



Published in final edited form as:

Obstet Gynecol. 2010 June ; 115(6): 1263–1266. doi:10.1097/AOG.0b013e3181dd22ef.

Ectopic Pregnancy and Emergency Contraceptive Pills: A Systematic Review

Kelly Cleland, MPA MPH^a, Elizabeth Raymond, MD MPH^b, James Trussell, PhD^{a,c}, Linan Cheng, MD^d, and Haoping Zhu, MD^e

^aOffice of Population Research, Princeton University, Wallace Hall, Princeton, NJ 08540, USA

^bFamily Health International, PO Box 13950, Research Triangle Park, NC 27709, USA

^cThe Hull York Medical School, University of Hull, Hull HU6 7RX, UK

^dShanghai Institute of Planned Parenthood Research, Xie Tu Rd, Shanghai 200032, People's Republic of China

^eMinhang Central Hospital, Shanghai Jiaotong University, Shanghai 201100, People's Republic of China

Abstract

Objective—To evaluate the existing data to estimate the rate of ectopic pregnancy among emergency contraceptive pill treatment failures.

Data Sources—Our initial reference list was generated from a 2008 Cochrane review of emergency contraception. In August 2009, we searched Biosys Previews, the Cochrane Database of Systematic Reviews, Medline, Global Health Database, Health Source: Popline, and Wanfang Data (a Chinese database).

Methods of Study Selection—This study included data from 136 studies which followed a defined population of women treated one time with emergency contraceptive pills (either mifepristone or levonorgestrel), and in which the number and location of pregnancies were ascertained.

Results—Data from each article were abstracted independently by two reviewers. In the studies of mifepristone, 3 out of 494 (0.6%) pregnancies were ectopic; in the levonorgestrel studies, 3 out of 307 (1%) were ectopic.

Conclusion—The rate of ectopic pregnancy when treatment with emergency contraceptive pills fails does not exceed the rate observed in the general population. Since emergency contraceptive pills are effective in lowering the risk of pregnancy, their use should reduce the chance that an act of intercourse will result in ectopic pregnancy.

© Copyright 2010 American College of Obstetricians and Gynecologists.

Corresponding author: Kelly Cleland, Office of Population Research, Princeton University 218 Wallace Hall, Princeton, NJ 08544, Telephone: 609.258.1395; Fax: 609.258.1039; kcleland@princeton.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

At least 36% of all pregnancies worldwide are unintended (1). In the event of contraceptive mishap or non-use, or nonconsensual intercourse, emergency contraceptive pills provide women with a means of preventing unintended pregnancy after sex. Emergency contraceptive pills have been shown to be safe, effective and well-tolerated; according to the World Health Organization's Medical Eligibility Criteria, the benefits of their use always outweigh the medical risks (2).

The safety of emergency contraceptive pills has been extensively studied and is well-established (3). However, concern persists about whether their use increases the risk of ectopic pregnancy should treatment fail. This issue was first raised in New Zealand. Based on case reports of three ectopic pregnancies following use of levonorgestrel-only emergency contraceptive pills, the New Zealand Medicines and Medical devices Safety Authority warned in 2002 that "the possibility of an ectopic pregnancy should be considered" (4) if a pregnancy test is positive following use of levonorgestrel emergency contraceptive pills. In an editorial published a year later, the authors noted that 12 ectopic pregnancies in women who used levonorgestrel emergency contraceptive pills had been reported in the United Kingdom and that a handful of additional cases had been reported in other countries (5). As the authors acknowledge, this information cannot be used to calculate the probability that a pregnancy occurring after use of the treatment will be ectopic because the total number of pregnancies needed for the denominator of the calculation is unknown. Nevertheless, based on these case reports, Britain's Committee on Safety of Medicines also advised that if a woman who has used progestin-only emergency contraceptive pills becomes pregnant, "the possibility of an ectopic pregnancy should be considered" (6). Recent published case reports cite ectopic pregnancy as a known risk of using levonorgestrel emergency contraceptive pills (7,8). Several patient information websites, including one provided by the United States National Library of Medicine and National Institutes of Health, currently note a potential link between use of emergency contraceptive pills and ectopic pregnancy (9–12). In addition, the patient labeling information in Ireland for NorLevo (manufactured by Cardinal Health France), a dedicated levonorgestrel emergency contraceptive pill, lists previous ectopic pregnancy as a contraindication (13).

Among women who have not used emergency contraceptive pills, the chance that a pregnancy will be ectopic has been estimated at 0.8% to 2% of all reported pregnancies (14–20). This range likely reflects differences in how rates are calculated and reported (21) as well as true variation in incidence among populations. Ectopic pregnancy is a potentially life-threatening condition, and accurate assessment of its risk factors is an important step in helping clinicians, public health professionals and pharmaceutical regulatory bodies generate optimal guidelines for women's health.

Our prior review of 5 prospective efficacy trials of levonorgestrel-only emergency contraceptive pills suggested that the risk of ectopic pregnancy when that regimen fails is unlikely to be raised (22). Here we update that report with an additional 131 studies, including trials of emergency contraceptive regimens containing mifepristone as well as trials of levonorgestrel-only emergency contraceptive pills. These drugs are the active agents in most currently marketed dedicated emergency contraceptive products worldwide.

Sources

Our initial reference list was generated from a 2008 Cochrane review of emergency contraception (23). To ensure completeness and timeliness, we identified relevant studies by conducting computerized literature searches using the following databases and search terms:

BIOSYS PREVIEWS: (CC=(Pharmacology - Reproductive system OR Reproductive system - Physiology "and" biochemistry OR Reproductive system - General "and" methods) AND MC=(Reproduction OR Gynecology OR Oncology) AND PY=(2004 OR 2005 OR 2006 OR 2007 OR 2008 OR 2009) AND TS=(postcoit* or post-coit* or emergenc* same contracept* or morning same after or ru-486 or mifepristone or levonorgestrel or ulipristal or cbd-2914 or cdb2914) AND TA=(Hominidae)

COCHRANE DATABASE: (Topic: Fertility Regulation, Emergency Contraception); Medline ((MH "Contraceptives, Postcoital") not PT case report not PT comment not PT editorial not PT review; date of Publication from: 200401–201012; English Language; Human)

GLOBAL HEALTH: (emergency contracept* OR postcoit* contracept*)

EALTH SOURCE: (emergency contracept* OR postcoit* contracept*)

POPLINE: (emergency contracept*) & (ru-486 / mifepristone / levonorgestrel / ulipristal / cbd-2914 / cdb2914)

WANFANG DATA (Chinese): (emergency contraception, mifepristone, levonorgestrel)

Study Selection

Our review included any study published by August 2009 in English or Chinese with a defined population of women whom investigators treated one time with either levonorgestrel or mifepristone alone for emergency contraception, and in which the number and location of pregnancies were ascertained. We also included one large study with a levonorgestrel arm which we knew to have been completed by August 2009, but which was not published until February 2010. We did not include advance provision studies (in which emergency contraceptive pills are dispensed to study subjects in anticipation of future need) or repeat use studies. We did not include the newly-approved emergency contraceptive pill ulipristal acetate, which has been marketed in Europe since October 2009, as only three studies of this regimen had been published at the time of writing. We excluded studies of emergency contraceptive regimens containing both estrogen and progestin, as this regimen is now increasingly being replaced by the levonorgestrel-only regimen, and we also excluded studies of other combinations of drugs.

After appropriate studies were identified, data from each article were abstracted independently by two reviewers. If the study report did not explicitly state whether each pregnancy was intrauterine or ectopic, we contacted the authors to obtain this information. Each author whom we contacted responded to our queries, so we did not find it necessary to exclude any studies from the analysis based on missing information. We excluded from our analyses all subjects who were believed by the authors to have been pregnant before treatment. Discrepancies were identified and reconciled after reviewers re-assessed the original data.

Results

Our search identified 137 studies that fit our criteria. We excluded one study from our analyses because it was designed to measure bleeding effects of emergency contraceptive pills and explicitly excluded women who became pregnant after treatment (24). Among the remaining 136 studies, 114 were published in Chinese (25–138) and 22 were published in English (139–160). Mifepristone in doses from 10 mg to 600 mg was the most commonly-

studied regimen in our review (Table 1). One-third of the studies included a levonorgestrel-only regimen.

Of the included studies, 130 (95.6%) ascertained pregnancy by urine or serum hCG assay 7 to 10 days from the expected onset of menses (sensitivity level of tests was generally not specified), followed by ultrasound in the event of a positive test. One additional study specified that all pregnancies were confirmed to be intrauterine histologically after termination. These studies using high-certainty ascertainment methods (ultrasound or histology) contribute 716 (89.1%) of the pregnancies in this review, including all six ectopic pregnancies. For 85 (10.6%) pregnancies, the author did not specify how pregnancy location was determined, but stated (either in the paper or in follow-up communication with us) that the location was known to be intrauterine. In three cases (0.4% of all pregnancies), pregnancy location was classified as “unknown”, because the study authors were unable to designate whether the pregnancy was intrauterine or ectopic.

Among the mifepristone study subjects overall, 494 pregnancies of known location occurred after treatment, 3 of which were ectopic, resulting in an ectopic pregnancy rate of 0.6% (Table 2). Among the 307 pregnancies of known location occurring after treatment with levonorgestrel, 3 (1%) were ectopic. Results did not differ significantly between studies published in English and those published in Chinese for either regimen (for mifepristone studies, p -value for Fisher’s Exact test = 0.30; for levonorgestrel studies, p =1.00). A full table detailing results of each study is available from the authors upon request.

We performed a sensitivity analysis assuming that pregnancies of unknown location (two pregnancies following treatment with levonorgestrel and one following treatment with mifepristone) were ectopic. The proportion of pregnancies that were ectopic among levonorgestrel recipients was then 5/309, or 1.6% (95% CI = 0.6%–3.7%), and the proportion among those treated with mifepristone was then 4/495, or 0.8% (95% CI = 0.2%–2.1%).

Conclusion

Our results indicate that use of emergency contraceptive pills, in the two forms widely available today, does not increase the risk that a pregnancy after treatment will be ectopic. Available ectopic pregnancy rates range from 0.8% to 2% of all reported pregnancies; our study detected a range of 0.6% to 1.1%, depending on the medication used. Even when we analyzed the data under the most conservative possible scenario (assuming pregnancies of unknown location to be ectopic), we still found that the rate of ectopic pregnancy following use of levonorgestrel (1.6%) and mifepristone (0.8%) does not exceed the top of the range of rates of ectopic pregnancies among the general population. Indeed, the rate for mifepristone emergency contraceptive pills is at the bottom of that range.

In order to create as much consistency as possible across studies, we carefully considered our inclusion criteria in light of the data that were available to us from each study. We excluded pregnancies that were determined to have begun before emergency contraceptive pill treatment, but did not exclude those that may have begun after treatment had occurred as this information was not always reported. Some studies reported that subjects took additional doses of emergency contraceptive pills after the study treatment. However, because we did not have this information for every study, we did not exclude these subjects from our review.

Our review has several additional limitations. We could not include all women who were treated because some were lost to follow up, and unfortunately, we cannot assess the magnitude of this problem because not all studies reported the number of subjects who were

lost. In addition, the exact methods used to ascertain the existence and location of pregnancy are not entirely consistent from study to study. While most studies stated that ultrasound or histological examination was used, this is not explicitly specified in every study. For 10.6% of pregnancies, we relied upon the authors' assertion that the pregnancies were intrauterine. It is possible that ascertainment procedures vary from study to study, and that ectopic pregnancy is therefore under-diagnosed and underreported. Finally, we cannot be certain what the expected ectopic pregnancy rate would have been in the particular populations studied if subjects had not been treated with emergency contraceptive pills. We found it notable that two of the three ectopic pregnancies among the mifepristone recipients occurred in one study arm in which only six pregnancies were reported (151), but these pregnancies did not occur at the same study site and therefore do not in themselves raise particular concerns about differential ascertainment of pregnancy location.

Despite these limitations, this review provides the most comprehensive assessment to date of the risk of ectopic pregnancy when emergency contraceptive pill treatment fails. Based on our results, we conclude that no situations exist in which clinicians should counsel women against use of emergency contraceptive pills based solely on concerns about ectopic pregnancy. Likewise practitioners and women should have no heightened concern that if treatment fails, the pregnancy is more likely to be ectopic than a pregnancy occurring in the absence of emergency contraceptive pills. Previous studies show that emergency contraceptive pills reduce the likelihood that an act of intercourse will result in a pregnancy (3,23,161,162). Therefore, emergency contraceptive pills reduce the chance that an act of sexual intercourse will result in ectopic pregnancy.

Acknowledgments

Financial Disclosure: James Trussell, Elizabeth Raymond, Linan Cheng, and Kelly Cleland participated in the Data Safety Monitoring Board for two studies of ulipristal acetate conducted by HRA Pharma. Elizabeth Raymond: received research grants, consulting fees, or travel expenses from two pharmaceutical companies that sell emergency contraceptive pills. Linan Cheng: received research grants, travel expenses, or in-kind support from WHO and CHPFPC.

References

The references are available online at <http://links.lww.com/xx>.

Appendix. References

1. Singh, S.; Wulf, D.; Hussain, R.; Bankole, A.; Sedgh, G. Abortion worldwide: a decade of uneven progress. New York: Guttmacher Institute; 2009.
2. World Health Organization. Medical eligibility criteria for contraceptive use. Geneva, Switzerland: 2004.
3. Trussell, J.; Raymond, EG. Emergency contraception: a last chance to prevent unintended pregnancy. Office of Population Research, Princeton University; Available at: <http://ec.princeton.edu/questions/ec-review.pdf>. Retrieved December 3, 2009
4. New Zealand Medicines and Medical Devices Safety Authority. Progestogen-only emergency contraception and ectopic pregnancy. Available at: <http://www.medsafe.govt.nz/Profs/PUarticles/ectopic.htm>. Retrieved December 3, 2009
5. Harrison-Woolrych M, Woolley J. Progestogen-only emergency contraception and ectopic pregnancy. *J Fam Plann Reprod Health Care*. 2003; 29:5–6. [PubMed: 12626168]
6. Woolley J. Levonelle/Levonelle-2 emergency contraception: new advice. *CMO's Update*. 2003; 35:9.
7. Ghosh B, Dadhwal V, Deka D, Ramesan CK, Mittal S. Ectopic pregnancy following levonorgestrel emergency contraception: a case report. *Contraception*. 2009; 79:155–157. [PubMed: 19135575]

8. Cabar FR, Pereira PP, Zugaib M. Ectopic pregnancy following levonorgestrel emergency contraception. *Contraception*. 2009; 80:227. author reply 227–8. [PubMed: 19631798]
9. UK National Health Service. Emergency contraceptive pill. Available at: <http://www.nhs.uk/Conditions/Emergency-contraceptive-pill/Pages/Considerations.aspx>. Retrieved November 25, 2009
10. NHS Direct Wales. Emergency contraceptive pill. Available at: <http://www.nhsdirect.wales.nhs.uk/encyclopaedia/e/article/emergencycontraceptivepill/>. Retrieved November 25, 2009
11. UK National Health Service. Clinical knowledge summaries: emergency contraceptive pill. Available at: http://www.cks.nhs.uk/patient_information_leaflet/emergency_contraceptive_pill. Retrieved November 25, 2009
12. American Association of Pro Life Obstetricians and Gynecologists. Letter to the FDA regarding over-the-counter status for Plan B. Available at: <http://www.aaplog.org/PositionsAndPapers/EmergencyContraception.aspx?fileID=3>. Retrieved November 25, 2009
13. Laboratoire HRA Pharma. NorLevo 1.5 mg tablet, patient information. 2009
14. Centers for Disease Control. MMWR weekly: current trends in ectopic pregnancy — United States, 1990–1992. 1995
15. Egger M, Low N, Smith GD, Lindblom B, Herrmann B. Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. *Br Med J*. 1998; 316:1776–1780. [PubMed: 9624063]
16. Saraiya M, Berg CJ, Shulman H, Green CA, Atrash HK. Estimates of the annual number of clinically recognized pregnancies in the United States, 1981–1991. *Am J Epidemiol*. 1999; 149:1025–1029. [PubMed: 10355378]
17. Cagnacci A, Landi S, Volpe A. Rhythmic variation in the rate of ectopic pregnancy throughout the year. *Obstet Gynecol*. 1999; 180:1067–1071.
18. Irvine LM, Setchell ME. Declining incidence of ectopic pregnancy in a UK city health district between 1990 and 1999. *Hum Reprod*. 2001; 16:2230–2234. [PubMed: 11574521]
19. Wan F, Zhang H. A comparative study on ectopic pregnancy between internal migrants and residents in Shanghai. *Shanghai Medicine*. 2002; 25:472–475.
20. Rajkhowa M, Glass MR, Rutherford AJ, Balen AH, Sharma V, Cuckle HS. Trends in the incidence of ectopic pregnancy in England and Wales from 1966 to 1996. *Br J Obstet Gynaecol*. 2000; 107:369–374.
21. Salman G, Irvine LM. Ectopic pregnancy, the need for standardisation of rate. *J Obstet Gynaecol (Lahore)*. 2008; 28:32–35.
22. Trussell J, Hedley A, Raymond E. Ectopic pregnancy following use of progestin-only ECPs. *J Fam Plann Reprod Health Care*. 2003; 29:249. [PubMed: 14662065]
23. Cheng L, Guelmenzoglu AM, Piaggio G, Ezcurra E, Van LPFA. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2008:CD001324. [PubMed: 18425871]
24. Gainer E, Kenfack B, Mboudou E, Doh AS, Bouyer J. Menstrual bleeding patterns following levonorgestrel emergency contraception. *Contraception*. 2006; 74:118–124. [PubMed: 16860049]
25. Cao P, Li M, Xu J, Li Q. Different doses of mifepristone for emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics*. 1999; 15:295–296. [Chinese].
26. Chen G. Mifepristone for emergency contraception. *Journal of Guangxi Traditional Chinese Medical University*. 2001; 4:22–24. [Chinese].
27. Chen H, Min X. Mifepristone in combination with MTX for emergency contraception. *Strait Pharmaceutical Journal*. 2002; 14:51–52. [Chinese].
28. Chen HY. Clinical observation of emergency contraception with 10 mg mifepristone. *Sichuan Medical Journal*. 2005; 26:445–446. [Chinese].
29. Chen R, Li Q, Zhang Y, Huang M, Chen Y, Zhong X, et al. A comparative study of low-dose mifepristone for emergency contraception. *Shi Yong Yi Xue Zha Zi*. 2002; 18:1028–1029. [Chinese].
30. Chen S, An HB, Wang D, Jin FB. Two doses of mifepristone for emergency contraception. *China Health Care Nutrition: Clinical Journal*. 2009; 18:28–29. [Chinese].
31. Cheng L, Tong CH, Xiao ZH. Low doses of mifepristone for emergency postcoital contraception. *Chinese Journal of Obstetrics and Gynecology*. 1999; 34:335–338. [Chinese].

32. Cheng X. Clinical observation of prevention of pregnancy with Yu Ting. *Chin J Mod Drug Appl.* 2009; 3:147–148. [Chinese].
33. Ding G. Different doses of mifepristone for emergency contraception. *Journal of Practice Diagnosis and Treatment.* 2005; 19:226–227. [Chinese].
34. Dong JF. Clinical study of emergency contraception with two methods. *Shi Yong Zhong Xi Yi Lin Chuang.* 2009; 9:58–59. [Chinese].
35. Du J. Low dose of mifepristone for emergency contraception. *Yi Yao Xin Xi.* 2002; 10:14–15. [Chinese].
36. Du LY, Wang HX. Clinical observation of emergency contraception with mifepristone. *Journal of Qiqihar Medical College.* 2007; 28:1211–1212. [Chinese].
37. Duan JY, Li WX, Hou YJ. Clinical observation of emergency contraception with mifepristone. *Chinese Medical Journal of Metallurgical Industry.* 2007; 24:62–63. [Chinese].
38. Fan H, Cheng Y, Guo F, Wu S, Tan Y, Chen X, et al. Low dose of mifepristone for emergency contraception. *Hubei Yu Fang Yi Xue Zha Zi.* 2001; 23:52. [Chinese].
39. Fang Q, Guo X, Pan J, Xiao J, Li Y. A comparative study of different doses of mifepristone for emergency contraception. *Maternal and Child Health Care of China.* 2000; 15:48–49. [Chinese].
40. Fu X, Wang L, Jiang Q, Yang X. Anordrin and mifepristone for emergency contraception. *Journal of Qinghai Medical College.* 2000; 21:43–44. [Chinese].
41. Gai YM. Clinical observation of emergency contraception with mifepristone. *Chinese Journal of Trauma and Disability Medicine.* 2008; 16:62. [Chinese].
42. Gan S, Chang M, Hu S, Zhang P, Chang M, Xu X. A clinical study of 10 mg mifepristone for emergency contraception. *Reproduction & Contraception (China).* 1999; 19:311–313. [Chinese].
43. Gan SX, Li SS, Lu Y. Comparative study of the efficacy of mifepristone and levonorgestrel for emergency contraception. *Chinese Journal of Family Planning.* 2001; 9:178–181. [Chinese].
44. Gan XH, Jiang H, Li LP. Clinical observation of emergency contraception with a low dose of mifepristone. *Xian Dai Yi Yao Wei Sheng.* 2007; 23:1634. [Chinese].
45. Gu XY, Yie TF. Clinical study of the effect of Multiload 375 SL and levonorgestrel for emergency contraception. *Chinese Journal of Family Planning.* 2002; 10:740–742. [Chinese].
46. Han L, Ma Y, Li H. Low doses of mifepristone for emergency contraception. *Fudan University Journal of Medical Sciences.* 2001; 28:176–177. [Chinese].
47. Han X, Jin X, Weng L. A comparative study of mifepristone with levonorgestrel for emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics.* 1999; 15:294–6. [Chinese].
48. Han X, Weng L, Xiao B. Emergency contraception with mifepristone and anordrin. *Chinese Journal of Obstetrics and Gynecology.* 1996; 31:526–529. [Chinese].
49. Han X, Weng L, Zhang L, Zeng T, Xiao B. Clinical trial of mifepristone and anordrin for emergency contraception. *Journal of Reproductive Medicine.* 1995; 4:206–211. [Chinese].
50. Han Y. Clinical observation of low-dose mifepristone for emergency contraception. *Medical Information.* 2006; 19:1044–1045. [Chinese].
51. Hao XQ. Clinical observation of emergency contraception with a low dose of mifepristone. *Maternal and Child Health Care of China.* 2008; 23:3009–3010. [Chinese].
52. He AX. Clinical observation of emergency contraception with oral mifepristone. *China Medical Herald.* 2007; 4:70–71. [Chinese].
53. He FX. Clinical observation of emergency contraception with mifepristone. *Guide of Chinese Medicine.* 2009; 7:80. [Chinese].
54. Hu X, Lu C. A comparative study of mifepristone and levonorgestrel for emergency contraception. *Sichuan Medical Journal.* 2003; 24:F004. [Chinese].
55. Jiang DX, Wu ER. Effects of gestrinone (R2323) on emergency contraception: a clinical observation of 120 cases. *Journal of Reproductive Medicine.* 2002; 11:326–330. [Chinese].
56. Lai Z, Wang J, Zhou Z, Lu H, Song X, Sun J. A comparative study of low-dose mifepristone for emergency contraception. *Maternal and Child Health Care of China.* 2004; 19:36–38. [Chinese].
57. Lan CQ, Zheng HF. Clinical observation of emergency contraception with a low dose of mifepristone. *Acta Medicinæ Sinica.* 2002; 15:215–216. [Chinese].

58. Lan LQ. Clinical observation of emergency contraception with 10 mg mifepristone: 102-case report. *Maternal and Child Health Care of China*. 2008; 23:3140. [Chinese].
59. Li A, Zhang Y. Low dose of mifepristone for emergency contraception. *Journal of Guangxi Medical University*. 2000; 17:857. [Chinese].
60. Li F, Chen YX, Tang JH. Emergency contraception with low-dose mifepristone: observation of 150 cases. *Journal of First Military Medical University*. 2002; 22:466. [Chinese]. [PubMed: 12390720]
61. Li F, Qian X, Wu W. A comparative study of mifepristone with Cu-IUD for emergency contraception. *Journal of Practice Medicine*. 2005; 21:2313–2314. [Chinese].
62. Li H, Chang JP, Li J. A study of low-dose mifepristone for emergency contraception. *Heilongjiang Medical Journal*. 2000; 23:90. [Chinese].
63. Li J. A comparative study of mifepristone with levonorgestrel for emergency contraception. *Anthology of Medicine*. 2005; 24:754. [Chinese].
64. Li Q, Chen R, Zhang Y, Huang M, Chen RX, Zhong X. A comparative study of 25 mg and 50 mg mifepristone for emergency contraception. *Guangdon Medical Journal*. 2000; 22:884–885. [Chinese].
65. Li W. A comparative study of mifepristone with levonorgestrel for emergency contraception. *Guizhou Journal of Medicine*. 2002; 26:457. [Chinese].
66. Li WL. Clinical observation of emergency contraception with oral mifepristone. *Central Plains Medical Journal*. 2007; 34:59. [Chinese].
67. Li XY, Hu LY. A study of low-dose mifepristone for emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics*. 2001; 17:619–620. [Chinese].
68. Liang JZ, Zhou MR. A randomised comparative study of mifepristone and levonorgestrel for emergency contraception. *Heilongjiang Medical Journal*. 2001; 25:594. [Chinese].
69. Liao AH, Chang CF, Zhu JW. Randomized controlled prospective studies of mifepristone in small doses and levonorgestrel for emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics*. 2003; 19:25–27. [Chinese].
70. Lin N, Cheng W, Yang Y, Shao L. A comparative study of mifepristone and levonorgestrel for emergency contraception. *Tianjing Medical Journal*. 2000; 28:601–603. [Chinese].
71. Liu GZ, Lu XR, Zhang GC, Shi HT. Clinical observation of emergency contraception with a low dose of mifepristone. *Modern Medical Journal*. 2002; 30:183–184. [Chinese].
72. Liu JL, Liu LH, Li KZ, Liu HL. Comparative study of the efficacy of low-dose mifepristone and levonorgestrel for emergency contraception. *Practical Preventive Medicine*. 2000; 7:127. [Chinese].
73. Liu L, Chen A. A comparative study of mifepristone and Cu-IUD for emergency contraception. *Journal of Changzhi Medical College*. 2002; 61:198–199. [Chinese].
74. Liu L, Wang Z, Li L. Mifepristone and anordrin for emergency contraception. *Zhong Guo Yiu Sheng Yu Yi Chuan Zha Zi*. 2001; 19:108–111. [Chinese].
75. Liu Y, Chen X. A comparative study of mifepristone with Cu-IUD for emergency contraception. *Journal of Qiqihar Medical College*. 2002; 23:890–891. [Chinese].
76. Lou C. Low-dose mifepristone for emergency contraception. *Xian Dai Shi Yong Yi Xue*. 2002; 14:485. [Chinese].
77. Lou X, Ma L, Yang Y. Mifepristone and C53 contraceptive for postcoital contraception. *Journal of Chinese Modern Gynaecology and Obstetrics*. 2005; 2:405–406. [Chinese].
78. Ma J. A study of 110 cases of emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics*. 2001; 17:189. [Chinese].
79. Ma SF, Li WZ. Clinical observation of emergency contraception with a low dose of mifepristone. *Journal of Changzhi Medical College*. 2005; 9:116–118. [Chinese].
80. Pang YZ, Zhang Y. Clinical observation of emergency contraception with mifepristone. *Chinese Community Doctors*. 2006; 7:23. [Chinese].
81. Pei JH, Wang ZX. A randomized comparative study of mifepristone in small doses and levonorgestrel for emergency contraception. *Harbin Medicine*. 2001; 21:32–33. [Chinese].

82. Qi M, Wang Y, Yan L. A comparative study of low-dose mifepristone with levonorgestrel for emergency contraception. *Journal of Qinghai Medical College*. 2003; 24:255–256. [Chinese].
83. Qi Y, Zhang J, Cao Y, Yan W, Zhang Z. A clinical study of mifepristone at low dose for emergency contraception. *Chinese Journal of Family Planning*. 2000; 8:305–307. [Chinese].
84. Qi Y, Zhang J, Cao Y, Zhang Z. A comparative clinical trial of two low doses of mifepristone for emergency contraception. *Maternal and Child Health Care of China*. 2000; 15:701–704. [Chinese].
85. Qian L. Three doses of mifepristone for emergency contraception. *Chinese Journal of Family Planning*. 1999; 7:322–323. [Chinese].
86. Qin C. A clinical study of 137 cases of emergency contraception with mifepristone. *Zhejiang Journal of Clinical Medicine*. 2000; 2:302–303. [Chinese].
87. Sang GW, Shao Q, Zhang J, Zhang M, Chen S, Song S, et al. A randomized multicentre clinical trial of different doses of mifepristone alone and in combination with anordrin as emergency contraception. *Chinese Journal of Obstetrics and Gynecology*. 1999; 34:331–334. [Chinese].
88. Shao XY, Li JB, Lu YC, Li F, Liu FY. Three different approaches for emergency contraception. *Chinese Journal of Family Planning*. 2006; 1:51–53. [Chinese].
89. Sheng A. Clinical observation of the efficacy of mifepristone and levonorgestrel as emergency contraception. *Academic Journal of Jiangsu University (Medicine)*. 2002; 12:246–249. [Chinese].
90. Sheng SY. Clinical study of emergency contraception with oral contraceptive pills versus levonorgestrel. *Asia-Pacific Traditional Medicine*. 2008; 4:93–94. [Chinese].
91. Song ZH, Wang Y, Chen P, Wang D, Lu WH. Clinical comparative study of emergency contraception with mifepristone versus Cu-IUD. *Chinese Medicine of Factory and Mine*. 2007; 20:630–631. [Chinese].
92. Su W, Chui JY, Liu P. A comparative study of Cu-IUD with mifepristone and with levonorgestrel for emergency contraception. *Journal of Baotou Medicine*. 2001; 25:24. [Chinese].
93. Sun MX. Clinical observation of emergency contraception with oral contraceptive pills versus levonorgestrel. *Chinese Journal of Family Planning*. 2007; 6:366–367. [Chinese].
94. Sun P. Mifepristone for emergency contraception. *Journal of Chinese Practice Medicine*. 2003; 5:92. [Chinese].
95. Sun Y, Wang X. A clinical comparative study of mifepristone with anordrin for emergency contraception. *Chinese Journal of Family Planning*. 2000; 8:172–173. [Chinese].
96. Tan K, Mai T, He P, Lin H, Li S. Low doses of mifepristone for emergency contraception. *Chinese Journal of Family Planning*. 1999; 7:470–471. [Chinese].
97. Tan L, Zheng G, Li J. Mifepristone for emergency contraception. *Wei Sheng Zhi Yie Jiao Yu*. 2003; 21:138–139. [Chinese].
98. Tan LF, Zheng GP, Li J. Clinical observation of emergency contraception with mifepristone. *Wei Sheng Zhi Ye Jiao Yu*. 2003; 21:138–139. [Chinese].
99. Tian Q. A comparative study of mifepristone with Cu-IUD for emergency contraception. *Journal of Henan Medical College for Staff and Workers*. 2000; 12:51. [Chinese].
100. Wan LQ. Efficacy assessment of misoprostol for emergency contraception. *Modern Hospital*. 2009; 16:34–36. [Chinese].
101. Wang C, Tian M, Chang Y, Shao M. A clinical comparative observation of copper IUD, low-dose mifepristone and levonorgestrel for emergency contraception. *Journal of Chinese Physician*. 2000; 2:271–273. [Chinese].
102. Wang CP, Liu Y, Chang YF, Shao WQ. Clinical comparative study of emergency contraception with low-dose mifepristone versus Cu-IUD. *Journal of Reproductive Medicine*. 2006; 15:271–273. [Chinese].
103. Wang J. A comparative study of different doses of mifepristone for emergency contraception. *Journal Huaihai Medicine*. 2006; 24:19–20. [Chinese].
104. Wang L, Lv Y, Guan D, Zhang H, Yao L. 12.5 mg mifepristone for emergency contraception. 2004; 7:1477–1478. [Chinese].
105. Wang Q, Li A. A comparative study of levonorgestrel with low-dose mifepristone for emergency contraception. *Northwestern Pharmaceutical Journal*. 2000; 15:72. [Chinese].

106. Wang QJ, Chen Y. Clinical study of emergency contraception with mifepristone. *Chin J Misdiagn.* 2007; 17:242–243. [Chinese].
107. Wang SZ, Huang ZK, Li S. Clinical trial of mifepristone in different doses for emergency contraception. *Chinese Journal of Practical Gynecology and Obstetrics.* 2001; 17:271–279. [Chinese].
108. Wang TM. Clinical observation of emergency contraception with a low dose of mifepristone. *Journal of Henan Medical College for Staff and Workers.* 2007; 19:542–543. [Chinese].
109. Wang Y, Liu H. A comparative study of low doses of mifepristone with levonorgestrel for emergency contraception. *Chinese Journal of Family Planning.* 2003; 8:505–506. [Chinese].
110. Wang Z, Liu L, Liu Q, Zhang H. A clinical comparative study of mifepristone with anordrin for emergency contraception. *Chinese Journal of Family Planning.* 1999; 7:320–321. [Chinese].
111. Wei R. Low dose of mifepristone for emergency contraception: observation of 309 cases. *Jiangxi Medical Journal.* 2002; 37:102–104. [Chinese].
112. Wei RH. Low dose of mifepristone for emergency contraception. *Shanghai Sheng Wu Yi Xue Gong Cheng Zha Zi.* 2002; 23:39–42. [Chinese].
113. Wu C, Zhang Y. An extended study of a single dose of 25 mg mifepristone for emergency contraception. *Chinese Journal of Family Planning.* 1999; 7:358–360. [Chinese].
114. Wu XZ, Sao JY, Chen CQ, Yan Y, Fa YY, Liu JH. A comparative study on methods for emergency contraception. *Reproduction & Contraception (China).* 2002; 22:152–155. [Chinese].
115. Xie X, Liu Y, Lin X. A clinical study of 600 cases of mifepristone for emergency contraception. *Reproduction & Contraception (China).* 1998; 18:224–226. [Chinese].
116. Xu L, Wang Z. A comparative study of low-dose mifepristone with levonorgestrel for emergency contraception. *Chinese Journal of Family Planning.* 2000; 8:419–420. [Chinese].
117. Xu Y. Comparison of the efficacy of mifepristone and levonorgestrel for emergency contraception. *China Practical Medicine.* 2007; 2:11–12. [Chinese].
118. Xu Z. A comparative study of mifepristone, anordrin and levonorgestrel for emergency contraception. *Journal of Yichun Medical College.* 2000; 12:248–249. [Chinese].
119. Yang F. A comparative study of two low doses of mifepristone for emergency contraception. *J Clin Res.* 2003; 20:630–631. [Chinese].
120. Yang LJ. A comparative study of mifepristone, anordrin and danazol for emergency contraception. *Guangzhou Medical Journal.* 2001; 32:12–13. [Chinese].
121. Yang Y, Liang X, Liu X. Low dose of mifepristone for emergency contraception: observation of 106 cases. *Heilongjiang Medical Journal.* 2002; 26:283. [Chinese].
122. Yu L, Yang XY, Wang H, Cheng WY. Clinical effectiveness observation of low-dose mifepristone as an emergency contraceptive. *Journal of Tianjin Medical University.* 2001; 7:165–167. [Chinese].
123. Zhang J, Jing X, Wong L. Cu-IUD versus mifepristone for emergency contraception. *Chinese Journal of Obstetrics and Gynecology.* 1999; 34:569–570. [Chinese].
124. Zhang JQ. Emergency contraception in the highland. *Chinese Journal of Family Planning.* 2000; 8:552–554. [Chinese].
125. Zhang L, Lai L, Deng X. Single and small doses of mifepristone for emergency contraception. *Journal of Gannan Medical College.* 2005; 25:328–330. [Chinese].
126. Zhang X, Gao G, Shi J, Qu C, Leng Y. A clinical study of low doses of mifepristone for emergency contraception. *Chinese Journal of Family Planning.* 1999; 7:175–176. [Chinese].
127. Zhang X, Leng Y, Shi J, Gao G, Xu Y, Sun H. A study of levonorgestrel for emergency contraception. *Chinese Journal of Family Planning.* 1999; 7:375–376. [Chinese].
128. Zhang XL, Yang JZ. Clinical observation of emergency contraception with a low dose of mifepristone. *Maternal and Child Health Care of China.* 2005; 20:1274. [Chinese].
129. Zhang Y, Qiao G, Zhu P, Zhang S, Zhang J, Zhu N. Clinical observation of three lower doses of mifepristone for emergency contraception. *Chinese Journal of Family Planning.* 1998; 19:352–356. [Chinese].
130. Zhang Y, Wen L, Li S, Wang Y. Mifepristone for emergency contraception. *Henan YI Yao Xin XI.* 2002; 10:20–21. [Chinese].

131. Zhang Y, Zhang W, Wang L. Low dose of mifepristone and anordrin for emergency contraception. *Journal of Qiqihar Medical College*. 2002; 23:415. [Chinese].
132. Zhao J, Liu R, Li H, Zhang Y. Different doses of mifepristone for emergency contraception. *Journal of Shandong University (Health Sciences)*. 2003; 41:468. [Chinese].
133. Zheng A. Low dose of mifepristone for emergency contraception. *Youjiang Medical Journal*. 2005; 33:375–376. [Chinese].
134. Zheng MY, Zhu MF, Huang Y. Clinical observation of emergency contraception with a low dose of mifepristone. *Guo Ji Yi Yao Wei Sheng Dao Bao*. 2008; 14:68–70. [Chinese].
135. Zheng QL. Clinical observation of emergency contraception with a low dose of mifepristone at different times. *Capital Medicine*. 2000; 7:32–33. [Chinese].
136. Zheng XY. Clinical observation of emergency contraception with mifepristone combined with MTX. *Shi Yong Zhong Xi Yi Lin Chuang*. 2007; 7:62–63. [Chinese].
137. Zhu YH, Oyang LX. Three different approaches for emergency contraception. *J Med Theor & Prac*. 2007; 20:200–202. [Chinese].
138. Zuo SH, Wu J, Liu L, Liu J, Gao Y. A clinical trial of two low doses of mifepristone for emergency contraception. *Reproduction & Contraception (China)*. 1999; 19:352–356. [Chinese].
139. Arowojolu AO, Okewole IA, Adekunle AO. Comparative evaluation of the effectiveness and safety of two regimens of levonorgestrel for emergency contraception in Nigerians. *Contraception*. 2002; 66:269–273. [PubMed: 12413624]
140. Ashok PW, Stalder C, Wagaarachchi PT, Flett GM, Melvin L, Templeton A. A randomised study comparing a low dose of mifepristone and the Yuzpe regimen for emergency contraception. *BJOG-Int J Obstet Gyn*. 2002; 109:553–560.
141. Ashok PW, Wagaarachchi PT, Flett GM, Templeton A. Mifepristone as a late post-coital contraceptive. *Hum Reprod*. 2001; 16:72–75. [PubMed: 11139540]
142. Creinin MD, Schlaff W, Archer DF, Wan L, Frezieres R, Thomas M, et al. Progesterone receptor modulator for emergency contraception: a randomized controlled trial. *Obstet Gynecol*. 2006; 108:1089–1097. [PubMed: 17077229]
143. Esteve JLC, García R, Breto A, Llorente M. Emergency contraception in Cuba with 10 mg of mifepristone. *Eur J Contracept Reprod Health Care*. 2007; 12:162–167. [PubMed: 17559015]
144. Glasier AF. Mifepristone (RU 486) compared with high-dose estrogen and progestogen for emergency postcoital contraception. *N Engl J Med*. 1992; 327:1041. [PubMed: 1522839]
145. Glasier AF, Cameron S, Fine P, Logan S, Casale W, Van Horn J, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet*. 2010; 375:555–562. [PubMed: 20116841]
146. Hamoda H, Ashok PW, Stalder C, Flett GMM, Kennedy E, Templeton A. A Randomized trial of mifepristone (10 mg) and levonorgestrel for emergency contraception. *Obstet Gynecol*. 2004; 104:1307–1313. [PubMed: 15572495]
147. He CH, Gui YL, Yang J, Wang BS, Zheng EX, Gao ES, et al. A randomized comparative study on mifepristone alone and in combination with tamoxifen for emergency contraception. *Contraception*. 2002; 66:221–224. [PubMed: 12413615]
148. Ho PC, Kwan MSW. A prospective randomized comparison of levonorgestrel with the Yuzpe regimen in post-coital contraception. *Hum Reprod*. 1993; 8:389–392. [PubMed: 8473453]
149. Ngai SW, Fan S, Li SQ, Cheng LA, Ding JH, Jing XP, et al. A randomized trial to compare 24h versus 12h double dose regimen of levonorgestrel for emergency contraception. *Hum Reprod*. 2005; 20:307–311. [PubMed: 15567882]
150. Novikova N, Weisberg E, Stanczyk FZ, Croxatto HB, Fraser IS. Effectiveness of levonorgestrel emergency contraception given before or after ovulation—a pilot study. *Contraception*. 2007; 75:112–118. [PubMed: 17241840]
151. Okewole IA, Arowojolu AO. Single dose of 1.5 mg levonorgestrel for emergency contraception. *Int J Gynaecol Obstet*. 2005; 89:57–58. [PubMed: 15777904]
152. Piaggio G, von Hertzen H, Grimes D, Van Look PFA, Peregoudov S, Vucurevic M, et al. Comparison of three single doses of mifepristone as emergency contraception: a randomised trial. *Lancet*. 1999; 353:697–702. [PubMed: 10073511]

153. Taneepanichskul S. Emergency contraception with mifepristone 10 mg in Thai women. *J Med Assoc Thai.* 2009; 92:999–1002. [PubMed: 19694321]
154. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet.* 1998; 352:428–433. [PubMed: 9708750]
155. Tirelli A, Cagnacci A, Volpe A. Levonorgestrel administration in emergency contraception: bleeding pattern and pituitary-ovarian function. *Contraception.* 2008; 77:328–332. [PubMed: 18402847]
156. von Hertzen H, Piaggio G, Ding J, Chen J, Song S, Bartfai G, et al. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. *Lancet.* 2002; 360:1803–1810. [PubMed: 12480356]
157. Webb AMC, Russell J, Elstein M. Comparison of Yuzpe regimen, danazol, and mifepristone (RU486) in oral postcoital contraception. *Br Med J.* 1992; 305:927–931. [PubMed: 1458074]
158. Wu S, Wang C, Wang Y, Cheng W, Zuo S, Li H, et al. A randomized, double-blind, multicenter study on comparing levonorgestrel and mifepristone for emergency contraception. *J Reprod Med.* 1999; 8:43–46.
159. Xiao BL, von Hertzen H, Zhao H, Piaggio G. A randomized double-blind comparison of two single doses of mifepristone for emergency contraception. *Hum Reprod.* 2002; 17:3084–3089. [PubMed: 12456607]
160. Xiao BL, Zhao H, Piaggio G, von Hertzen H. Expanded clinical trial of emergency contraception with 10 mg mifepristone. *Contraception.* 2003; 68:431–437. [PubMed: 14698073]
161. Bastianelli C, Farris M, Benagiano G. Emergency contraception: a review. *European Journal of Contraception and Reproductive Health Care.* 2008; 13:9–16. [PubMed: 18283598]
162. von Hertzen H, Godfrey EM. Emergency contraception: the state of the art. *Reprod Biomed Online.* 2009; 18:28–31. [PubMed: 19281661]

Table 1

Number of studies included in review, by regimen

Regimen	Dose	Studies*
Mifepristone	10 mg – 600 mg	124
Levonorgestrel	0.75 mg × 2 or 1.5 mg	46

* Because many studies included more than one regimen, the number of studies in this table exceeds the total number of studies in our review.

Table 2

Results by regimen (pregnancies of known location only)

Regimen	Population*	Pregnancies	Ectopic	% of pregnancies that were ectopic (95% CI)
Mifepristone (all)	35,867	494	3	0.6% (0.1% – 1.8%)
English studies	14,669	179	2	1.1% (0.1% – 4.0%)
Chinese studies	21,197	315	1	0.3% (0.0% – 1.8%)
Levonorgestrel (all)	15,696	307	3	1.0% (0.2% – 2.8%)
English studies	11,405	201	2	1.0% (1.2% – 3.5%)
Chinese studies	4,291	106	1	0.9% (0.0% – 5.1%)

† Excludes women who received treatment but either were known to have been pregnant before treatment or were lost to follow-up after treatment.