Reproductive health research at WHO

Paul F.A. Van Look, MD PhD FRCOG

Department of Reproductive Health and Research
World Health Organization

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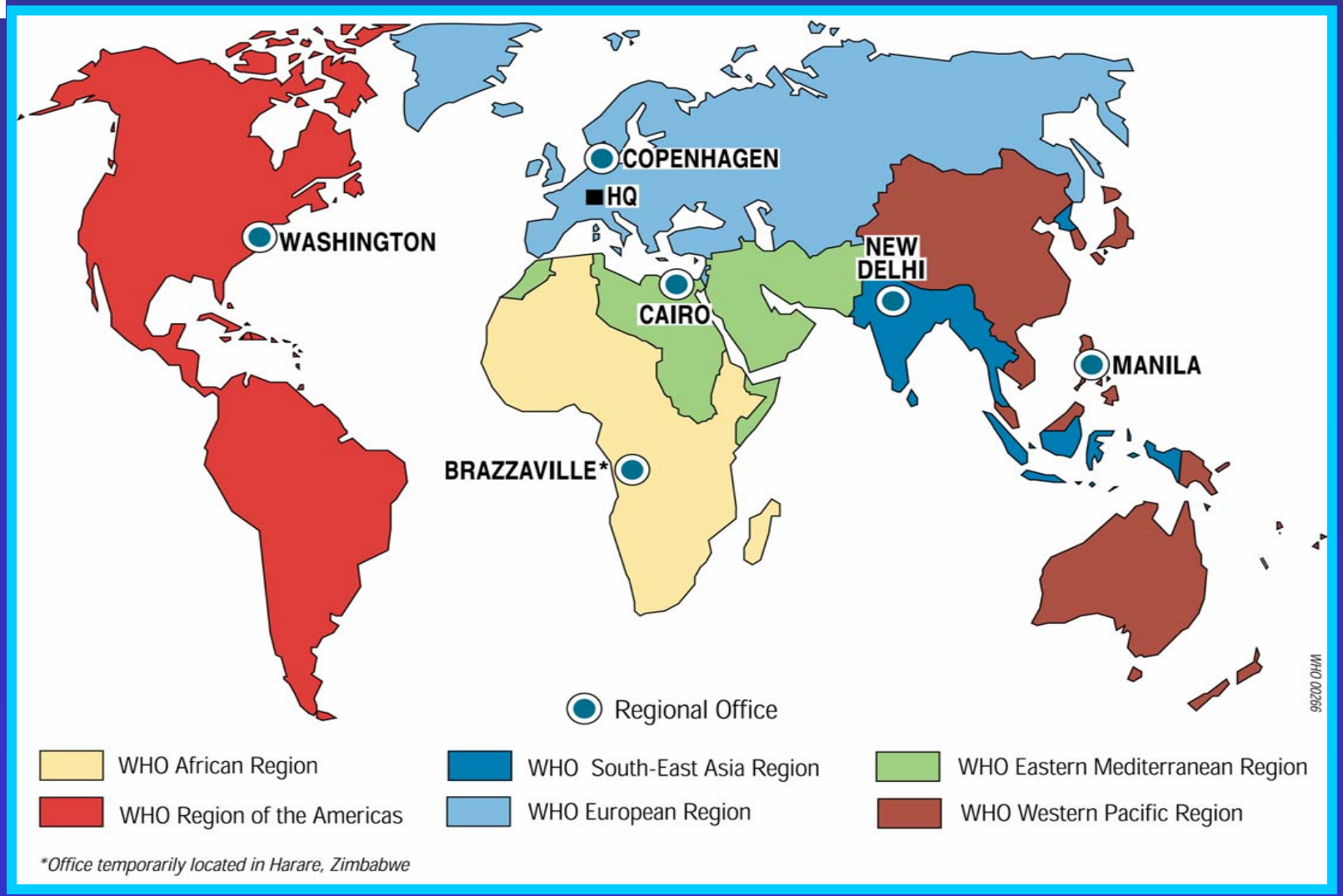
"Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."

7 April 1948

World Health Organization



191 Member States (as of September 2001)

Mission

"The objective of the World Health Organization shall be the attainment by all peoples of the highest possible level of health."

(WHO Constitution, Article 1)

Functions

"In order to achieve its objective, the functions of the Organization shall be:

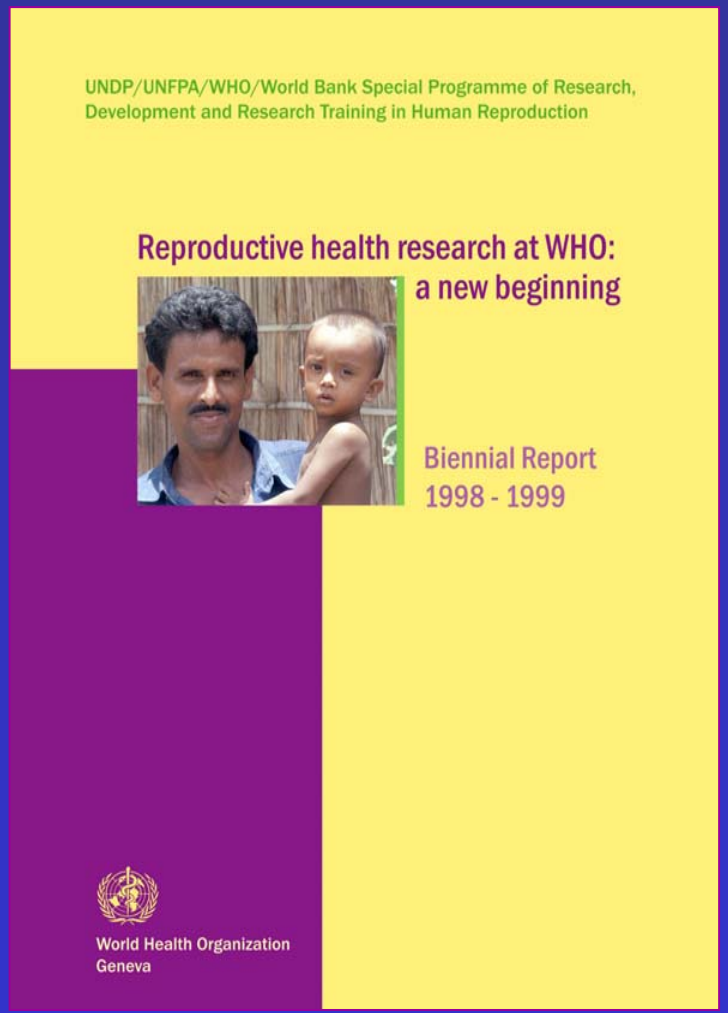
(a) to act as the directing and co-ordinating authority on international health work;

...

(n) to promote and conduct research in the field of health;

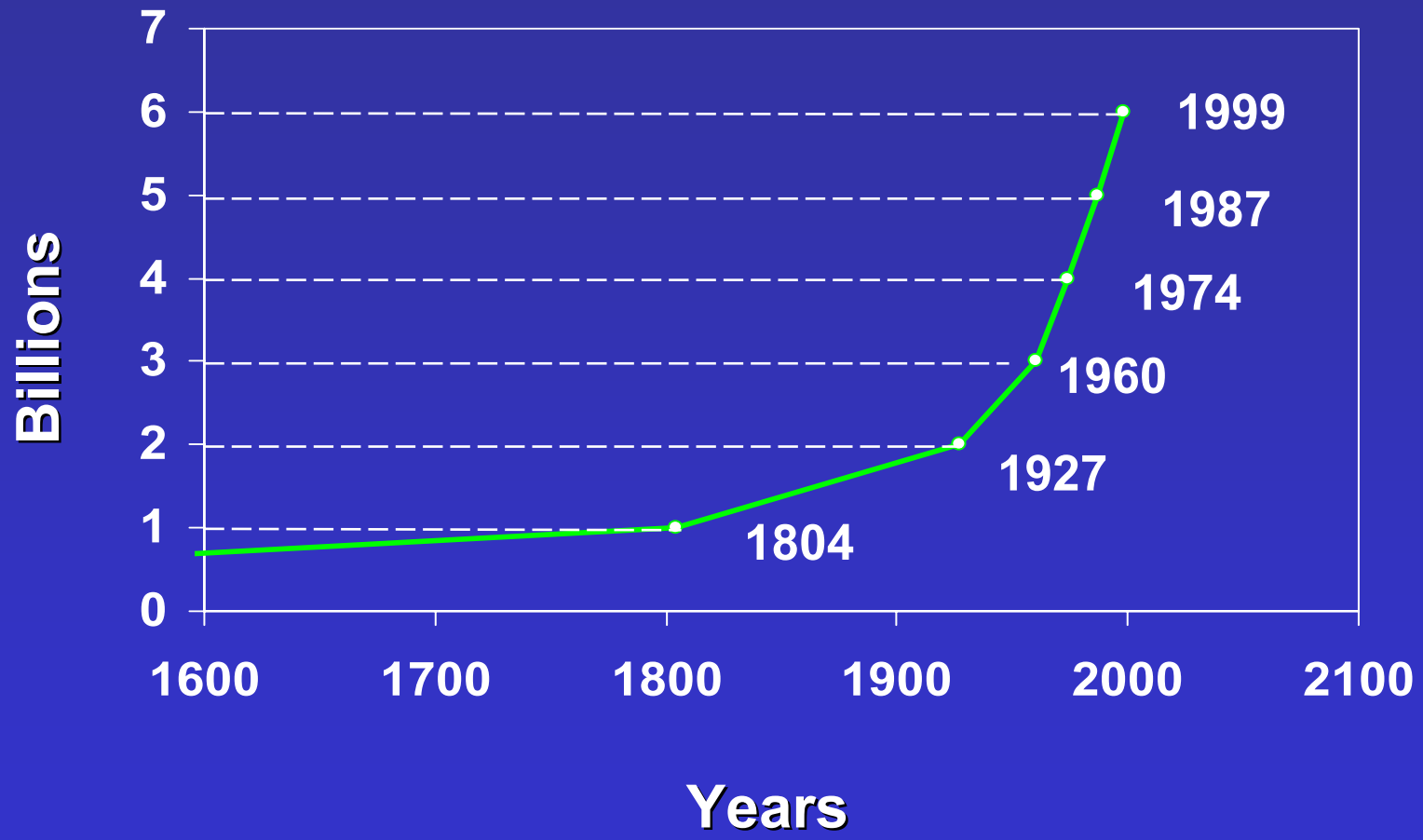
..."

(WHO Constitution, Article 2)



"To coordinate, promote, conduct and evaluate international research in human reproduction."

Growth of total world population



The Programme's history

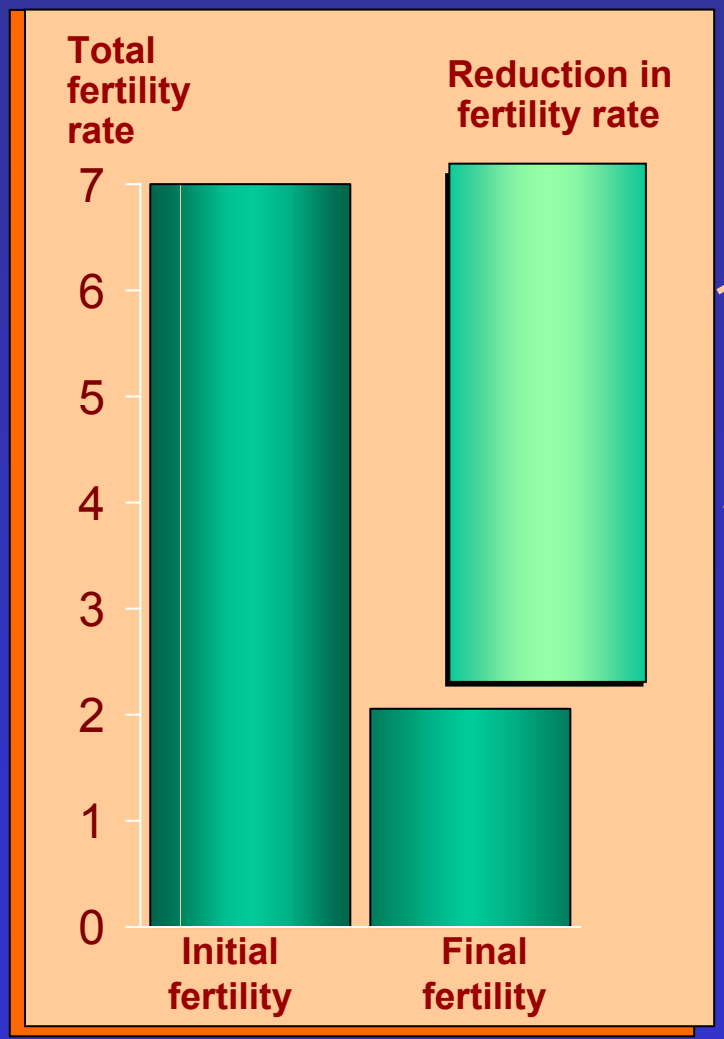
1971: Feasibility study

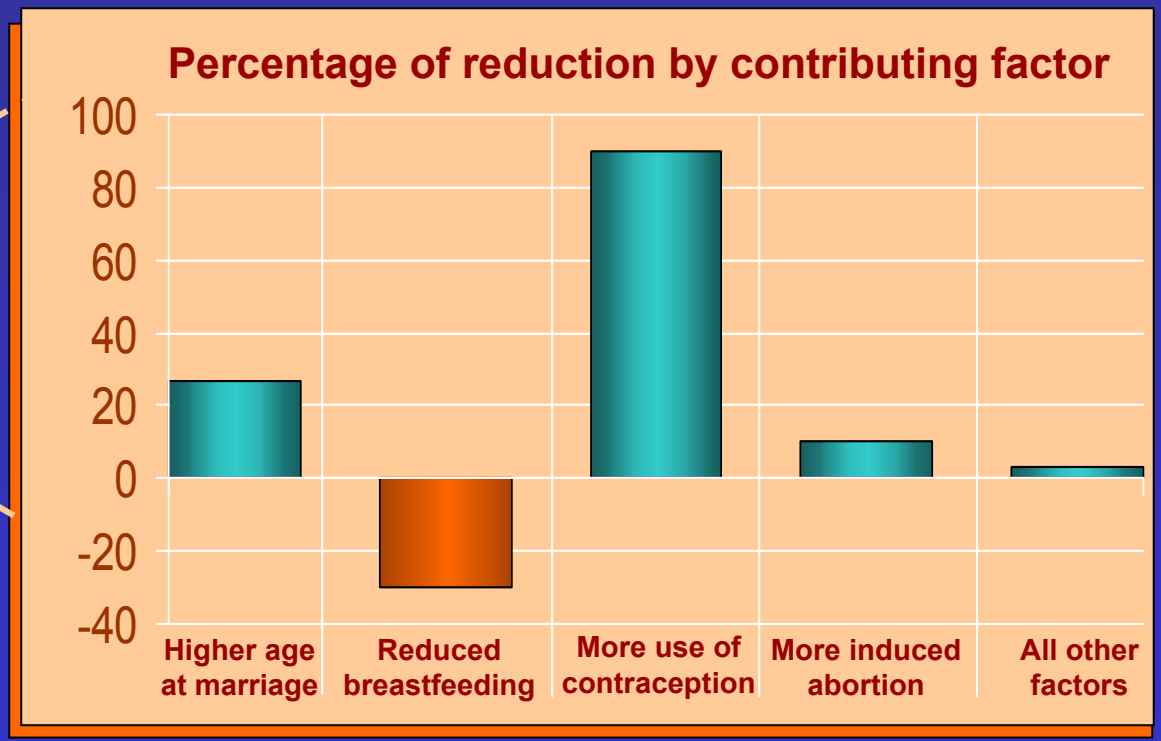
→ Expanded (Special) Programme of Research, Development and Research Training in Human Reproduction (HRP)

1972-1988: WHO Special Programme

1988-present: UNDP/UNFPA/WHO/World Bank cosponsored Special Programme

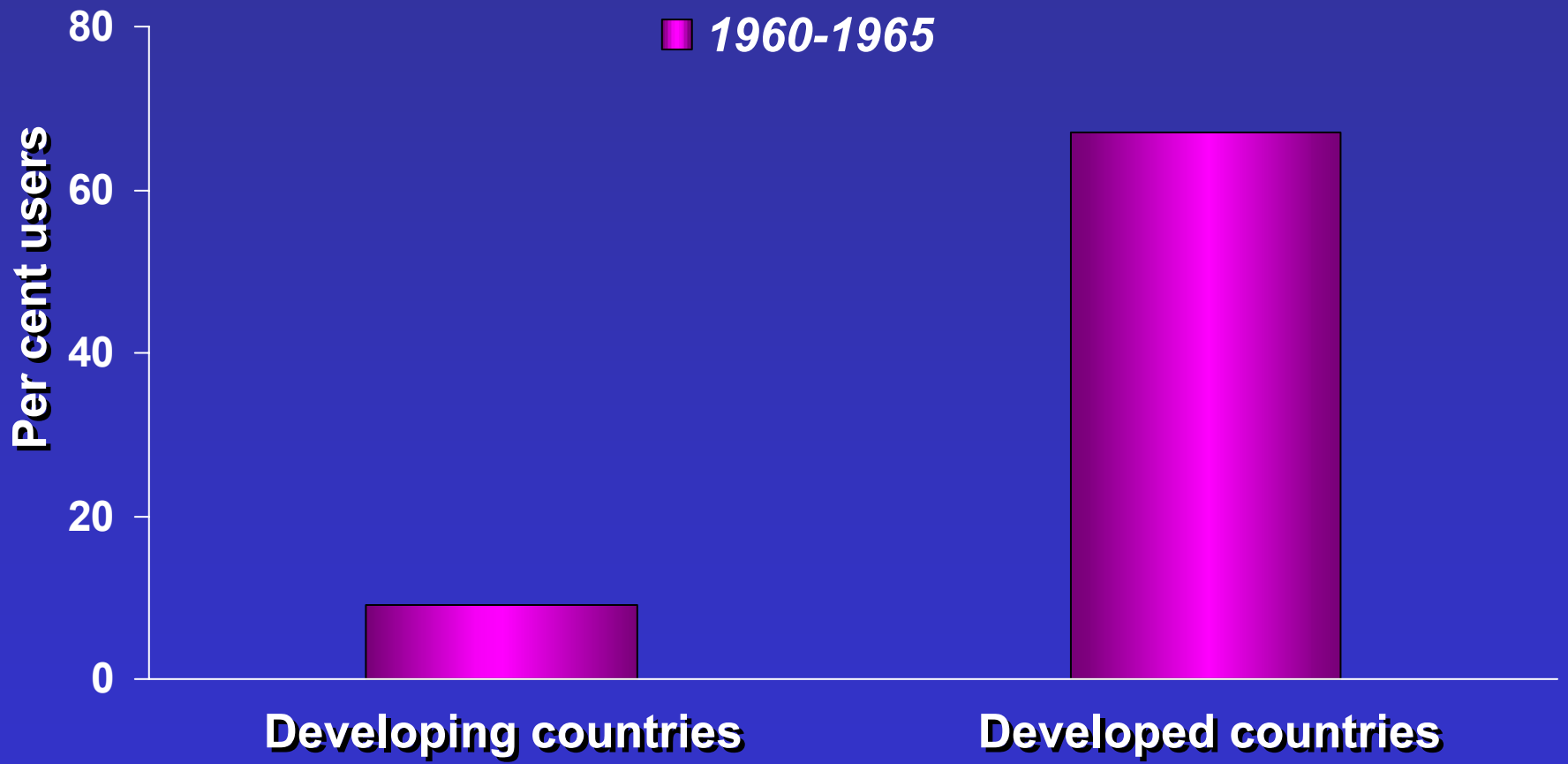
Factors contributing to fertility decline





(Source: World Bank, 1984)

Trends in use of contraception



(Source: United Nations, 1991 and 1999)

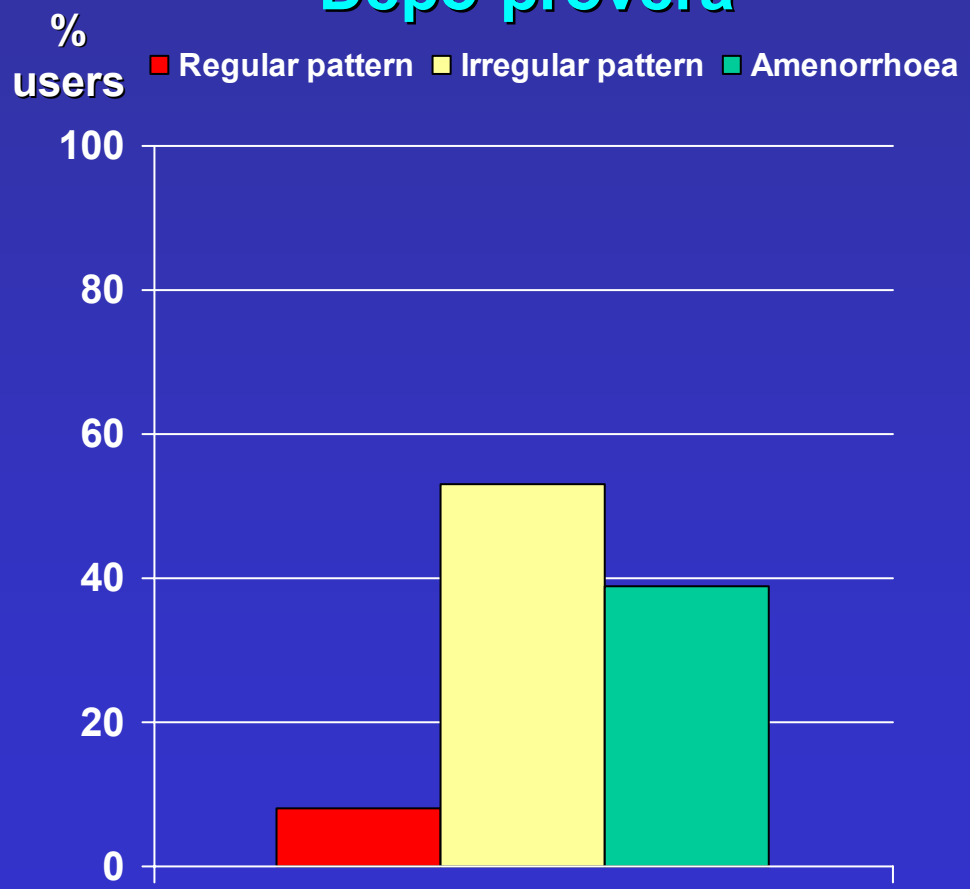
Once-a-month injectables developed by the Programme

Mesigyna® : **50 mg norethisterone enantate + 5 mg estradiol valerate**

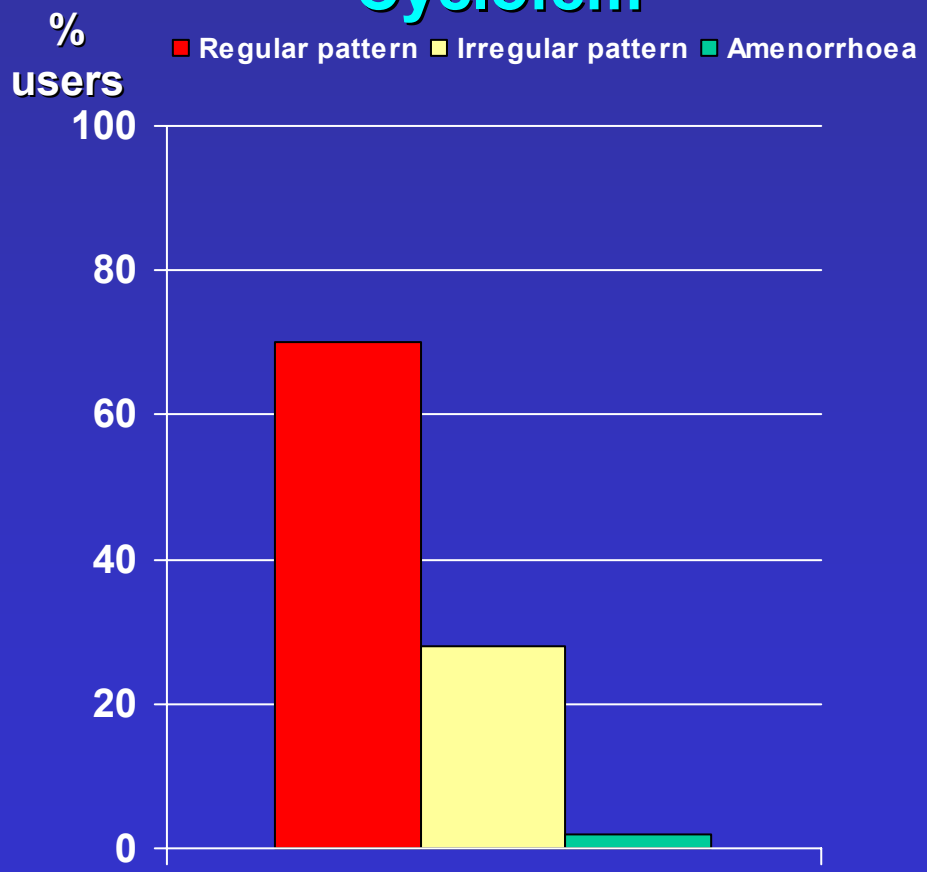
Cyclofem® : **25 mg medroxyprogesterone acetate + 5 mg estradiol cypionate**

Bleeding patterns experienced by injectable users at 1 year of use

Depo-provera

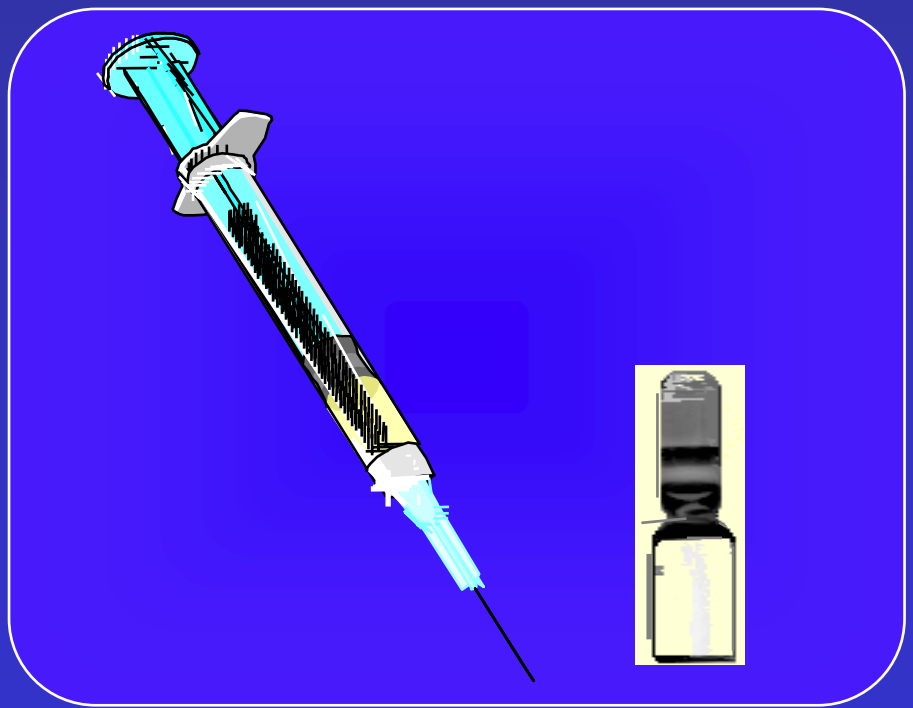


Cyclofem



Once-a-month injectables for women

Mesigyna



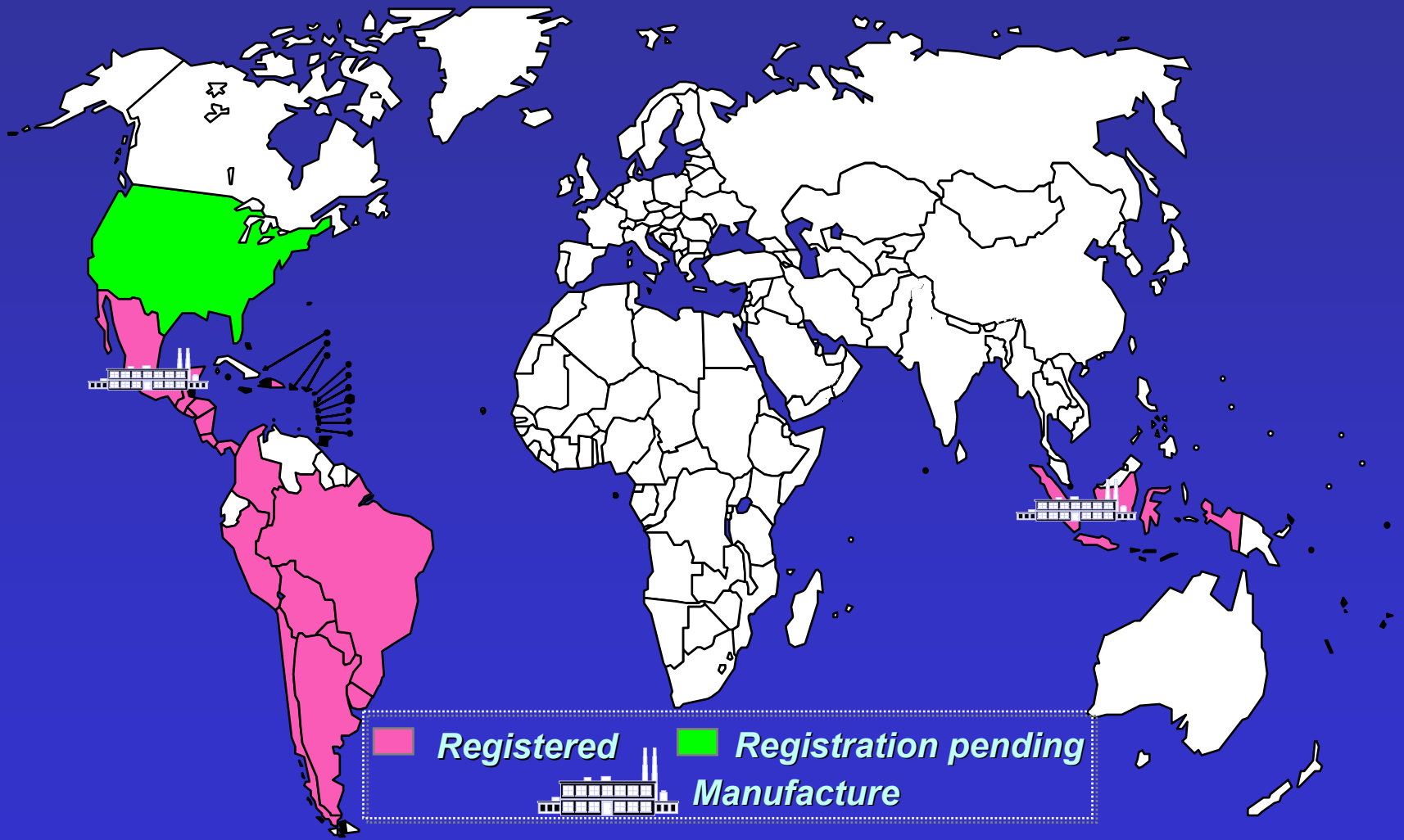
- licensed to **Schering**

  (low public sector price)

- currently registered in
  - *Caribbean and Latin America (44 countries)*
  - *Egypt*
  - *Kenya*
  - *Tanzania*
  - *Turkey*

CYCLOFEM

25 mg medroxyprogesterone acetate + 5 mg estradiol cypionate



Levonorgestrel for emergency contraception: efficacy

Group	Number of women	Observed pregnancies	Pregnancy rate (%)	95% CI
Yuzpe	979	31	3.2	(2.2, 4.5)
LNG	976	11	1.1	(0.6, 2.0)

Relative risk (RR) of pregnancy for LNG compared with Yuzpe:

RR	95% CI
0.36	(0.18, 0.70)

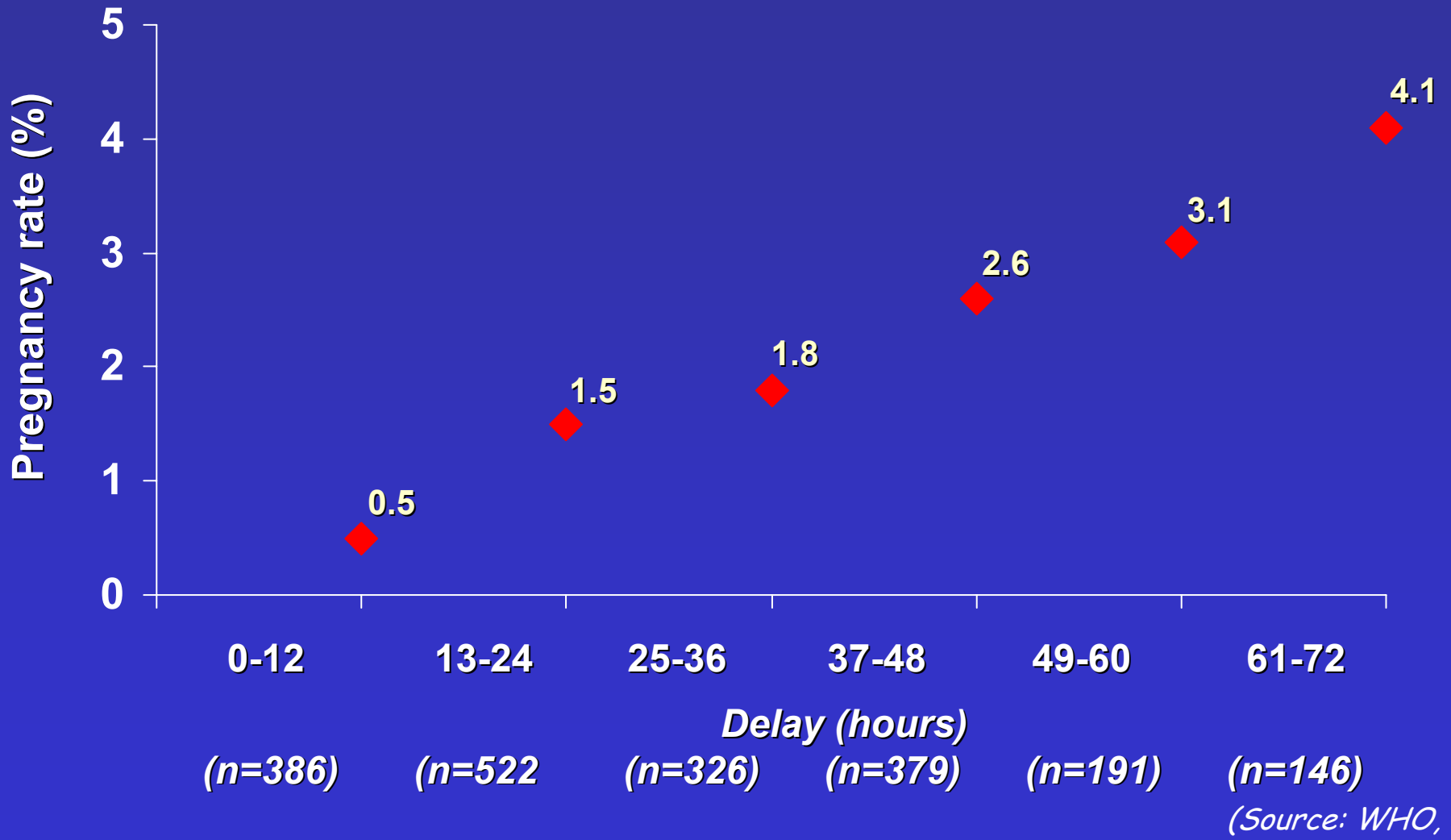
(Source: WHO, 1998)

Levonorgestrel for emergency contraception: side-effects

	Yuzpe	LNG	
Side effect	**No. (%) of cases**	**No. (%) of cases**	**p-value**
Nausea	494 (50.5)	226 (23.1)	<0.01
Vomiting	184 (18.8)	55 (5.6)	<0.01
Headache	198 (20.2)	164 (16.8)	0.06
Dizziness	163 (16.7)	109 (11.2)	<0.01
Fatigue	279 (28.5)	165 (16.9)	<0.01

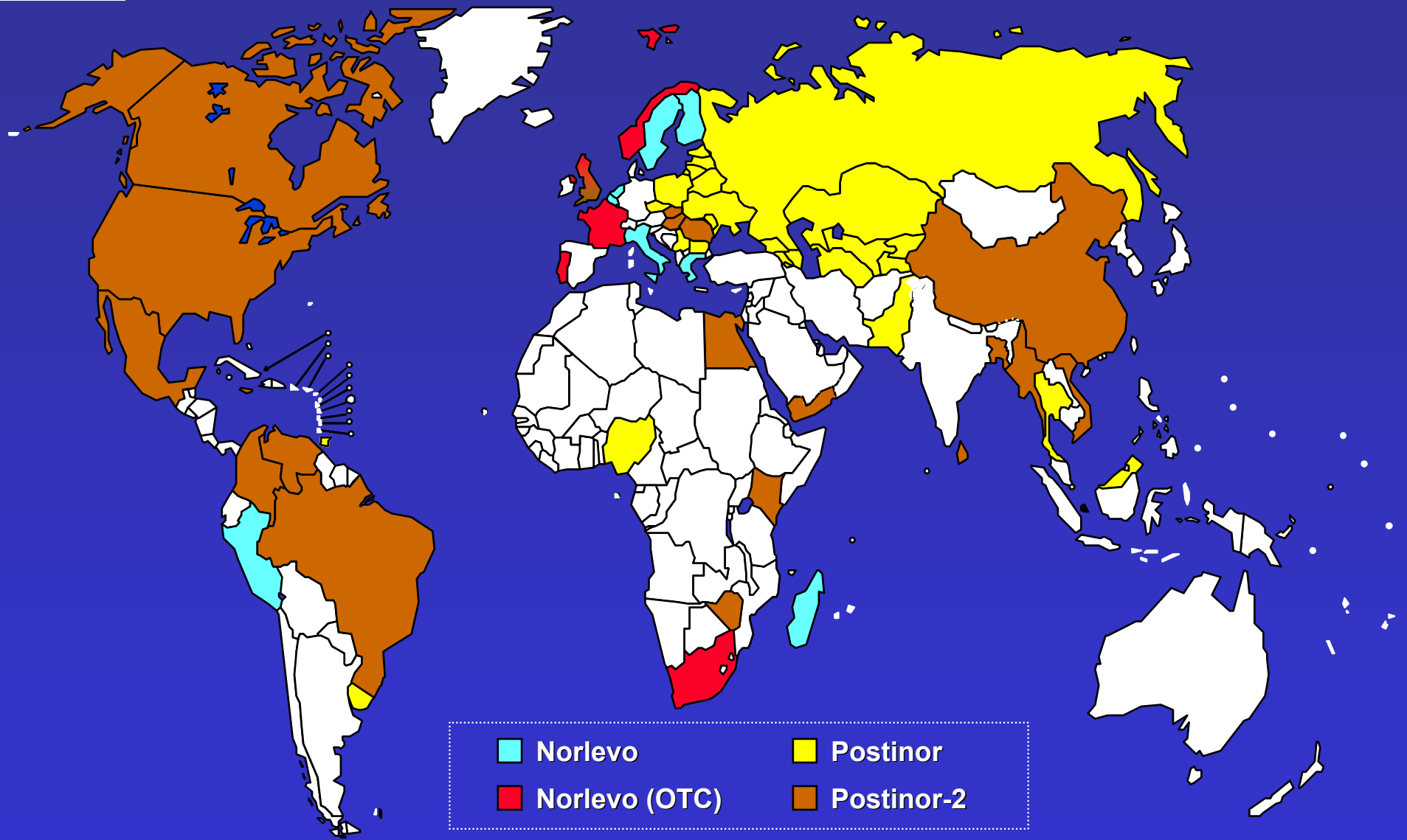
(Source: WHO, 1998)

Effect of delay on pregnancy rates



(Source: WHO, 1999)

Availability of levonorgestrel preparations for emergency contraception (as of end March 2001)



Mifepristone research

- pregnancy termination (first and second trimester)
- cervical ripening
- menses induction
- ovulation blocking
- luteal contraception
- emergency contraception

Mifepristone for emergency contraception

	Mifepristone	Yuzpe regimen
Number of women treated	597	589
Expected number of pregnancies	35	34
Observed number of pregnancies	0 (3)	9

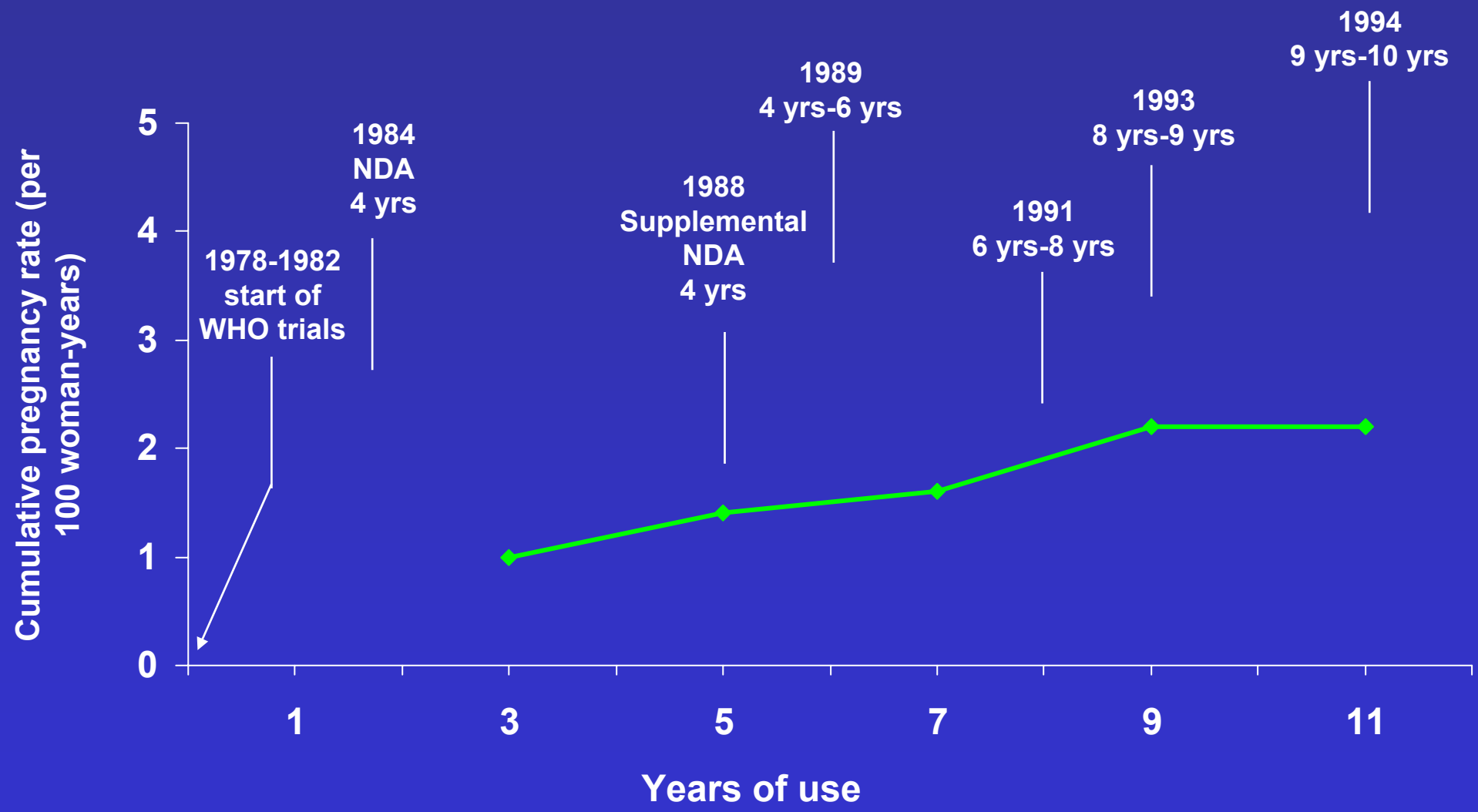
(after Glasier et al., 1992 and Webb et al., 1992)

Efficacy of three doses of mifepristone in emergency contraception

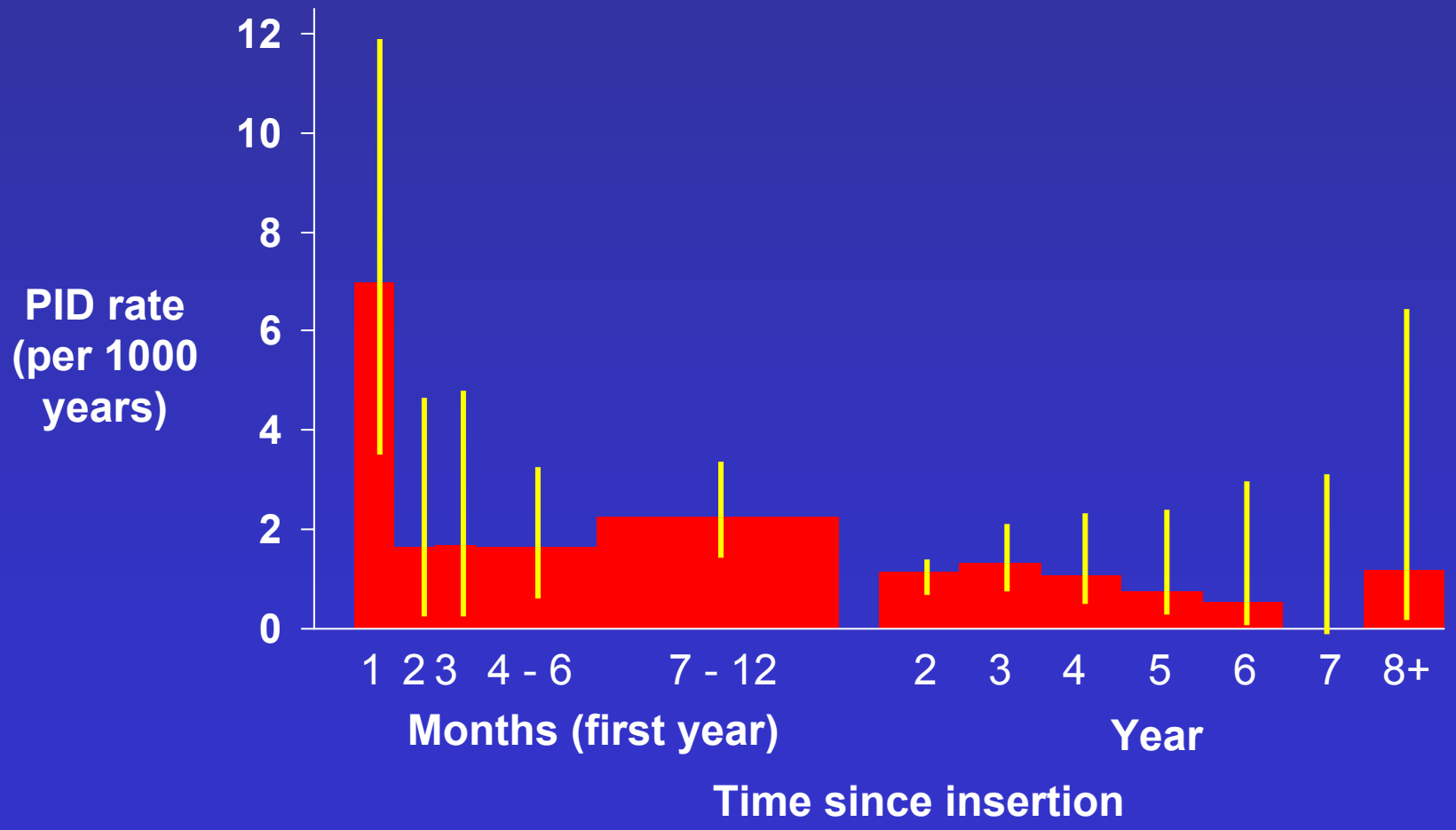
Dose	Number of women	Number of observed pregnancies	Pregnancy rate	Number of expected pregnancies*	Efficacy (%)
10 mg	565	7	1.2	48	85
50 mg	560	6	1.1	43	86
600 mg	559	7	1.3	45	84
ALL	1684	20	1.2	136	85%

* according to Trussell et al., Contraception 1998; 57:363-69

TCu 380A IUD : US FDA APPROVALS



PID INCIDENCE RATE
(95% confidence interval)



Important new knowledge about safety/efficacy of hormonal fertility-regulating methods

- Oral contraceptives and cancer (benefits and risks)
- Oral contraceptives and cardiovascular disease
- Oral contraceptives and breast cancer
- DMPA and breast cancer
- Safety and efficacy of mifepristone
- Third-generation oral contraceptives and venous thromboembolism
- Long-term safety and efficacy of Norplant®

Post-marketing surveillance of Norplant®

Cumulative pregnancy rate at five years

	Norplant®	Copper IUD	Non-Copper IUD	Sterilization
Woman-years	32,977	24,289	2619	6905
Events	88	215	77	10
Rate (SE)	1.46 (0.16)	4.19 (0.28)	13.00 (1.39)	0.72 (0.23)

(Source: WHO, 2001)

Post-marketing surveillance of Norplant®

Selected side-effects
(Rate ratios Norplant® /controls adjusted for clinic and age)

Bleeding disturbances				
- excessive /irregular, hospitalised	Norplant®			
	IUD	1.14	(0.39, 3.31)	0.82
	Sterilisation	2.33	(0.28, 19.7)	0.44
- excessive/irregular	Norplant®			
	IUD	2.72	(2.49, 2.97)	P<0.001
	Sterilisation	11.39	(8.49, 15.3)	P<0.001
- amenorrhoea	Norplant®			
	IUD	4.80	(3.88, 5.95)	P<0.001
	Sterilisation	6.69	(4.07, 11.0)	P<0.001
Anaemia				
Haemoglobin <10g/dl	Norplant®			
	IUD	0.78	(0.53, 1.13)	0.19
	Sterilisation	1.10	(0.40, 3.02)	0.85

(Source: WHO, 2001)

Main areas of ongoing research in fertility regulation

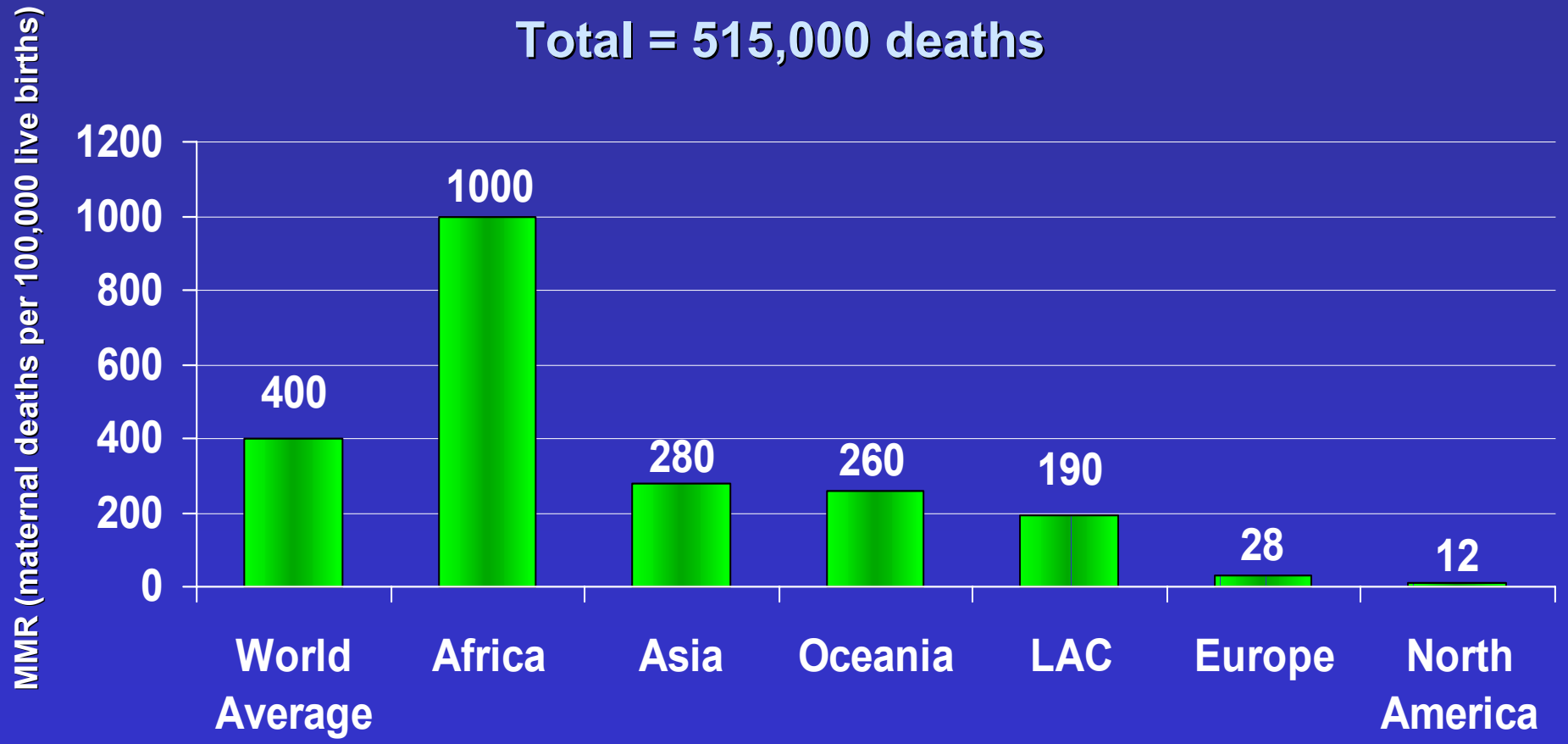
Method development

1. Male hormonal contraception
2. Improved progestogen-only injectable for women
3. Dual protection methods (non-latex male condom; female condom; microbicides/spermicides)
4. Immunocontraception

Surveillance

1. Long-term IUD safety and efficacy
2. Hormonal contraceptives and bone mineral density
3. Hormonal contraceptives and HIV
4. Contraceptive use and cervico-vaginal HIV shedding
5. Male condom efficacy against STIs
6. Female condom efficacy against pregnancy and STIs

Estimated maternal mortality ratios, by region, 1995



(WHO/UNICEF/UNFPA,2001)

Interventions evaluated during 1999-2000 with leading/active role of the Programme

	CENTRES	WOMEN	STATUS
Antenatal care	5	24,678	Published (2001)
Postpartum haemorrhage	9	18,530	Published (2001)
Caesarean section	5	149,206	For publication
Treatment of pre-eclampsia	28	10,000	Ongoing
Prevention of pre-eclampsia	6	8,500	Ongoing

Primary outcome	New model	Standard model	Adjusted odds ratio (95% CI)
Low birthweight (<2500g)	7.68 %	7.14 %	1.06 (0.97-1.15)
Pre-eclampsia/ eclampsia	1.69 %	1.38 %	1.26 (1.02-1.56)
Postpartum anaemia	7.59 %	8.67 %	1.01[a]
Treated urinary tract infection	5.95 %	7.41 %	0.93 (0.79-1.10)

[a] Confidence interval not computed because of heterogeneity between sites and strata

WHO Misoprostol Trial

Primary outcomes

Outcome	Misoprostol	Oxytocin	RR (95% CI)
Blood loss ≥ 1000 ml	4.0 %	2.9 %	1.39 (1.19-1.63)
Need for additional uterotonics	15.2 %	10.9 %	1.40 (1.29-1.51)

WHO Misoprostol Trial
Side-effects

Side-effect	Misoprostol	Oxytocin	RR (95% CI)
Any shivering	17.6 %	5.0 %	3.48 (3.15-3.84)
Severe shivering	1.3 %	0.2 %	8.58 (4.93-14.91)
Body temperature >38°C	6.1 %	0.8 %	7.17 (5.67-9.07)
Nausea	0.8 %	0.4 %	2.27(1.52-3.39)
Vomiting	0.7 %	0.3 %	2.64 (1.67-4.18)
Diarrhoea	0.4 %	0.1 %	4.38 (2.03-9.43)

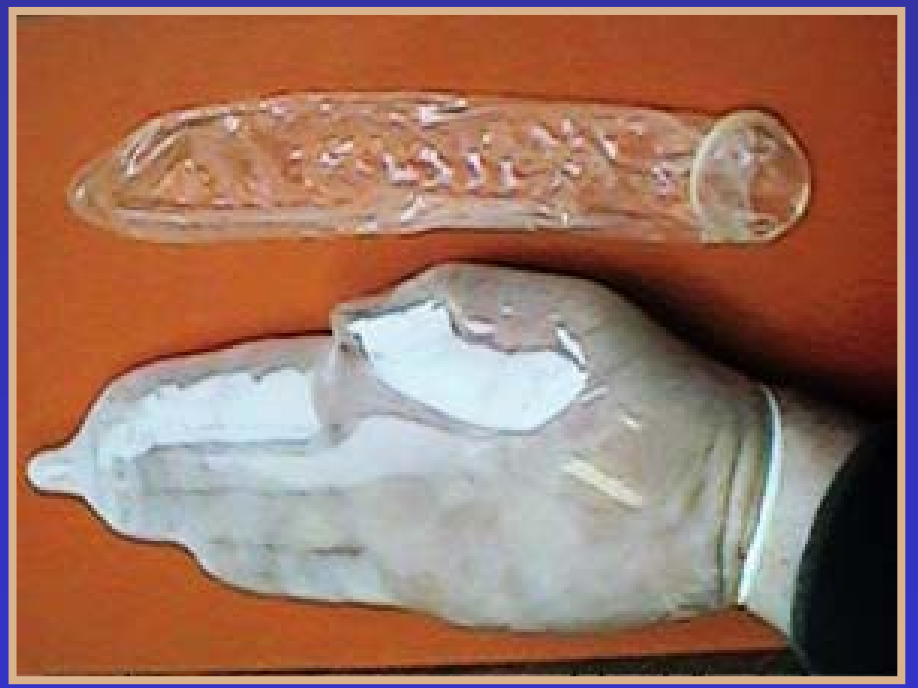
Acceptability of Male Condom : Key Findings

Countries: Kenya, Nigeria, Tanzania, Uganda, Zambia

Key findings:

- use of condom within marriage is constrained by lack of interspousal communication and misperceptions about safety of condom
- men report loss of pleasure, inconvenience and embarrassment as reasons for not using it
- potential for increased condom use, especially outside marriage and for prevention of STD/HIV

Non-latex Male Condom



Female Condom

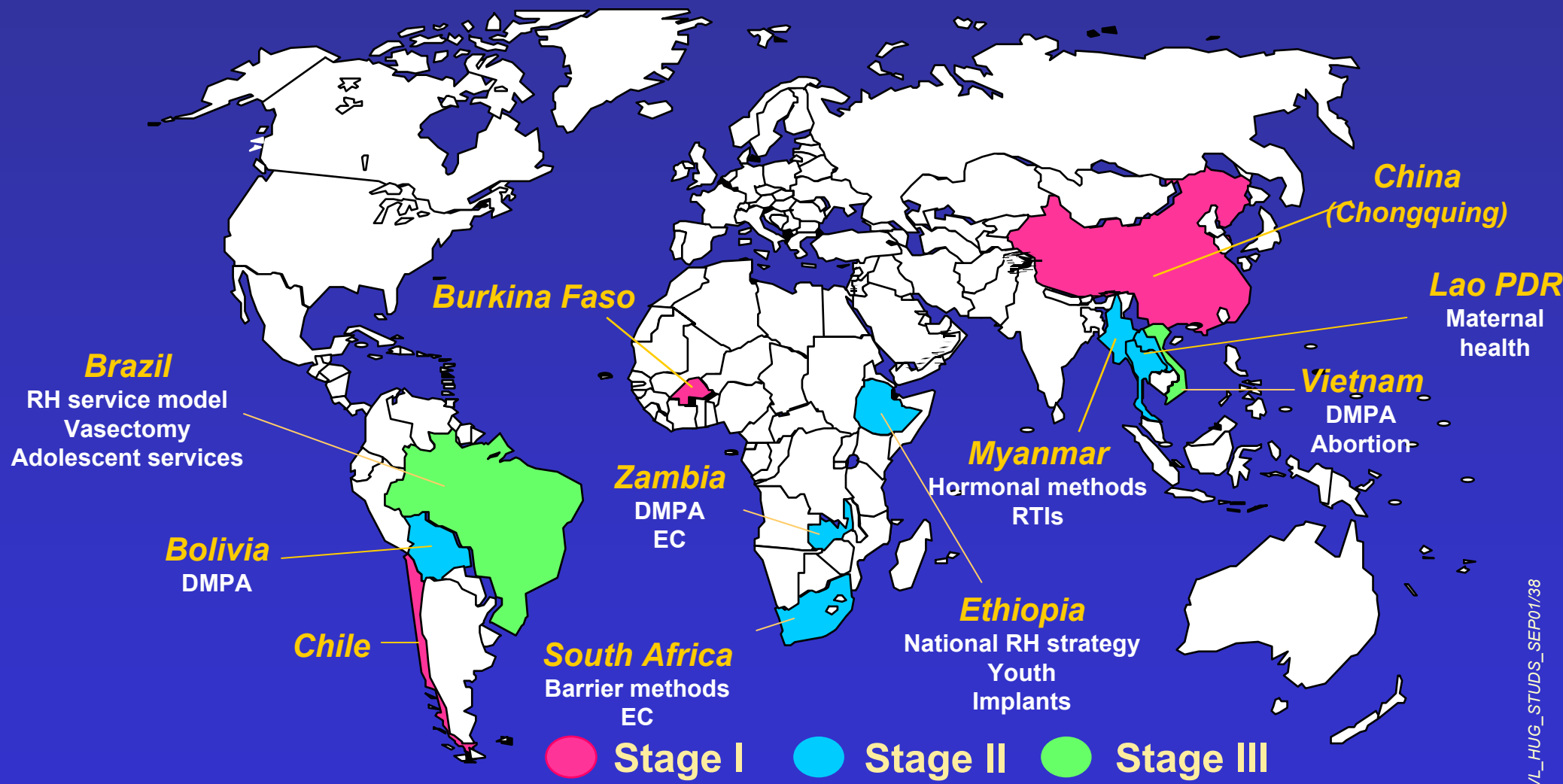
Activities in HIV during 2000

- male and female condoms
- dual protection
- COL-1492 (nonoxynol-9)
- cellulose sulphate as microbicide
- nevirapine and prevention of MTCT of HIV
- infant feeding and MTCT of HIV
- male circumcision and HIV transmission
- post-exposure prophylaxis

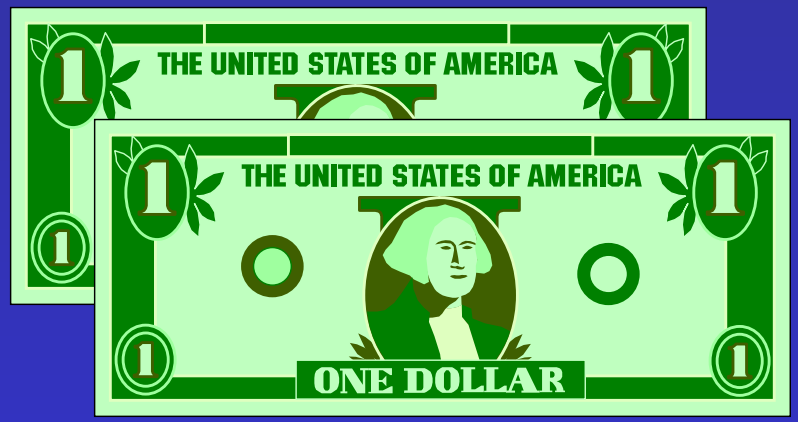
Global research initiatives in social sciences

1. Attitudes towards male condom use
2. Determinants and consequences of induced abortion
3. Role of men in reproductive health
4. Fertility regulation in the era of HIV/AIDS
5. Adolescent sexual and reproductive health
6. Quality of care in reproductive health

Broadening choices and improving quality of care of reproductive health services



Emphasis on Research Capability Strengthening



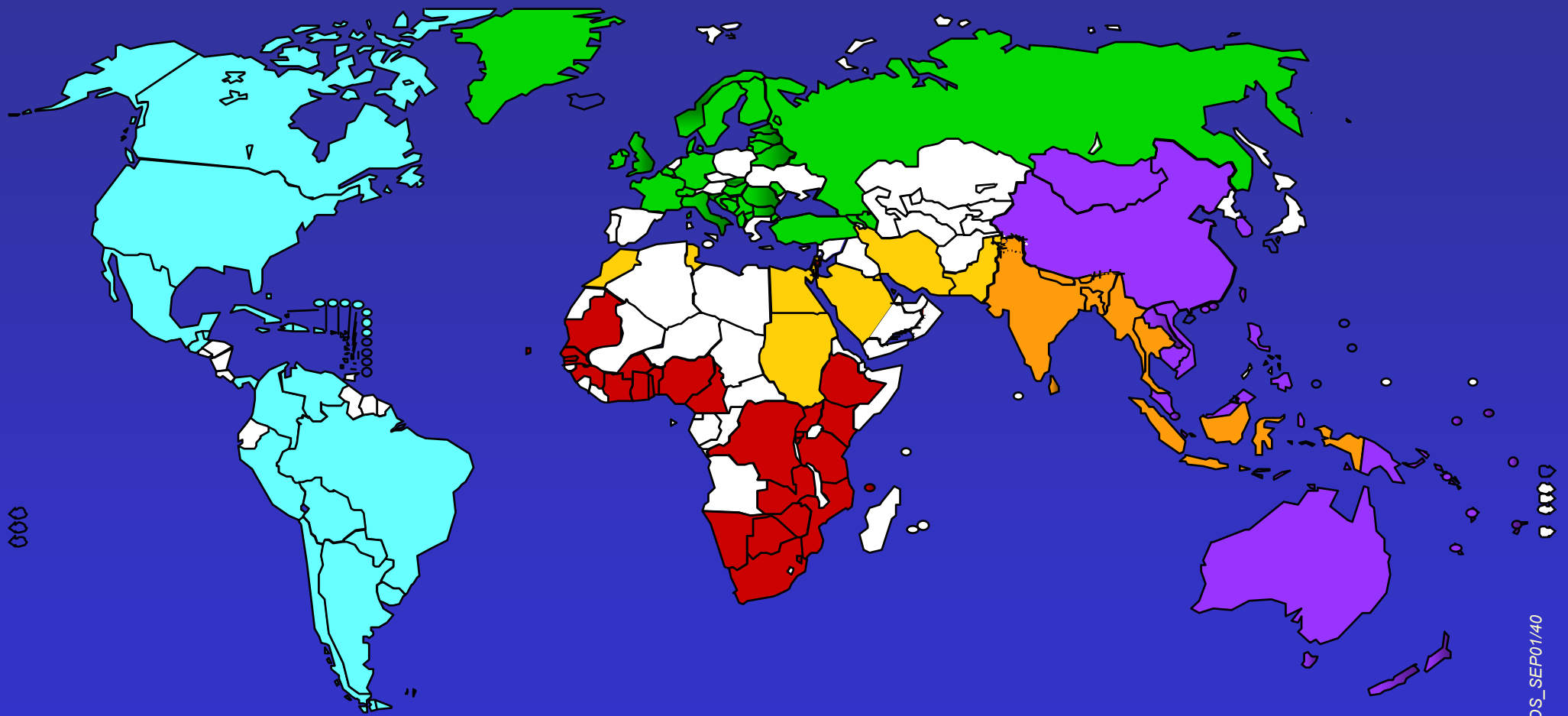
US$ 2

Research and Development

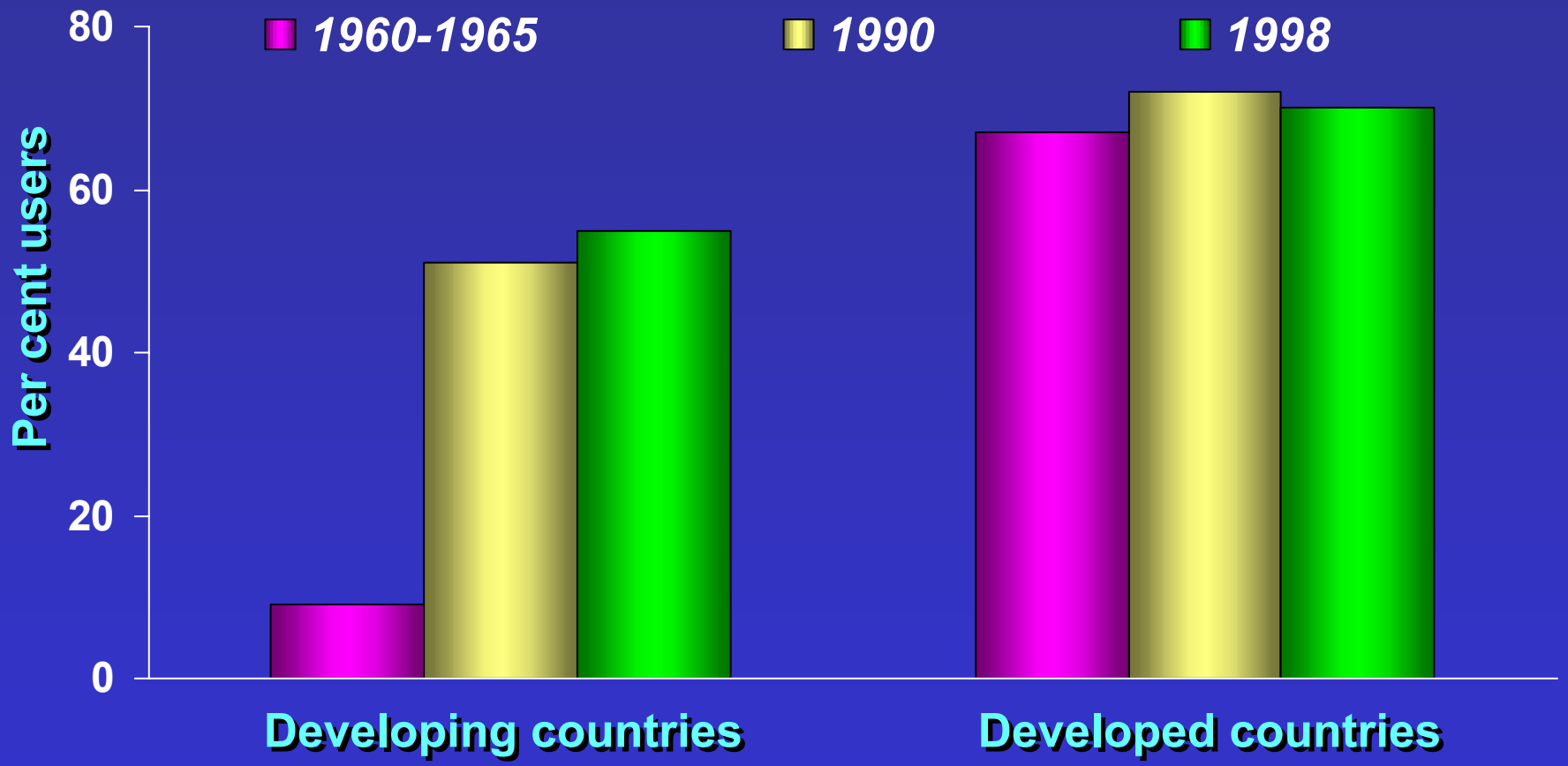
US$ 1

Research Capability Strengthening

Countries Collaborating with the Programme in the year 2000 (N = 81 countries)

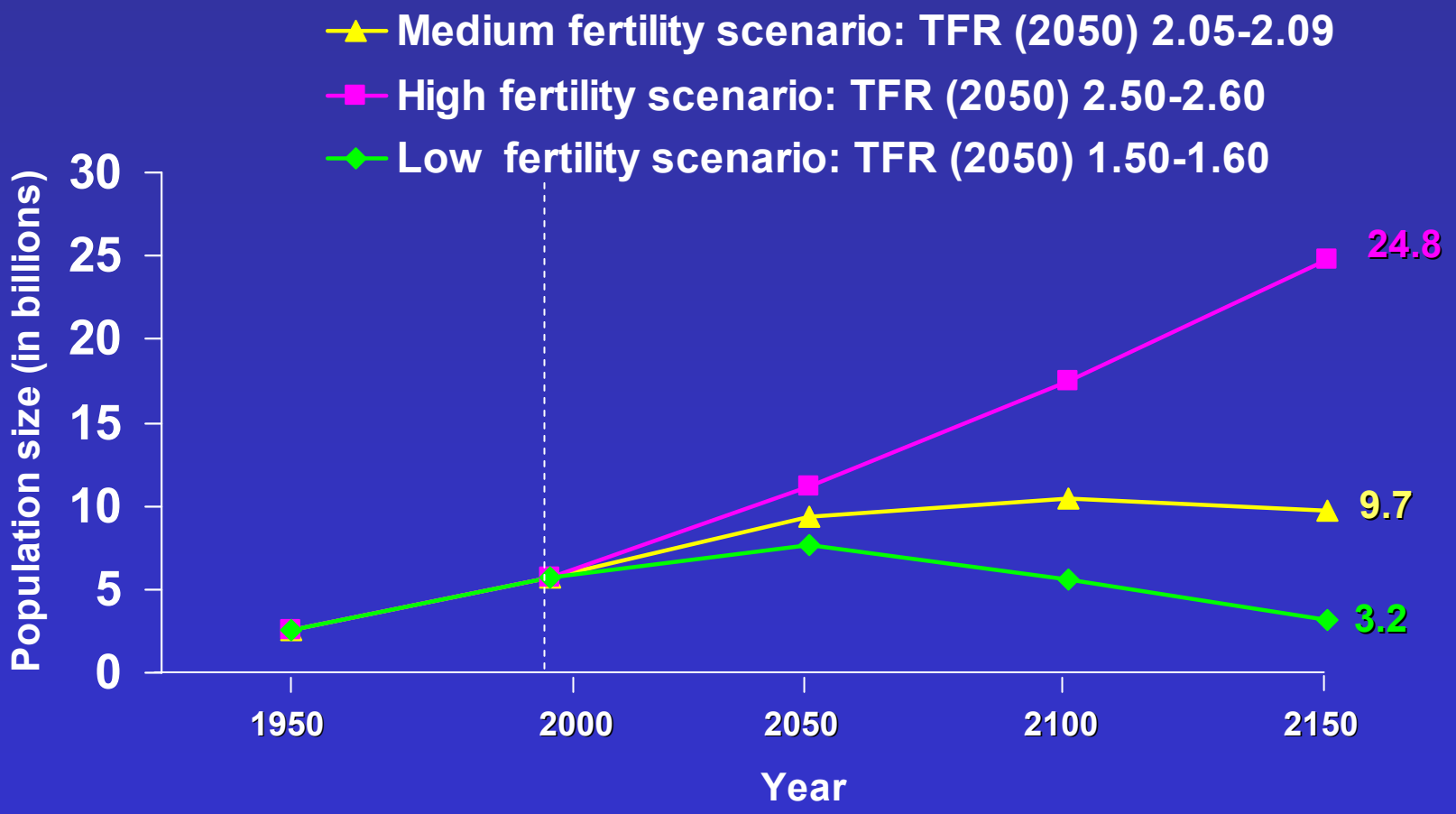


Trends in use of contraception



(Source: United Nations, 1991 and 1999)

World population size according to the main fertility scenarios, 1950-2150

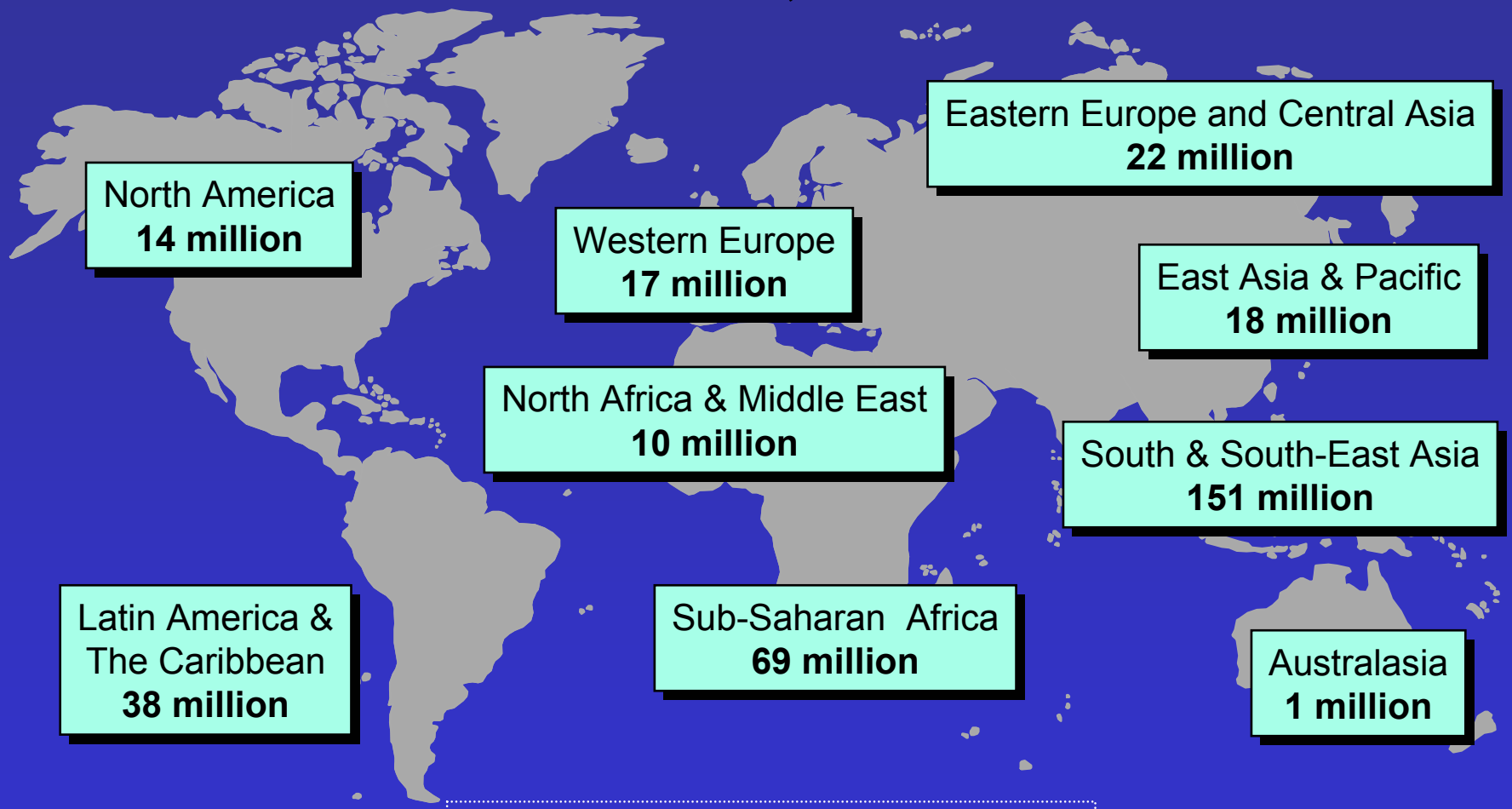


(Source: United Nations, 2000)

Increasing contraceptive prevalence

1. Better access to family planning services
2. Improved quality of care in service provision
3. Wider choice of acceptable and affordable methods
4. Availability of new and improved methods

Estimated new cases of curable STI* among adults, 1999



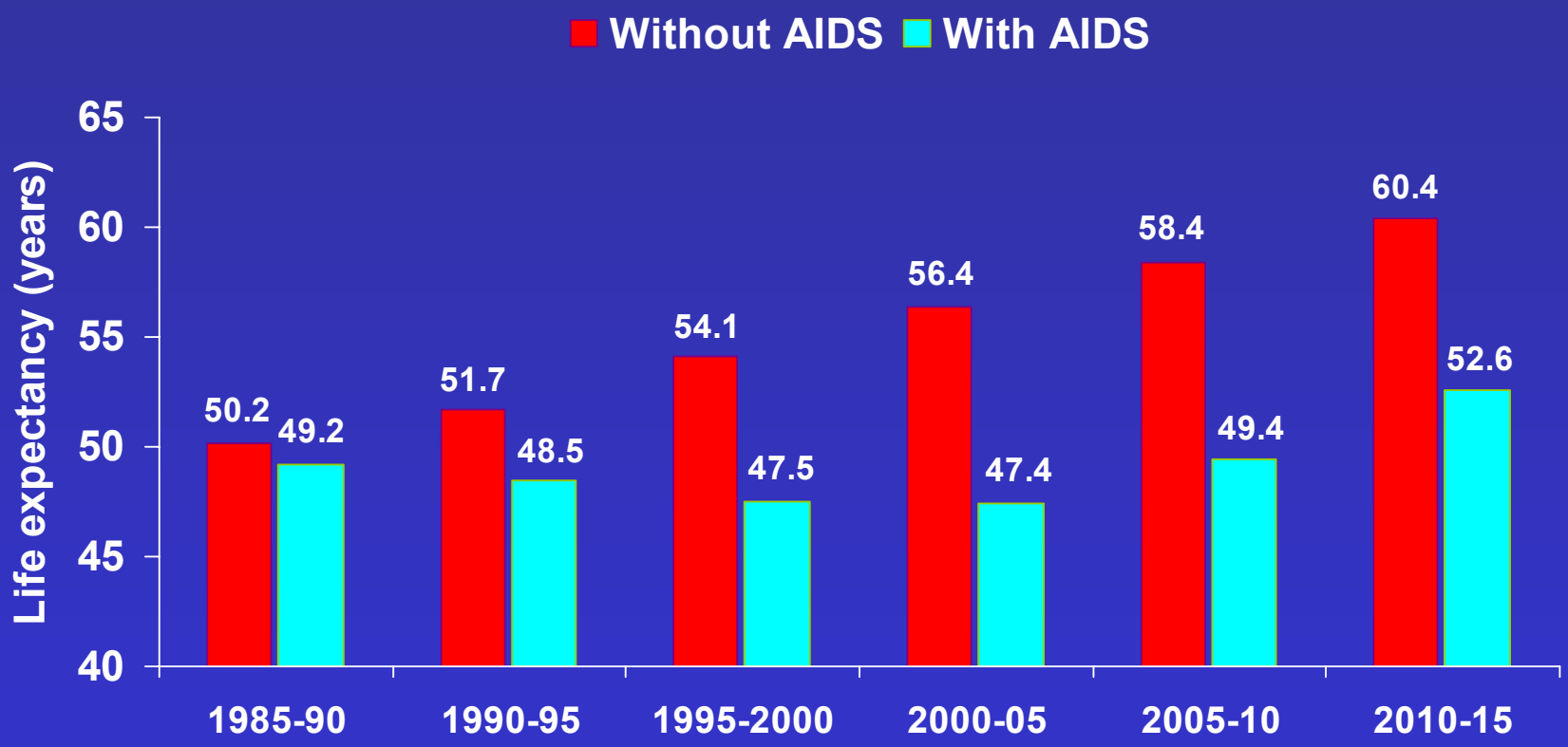
Global total: 340 million

*** gonorrhoea, chlamydial infection, syphilis and trichomoniasis**

About 15 000 new HIV infections a day in 2000

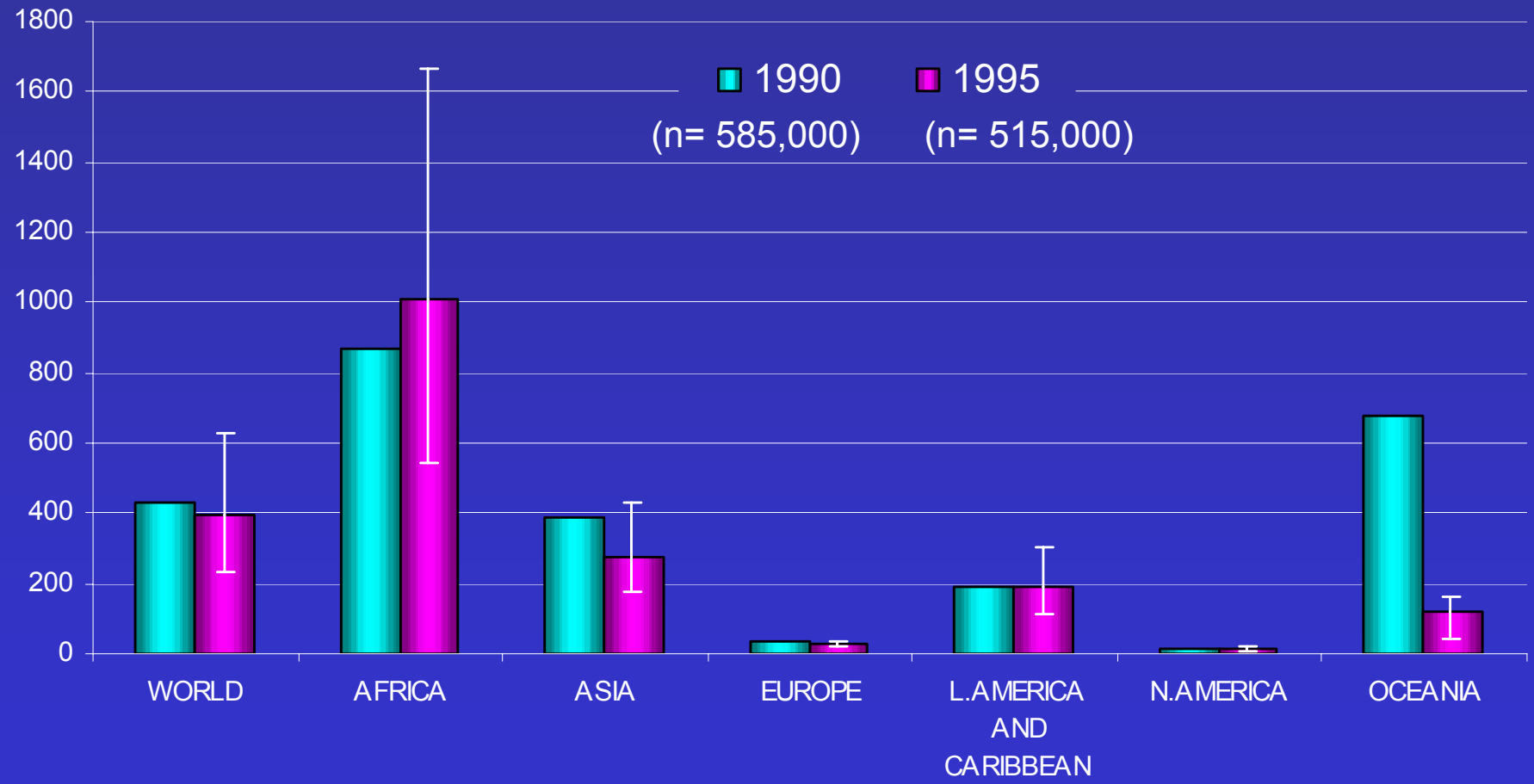
- More than 95% are in developing countries
- About 1700 are in children under 15 years of age
- About 13 000 are in persons aged 15 to 49 years, of whom:
  - 47% are women
  - over 50% are 15-24 year olds

Life expectancy at birth in 29 African countries with and without AIDS



(Source: UNAIDS, 2000)

Estimated maternal mortality ratios (per 100 000 live births)



"Eradicating polio, curbing the tobacco epidemic, stimulating research in the developing world — this is our corporate strategy in practice."

Dr Gro Harlem Brundtland, Statement
to the Executive Board at its 105th session,
29 January 2000