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Unintended pregnancy: introducing medication abortion

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Outline

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Introduction

Medication abortion: the evidence

Choosing a method of abortion

Service organization

Mifepristone: the international story

Mifepristone: the story in Australia

Worldwide context[1, 2]

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- ~42 million induced abortions annually
- ~29/1000 women aged 15-44
- 1/3 to ½ of all women in lifetime

- 20 million illegal (unsafe)
- ~68 000 women die from unsafe abortions
- ~13% global maternal mortality

Many more are permanently harmed

Estimates only: variable reporting and legality

Local challenges

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Prevention

Best practice:

- Access
- Options
- Service development

Data/monitoring/research

Training/continuing education

Legal/political

Medication abortion: what is it?

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200mg mifepristone (RU486)

2 days later 800mcg (4 tabs) misoprostol PV or SL

Complete miscarriage within a few hours for 95% in the first 9 weeks of pregnancy

Pain and bleeding to be expected, also gastrointestinal side effects of misoprostol

Need follow up to ensure complete

After 9 weeks gestation

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- takes longer
- more doses of misoprostol needed (400mcg 3 hourly)
- more pain and need for analgesia
- higher ongoing pregnancy rate
- increasing rates of surgery

Mifepristone

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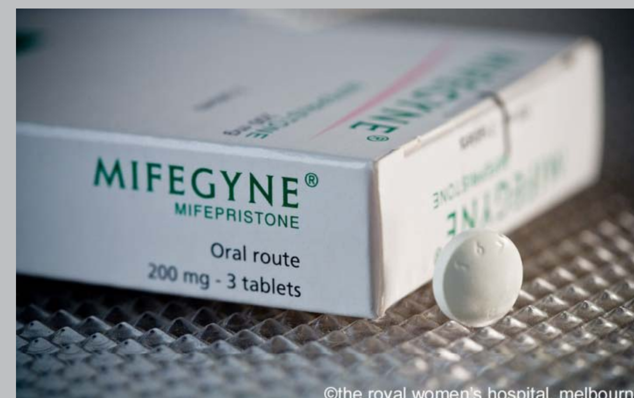
Formerly known as RU486 (Roussel Uclaf)

Anti-progesterone

- Softens cervix
- Increases myometrial sensitivity to prostaglandins
- Increases decidual prostaglandin production

Developed in France

First registered in 1988



Alternatives to mifepristone

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Surgical abortion

- Suitable if available and acceptable to women
- Less available at more advanced gestation

Other medication regimens

- Prostaglandin alone
- With methotrexate in early pregnancy

Outcomes of other medication regimens

- Take longer to work
- Higher failure rates
- RCOG: "Single agent regimens are not considered to have a role in UK practice, where mifepristone is readily available."

Medication vs surgical abortion (T1)

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Advantages:

- Avoids anaesthesia/surgical procedure for 95%
- May be perceived as more "natural"
- Can be done earlier than surgical
- Better satisfaction if it's the woman's preference

Disadvantages:

- Longer duration of bleeding than surgical
- Up to 5% don't respond to initial course, may require surgery anyway
- Less acceptable with increasing gestation

Potential for better geographic access and earlier abortion

Second trimester outcomes

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Variable selection and regimens

Mifepristone and prostaglandin

- 95% delivered within 24 hours of 1st PG dose
- Mean, median 6-10 hours
- Surgical evacuation ~10%

Prostaglandin alone

- 60-80% delivered within 24 hours
- Mean, median 14-24 hours
- Surgical evacuation 10-60%

Safety and effectiveness

Mifepristone with prostaglandin

- extensive published research and clinical experience
- approved France (1988), China, UK (1991), USA (2000), NZ (2001)
- several million women have been treated worldwide

Misoprostol

- extensive published research available
- part of USA and NZ approved regimens
- in RCOG recommended regimens
- available in Australia for other indications
- widely used for cervical priming and for second trimester abortion

Contraindications

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- Adrenal insufficiency
- Steroid use/dependence
- Uncontrolled asthma
- Porphyria
- Breastfeeding
- Caution with cardiac/renal/liver problems
- Known allergy to mifepristone or prostaglandin

4132 cases ≤63 days[3]

4132 took mifepristone

- 1 changed mind (term birth)
- 95 (2.3%) aborted <48 hours (without misoprostol)

Of the remaining 4036

- 94.9% passed products in ward
- 4.0% passed products later (no surgery)
- 1.1% proceeded to surgical evacuation

Total of 94 (2.3%) had surgery

Time to abortion[3]

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Determined for 3457 women (85.7% of total)

Of these:

- 65.1% <4 hours
- 91.8% <6 hours
- 98.6% <8 hours
- 99.9% <10 hours

Mean 4.0 hours (SD 2.6)

Longer with gestations 50-63/7 than ≤49

Failure and complications[3]

2.3% (94) needed surgery

- 1.6% (66) incomplete abortion
- 0.3% (11) missed abortion
- 0.3% (13) continuing pregnancy
- 0.1% (4) at laparoscopy to exclude ectopic

0.2% (10) evacuations to achieve haemostasis

0.2% (8) blood transfusions; 2 on day of procedure, 5 later within 14 days

2.7% (76/2778) with known follow up prescribed antibiotics

Side effects[3]

Analgesia: data for 3146 (77%)

- 36.7% nil
- 58.6% oral (paracetamol/codeine)
- 4.7% parenteral opiates

More for nullipara and higher gestations

GI side effects not reported in this study, but up to 40% diarrhoea, nausea, vomiting

9^{1}-13^{0} weeks (483 cases 64-91/7)[4]

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54.2% of total 891 women having abortions at this gestation

94.8% success (complete without surgery)

5.2% surgery

- 1.7% continuing
- 0.6% missed abortion
- 2.7% incomplete
- 0.2% bleeding

Other features[4]

Induction-abortion interval increased with gestation

Surgical intervention more common with increasing gestation and older women

81% needed oral analgesia, 1 parenteral opiates and 18% no analgesia

2.3% prolonged bleeding, no blood transfusion

Mortality [5]

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Several cases in USA of toxic shock due to clostridium sordellii infection

Not reported in Europe

Estimated death rates 1:100,000 medication abortions (surgical abortion similar, childbirth 1:10,000)

NB consider possibility of ectopic pregnancy

Ensuring effectiveness

All women need:

- Information re what to expect
- Contact information (24 hours)

Need to exclude ongoing pregnancy (1%)

Patient report of POCs usually accurate

US prior to discharge or at 1-2 weeks (will find POCs; don't treat test results)

ßHCG level on discharge and at follow up

Refining the protocols

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Dosage regimens

Interval mifepristone-misoprostol

Route of administration of misoprostol

- PV, SL, PO
- Effectiveness
- Side effect profile
- Staff and patient preferences
- Infection?

Location of procedure

Women's experience of medication abortion

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best features

- no surgery
- natural
- less pain/cramping
- simpler/faster
- safer/few SEs
- privacy/convenience
- emotionally easier

worst features

- failure
- uncertainty/waiting
- pain/cramping
- more visits/time
- more SEs/bleeding
- nausea/vomiting/ diarrhoea

Medication vs surgical abortion[6]

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363 Scottish women:

- 73 chose medical, 95 chose surgical (168)
- 99 and 96 randomized (195)

- more chose surgical if living further away
- higher pain scores on discharge for medication
- longer bleeding with medication
- more time off work with surgical
- return to normal activities same time

Reasons for choosing[7]

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Medication

- afraid of anaesthesia/ surgery(59%)
- want to be aware (8%)
- better time scale (21%)
- less invasive/more natural (15%)
- psychologically better (4%)

Surgical

- want to be unconscious (39%)
- better time scale (40%)
- fear of medical side effects (23%)
- psychologically better (1%)

Medication vs surgical abortion[7]

- satisfaction with method greater if chosen by woman (9% surgical and 11% medical would choose different method)
- of randomized, 13% (surgical) and 36% (medication) would choose different method in future
- after 50 days, less satisfaction with medication

Medication vs surgical abortion[8]

1373 women in China, Cuba and India who chose their method

- more women chose medication abortion
- satisfaction rates comparable
- most would choose same method again
- more medication would choose same method

Choice of method

Little flexibility in Australia because limited access to mifepristone (RU486)

Where choice available around half prefer medication and half surgical

Medication more "natural" like miscarriage, no surgery

Surgical over quickly, no waiting, no awareness

Service organization and facilities

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Choice means more counselling time

Possibly increased requirement for ultrasound

Multiple visits required

- pre-treatment
- treatment x 2
- follow-up/confirm complete

Observation/waiting area

Shift from surgical/anaesthetic/theatre staff to nursing staff

24 hour back up including surgical

Location of procedure

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- Inpatient, ambulatory or home
- Clinical factors including pain management
- Social support
- Access to emergency care
- Facilities
- Legal considerations
- Cost

Changes to GP role

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Usual role in abortion care continues:

- Information, counselling, support, referral, contraception

Added information about the medication option

Potentially greater role in follow up care:

- Ideally need information from service providers re passage of POCs
- Be aware of possibility of ongoing pregnancy
- Generally manage like miscarriage
- Treat symptoms not tests; be slow to use US for RPOCs
- Teamwork/communication will be important

Service implications[9]

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Overall abortion rates do not increase

May encourage earlier presentation

May achieve better geographical access

Change service structure and organization

Cost considerations comparable to surgical

More women able to have their preference

Greater satisfaction with treatment

Provider issues

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Experience/familiarity with methods and side effects

Built in “failure” rate

Concern re effects of drugs on continuing pregnancies

Anxiety about pharmaceutical statements and responsibilities (medicolegal)

Changing medical, surgical, nursing roles

Shifting responsibility/control towards patient

Orientation/preference

UK only 33% centres offer both methods in first trimester

International story

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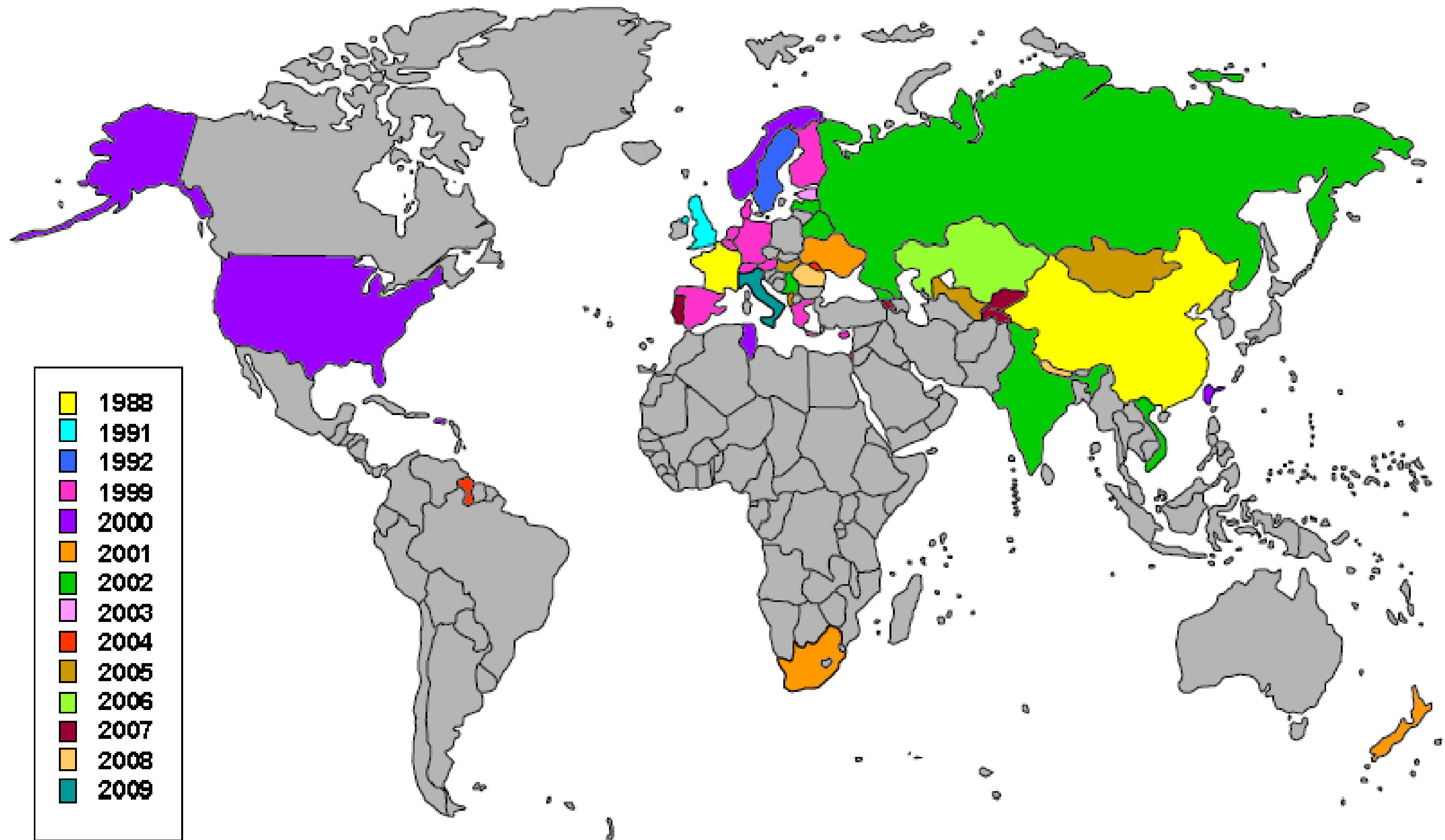
- Growing research evidence and practice guidelines WHO, RCOG, ACOG
- Pharmaceutical company attempts to withdraw
- USA presidential ban (Bush snr) and reversal (Clinton)
- Searle advisory against use of misoprostol in pregnancy

Mifepristone Approved



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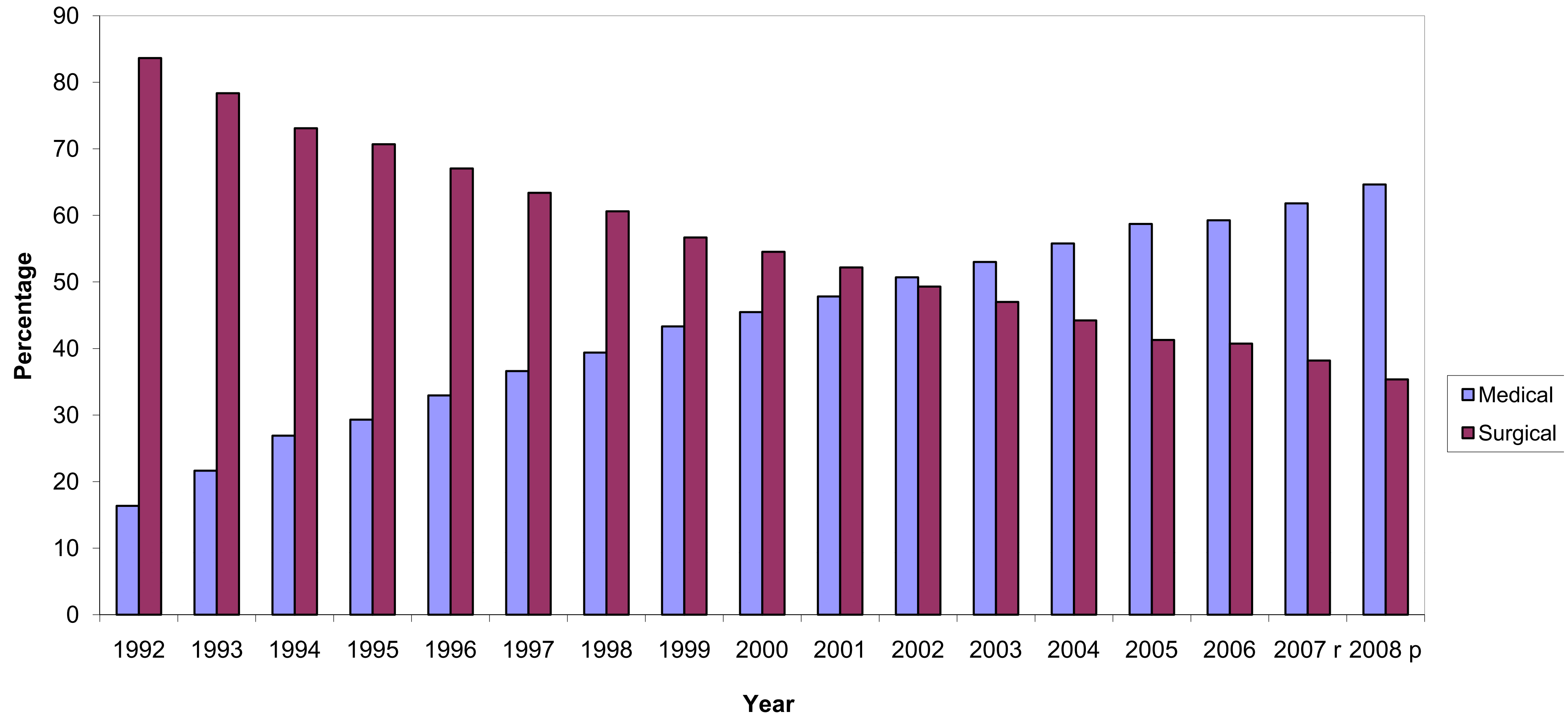
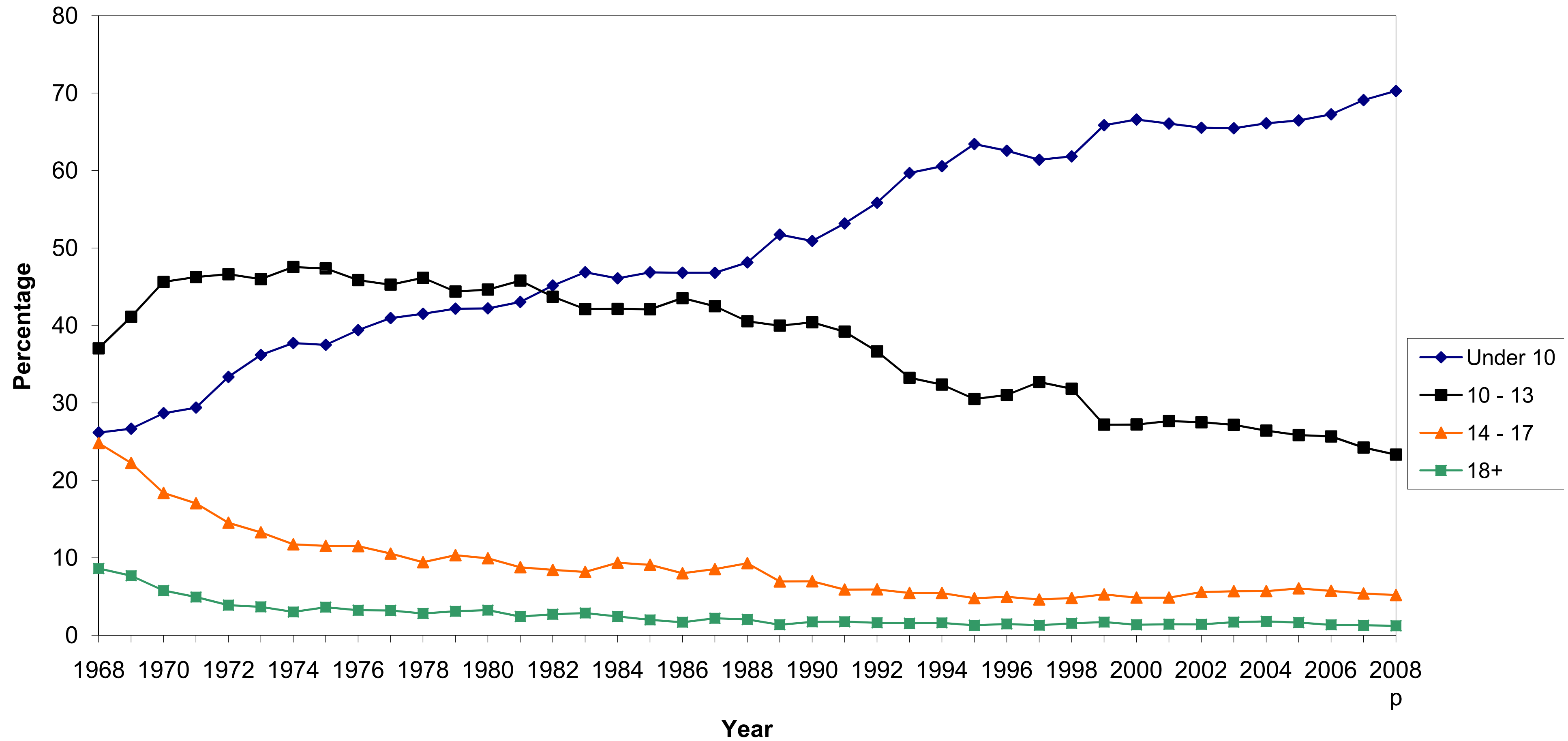


1 Refers to therapeutic abortions notified in accordance with the Abortion Act 1967.
p Provisional.
Source : Notifications (to the Chief Medical Officer for Scotland) of abortions performed under the Abortion Act 1967
ISD Scotland

Reference 10

Abortions performed in Scotland by estimated gestation (weeks), 1968-2008p



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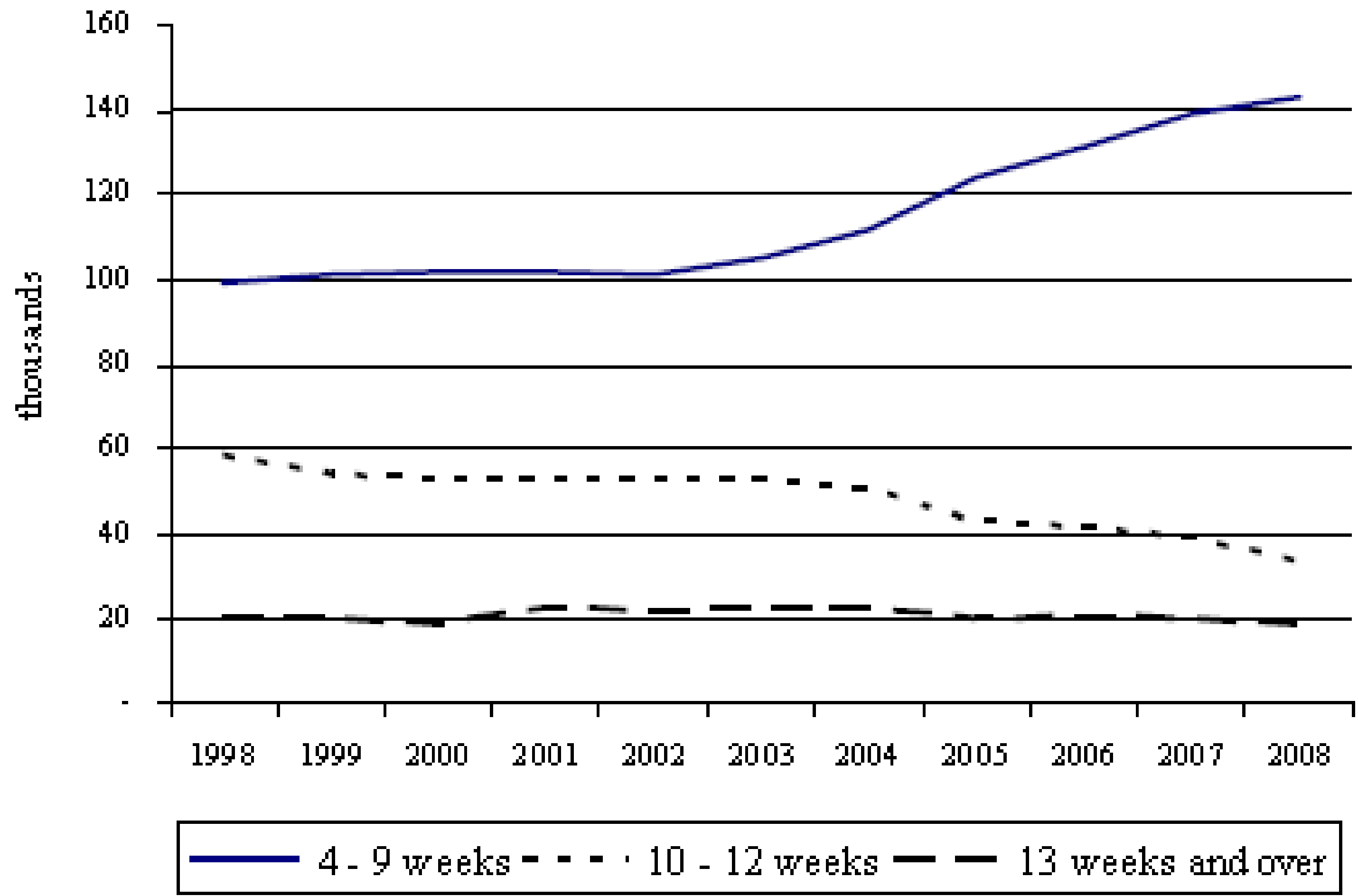
Abortions in England and Wales: gestation



Reference 11

Mifepristone in Australia to 1996

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No pharmaceutical application

1980s for women after fetal death

1994 WHO trials for abortion and emergency contraception

Halted by Health Minister Lawrence (later resumed)

Review of Ethics Committees

1996 “Harradine amendment” to Therapeutic Goods Act

Australia[12]

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- 50 women who chose medical TOP
- WHO dose-finding study for mifepristone/misoprostol
- 38 completed follow up questionnaire
- mean satisfaction 4.5/5 (range 1-5)
- 15 women with previous surgical TOP found medical more acceptable: mean 4.5/5 (range 3-5)

Mifepristone in Australia 1996-2005

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Ministerial approval required for import of specified ‘restricted goods’, notification of both houses of Parliament within 5 days

Strong disincentive to pharmaceutical companies: no application

Subsequent Special Access Scheme use (meningiomas)

Subsequent research use (contraception/abnormal bleeding)

Parliament 2005-6

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4 ♀ cross party private members' bill

Therapeutic Goods Amendment (repeal of Ministerial responsibility for approval of RU-486) Bill 2005

Senate inquiry and community debate

Now TGA must consider as for any other drug

Application for registration awaited

TGA: RU486		For	Against	%
Senate	Men	21	25	46:54
	Women	24	3	89:11
	Total	45	28	62:38
House	Men	61-68	49-42	55:45-62:38
(amendments only)	Women	29	7	81:19
	Total	90-97	56-49	62:38-66:34

Authorized prescriber process

Individual prescribers apply to TGA

Need HREC approval of individual as suitable

Evidence of safety and efficacy

Clinical justification for use instead of available alternatives to unapproved product

Review patient information and consent form

RWH approved indication: initially when surgical abortion contraindicated or unavailable

Current status

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Approvals in Qld 2006, Vic 2007, NSW 2007, WA 2007, SA 2008

Still awaiting pharmaceutical application

Prepare for eventual registration

Most women still don't have access to medication abortion

RWH application renewed with revised protocols

"Termination of pregnancy where medical abortion is assessed clinically as the most appropriate method for the woman, including when surgical abortion is not available"

Broader issues

Legal complexities

Timely investigation and referral

Equitable access to comprehensive services

Managing demand/sharing the load

Supporting staff

Training/succession planning

Research

Abortion as a health issue