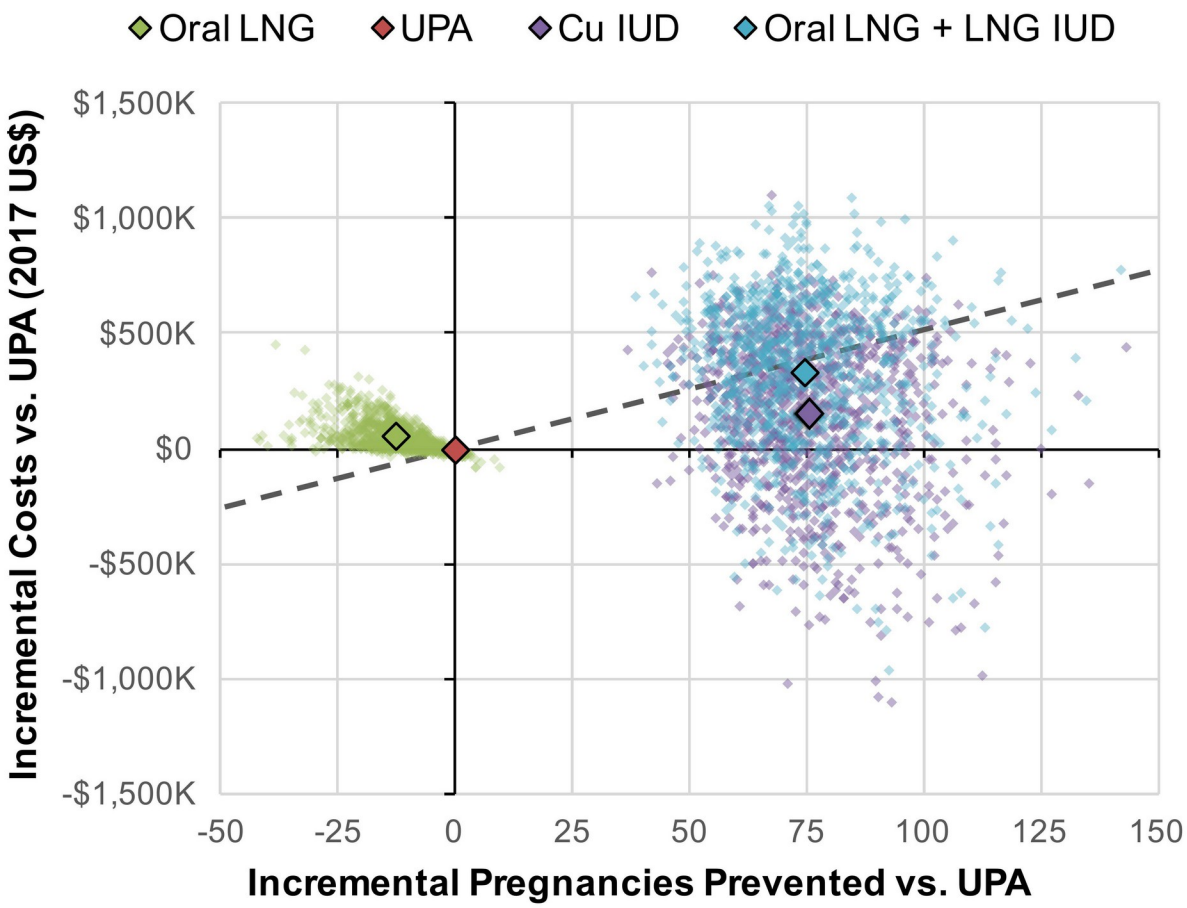
*ICER is interpreted as the cost to prevent one additional pregnancy

**Willingness-to-pay to determine if an option was cost-effective was set at $5167 to prevent a pregnancy based on the calculated weighted average cost of any pregnancy outcome if no EC was used.

25

462***Figure 2: Cost-effectiveness of emergency contraception over one year***

463***A) Incremental cost-effectiveness scatterplot for each strategy vs. ulipristal acetate***

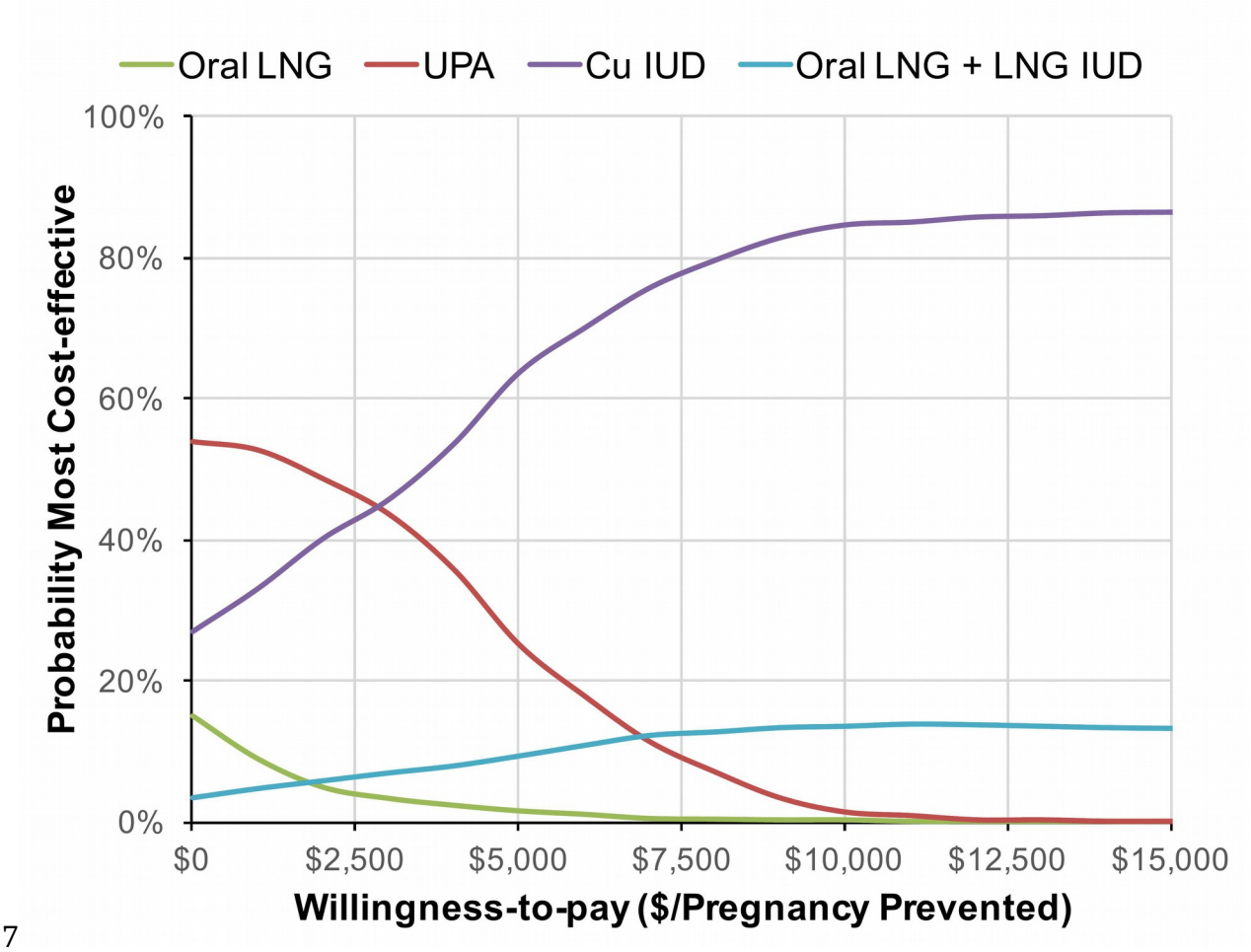


464

465

26

B) Probability of emergency contraception cost-effectiveness



Acronyms/abbreviations: Cu – copper, IUD – intrauterine device, LNG – levonorgestrel, UPA – ulipristal acetate.

Notes: Panel A shows the incremental cost-effectiveness scatterplot of each emergency contraception (EC) strategy vs. UPA in model 1000 iterations. Each point on the scatterplot represents the mean incremental costs and incremental pregnancies prevented in 1000 women in one iteration of the model compared to UPA. The larger diamonds represent the mean incremental costs and mean incremental pregnancies prevented over all 1000 model iterations. The dashed line represents the willingness-to-pay threshold of $5167 to prevent a pregnancy. Panel A shows that, on average, Oral LNG cost more and was less effective than UPA. In contrast, on average Cu IUD cost more than UPA, but also prevents more pregnancies and does so at an acceptable cost. Panel B shows the cost-effectiveness acceptability curve (CEAC). The CEAC shows the probability that each EC strategy is the most cost-effective across a range of willingness-to-pay (WTP) values over the 1000 model iterations. Panel B shows the Cu

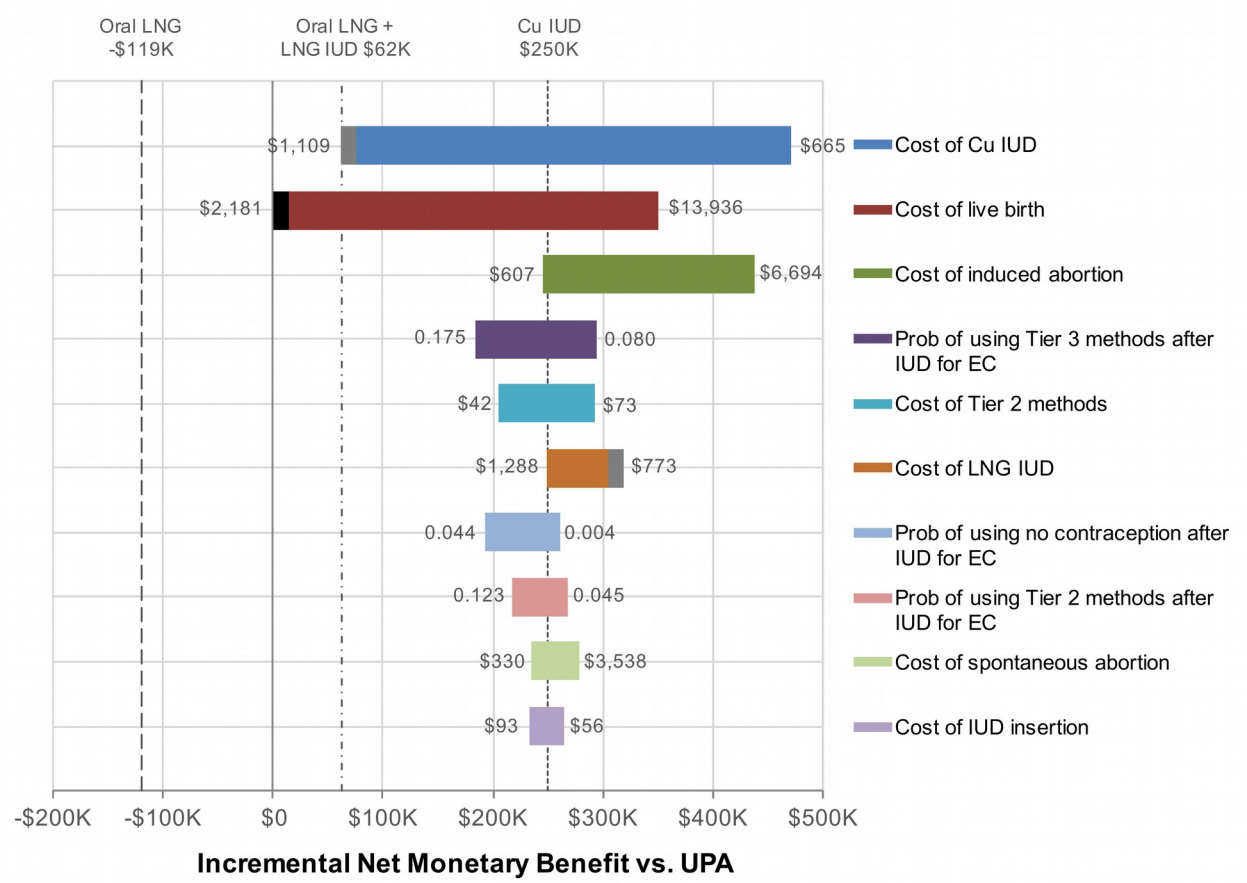
27

478IUD had the highest probability of being the most cost-effective EC when the WTP to prevent a pregnancy was
479above about $3000.

480

28

Figure 3: One-way sensitivity analysis – incremental net monetary benefits vs. UPA tornado diagram



Acronyms/abbreviations: Cu – copper, EC – emergency contraception, IUD – intrauterine device, LNG – levonorgestrel, Prob – probability, UPA – ulipristal acetate.

Notes: The figure shows the results of the one-way sensitivity analyses as a tornado diagram. The ten most influential variables are shown using the incremental net monetary benefit (INMB) framework with UPA as the reference group. The horizontal bars represent the range of the highest INMBs obtained with any EC strategy when that variable was varied across the range shown at the ends of each bar. The dotted and dashed lines represent the deterministic INMB for each EC strategy vs. UPA. The Cu IUD was the preferred strategy (i.e., most cost-effective) across nearly all of the one-way sensitivity analyses. The solid black and gray bars represent when there was a change in the preferred EC strategy, with the black bars representing when UPA was the preferred strategy and the

29

493gray bars when Oral LNG + LNG IUD was. In this analysis, a change in the preferred strategy only occurred at the
494extreme values in the one-way sensitivity analyses. Tier 1 methods include IUDs and implants; Tier 2 methods
495include injection, pill, patch, ring; and Tier 3 includes barrier methods.

496