Civico Di Cristina Benfratelli
Azienda di Rilievo Nazionale ad Alta Specializzazione

*Terza sessione: DIABETE E FERTILITA'*


# La Contraccezione

Antonio **Maiorana**

Ambulatorio per la diagnosi e cura dell'endometriosi

U.O.C. di Ginecologia e Ostetricia Direttore: L. Alio

A.R.N.A.S. Ospedale Civico – Palermo

Palermo, 29 Novembre 2018

# Conflitto d’interessi

- Dichiaro di avere avuto negli ultimi due anni rapporti di collaborazione con le seguenti aziende famaceutiche:
  - Bayer in qualità di consulente scientifico
  - Gedeon Richter in qualità di consulente scientifico

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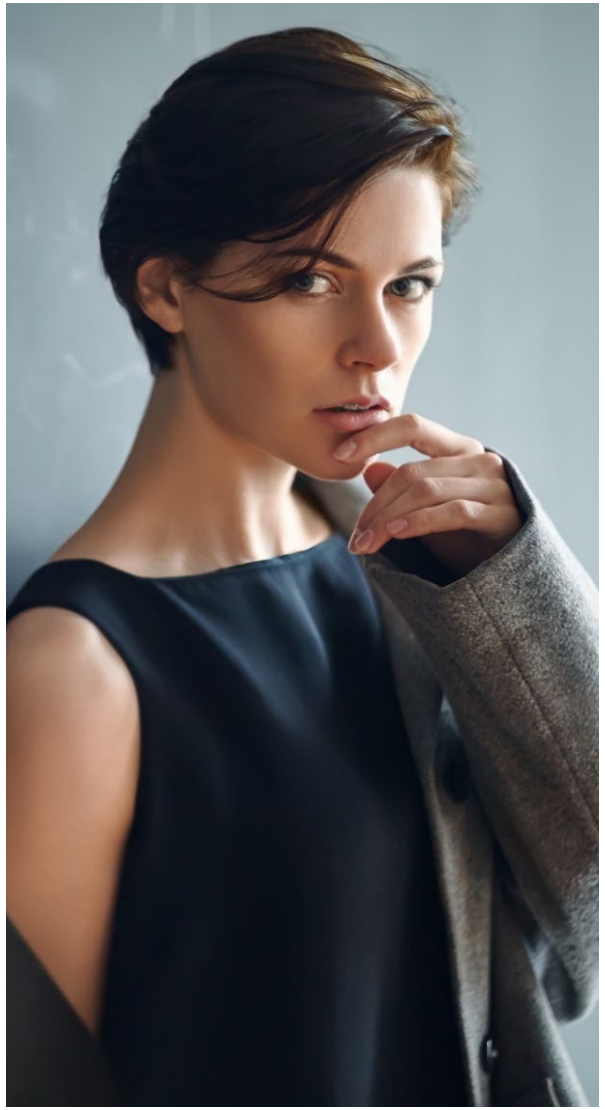
# Background



Diabetes mellitus (DM), the most common of metabolic disorders, is a global public health concern.

*Gourdy P. Diabetes and oral contraception. Best Pract Res Clin Endocrinol Metab. 2013;27:67–76.*

By 2035, numbers are set to increase by 55% with 592 million people becoming affected worldwide.

*International Diabetes Federation (IDF). IDF Diabetes Atlas. 6th ed; International Diabetes Federation: 2013. Available from: https://www.idf.org/sites/August 19, 2015.*

The rise in cases includes increasing numbers of women of reproductive age whose reproductive health and contraceptive needs must be carefully considered as DM has serious implications for pregnancy.

*Diabetes UK. Diabetes: Facts and Stats. Version 4. London: Diabetes UK; Revised 2015.*

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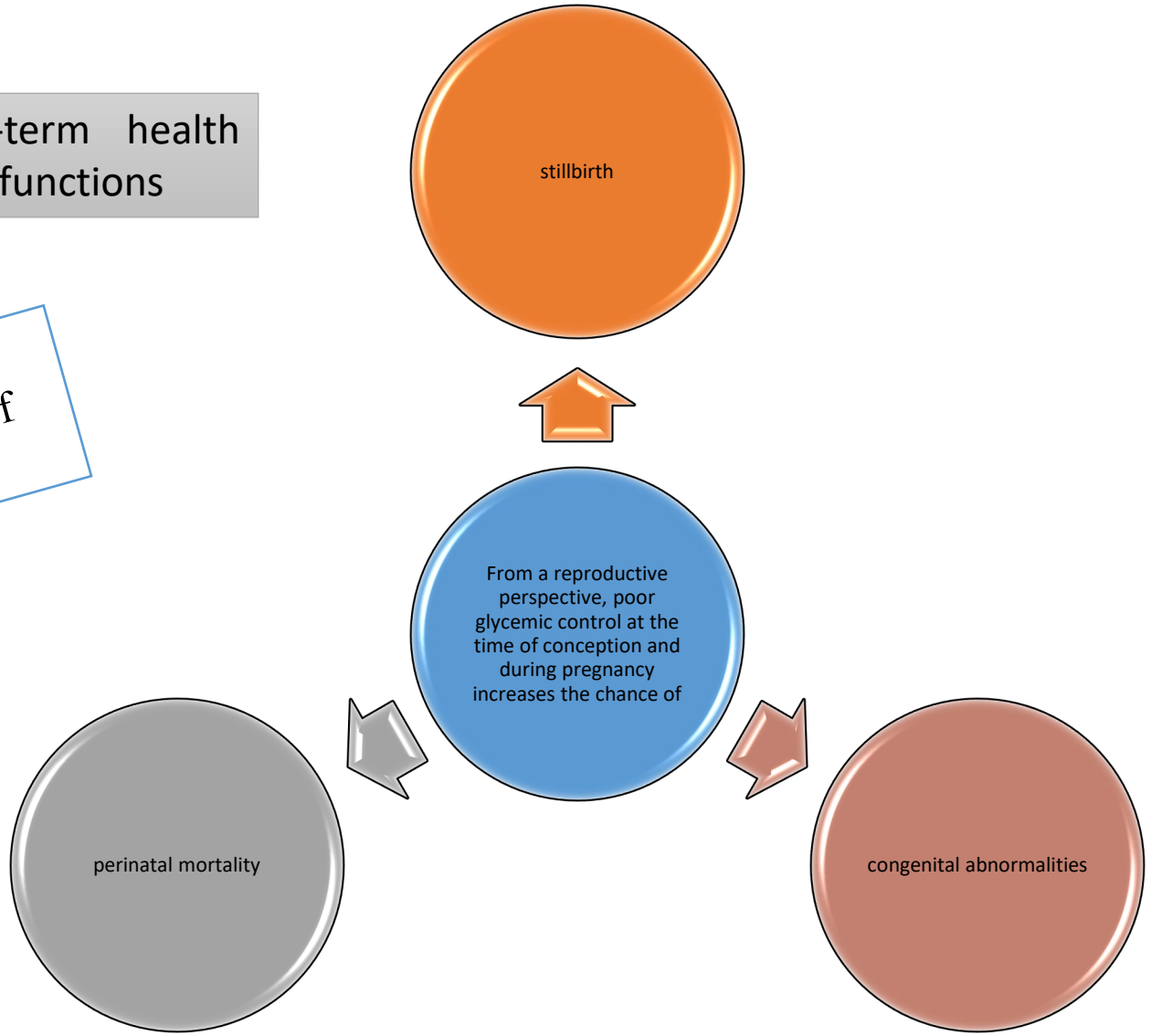
# Diabete and Pregnancy

DM can lead to numerous complications with long-term health implications on vascular, neurological, renal, and ophthalmic functions

Neonates born to women with DM are "five times as likely to be stillborn, three times as likely to die in their first months of life, and twice as likely to have a major congenital anomaly"




*Schwarz EB, Postlethwaite D, Yun-Yi Hung, Lantzman E, Armstrong MA, Horberg MA. Provision of contraceptive services to women with diabetes mellitus. J Gen Intern Med. 2011;27(2):196–201.*

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# Background

NICE National Institute for Health and Care Excellence

NICE guideline

**Diabetes in pregnancy: management from preconception to the postnatal period**

NICE guideline
Published: 25 February 2015
nice.org.uk/guidance/ng3

Monitoring and improving maternal health whilst encouraging adequate inter-pregnancy spacing and the use of effective contraception forms an integral part of pre-pregnancy care.

**In order to minimize complications, safe and effective contraception to prevent unintended pregnancy and preconception care is paramount for all women with DM.**

*National Institute for Health and Care Excellence (NICE). Management of Diabetes and Its Complications from Preconception to the Postnatal Period, (NG3). London: NICE; 2015.*

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# DM and Female Sexual Dysfunction

Despite the fact that more women suffer from DM than men, and that women share similar risks for diabetic complications with men, less attention has been given to sexual function in women with DM. **The prevalence of female sexual dysfunction (FSD) and associated risk factors in diabetic women are less clear than in men** (Bhasin et al., 2007).

# The Effect of DM on Sexual Function

***Sexual problems in women with DM may be explained by several possible mechanisms***

- Hyperglycemia may reduce the **hydration** of mucous membranes in the vagina, leading to decreased lubrication and dyspareunia.
- Increased risk of **vaginal infections** increases the risk of vaginal discomfort and dyspareunia.
- **Vascular damage and neuropathy** may result in decreased genital blood flow, leading to impaired genital arousal response.
- **Psychosocial factors** such as adjustment to the diagnosis of DM, the burden of living with a chronic disease, and depression may impair sexual function.

# Facing the challenges


1. *Cartwright A, Wallymahmed M, Macfarlane I, Ca… I. What do women with diabetes know abo… and contraception? Pract Diabetes… 242.*

2. *Murphy HR, T… psych… …. Education and …l experiences of women …ot attend pre-pregnancy care. …010;27:92–100.*

*…usgharzadeh A, Aghamohammadzadeh N, Mobasseri M, et al. Study of contraception status of female diabetic patients in childbearing years. Res J Biol Sci. 2008;3(7):710–715.*


The challenge is to support women with type 1 and type 2 DM in making a choice of contraception based on their individual needs and associated risk factors. J. Cleland. Contraception and health THE LANCET 2012

# Facing the challenges

Guidance about contraception needs to be offered holistically and a trusting relationship between practitioner and client is advocated.

*Shawe J. Contraceptive choices for women with diabetes'. Primary Care Women's Health Journal. 2013; 5(1):29–32.*

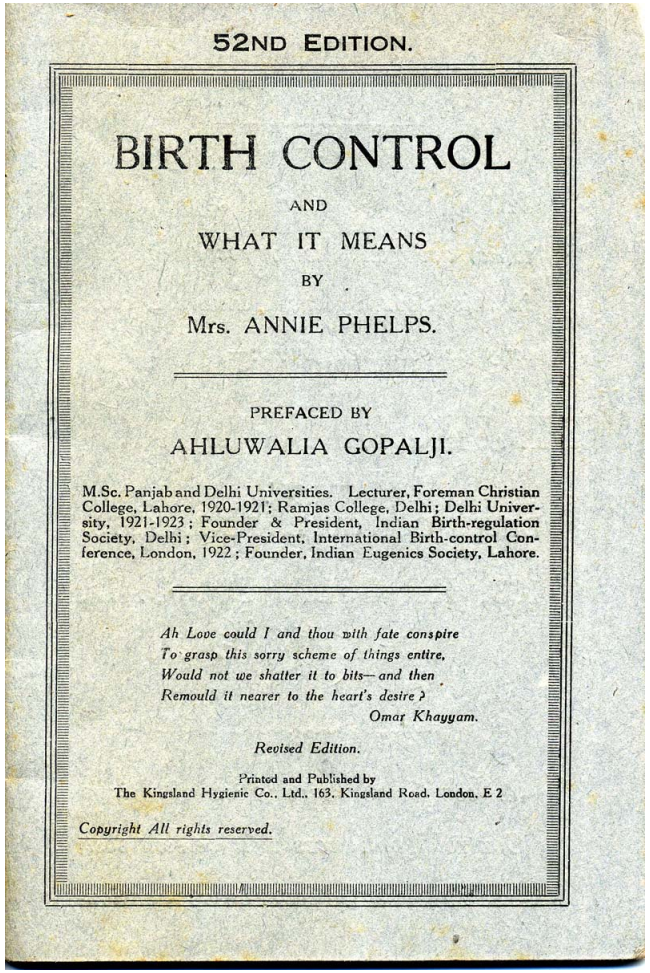
Choice of contraception should be made on the preference of the woman and individual risk factors identified such as the presence of vascular, nephropathy, neuropathy, or retinal disease.

*WHO. WHO Medical Eligibility Criteria for Contraceptive Use; Geneva: 2015*

**Table 2** WHO Medical Eligibility Criteria for Contraceptive Use (2015)

| Category | With clinical judgment |
|---|---|
| 1 | Use method in any circumstance |
| 2 | Generally use method |
| 3 | Use of method not usually recommended unless other more appropriate methods are not available or not acceptable |
| 4 | Method not to be used |

# Combined hormonal contraception

52ND EDITION.

BIRTH CONTROL

AND

WHAT IT MEANS

BY

Mrs. ANNIE PHELPS.

PREFACED BY

AHLUWALIA GOPALJI.

M.Sc. Panjab and Delhi Universities. Lecturer, Foreman Christian College, Lahore, 1920-1921; Ramjas College, Delhi; Delhi University, 1921-1923; Founder & President, Indian Birth-regulation Society, Delhi; Vice-President, International Birth-control Conference, London, 1922; Founder, Indian Eugenics Society, Lahore.

*Ah Love could I and thou with fate conspire*
*To grasp this sorry scheme of things entire,*
*Would not we shatter it to bits—and then*
*Remould it nearer to the heart's desire?*
*Omar Khayyam.*

*Revised Edition.*

Printed and Published by
The Kingsland Hygienic Co., Ltd., 163, Kingsland Road, London, E 2

1960

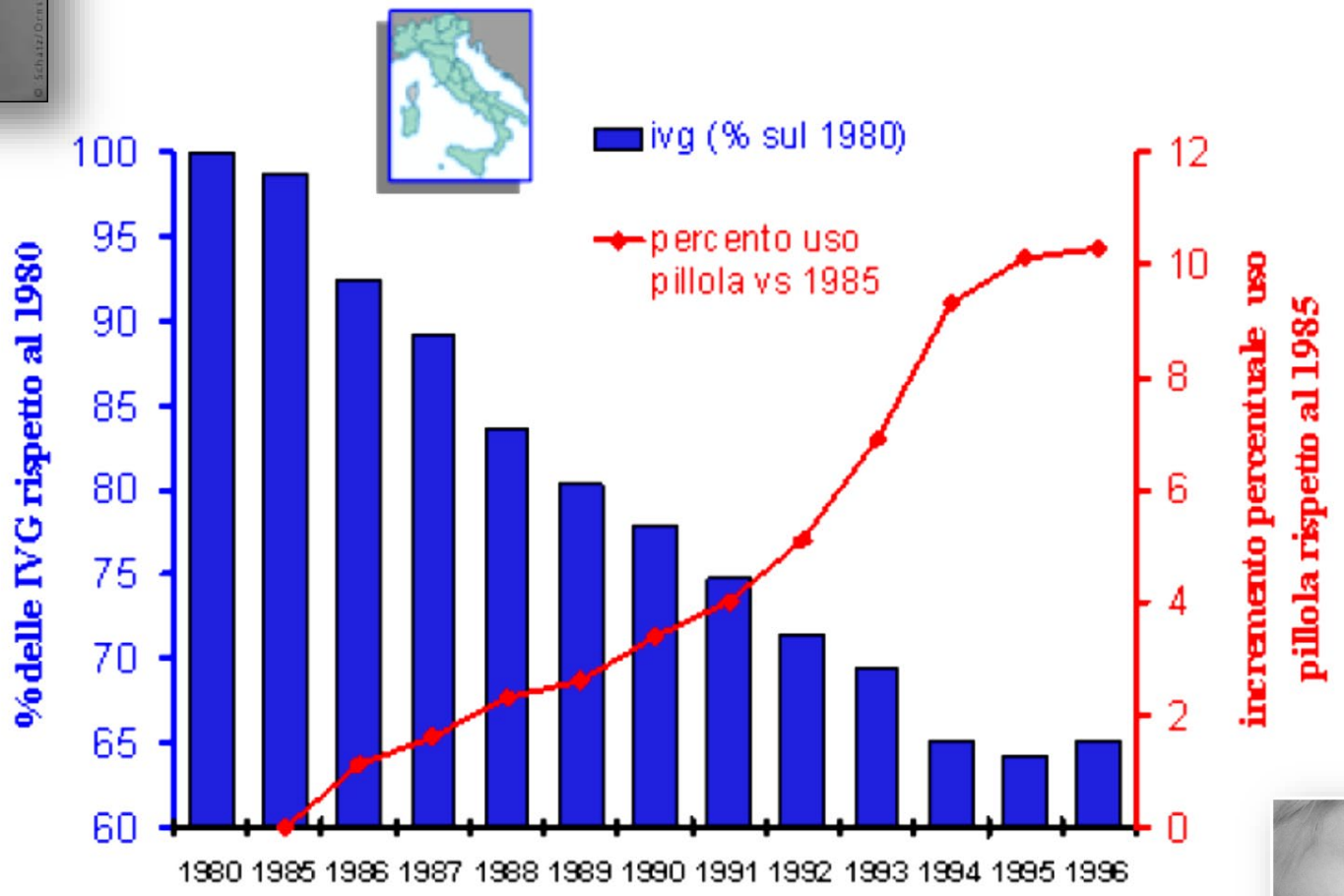

1968


It was a medical breakthrough many years in the making, the most convenient and reliable form of birth control ever invented — but it quickly became much more. Arriving at a moment of social and political upheaval, the Pill became a handy proxy for wider trends: **the rejection of tradition, the challenge to institutions, the redefinition of women's roles**."

1993


2010

# E/P vs IVG

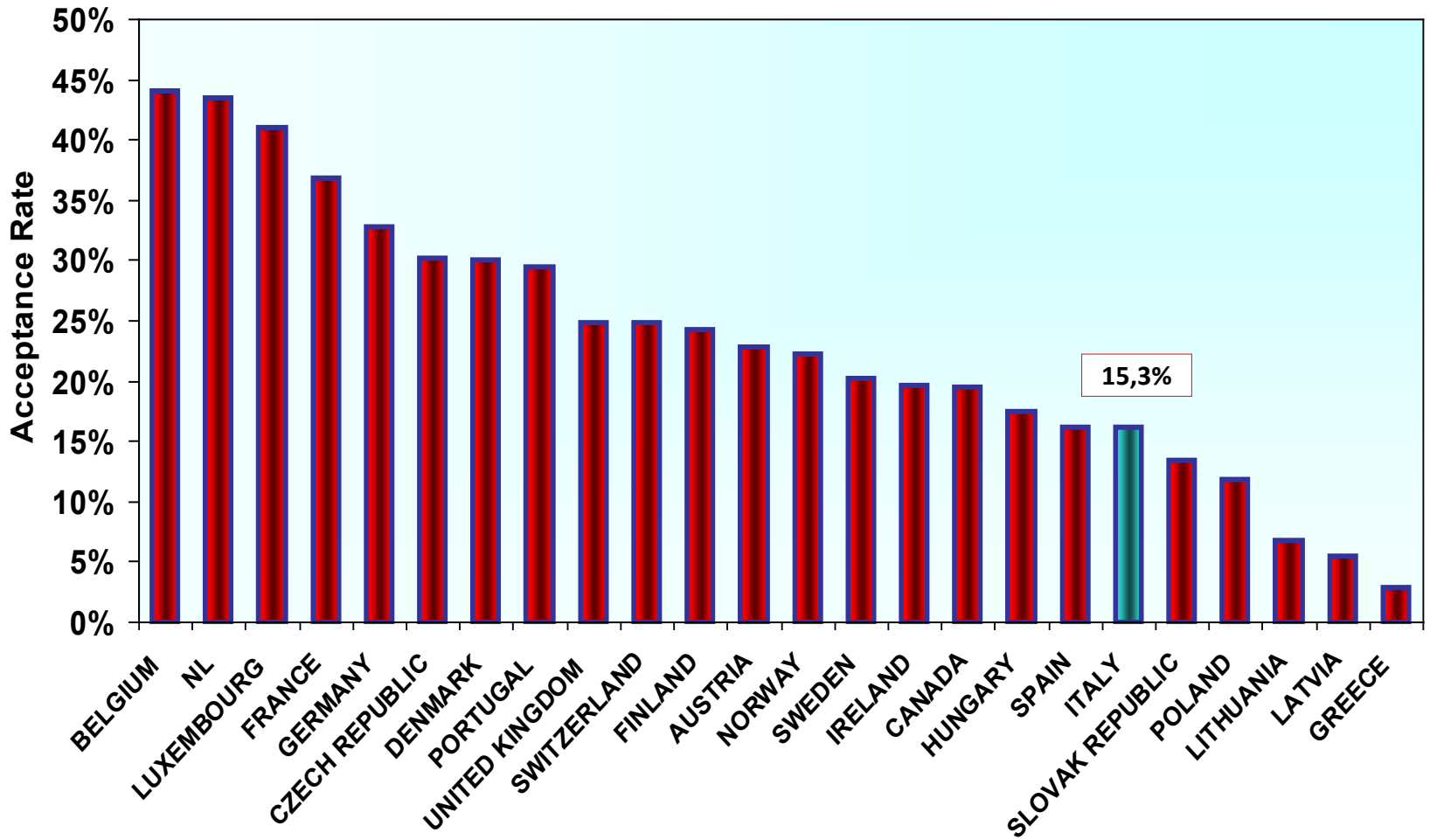



Variazioni percentuali delle IVG in Italia in funzione del progressivo incremento dell'uso della contraccezione ormonale (dati ISTAT 2002)

# Evoluzione della contraccezione ormonale

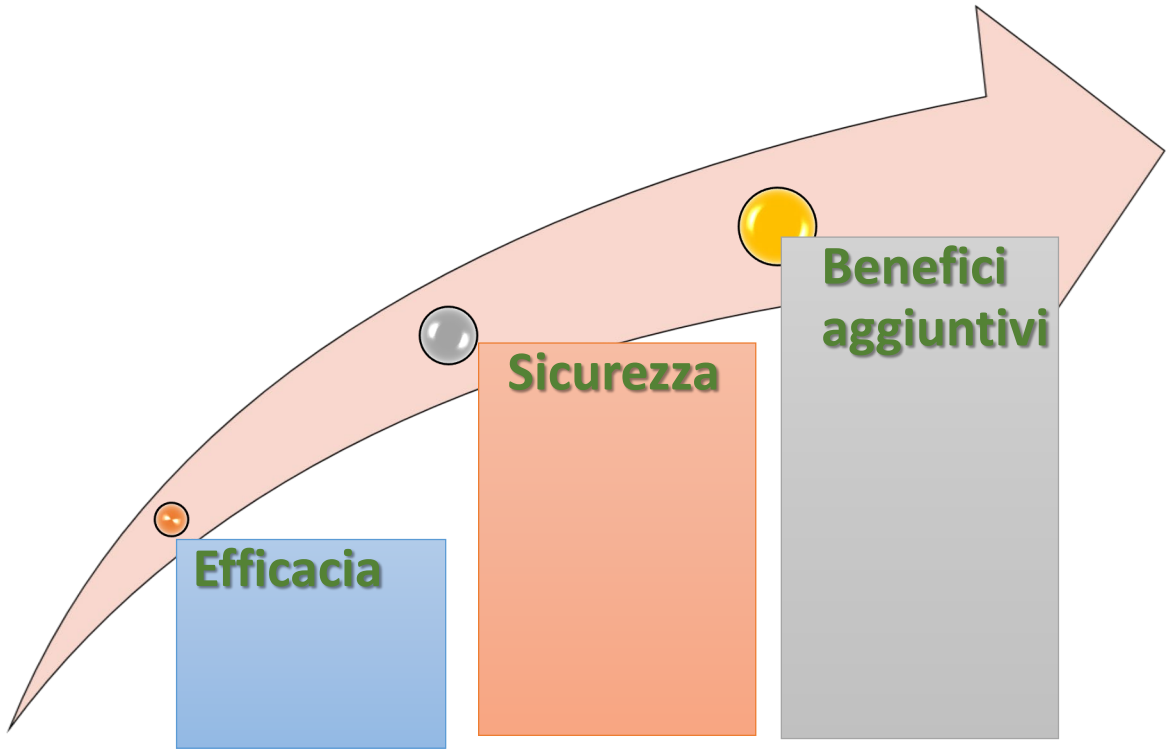
## Uso dei contraccettivi in Italia

Indice di utilizzo della contraccezione ormonale in Italia rispetto agli altri Paesi

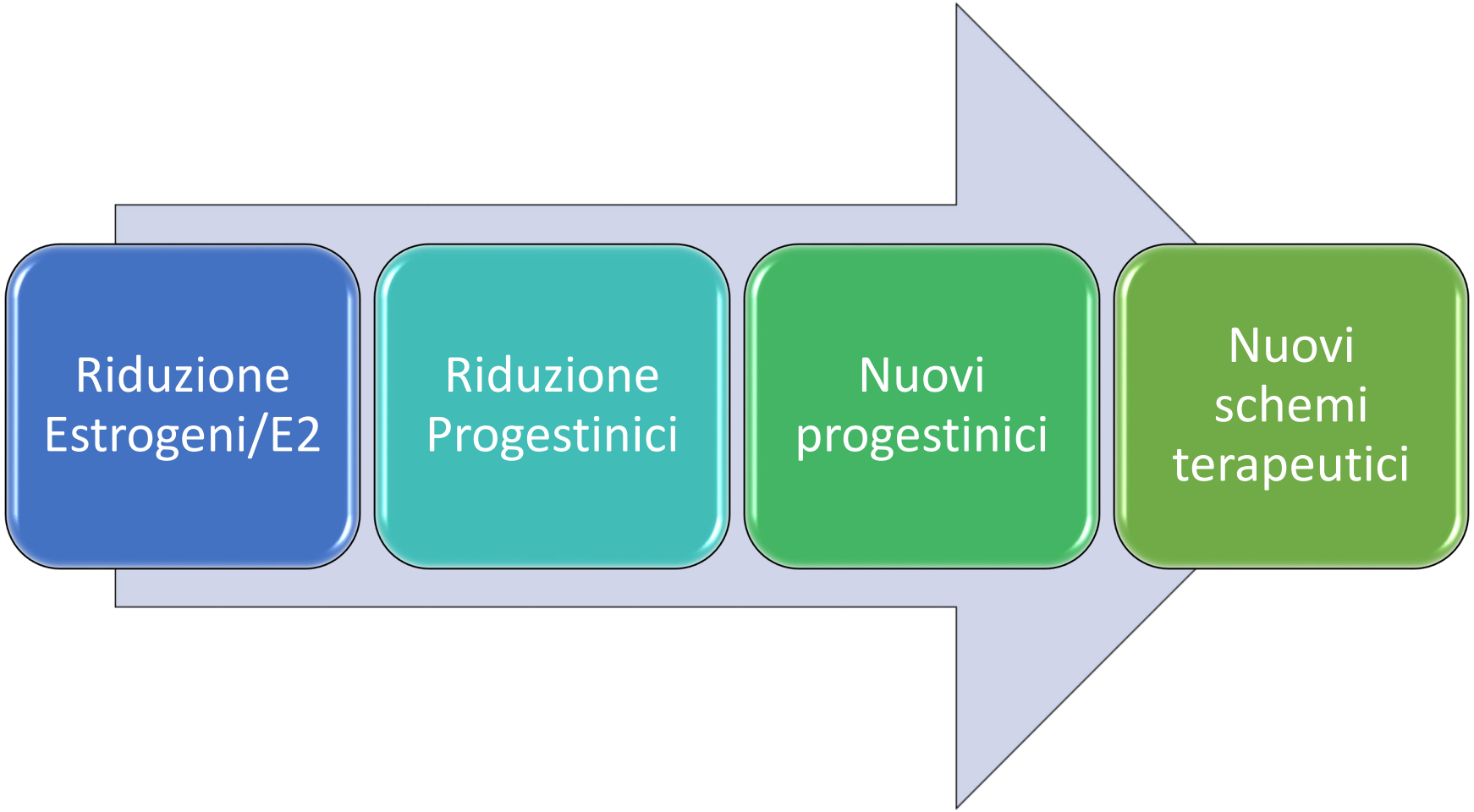


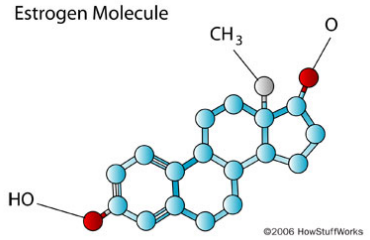

*Source: population World Bank; cycles IMF – ANNO 2012*

# E/P : Evoluzione




# Combined hormonal contraception





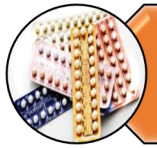


The "**total estrogenicity**" rises with increasing dose of estrogen but decreases with increasing antiestrogenic activity of progestogen compound.

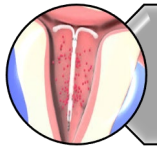
It was suggested that **third generation progestogens**, as well as **drospirenone and cyproterone acetate possess** a weaker anti-estrogenic activity **than levonorgestrel** and, therefore, are less potent in the counterbalancing the prothrombotic effects of estrogen.

S.N. Tchaikovski, J. Rosing / Thrombosis Research 126 (2010) 5–11

# Combined hormonal contraception

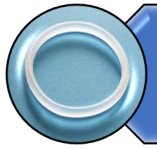


Contraccettivo Orale Combinato(Estroprogestinico)



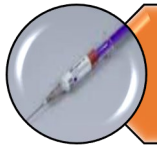
Spirale ormonale (Progestinico)

Cerotto (Estroprogestinico)



Anello Vaginale (Estroprogestinico)

POP (Pillola con solo progestinico)



Iniezione Trimestrale (solo progestinico)

Impianto sottocutaneo (solo progestinico)

# Combined hormonal contraception

Cochrane Library

Cochrane Database of Systematic Reviews

**Hormonal versus non-hormonal contraceptives in women with diabetes mellitus type 1 and 2 (Review)**

Visser J, Snel M, Van Vliet HAAM

Visser J, Snel VJ, Van Vilet HA. Hormonal versus non-hormonal contraceptives in women with diabetes mellitus type 1 and 2 (review). Cochrane Database Syst Rev. 2013;3:CD003990.

This review was performed to identify the most effective type of contraception with the least adverse effects.

- Four randomized controlled trials were included.
- Two studies compared hormonal (combined oral contraceptives) and LNG-releasing IUD versus non-hormonal (copper IUD) contraceptives.
- The two other studies compared combined oral contraceptives with progestogen-only pills.
- None of the studies compared low-dose combined oral contraceptives with high-dose oral contraceptives.

**The results of a Cochrane review of randomized controlled trials by Visser et al was inconclusive in determining whether hormonal contraception affected carbohydrate and lipid metabolism and long-term complications in women with DM.**

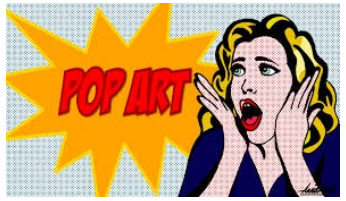
# Combined hormonal contraception

A recent review of evidence emphasized that CHC containing less than 35 μg of ethinyl-estradiol did not alter blood glucose concentrations and insulin secretion. In relation to diabetic retinopathy, macular edema, and nephropathy, there was no increase in risk or acceleration of disease in women taking oral CHC

Gourdy P. Diabetes and oral contraception. Best Pract Res Clin Endocrinol Metab. 2013;27:67–76.

In cases of DM complicated by cardiovascular or microvascular disease, the risks of prescribing CHC outweigh any advantages and a WHO Medical Eligibility Criteria (MEC) 3/4 would be awarded. CHC is also unlikely to be suitable for women with risk factors such as smoking, obesity, or hypertension due to increased risk of venous thromboembolism, myocardial infarction, and stroke

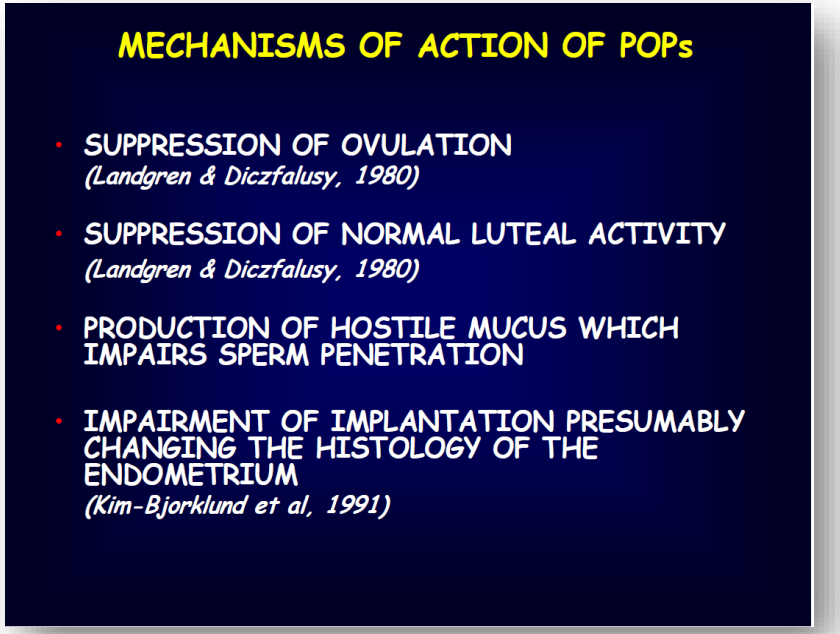
Faculty of Sexual and Reproductive Health Care (FSRH). Member's Enquiry Response EdME0040. London: FSRH; 2014.




# POP

Progestin Only Pill

# Progestin only pill



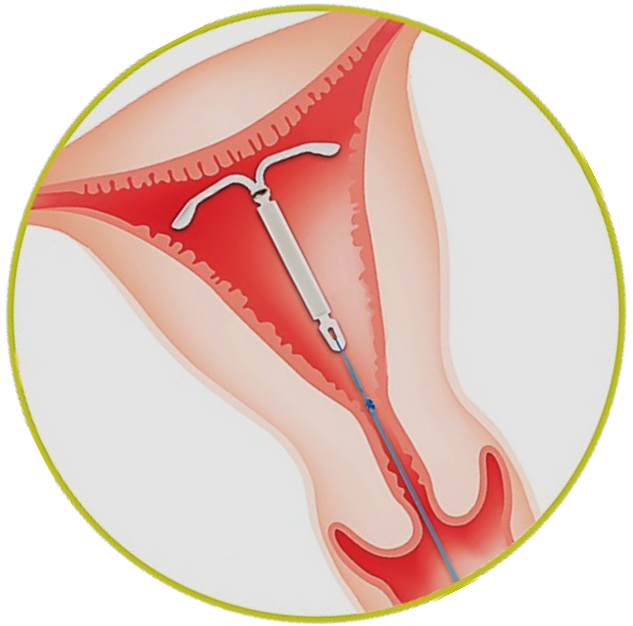

The progestogen-only pill (POP) is regarded as a safe option for women with DM of any age with or without complications.

The POP needs to be taken within a daily set time period but compliance is likely to be good if scheduled with routine insulin or oral hypoglycemic medication.

Desogestrel has the benefit of inhibiting ovulation in 97% of cases and a 12 hours dosing period, and therefore may be a more reliable choice especially for younger people with DM.

Faculty of Sexual and Reproductive Health Care (FSRH). Progestogen Only Pills. London:FSRH; 2009.


# Long-acting reversible contraception



# Long-acting reversible contraception

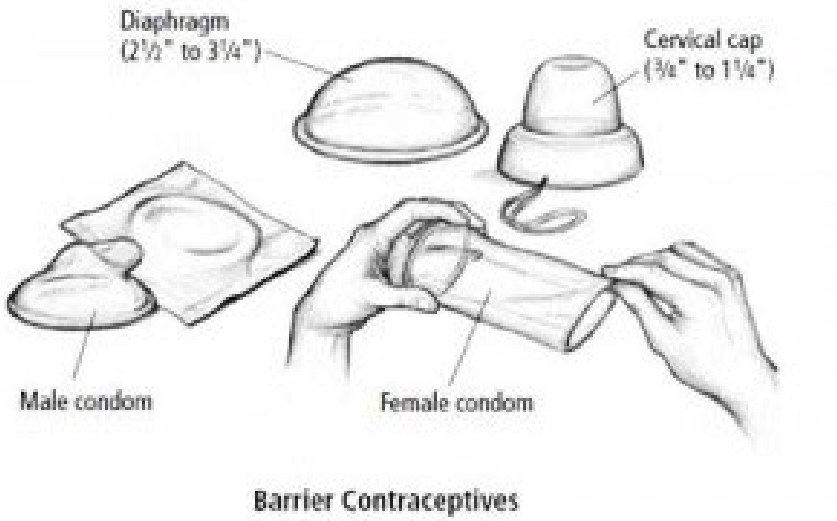

Long-acting reversible contraceptives (LARC) are not memory-dependent and have high efficacy, which can make them a good choice for women with DM.

Goldstuck and Steyn published a systematic review focusing on the efficacy of the IUD and IUS for women with DM.

Analysis resulted in the reassurance that the copper IUD and IUS were suitable for women with type 1 and type 2 DM, although the IUS needed further monitoring from a metabolic perspective in relation to type 2 DM.

Goldstuck ND, Steyn PS. The intrauterine device in women with diabetes mellitus type I and II: a systematic review. ISRN Obstet Gynecol. 2013;2013:814062.

# Barrier and natural methods of contraception




Barrier Contraceptives

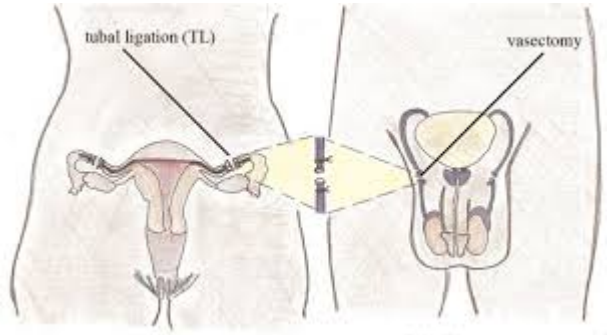
The decision to use a barrier method comes down to personal acceptability and efficacy; a male condom, for example, is 98% effective with proper use, a female condom 95%, and a diaphragm with spermicide is 92%–96% effective

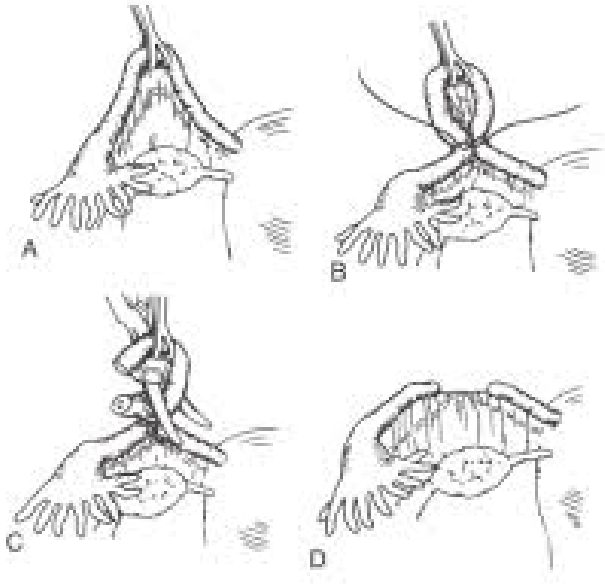
However, there appear to be no studies contraindicating the use of spermicide from a diabetic perspective

Using barrier methods alone may be too unreliable in preventing pregnancy for women with DM, especially if she is trying to lose weight or reduce her $HbA_{1c}$ levels

National Institute for Health and Care Excellence (NICE). Guidance on Long-Acting Reversible Contraception (Update). London: NICE; 2014. Accessed from: http://www.nice.org.uk/CG30. Accessed August 19, 2015.

# Male and female sterilization




The failure rate for female sterilization is one in 200 and one in 2,000 for men following a vasectomy.

Family Planning Association (FPA). Advice on Choice of Contraceptive Method from The Family Planning Association; London: 2010

Since both procedures involve an operative intervention, however, minor, glycemic control needs consideration since it can affect the chances of acquiring a postoperative infection.

Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C. Prevalence and clinical outcome of hyperglycemia in the perioperative period in non-cardiac surgery. Diabetes Care, 2010;33:1783–1788.

Guidance from a diabetic physician regarding the safest operative location as well as prophylactic antibiotics are advisable if a couple decides that sterilization is the right choice

# Emergency contraception

Emergency contraception provides all women with additional choice for prevention of pregnancy.

The global rate of unplanned pregnancy in 2012 was 53 per 1,000 women aged between 15 years and 44 years.

Sedgh G, Singh S, Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. Stud Fam Plann. 2014;45(3):301–314.

**Women with DM, at risk and not wanting to be pregnant, are advised to seek emergency contraception at the earliest opportunity.**

From a diabetic perspective, there are no contraindications to taking emergency progestogen-only contraceptive pills within the recommended time frame or to the use of the copper-bearing IUD within 5 days of unprotected intercourse or when ovulation is known, no more than 5 days after ovulation

Mugglestone MA. Management of diabetes from preconception to the postnatal period: summary of NICE guidance. BMJ. 2008;336:714–717.

World Health Organization

# Key solutions

**Table 2** WHO Medical Eligibility Criteria for Contraceptive Use (2015)

| Category | With clinical judgment |
|---|---|
| 1 | Use method in any circumstance |
| 2 | Generally use method |
| 3 | Use of method not usually recommended unless other more appropriate methods are not available or not acceptable |
| 4 | Method not to be used |

**Table 3** Contraceptive methods and diabetes

| Condition | CHC | POP | DMPA/ NET-EN | IMP | Cu IUD | IUS |
|---|---|---|---|---|---|---|
| History of gestational diabetes | 1 | 1 | 1 | 1 | 1 | 1 |
| Nonvascular disease | | | | | | |
| i. Noninsulin dependent | 2 | 2 | 2 | 2 | 1 | 2 |
| ii. Insulin dependent | 2 | 2 | 2 | 2 | 1 | 2 |
| Neuropathy/retinopathy/ neuropathy | 3/4 | 2 | 3 | 2 | 1 | 2 |
| Other vascular disease | 3/4 | 2 | 3 | 2 | 1 | 2 |

**Tab. I Definizione delle categorie WHO 2009**

| | |
|---|---|
| CATEGORIA 1 | Condizione nella quale non vi è restrizione all'uso del metodo contraccettivo. |
| CATEGORIA 2 | Condizione nella quale i vantaggi dati dall'uso del metodo generalmente superano i rischi teorici o provati. |
| CATEGORIA 3 | Condizione nella quale i rischi teorici o provati generalmente superano i vantaggi dati dall'uso del metodo. |
| CATEGORIA 4 | Condizione che rappresenta un rischio inaccettabile per la salute se il contraccettivo è utilizzato. |

Vengono, inoltre, classificati separatamente l'inizio o la continuazione di un metodo contraccettivo:

| | |
|---|---|
| Inizio (I) | Inizio di un metodo contraccettivo da parte di una donna con una specifica condizione medica. |
| Continuazione (C) | Continuazione di un metodo contraccettivo già usato da parte di una donna che sviluppa ex-novo una condizione medica. |

S.I.C.

**Tabella I.** Indicazioni contraccettive nella donna con diabete: classi di rischio secondo WHO (da WHO, 2010, mod.)

| CONDIZIONE | COC P/R | POP | DMPA NET-EN | LNG ETG impianti | Cu-IUD | LING-IUD |
|---|---|---|---|---|---|---|
| Diabete | | | | | | |
| Storia di diabete gestazionale | 1 | 1 | 1 | 1 | 1 | 1 |
| Diabete mellito tipo 1 senza complicanze vascolari | 2 | 2 | 2 | 2 | 1 | 2 |
| Diabete mellito tipo 2 senza complicanze vascolari | 2 | 2 | 2 | 2 | 1 | 2 |
| Diabete con nefropatia e/o neuropatia e/o retinopatia | 3/4 | 2 | 3 | 2 | 1 | 2 |
| Diabete con malattia vascolare o diabete > 20 anni | 3/4 | 2 | 3 | 2 | 1 | 2 |
| Malattie cardiovascolari | 3/4 | 2 | 3 | 2 | 1 | 2 |
| Fattori di rischio multipli per CVD (età, fumo, diabete, ipertensione, obesità) | 3/4 | 2 | 3 | 2 | 1 | 2 |

COC: contraccettivo orale combinato; P: cerotto contraccettivo combinato; R: anello vaginale combinato; POP: pillola di solo progestinico; DMPA: deposito di medrossiprogesterone acetato; NET-EN: deposito di noretisteroneenantato; LNG/ETG: impianti di levonorgestrel e impianti di etonogestrel; Cu-IUD: dispositivo intrauterino al rame; LNG-IUD: dispositivo intrauterino al levonorgestrel.

S.I.C.

S.I.C.

Nella donna con diabete la contraccezione ormonale può essere prescritta secondo le seguenti indicazioni:

- La contraccezione estoprogestinica può essere utilizzata solo se in presenza di diabete senza complicanze vascolari (Livello di Evidenza I, Forza della Raccomandazione A).
- La contraccezione solo progestinica (POP, impianto sottocutaneo, IUS) può essere utilizzata sempre anche in presenza di complicanze vascolari (Livello di Evidenza I, Forza della Raccomandazione A).
- In presenza di comorbidità, la contraccezione estroprogestinica è quasi sempre controindicata (Livello di Evidenza I, Forza della Raccomandazione A).
- In presenza di comorbidità può essere utilizzata una contraccezione solo progestinica (POP, impianto sottocutaneo, IUS) (Livello di Evidenza I, Forza della Raccomandazione A)

S.I.C.

S.I.C.

**Raccomandazioni per la Contraccezione Ormonale nella donna con Diabete.**

Sulla scorta dei dati della letteratura si è scelto di adeguare le nostre raccomandazioni a quelle stilate dalla OMS e per buona parte accolte anche negli Stati Uniti (Curtis et al, 2010).

Pertanto, alcune raccomandazioni sono auspicabili durante il primo "counseling" contraccettivo (Livello di Evidenza I, Forza della Raccomandazione A)

1. Anamnesi personale, per stabilire l'esistenza di eventuali controindicazioni assolute.
2. Familiarità per malattie cardiovascolari in età giovanile (<50 aa per uomini e donne).
3. Durata della malattia diabetica.
4. Valutazione delle complicanze del diabete.
5. Valutazione della PA.
6. Valutazione del BMI.

# CONCLUSIONS

- Practitioners need to make reference to the WHO Medical Eligibility Criteria for Contraceptive Use.
- Women should be informed of all methods available including LARC methods which have higher efficacy

# CONCLUSIONS

- Recent data highlight the safety of hormonal contraception in relation to women with DM without complications of cardiovascular or microvascular risk factors

# CONCLUSIONS

- Natural and barrier methods of contraception are not contraindicated for women looking for a nonhormonal method of birth control.
- Male and female sterilization remains an option; however, infection control is paramount and specialist referral is recommended.

# CONCLUSIONS

The progestogen-only pill (POP) is regarded as a safe option for women with DM of any age with or without complications. (MEC 1/2).

# CONCLUSIONS

- The copper IUD and IUS are suitable for women with type 1 and type 2 DM (MEC 1/2).

# CONCLUSIONS

- There is a need for an integrated approach to diabetes and reproductive health with improved communication between women with DM and their health care providers.


Grazie!