Expanding access to injectable contraception

Current use of injectables worldwide

The first injectable contraceptive became available in the mid-1960s. This was the three-monthly injectable depot-medroxyprogesterone acetate (DMPA) given intramuscularly at a dose of 150mg. By now, eight injectable preparations are used by an estimated 32 million women, i.e about 3% of contraceptive users worldwide. The majority, estimated at 26 million women, use DMPA; about 6 million women use once-a-month combined injectables; and less than 1 million women use the progestin-only injectable northisterone enanthate (NET-EN). Injectables currently available are listed on Table 1.

There are great regional variations in injectable contraceptive use, with overall prevalence of these methods being <1% in the developed world, vs about 3% in the developing world. Within region, there are marked differences (Figure 1). In some countries of sub-Saharan Africa, Latin America and south-east Asia, injectable use represents a significant share of modern method use (e.g. as much as 71% in Ethiopia) (Figure 2).

Efficacy of injectable methods

Injectable contraceptives are among the most effective contraceptive methods, after IUDs, implants and sterilization (Table 2).

The injection schedule needed to maintain effectiveness is shown for each method in Table 1. Of note, recent data have allowed to extend the re-injection window of DMPA to four weeks beyond the three months injection interval.

Eligibility / risk

WHO guidance recommends that, for persons who are presumed to be healthy, screening for eligibility to use an injectable contraceptive should include a medical history and blood pressure measurement before initiation. However, in settings where blood pressure measurement is unavailable, often pregnancy morbidity and mortality risks are high and hormonal methods are among the few methods available. In such settings, injectables should not be denied because blood pressure cannot be measured.

Safety among healthy women

In healthy women, pregnancy needs to be ruled out before initiation of injectables to avoid possible fetal exposure in very early pregnancy.

For postpartum women, combined injectable contraceptives should not be given during the first 3 weeks postpartum because of a concern of increased risk of thrombosis.

For postpartum lactating women, initiation of injectable contraception should not be before six weeks for progestogen-only methods (DMPA, NET-EN), and before six months for combined injectable methods.

For adolescent girls (below 18 y/o), there is a concern that prolonged use of progestogen-only injectables, particularly DMPA, may prevent them from reaching peak bone mass, putting them at risk of osteoporosis later in life. However, the overall advantages of using DMPA at that age outweigh the risks.

Safety among women with chronic conditions

Women whose health may be put at risk by receiving an injectable contraceptive are those with conditions labelled 3 and 4 in Table 3. They include women with cardio-vascular disease (Ischemic heart disease, DVT/PE, stroke, migraine headaches, hypertension) or at risk (early postpartum, smoker and above 35 y/o, diabetic), women with breast cancer (current or past) and those with certain liver diseases.

The prevalence of these conditions varies between regions and these risks need to be compared to those of an unwanted pregnancy and of maternal mortality in a given setting. Table 4 and Figure 3 illustrate the great variations in causes of mortality and disease burden between regions and between developed and developing countries, and the relative importance of maternal causes vis-à-vis cardiovascular disease and cancer, among women of reproductive age. Examples of the variety of country situations are given in Table 5.

Means of expanding access to injectable contraception

A number of technological developments can make injections safer for administration, whether by health personnel, trained community workers or the women themselves:

- sub-cutaneous injections, which have less complications than intra-muscular injections
- non-reusable disposable syringes

Distribution by community health workers needs special attention to:

- the possibility that a woman is already pregnant (or seeking an abortion by using an injectable)
- the screening of women with pre-existing conditions or on medications
- the need for counselling for side-effects (in particular: vaginal bleeding irregularities, amenorrhea, weight gain, delay in return to fertility)
- the safety of injections to the woman and to the health worker
- the possible confusion between different injectables - provided by public and private sectors

To complement pre-service and in-service training, a number of job aids are available to support community workers providing injectables:

- medical eligibility criteria wheel to screen for eligibility
- pregnancy checklist
- simplified material for the management of side-effects (bleeding, amenorrhea, weight changes, etc)

Table 1. *Formulation, Injection Schedule, and Availability of Injectable Contraceptives*

Formulation	*Developer*	*Brand Name/ Manufacturer*	*Injection Schedule*	*Availability*
1 - *Progestin only: 150 mg depot medroxy-progesterone acetate (DMPA)*	*The Upjohn Company*	*Depo-Provera/Pfizer Megestron/Schering-Plough Various generic manufacturers*	*IM, every 3 months (can be up to 2 weeks early or 4 weeks late)*	*Registered in over 170 countries; available in both public and private sectors.*
2 - *Progestin only: 104 mg depot medroxy-progesterone acetate (DMPA-SC)*	*Pfizer*	*Depo-subQ provera 104*	*SC, every 3 months ± 2 weeks*	*Registered in USA and EU.*
3 - *Progestin only: 200 mg norethindrone (norethisterone) enanthate (NET EN)*	*Schering AG*	*Noristerat, Norigest/Bayer Doryxas/ Richter Gedeon Ltd.*	*IM, every 2 months ± 2 weeks*	*Registered in over 90 countries; available in both public and private sectors.*
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4 - *Progestin + Estrogen: 25 mg DMPA + 5 mg estradiol cypionate*	*The Upjohn Company, WHO*	*Cyclofem/Aplicaci6nes Farmaceuticas (Mexico); Cyclo Geston/PT Tunggal, PT Harssen, PT Triyasa Nagamas Farma (Indones.); Iran Hormone (Iran); Sun Pharmaceuticals (India)*	*IM, every 4 weeks ± 7 days*	*Registered in 18 countries; available in both public and private sectors.*
5 - *Progestin + Estrogen: 50 mg NET EN + 5 mg estradiol valerate*	*WHO*	*Mesigyna, Norigynon Bayer*	*IM, every 4 weeks ± 7 days*	*Registered in 35 countries.*
6 - *Progestin + Estrogen: 150 mg Dihydroxy Progesterone Acetophenide + 10 mg estradiol enanthate*	*Squibb Pharmaceutical Company*	*Perlutan, Topasel, Agurin Horprotal, Uno-Ciclol/ Various manufacturers in Latin America*	*IM, every month*	*Available in pharmacies in many Latin American countries and Spain; generally not available in public FP programmes.*
7 - *Half-dose: 75 mg Dihydroxy Progesterone Acetophenide + 5 mg estradiol enanthate*		*Anafertin, Yectames/ Various manufacturers in Latin America*	*IM, every month*	*Latin America*
8 - *Progestin + Estrogen: 250 mg 17∝-hydroxy-progesterone caproate + 5 mg estradiol valerate*	*Chinese researchers; Squibb Pharmaceutical Company*	*Chinese Injectable No. 1*	*IM, every month, 2 injections in first month*	*China*

Table 2

Method	% of women experiencing an unintended pregnancy within the first year of use		% women continuing at one year
	Typical use	Perfect use	
No method	85	85	
Spermicides	29	18	42
Withdrawal	27	4	43
Periodic abstinence	25	1-9	51
Cap	16-32	9-26	46-57
Sponge	16-32	9-20	46-57
Diaphragm	16	6	57
Condom - female	21	5	49
Condom - male	15	2	53
Combined pill and minipill	8	0.3	68
Combined hormonal patch (Evra)	8	0.3	68
Combined hormonal ring (Nuvaring)	8	0.3	68
DMPA (Depo-provera)	**3**	**0.3**	56
Combined injectable (Lunelle)	**3**	**0.05**	56
IUD - Copper-releasing (Paragard)	0.8	0.6	78
IUS - Levonorgestrel-releasing (Mirena)	0.1	0.1	81
Levonorgestrel implants	0.05	0.05	84
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

Source: Trussell J (2004)

Table 3. *WHO Eligibility Classification for use of progestin only (DMPA and NET-EN) and combined injectable contraceptives (products 4 and 5 in Table 1 only) by key health condition. Ref: WHO 2008*

		DMPA & NET-EN	*Combined injectables*
Age	• *menarche to 18 years*	*2*	*1*
	• *18-45 years*	*1*	*1*
	• *≥ 45 years*	*2*	*2*
Obesity	• *≥ 30 kg/m² body mass index*	*2*	*1*
	• *≥ 30 kg/m² body mass index and menarche to 18 years*	*2 (DMPA) 1 (NET-EN)*	*1*
Smoking	• *age < 35 years*	*1*	*2*
	• *age ≥ 35 years, light (< 15 cigarettes/day)*	*1*	*2*
	• *age ≥ 35 years, heavy (≥ 15 cigarettes/day)*	*1*	*3*
Parity	• *any*	*1*	*1*
Pregnancy		*N/A*	*N/A*
History of high blood pressure during pregnancy	*1*		*2*
Past ectopic pregnancy		*1*	*1*
Breast feeding	• *< 6 weeks post-partum*	*3*	*4*
	• *6 weeks to <6 month post-partum*	*1*	*3*
	• *≥ 6 months post-partum*	*1*	*2*
Post partum	• *< 21 days*	*1*	*3*
(in non-breast-feeding women)	• *≥ 21 days*	*1*	*1*
Post abortion	*(first trimester, second trimester, post-septic abortion)*	*1*	*1*
Vaginal bleeding patterns	• *irregular pattern without heavy bleeding*	*2*	*1*
	• *with heavy or prolonged bleeding (includes regular and irregular patterns)*	*2*	*1*
Unexplained vaginal bleeding (suspicious for serious underlying condition) - before evaluation		*3*	*2*
Severe dysmenorrhea		*1*	*1*
Breast disease	• *undiagnosed mass*	*2*	*2*
	• *benign breast disease*	*1*	*1*
	• *family history of breast cancer*	*1*	*1*
	• *current breast cancer*	*4*	*4*
	• *cancer - past and no evidence of current disease for 5 years*	*3*	*3*
Cervical intraepithelial neoplasia (CIN)		*2*	*2*
Cervical cancer (awaiting treatment)		*2*	*2*
Cervical ectropion		*1*	*1*
Benign ovarian tumours (including cysts)		*1*	*1*
Endometrial, ovarian cancer		*1*	*1*
Uterine fibroids		*1*	*1*
Endometriosis		*1*	*1*
Trophoblast disease (benign or malignant)		*1*	*1*
Prior pelvic surgery		*-*	*1*
Pelvic inflammatory disease (current or past, with or without subsequent pregnancy)		*1*	*1*
STIs (at increased risk, current or recent disease)		*1*	*1*
HIV/AIDS (high risk of HIV, HIV positive, AIDS)		*1*	*1*

Table 3. *Continued*

		DMPA & NET-EN	Combined injectables
Hypertension	• *history of - (where blood pressure cannot be evaluated)*	*2*	*3*
	• *adequately controlled hypertension*	*2*	*3*
	• *systolic 140-159 or diastolic 90-99*	*2*	*3*
	• *systolic ≥ 160 or diastolic ≥ 100*	*3*	*4*
	• *vascular disease*	*3*	*4*
Multiple risk factors for arterial cardiovascular disease (such as older age smoking, diabetes and hypertension)		*3*	*3/4*
Known thrombogenic mutations		*2*	*4*
Deep Venous Thrombosis (DVT) Pulmonary Embolism (PE)	• *history of DVT/PE*	*2*	*4*
	• *family history of DVT/PE*	*1*	*2*
	• *acute DVT/PE*	*3*	*4*
	• *DVT/PE and established on anticoagulant therapy* *2*	*4*	
	• *major surgery with prolonged immobilization*	*2*	*4*
	• *major surgery without prolonged immobilization*	*1*	*2*
	• *minor surgery without immobilization* *1*	*1*	
Superficial venous thrombosis	• *varicose veins*	*1*	*1*
	• *superficial thrombophlebitis*	*1*	*2*
Ischemic heart disease (current or history of -)		*3*	*4*
Stroke (history of cerebro-vascular accident)		*3*	*4*
Known hyperlipidemias		*2*	*2/3*
Valvular heart disease	• *uncomplicated*	*1*	*2*
	• *complicated (pulmonary hypertension, risk of atrial fibrillation, history of sub-acute bacterial endocarditis)*	*1*	*4*

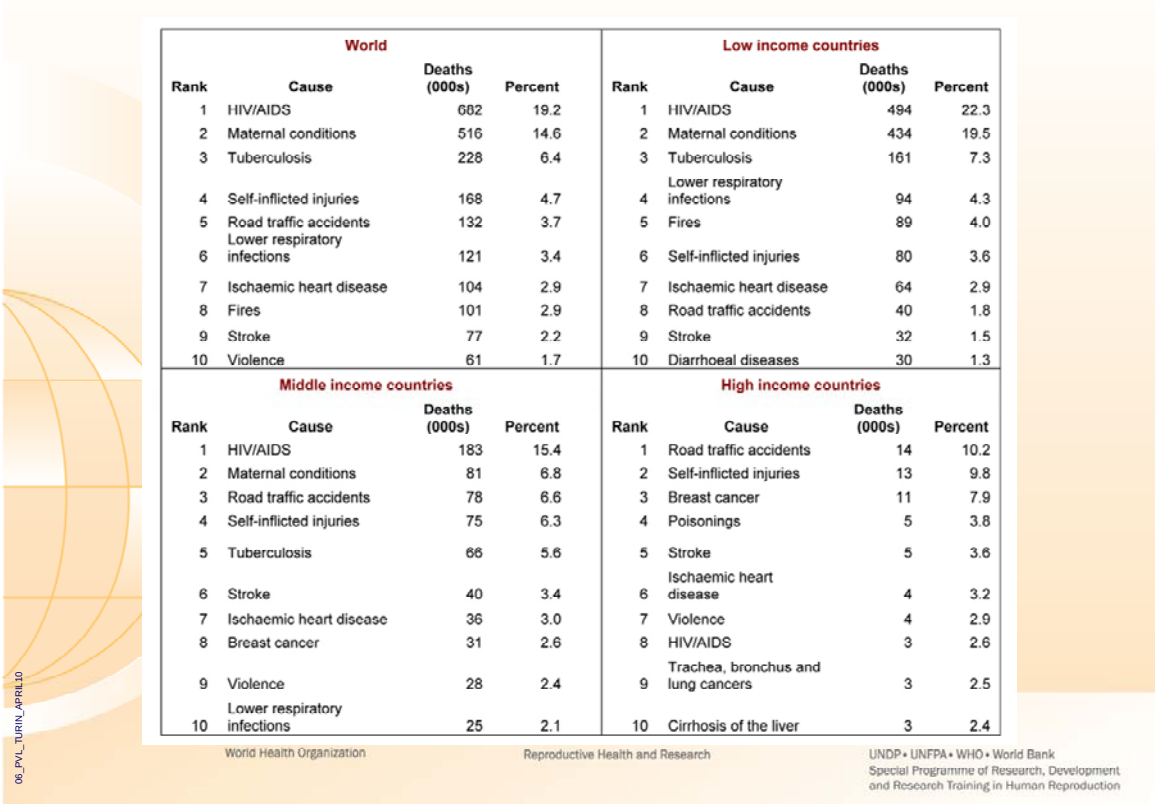
Headaches			*Init*	*Cont*	*Init*	*Cont*
	• *non-migrainous (mild or severe)* *1*		*1*	*1*	*2*	
	• *migraine:*					
	without aura, age <35		*2*	*2*	*2*	*3*
	without aura, age ≥35		*2*	*2*	*3*	*4*
	with aura, any age		*2*	*3*	*4*	*4*
Diabetes	• *hx of gestational disease*		*1*		*1*	
	• *non-vascular disease,*		*2*		*2*	
	• *nephropathy/retinopathy/neuropathy*		*3*		*3/4*	
	• *other vascular disease or diabetes of > 20 years' duration*		*3*		*3/4*	
Epilepsy			*1*		*1*	
Depressive disorders			*1*		*1*	
Systemic lupus erythematosus	• *positive (or unknown) antiphospholipid Antibodies*	*Init* *3*	*Cont* *3*		*4*	
	• *severe thrombocytopenia*	*3*	*2*		*2*	
	• *immunosuppressive treatment*	*2*	*2*		*2*	
	• *none of the above*	*2*	*2*		*2*	

Table 3. *Continued*

		DMPA & NET-EN	*Combined injectables*	
Gall bladder disease (current or treated, asymptomatic)		*2*		*2*
History of cholestasis	• *pregnancy-related*	*1*		*2*
	• *past combined oral contraceptive-related*	*2*		*2*
			Init	*Cont*
Viral hepatitis	• *acute or flare*	*1*	*3*	*2*
	• *carrier*	*1*	*1*	*1*
	• *chronic*	*1*	*1*	*1*
Cirrhosis	• *mild (compensated)*	*1*		*1*
	• *severe (decompensated)*	*3*		*3*
Liver tumours	• *benign (focal nodular hyperplasia)*	*2*		*2*
	• *benign (hepatocellular adenoma)*	*3*		*3*
	• *malignant (hepatoma)*	*3*		*¾*
Thyroid disease	• *(simple goitre, hypothyroidism, hyperthyroidism)*	*1*		*1*
Sickle cell disease		*1*		*2*
Iron deficiency anemia		*1*		*1*
Thalassemia		*1*		*1*
Schistosomiasis (any stage)		*1*		*1*
Malaria		*1*		*1*
Tuberculosis		*1*		*1*
Drug interactions	• *antimicrobial therapy*			
	- *broad-spectrum antibiotics*	*1*		*1*
	- *antifungals, antiparasitics*	*1*		*1*
	- *rifampicin or rifabutin*	*1 (DMPA)* *2 (NET-EN)*		*2*
	• *anticonvulsants*			
	- *certain anticonvulsants (phenytoin, carbamazeptine, barbiturates, primidone, topiramate, oxcarbazepine)*	*1 (DMPA)* *2 (NET-EN)*		*2*
	- *lamotrigine*	*1*		*3*
	• *antiretroviral therapy*			
	- *nucleoside reverse transcriptase inhibitors (NRTIs)*	*1*		*1*
	- *non- nucleoside reverse transcriptase Inhibitors (NNRTIs)*	*1 (DMPA) 2* *2 (NET-EN)*		
	- *ritonavir-boosted protease inhibitors*	*1 (DMPA) 3* *2 (NET-EN)*		

Table 4

Ten leading causes of death in women aged 15-44 years by country income group, 2004



World

Rank	Cause	Deaths (000s)	Percent
1	HIV/AIDS	662	19.2
2	Maternal conditions	516	14.6
3	Tuberculosis	228	6.4
4	Self-inflicted injuries	168	4.7
5	Road traffic accidents	132	3.7
6	Lower respiratory infections	121	3.4
7	Ischaemic heart disease	104	2.9
8	Fires	101	2.9
9	Stroke	77	2.2
10	Violence	61	1.7

Low income countries

Rank	Cause	Deaths (000s)	Percent
1	HIV/AIDS	494	22.3
2	Maternal conditions	434	19.5
3	Tuberculosis	161	7.3
4	Lower respiratory infections	94	4.3
5	Fires	89	4.0
6	Self-inflicted injuries	80	3.6
7	Ischaemic heart disease	64	2.9
8	Road traffic accidents	40	1.8
9	Stroke	32	1.5
10	Diarrhoeal diseases	30	1.3

Middle income countries

Rank	Cause	Deaths (000s)	Percent
1	HIV/AIDS	183	15.4
2	Maternal conditions	81	6.8
3	Road traffic accidents	78	6.6
4	Self-inflicted injuries	75	6.3
5	Tuberculosis	66	5.6
6	Stroke	40	3.4
7	Ischaemic heart disease	36	3.0
8	Breast cancer	31	2.6
9	Violence	28	2.4
10	Lower respiratory infections	25	2.1

High income countries

Rank	Cause	Deaths (000s)	Percent
1	Road traffic accidents	14	10.2
2	Self-inflicted injuries	13	9.8
3	Breast cancer	11	7.9
4	Poisonings	5	3.8
5	Stroke	5	3.6
6	Ischaemic heart disease	4	3.2
7	Violence	4	2.9
8	HIV/AIDS	3	2.6
9	Trachea, bronchus and lung cancers	3	2.5
10	Cirrhosis of the liver	3	2.4

Table 5

Country	*CPR (%)*		*Unmet need for contra-ception (%)*	*TFR*	*MMR (per 100 000 live births)*	*Lifetime risk of maternal death (1 in x)*	*Life expectancy at birth for females*
	Modern methods	*(injectables)*					
Paraguay	*60.5*	*(10.4)*	*6.6*	*3.8*	*150 (99-200)*	*170*	*74*
South Africa	*60.3*	*(28.4)*	*15.0*	*2.8*	*400 (270-530)*	*110*	*49*
Indonesia	*56.7*	*(27.8)*	*8.6*	*2.3*	*420 (240-600)*	*97*	*68*
Sri Lanka	*49.6*	*(10.8)*	*8.0*	*1.9*	*58 (39-77)*	*850*	*75*
Peru	*47.6*	*(14.6)*	*8.1*	*2.8*	*240 (170-310)*	*140*	*73*
Bangladesh	*47.3*	*(9.7)*	*11.3*	*3.2*	*570 (380-760)*	*51*	*63*
Namibia	*42.6*	*(18.7)*	*25.1*	*3.8*	*210 (110-300)*	*170*	*55*
Malawi	*38.9*	*(22.9)*	*27.6*	*6.0*	*1100 (720-1500)*	*18*	*41*
Bolivia	*34.9*	*(8.0)*	*22.7*	*3.8*	*440 (160-970)*	*55*	*66*
Philippines	*33.4*	*(3.1)*	*17.3*	*3.1*	*230 (60-700)*	*140*	*72*
Myanmar	*32.8*	*(14.8)*	*19.1*	*2.3*	*380 (260-510)*	*110*	*63*
Kenya	*31.5*	*(14.3)*	*24.5*	*5.0*	*560 (340-800)*	*39*	*50*
Zambia	*22.6*	*(4.5)*	*27.4*	*5.5*	*830 (520-1200)*	*27*	*40*
Pakistan	*20.2*	*(2.6)*	*37.5*	*4.1*	*320 (99-810)*	*74*	*63*
Ghana	*18.7*	*(5.4)*	*34.0*	*4.2*	*560 (200-1300)*	*45*	*58*
Mozambique	*11.8*	*(4.8)*	*18.4*	*5.4*	*520 (360-680)*	*45*	*46*
Gabon	*11.8*	*(0.5)*	*28.0*	*3.9*	*520 (290-760)*	*53*	*59*
Niger	*5.0*	*(1.5)*	*15.8*	*7.8*	*1800 (840-2900)*	*7*	*41*

Sources: World Contraceptive Use 2007. UN Population Division. 2008
Maternal mortality in 2005. WHO, UNICEF, UNFPA, The World Bank. 2008

Figure 1

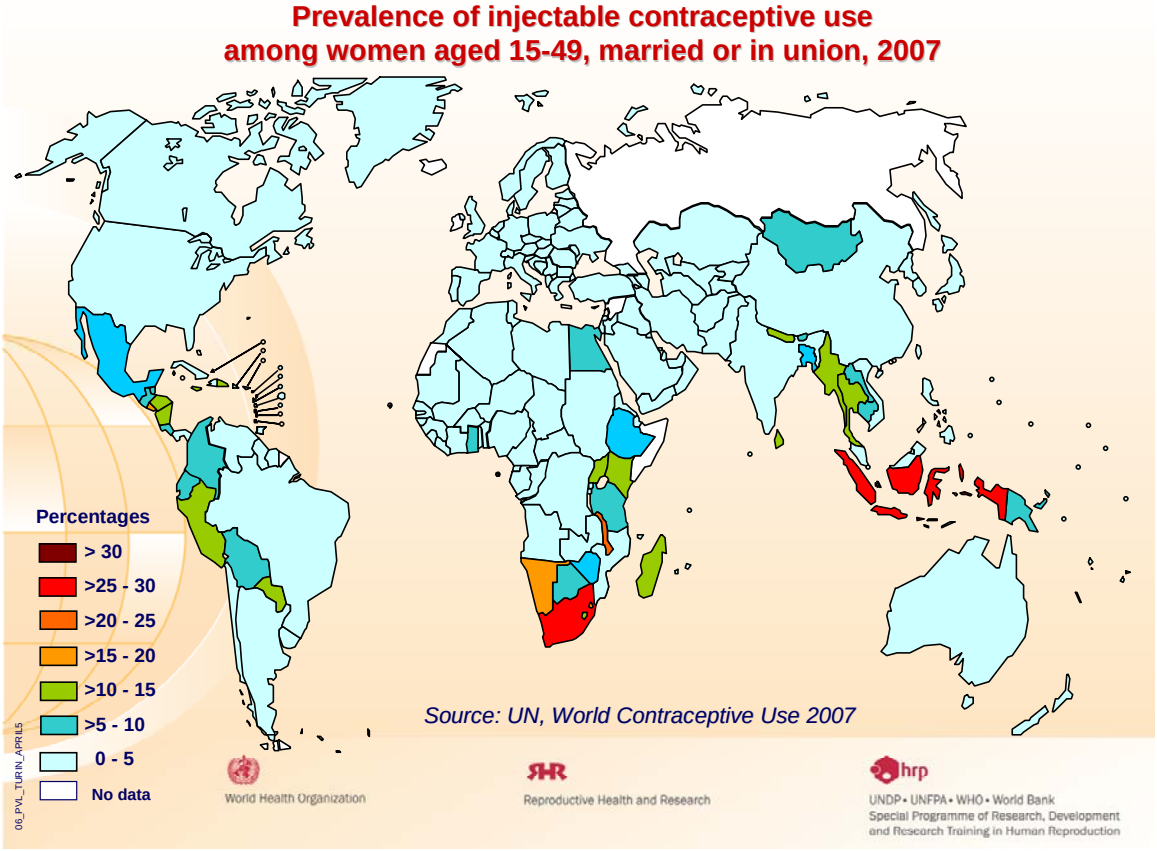

Prevalence of injectable contraceptive use
among women aged 15-49, married or in union, 2007
Percentages
> 30
>25 - 30
>20 - 25
>15 - 20
>10 - 15
>5 - 10
0 - 5
No data
Source: UN, World Contraceptive Use 2007
World Health Organization
Reproductive Health and Research
hrp
UNDP • UNFPA • WHO • World Bank
Special Programme of Research, Development
and Research Training in Human Reproduction
06_PVL_TURN_APR15

Figure 2

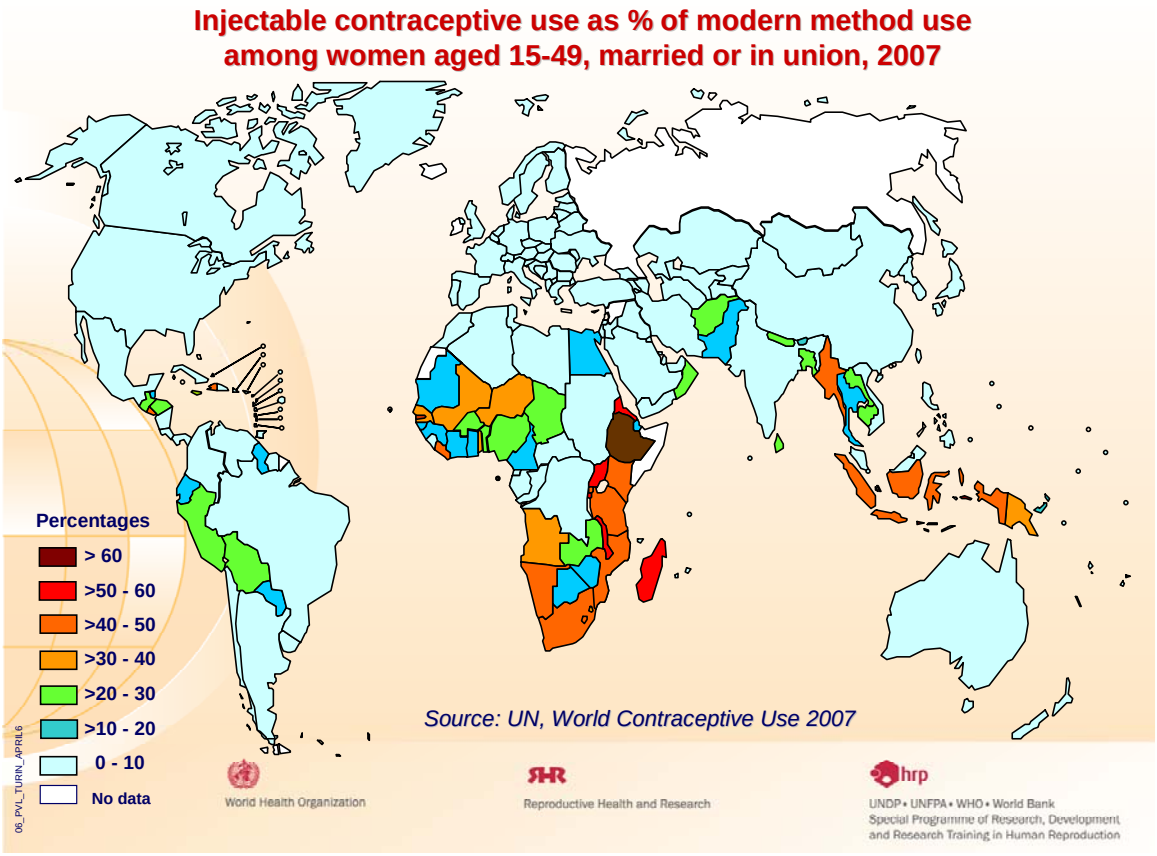
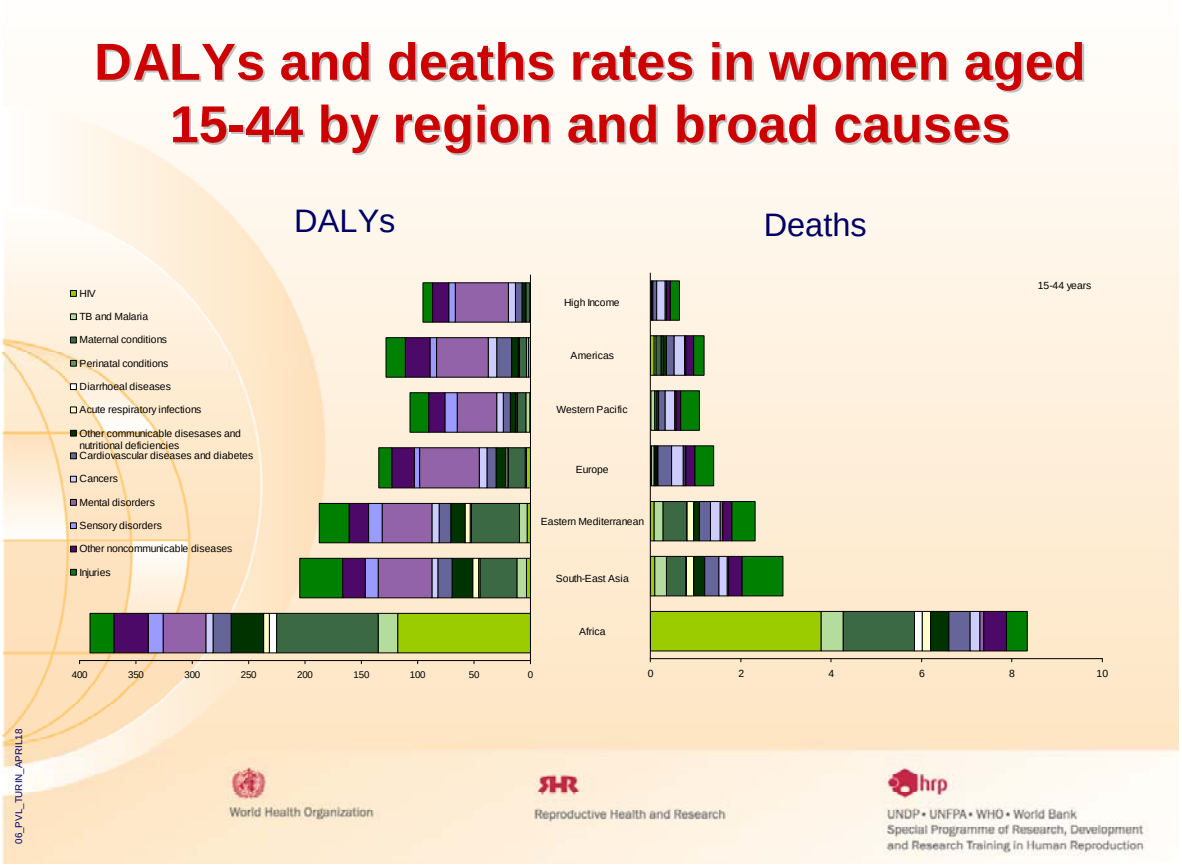

Injectable contraceptive use as % of modern method use among women aged 15-49, married or in union, 2007
Percentages
> 60
>50 - 60
>40 - 50
>30 - 40
>20 - 30
>10 - 20
0 - 10
No data
Source: UN, World Contraceptive Use 2007
World Health Organization
Reproductive Health and Research
hrp
UNDP • UNFPA • WHO • World Bank
Special Programme of Research, Development and Research Training in Human Reproduction
06_PVL_TURIN_APRIL6

Figure 3


DALYs and deaths rates in women aged 15-44 by region and broad causes
DALYs
Deaths
15-44 years
HIV
TB and Malaria
Maternal conditions
Perinatal conditions
Diarrhoeal diseases
Acute respiratory infections
Other communicable disesases and nutritional deficiencies
Cardiovascular diseases and diabetes
Cancers
Mental disorders
Sensory disorders
Other noncommunicable diseases
Injuries
High Income
Americas
Western Pacific
Europe
Eastern Mediterranean
South-East Asia
Africa
400 350 300 250 200 150 100 50 0
0 2 4 6 8 10
World Health Organization
Reproductive Health and Research
hrp
UNDP • UNFPA • WHO • World Bank
Special Programme of Research, Development and Research Training in Human Reproduction
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