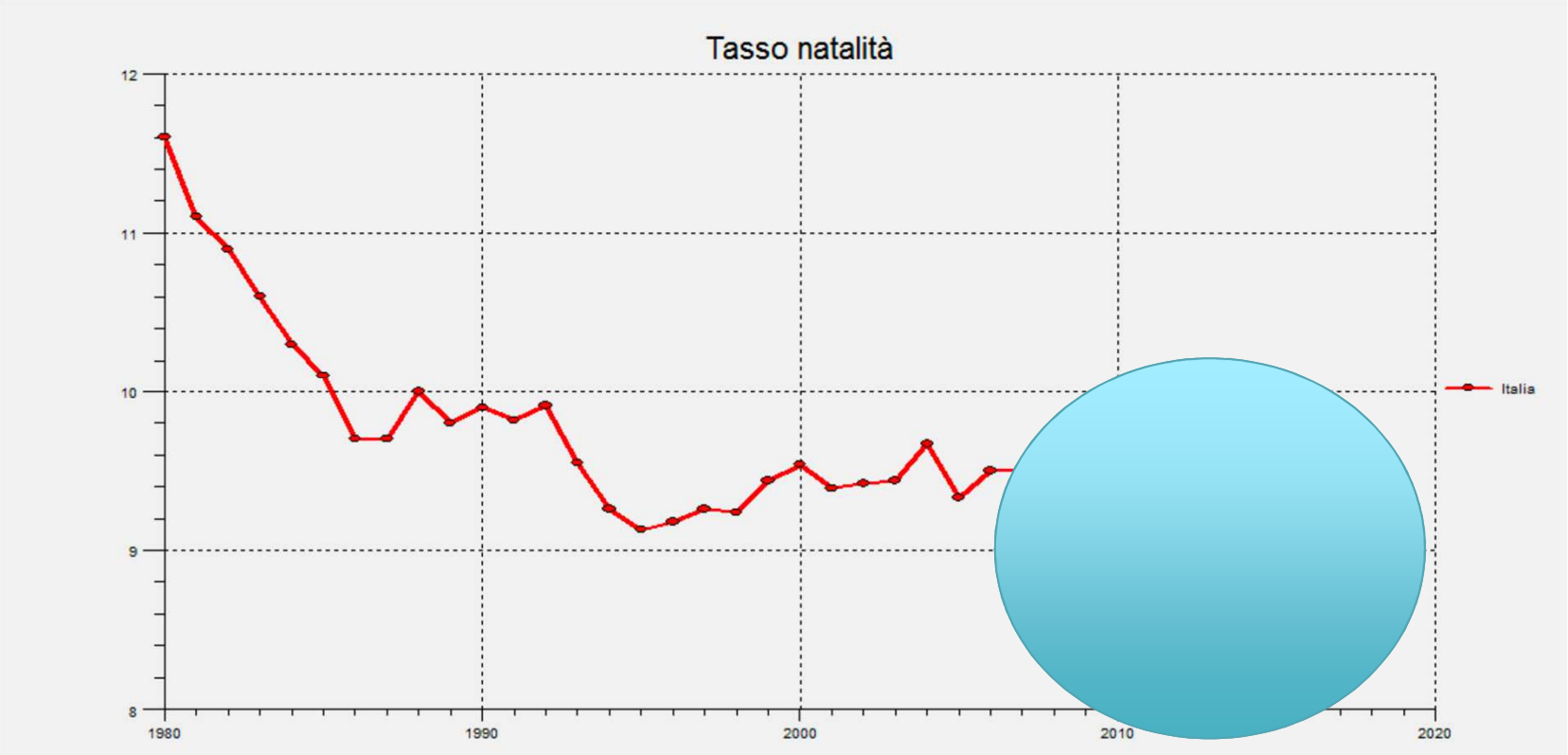
Inquinamento ambientale ed (in)fertilità

Agostino DI CIAULA
Comitato Scientifico ISDE Italia

Arezzo, 29 Settembre 2017

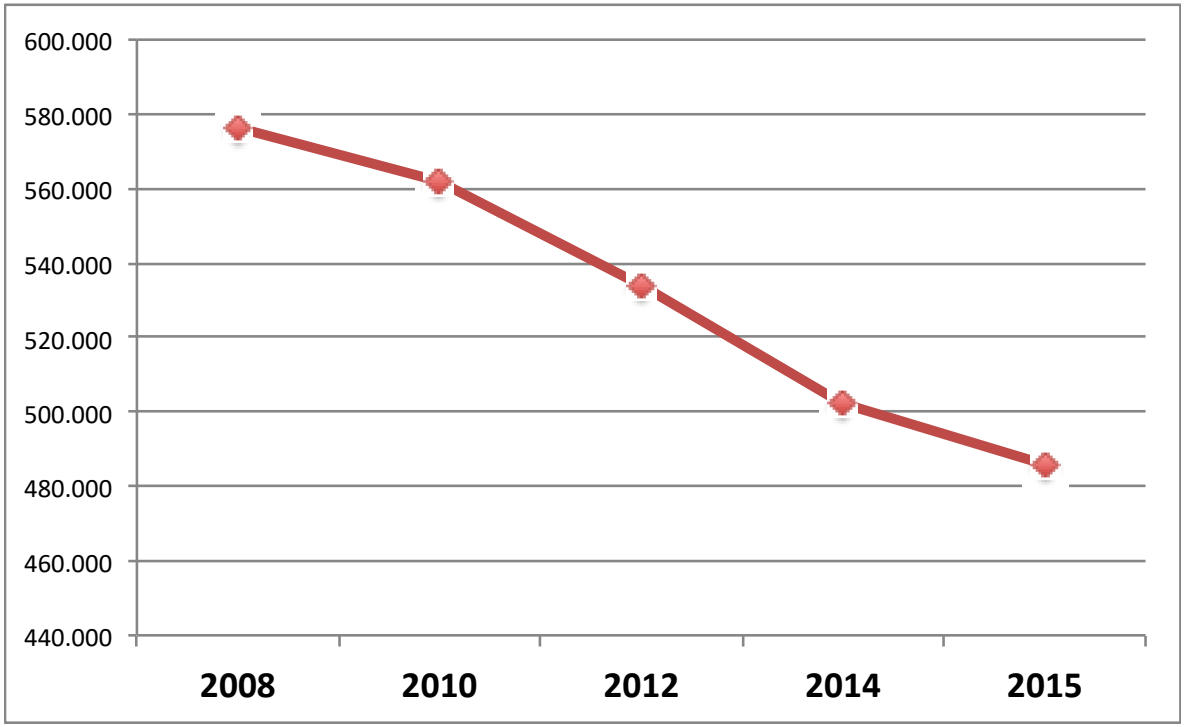
Italia – Tasso natalità
Anni 1980-2015



Fonte: ISTAT

Anni 2008-2015

Numero nati in Italia
Periodo 2008 - 2015



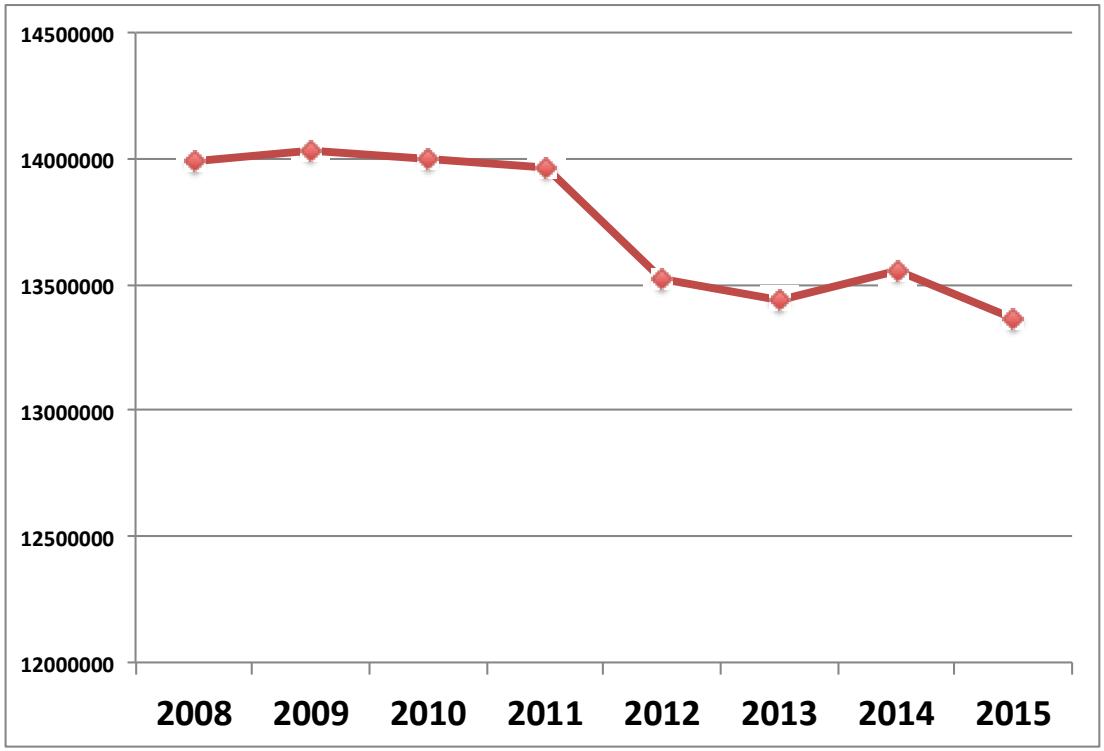
Fonte: ISTAT

Differenza 2008-2015:
- 90.879 nascite

(-16%)

- Cause strutturali (riduzione popolazione femminile in età feconda)
- Abortività volontaria
- Cause socio-economiche
- Cause organiche

Numero donne in età fertile (15-49 anni) Italia – anni 2008 - 2015



Fonte: ISTAT

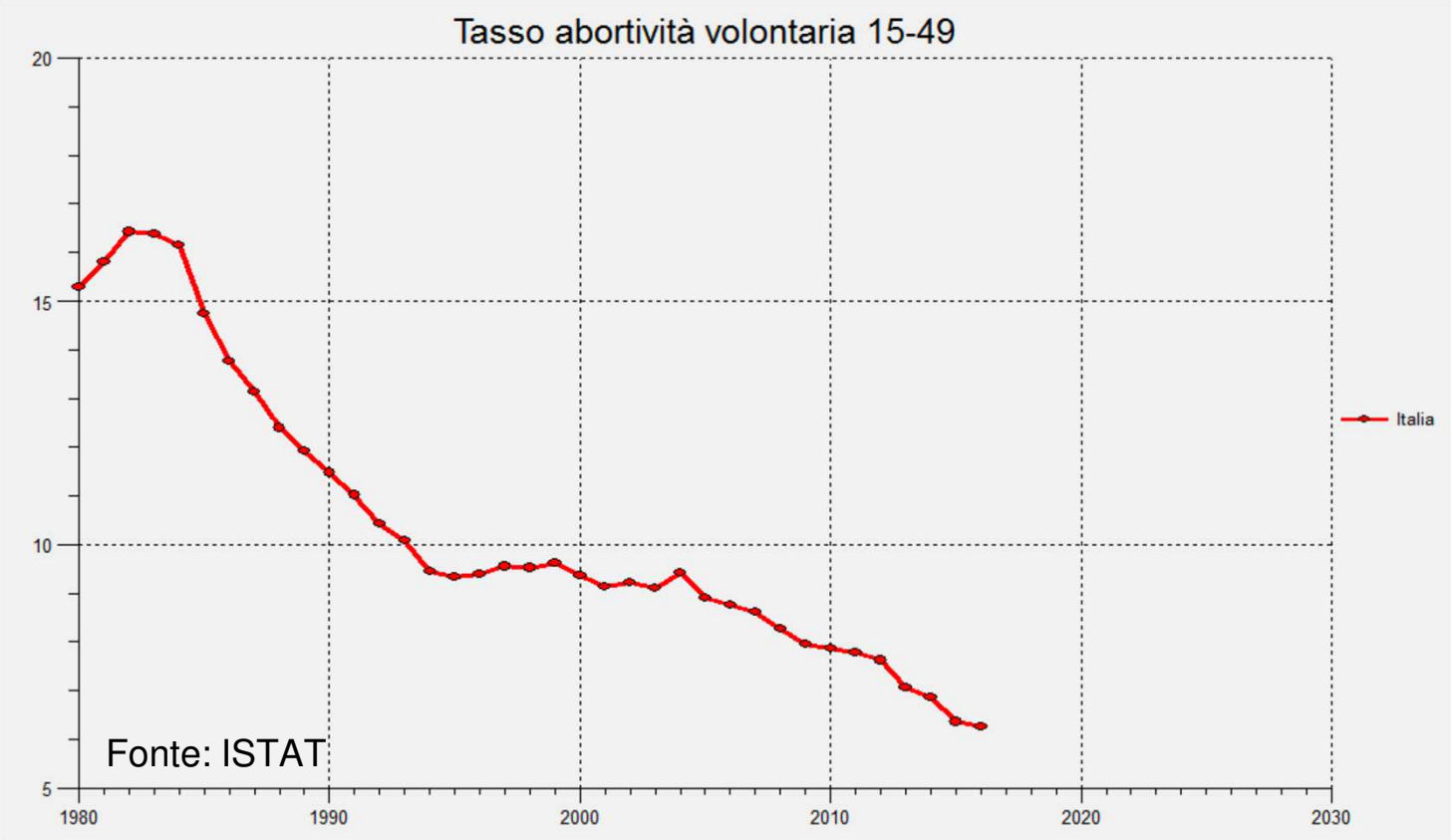
Differenza 2008-2015:

-5%

"peso relativo" scarso e a sua volta parzialmente dipendente dal calo demografico

(conseguenza del calo di fecondità nel ventennio 1976-1995)

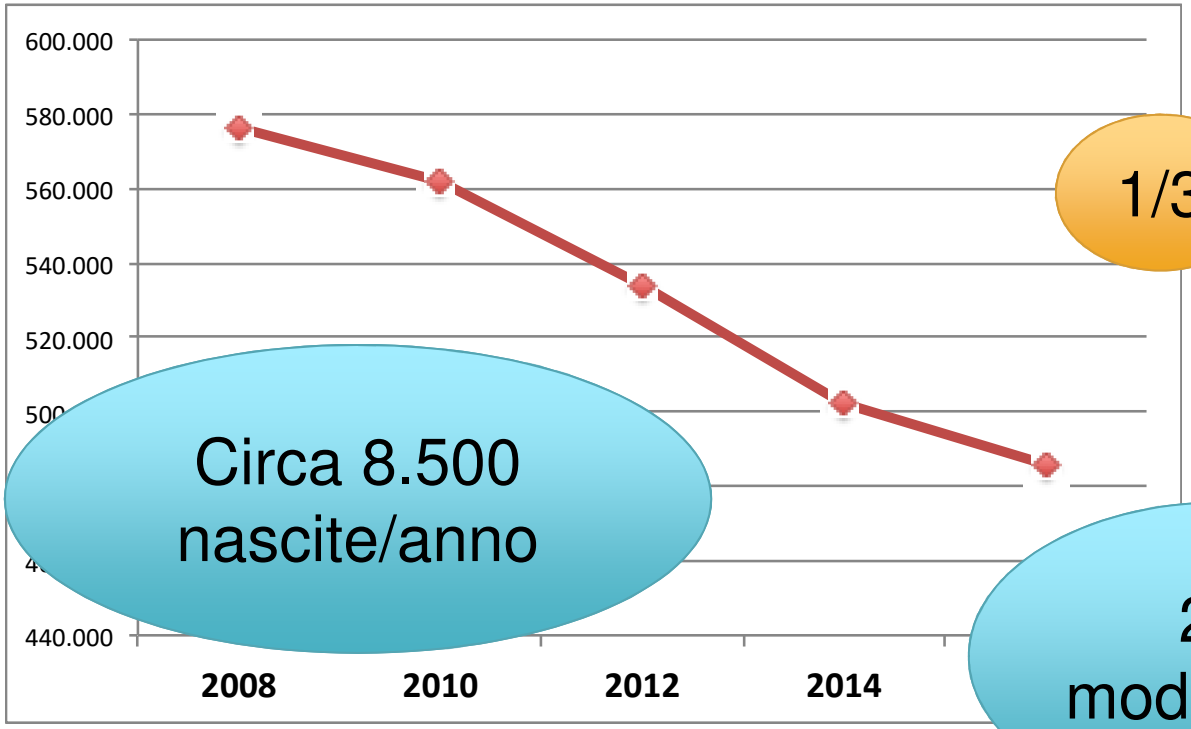
Tasso di abortività volontaria in Italia
Periodo 2008 - 2015



Riduzione progressiva e costante

Ininfluente tra le cause del ridotto tasso di natalità

Numero nati in Italia
Periodo 2008 - 2015



Differenza 2008-2015:
- 90.879 nascite

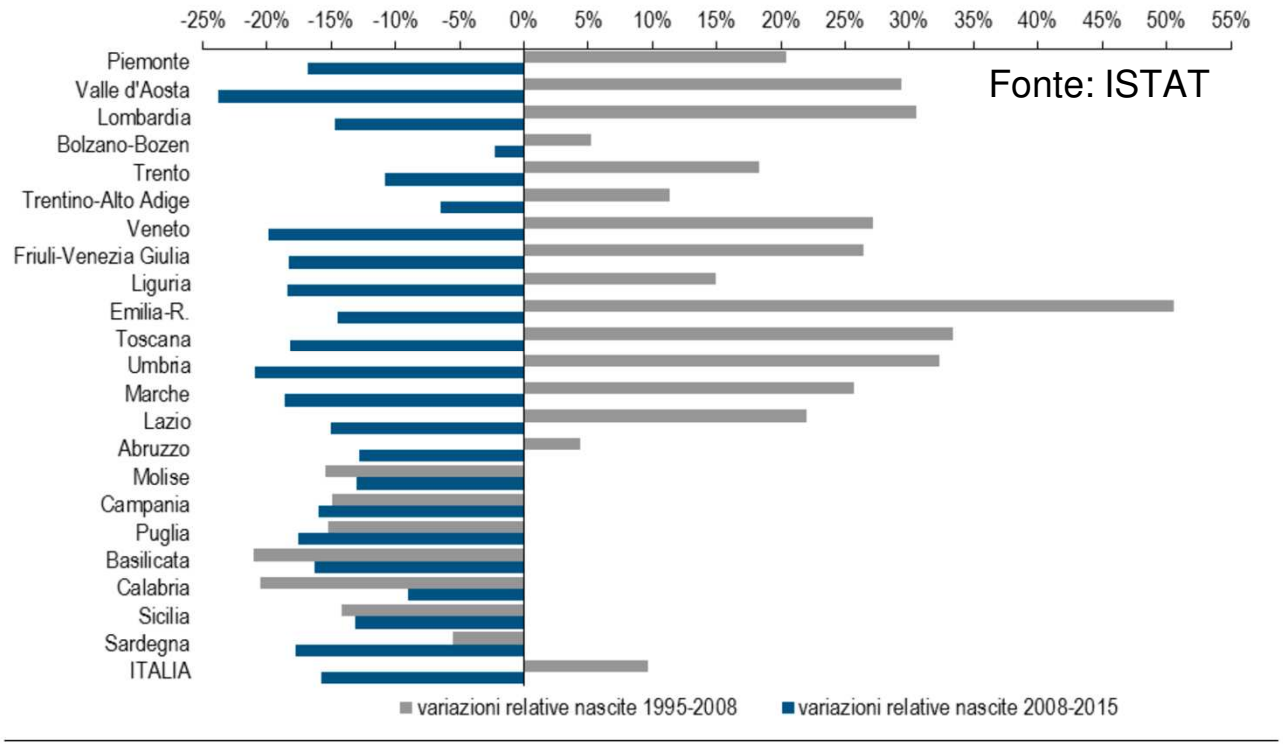
(-16%)

1/3

Circa 8.500 nascite/anno

2/3 modificabili

FIGURA 2. VARIAZIONI PERCENTUALI DELLE NASCITE PER REGIONE. Periodi 1995-2008 e 2008-2015



Fonte: ISTAT

Calo delle nascite costante nelle regioni meridionali dal 1995, presente anche nelle regioni centro-settentrionali solo a partire dal 2008

Cause socio-economiche hanno sicuramente influenzato questo dato.
Ma quanto ?

Human Reproduction Update, Vol.16, No.6 pp. 590–602, 2010
Advanced Access publication on July 4, 2010 doi:10.1093/humupd/dmq023

human reproduction update

Europe the continent with the lowest fertility

The ESHRE Capri Workshop Group*,†

*Correspondence address. P.G. Crosignani, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via M. Fanti, 6, Milano 2012
Italy. E-mail: piergiorgio.crosignani@unimi.it.

- Europe is the continent with the lowest total fertility rate (TFR)
- Effect independent from contraception
- Government policies that transfer cash to families for pregnancy and child support have small effects on the TFR

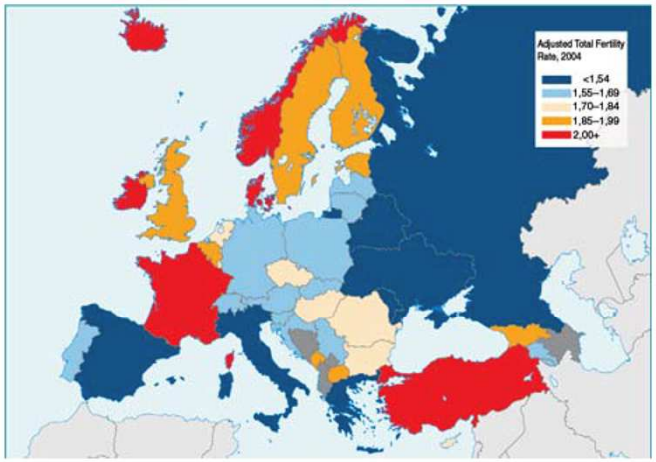


Figure 2 Adjusted total fertility rate (TFR) for European countries (Lutz *et al.*, 2008b). (The values have been adjusted for the tempo effect arising from postponement of childbearing which depresses the values of the conventional period TFR) The lowest fertility rates in 2004 were registered in Eastern Europe, Italy, Greece and Spain.

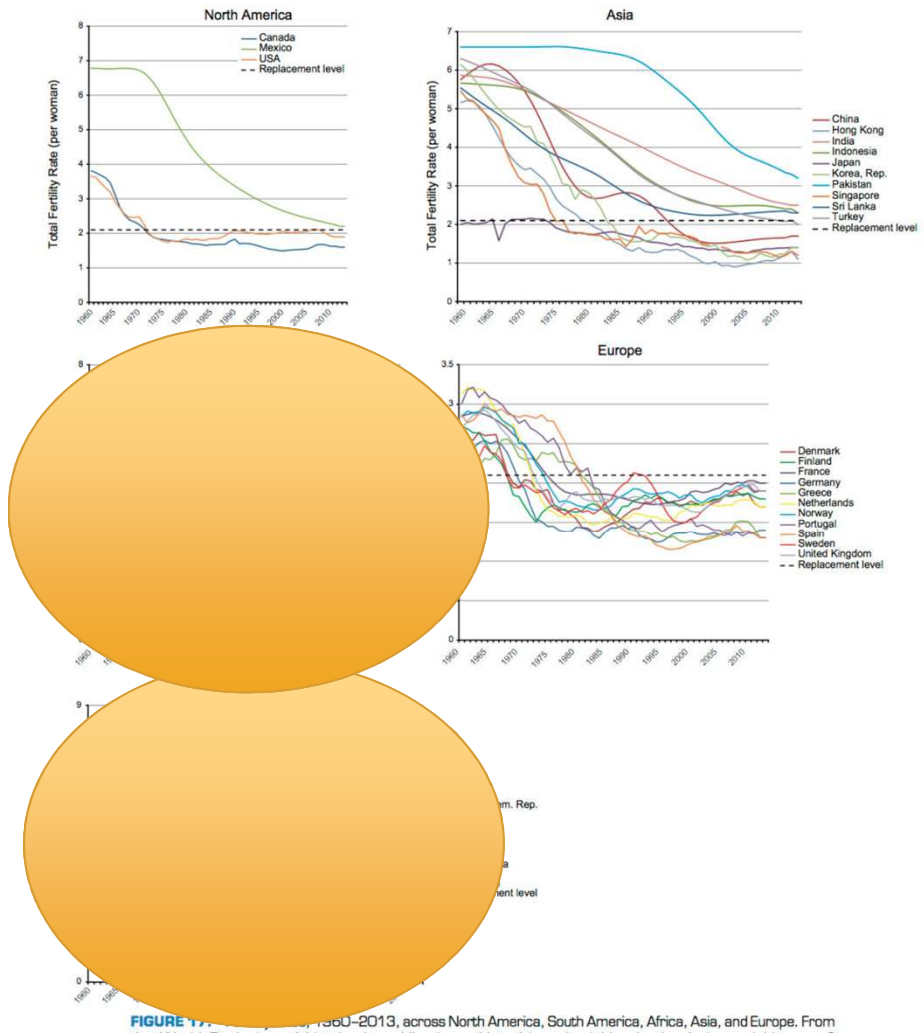


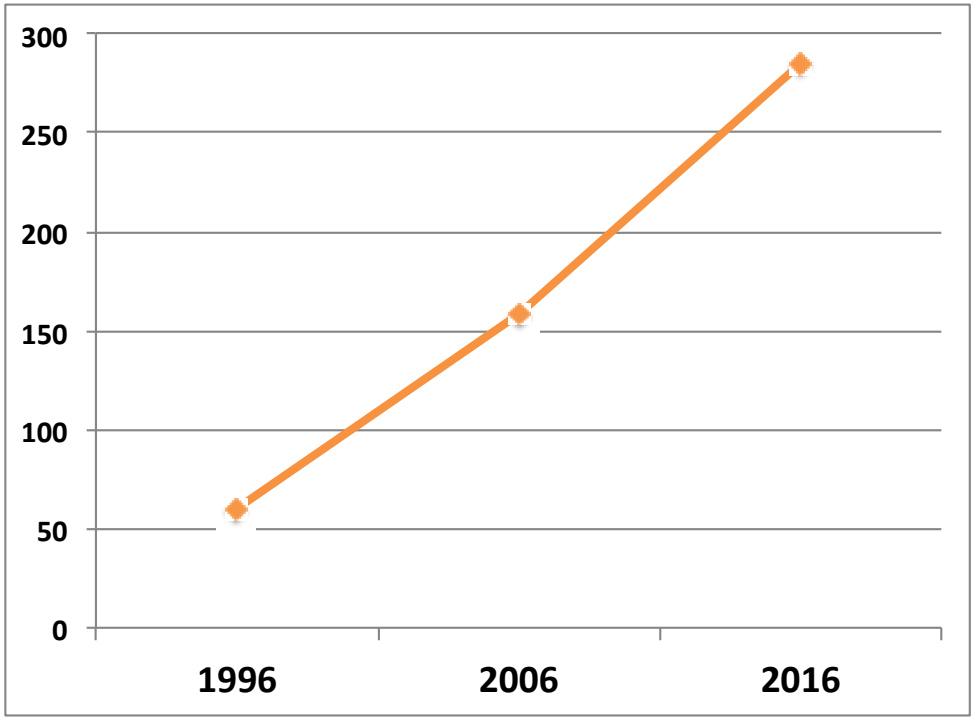
FIGURE 1 ... 1960–2013, across North America, South America, Africa, Asia, and Europe. From the World Bank: http://databank.worldbank.org/data/views/variableselection/selectvariables.aspx?source=world-development-indicators.

Soglia di sostituzione: tasso di fertilità femminile del 2.1, limite al di sotto del quale la popolazione non può essere sostenuta (Fonte: World Bank)

A livello internazionale la riduzione dei tassi di fertilità è una tendenza comune ma è molto meno marcata nelle aree meno ricche e meno industrializzate (Africa, America Latina), che sono le sole a mantenersi al di sopra della soglia di sostituzione

Fattori socio-economici che generano DISUGUAGLIANZE hanno certamente un ruolo rilevante ma NON SUFFICIENTE a spiegare il vistoso calo di fertilità registrato oggi in ogni area del nostro Paese ed a livello internazionale

Pollution and reproduction



4232
(August 2017)

PubMed.gov
US National Library of Medicine
National Institutes of Health

No. of papers

Adult air pollution exposure and risk of infertility in the Nurses' Health Study II

Hum. Reprod. (2016) 31 (3): 638-647 first published online January 2, 2016

"We observed an association between all size fractions of PM exposure… and incidence of infertility".

inquinanti atmosferici
(particolato, inquinanti gassosi)

Urinary Concentrations of Organophosphate Flame Retardant Metabolites and Pregnancy Outcomes among Women Undergoing *in Vitro* Fertilization

Courtney C. Carignan,[1] Lidia Mínguez-Alarcón,[1] Craig M. Butt,[2] Paige L. Williams,[3,4] John D. Meeker,[5] Heather M. Stapleton,[2] Thomas L. Toth,[6] Jennifer B. Ford,[1] and Russ Hauser[1,4,6] for the EARTH Study Team

"Using IVF … we found that concentrations of some urinary PFR metabolites were negatively associated with proportions of successful fertilization, implantation, clinical pregnancy, and live birth " *(EHP Aug 2017)*

contaminanti alimentari
(pesticidi, EDCs)

Effect of electromagnetic field exposure on the reproductive system

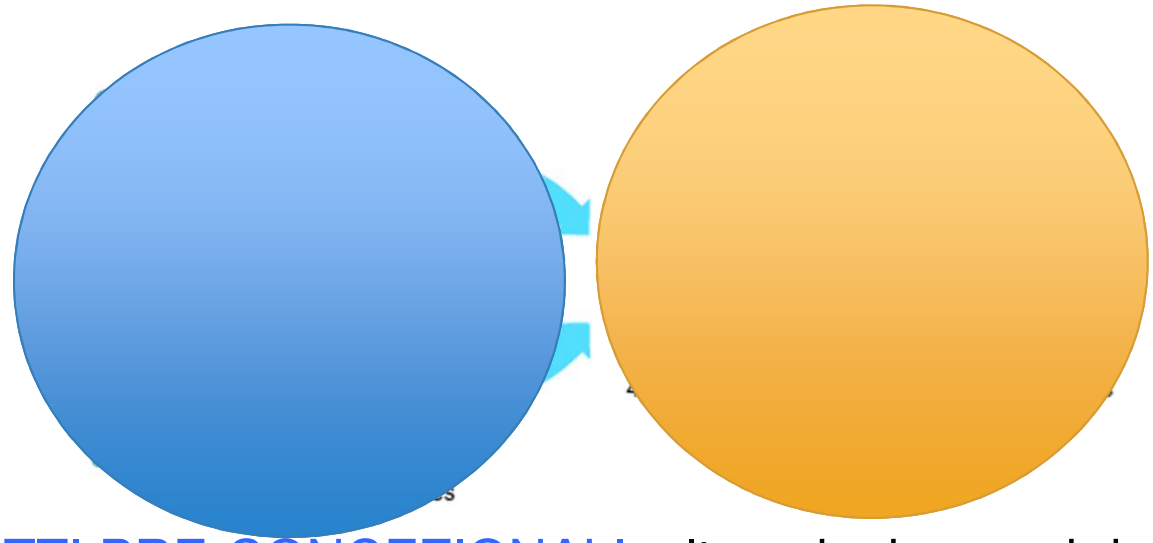
Clin Exp Reprod Med 2012;39(1):1-9

Myung Chan Gye, Chan Jin Park

"Reproductive parameters reported to be altered by EMF exposure include male germ cell death, the estrous cycle, reproductive endocrine hormones, reproductive organ weights, sperm motility, early embryonic development, and pregnancy success. ".

EMF

Inquinamento e fertilità



- EFFETTI PRE-CONCEZIONALI: alterazioni ormoni della riproduzione, alterazione genetiche o epigenetiche dei gameti

- EFFETTI POST-CONCEZIONALI: capacità degli inquinanti di causare infiammazione endometriale, di attraversare placenta, membrane cellulari e nucleari e di determinare effetti su gravidanza, organogenesi e sviluppo fetale

Carré *et al. Environmental Health* (2017) 16:82
DOI 10.1186/s12940-017-0291-8

Environmental Health

Aug 2017

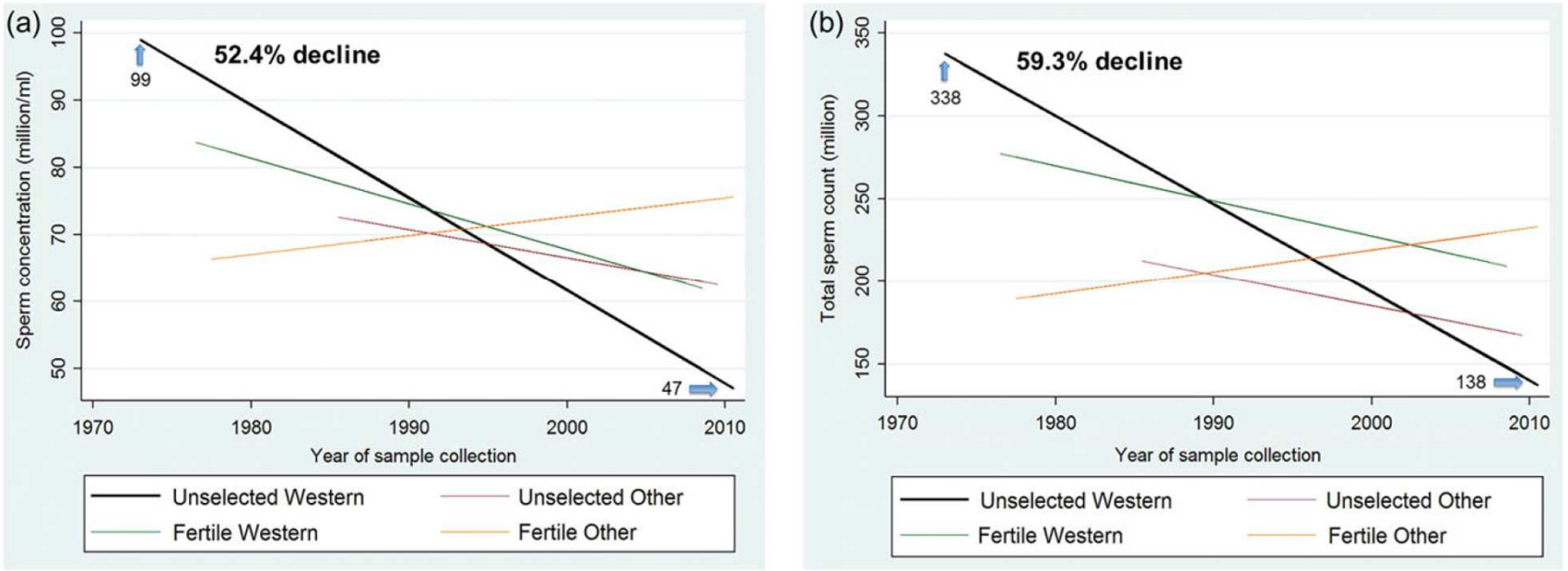
REVIEW Open Access

Does air pollution play a role in infertility?: a systematic review

Julie Carré[1], Nicolas Gatimel[1,2], Jessika Moreau[1,2], Jean Parinaud[1,2,3*] and Roger Léandri[1,2]

*"**Conclusion**: Both animal and human epidemiological studies support the idea that air pollutants cause defects during gametogenesis leading to a drop in reproductive capacities in exposed populations. Air quality has an impact on overall health as well as on the reproductive function, so increased awareness of environmental protection issues is needed among the general public and the authorities"*

Negli uomini occidentali il numero e la concentrazione degli spermatozoi si sono ridotti di oltre il 50% rispetto al 1973



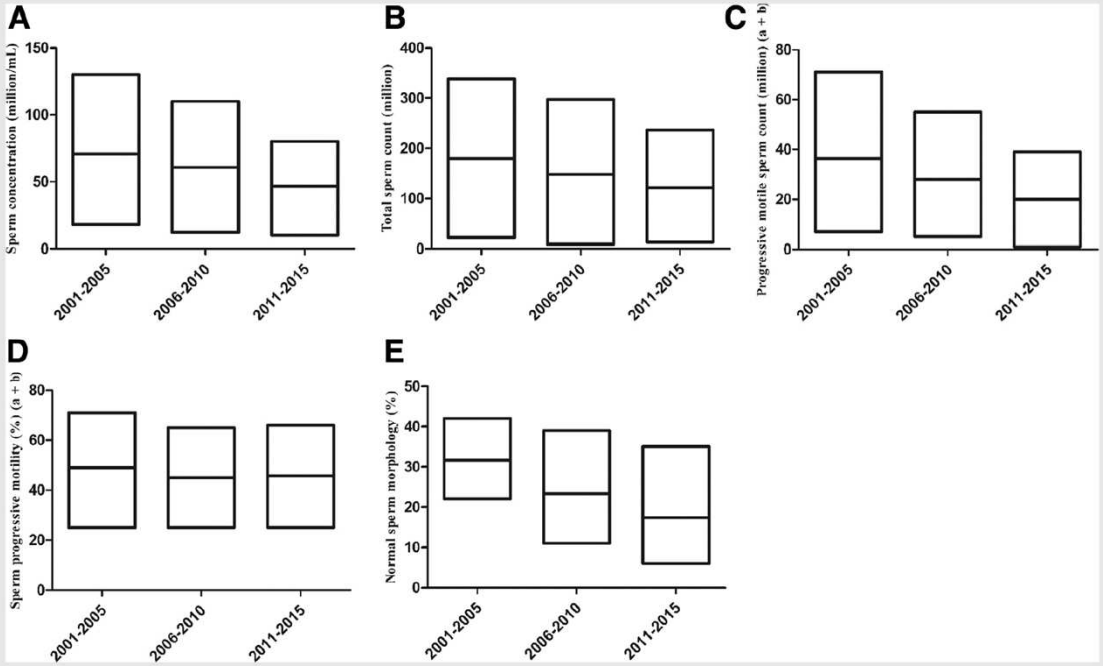
Levine et al, Human Reproduction Update, 2017

Decline in semen quality among 30,636 young Chinese men from 2001 to 2015

Chuan Huang, Ph.D.,[a] Baishun Li, B.S.,[b] Kongrong Xu, M.S.,[a] Dan Liu, M.S.,[a] Jing Hu, M.S.,[b] Yang Yang, B.S.,[b] HongChuan Nie, M.D., Ph.D.,[b] Liqing Fan, M.D., Ph.D.,[a,b] and Wenbing Zhu, M.D., Ph.D.[a,b]

Fertility and Sterility® Vol. 107, No. 1, January 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2016.09.035



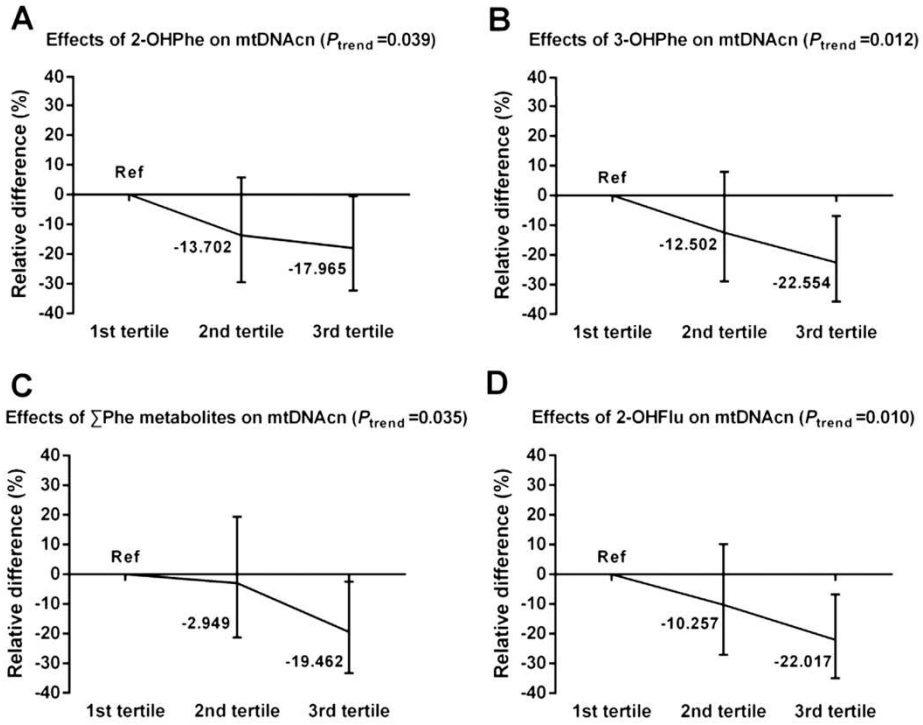
Semen quality of 30,636 young men from the general population in Hunan, China. Semen parameters of Chinese young men from the general population. The bars show the 5th to 95th percentiles with median lines. (**A**) Sperm concentration, (**B**) total sperm count, (**C**) progressive motile sperm count, (**D**) sperm progressive motility, and (**E**) normal sperm morphology decreased during the 15-year period.

Huang. Declining semen quality in Chinese men. Fertil Steril 2016.

Nei giovani cinesi la concentrazione degli spermatozoi si è ridotta di circa il 30% negli ultimi 15 anni, con riduzione della motilità e alterazioni della morfologia

Polycyclic aromatic hydrocarbons exposure decreased sperm mitochondrial DNA copy number: A cross-sectional study (MARHCS) in Chongqing, China☆

Xi Ling [a], Guowei Zhang [a], Lei Sun [a], Zhi Wang [a], Peng Zou [a], Jianfang Gao [a], Kaige Peng [a], Qing Chen [a], Huan Yang [a], Niya Zhou [a], Zhihong Cui [a], Ziyuan Zhou [b], Jinyi Liu [a], Jia Cao [a], Lin Ao [a, *]



Ling X et al, Environmental pollution 220(2017):680

2017

Contents lists available at ScienceDirect
Environmental Pollution
journal homepage: www.elsevier.com/locate/envpol

L'esposizione a bassi livelli di IPA può causare anormalità nei mitocondri di spermatozoi umani (danno e disfunzione mitocondriale)

Exposure to ambient air pollution-does it affect semen quality and the level of reproductive hormones?

Michał Radwan[1], Joanna Jurewicz[2], Kinga Polańska[2], Wojciech Sobala[2], Paweł Radwan[1], Michał Bochenek[3], Wojciech Hanke[2]

Annals of Human Biology 2015
Journal of the Society for the Study of Human Biology

Ann Hum Biol, Early Online: 1–7
 DOI: 10.3109/03014460.2015.1013986

"The statistically significant association was observed between abnormalities in sperm morphology and exposure to all examined air pollutants (PM10, PM2.5, SO2, NOX, CO). Exposure to air pollutants (PM10, PM2.5, CO, NOx) was also negatively associated with the level of testosterone. Additional exposure to PM2.5, PM10 increase the percentage of cells with immature chromatin (HDS)".

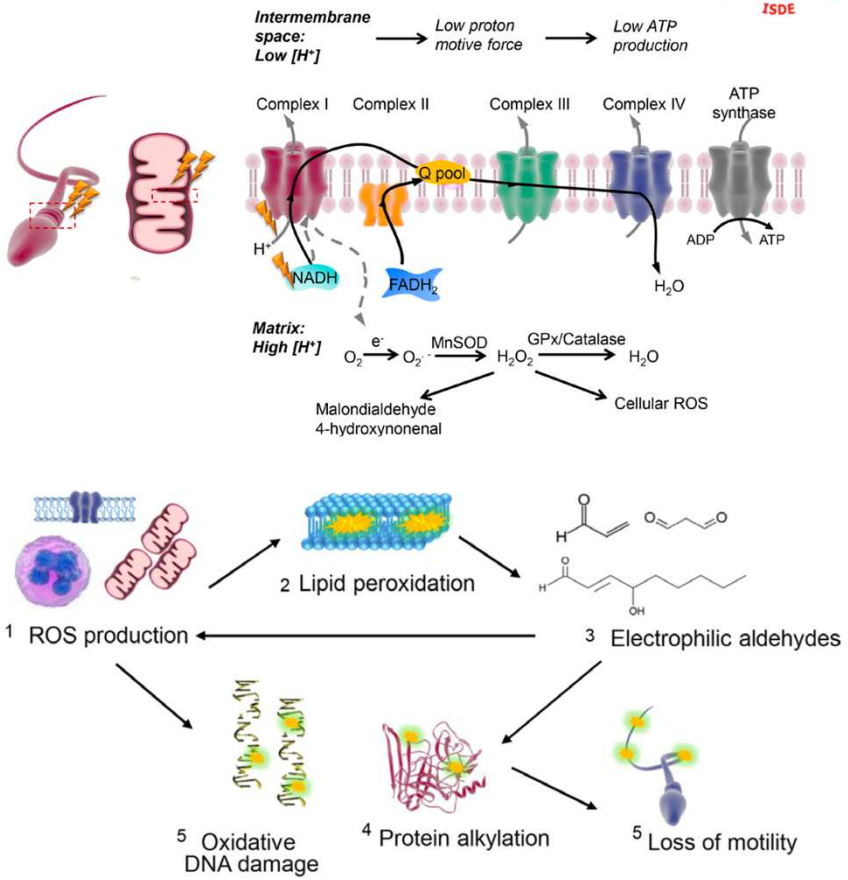
REPRODUCTION
REVIEW

The effects of radiofrequency electromagnetic radiation on sperm function

B J Houston[1], B Nixon[1], B V King[2], G N De Iuliis[1,*] and R J Aitken[1,*]

Houston et al, Reproduction. 2016;152(6):R263-R276

- Effetti negativi in 21 studi su 27
- Ridotta motilità spermatica (11/15)
- Elevata produzione ROS (7/7)
- Ridotto livello antiossidanti (6/6)
- Danno al DNA (4/5)



HUMAN FERTILITY, 2017
https://doi.org/10.1080/14647273.2017.1358828

2017

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

Exposure to modern, widespread environmental endocrine disrupting chemicals and their effect on the reproductive potential of women: an overview of current epidemiological evidence

Anetta Karwacka[a], Dorota Zamkowska[b], Michał Radwan[a] and Joanna Jurewicz[c]

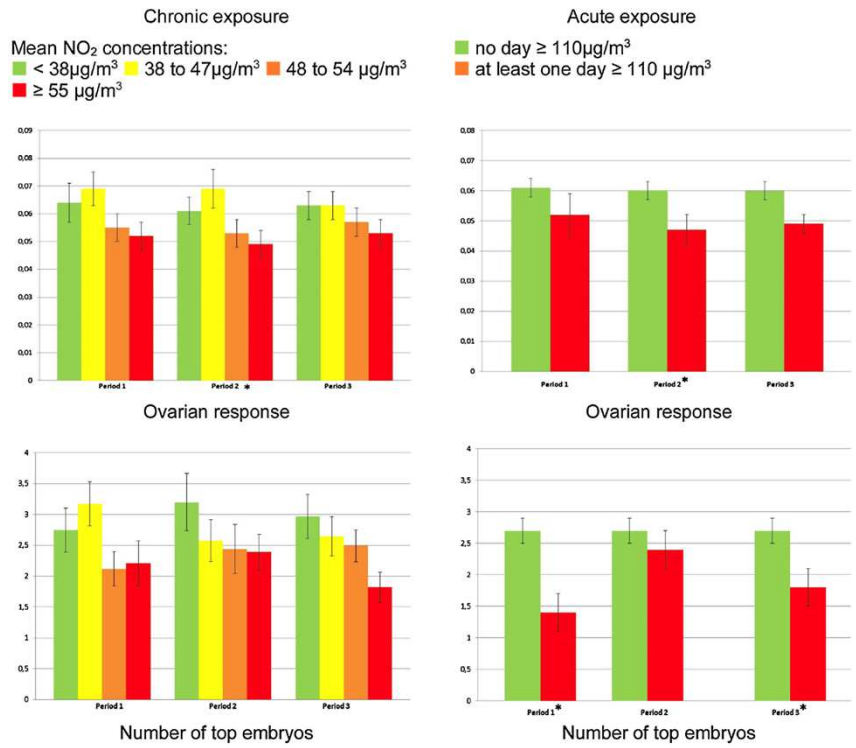
Exposure to environmental endocrine disrupting chemicals decrease:

(i) oestradiol levels (BPA);
(ii) anti-Müllerian hormone concentrations (PCBs);
(iii) antral follicle count (BPA, parabens, phthalates);
(iv) oocyte quality (BPA, triclosan, phthalates, PCBs);
(v) fertilization rate (PFCs, PCBs);
(vi) implantation (BPA, phthalates, PCBs);
(vii) embryo quality (triclosan, PCBs, BPA);
(viii) rate of clinical pregnancy and live births (parabens, phthalates).

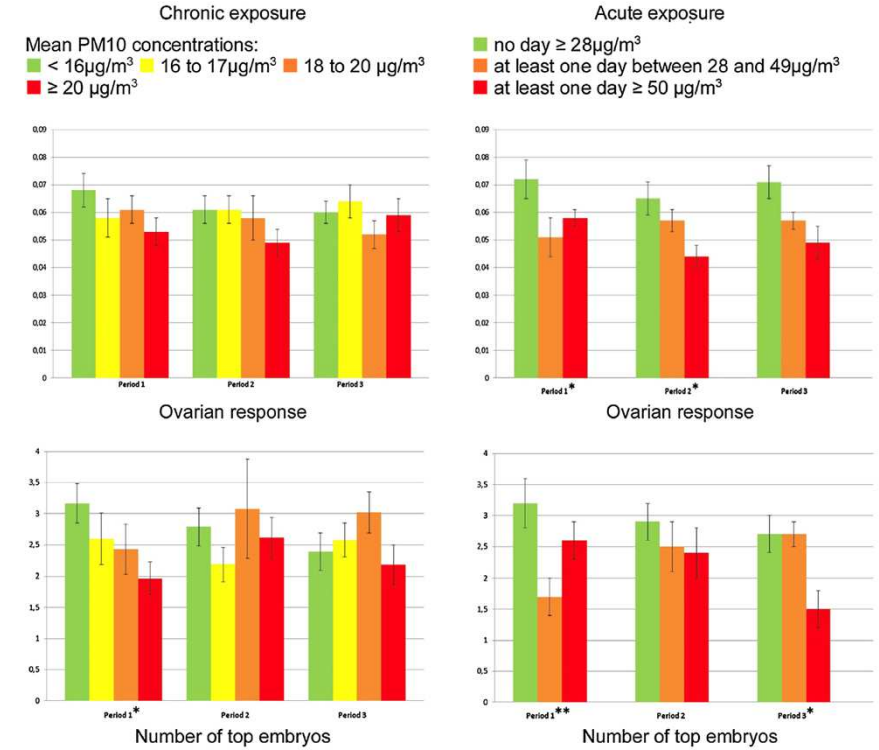
IVF: l'esposizione acuta e cronica ad elevate concentrazioni atmosferiche di NO2 e PM10 peggiora la risposta ovarica a stimolazione e riduce il numero di embrioni di qualità migliore

*(Carrè et al, European Journal of Obstetrics & Gynecology and Reproductive Biology 210 (**2017**) 116–122)*

NO2



PM10



PM2.5 e **infiammazione intrauterina**
anche per esposizioni modeste

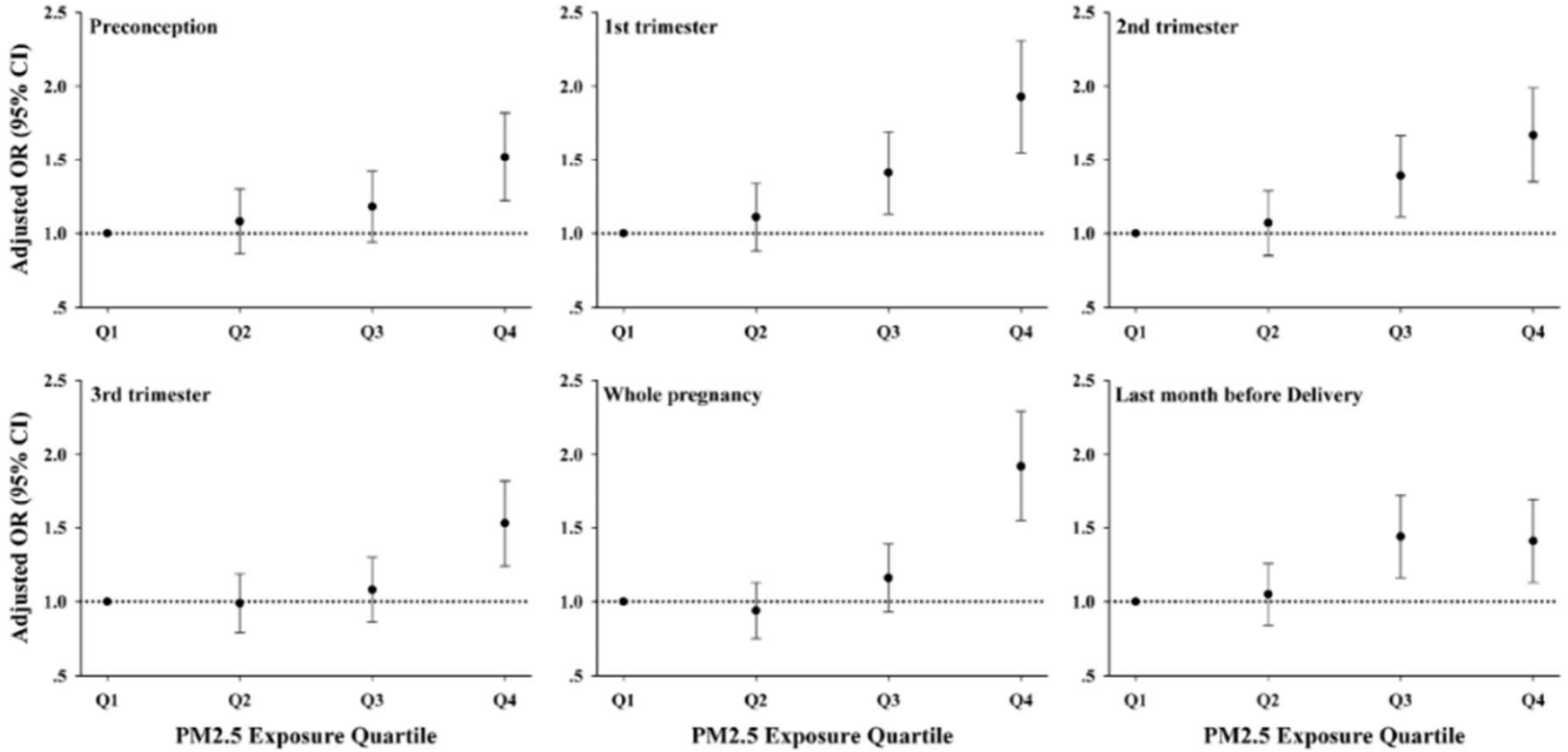


Figure 2. Adjusted ORs quantifying associations between $PM_{2.5}$ exposure and IUI by quartile and period of prepregnancy or pregnancy in 5,059 mothers from 1999 to 2012.

Nachman et al, EHP 2016


Rapporto abortività spontanea 15-49
150
140
130
120
110
100
90
80
1980
1990
2000
2010
2020
Italia

Inquinamento e aborti spontanei

Relationships between mild PM10 and ozone urban air levels and spontaneous abortion: clues for primary prevention

Agostino Di Ciaula[a]* and Massimo Bilancia[b]

Table 4. Adjusted risk rate, effect estimates, approximate significance of smooth terms and global model scores in the selected best model.

Approximate significance of parameter estimates					
	Adj. RR (CI)	Estimate	Std. Error	*Z*-value	*p*
(Intercept)		−0.317	0.450	−0.71	NS
PM10	1.20 (1.08–1.34)	0.018	0.006	3.26	<0.01
NO_2	0.96 (0.87–1.05)	−0.004	0.005	−0.82	NS
O_3	1.34 (1.26–1.42)	0.029	0.003	9.33	<0.001
Approximate significance of smooth terms					
	Edf*	X^2 value**		*p***	
s (temperature, δ_1)	8.37	8.84		<0.001	
s (humidity, δ_2)	7.59	8.47		<0.001	
Global scores					
R^2 (adj)	Dev. explained			UBRE score	
0.34	51.8			3.61	
*Test on the basis dimension used for smooth terms****					
		k'		*k*-index	
s (temperature, δ_1)		9.00		1.14	
s (humidity, δ_2)		9.00		1.14	

A. Di Ciaula, M.Bilancia. IJEHR 2015

Effetti post-concezionali (esposizione *in utero*)

- Aborto spontaneo
- Morte fetale
- Basso peso alla nascita
- Ridotta circonferenza cranica
- Nascita pretermine
- Malformazioni congenite

Indicatori sensibili di danno sanitario da esposizioni ambientali

Conclusioni

- L'incremento epidemiologico dell'infertilità è da mettere in relazione a cause strutturali e socio-economiche ma anche a inquinanti introdotti attraverso aria, acqua e cibo
- I 2/3 dei fattori causali dell'infertilità sono modificabili
- Il "peso relativo" delle cause ambientali sembra essere prevalente rispetto a quello delle cause strutturali e questo impone l'applicazione di misure preventive

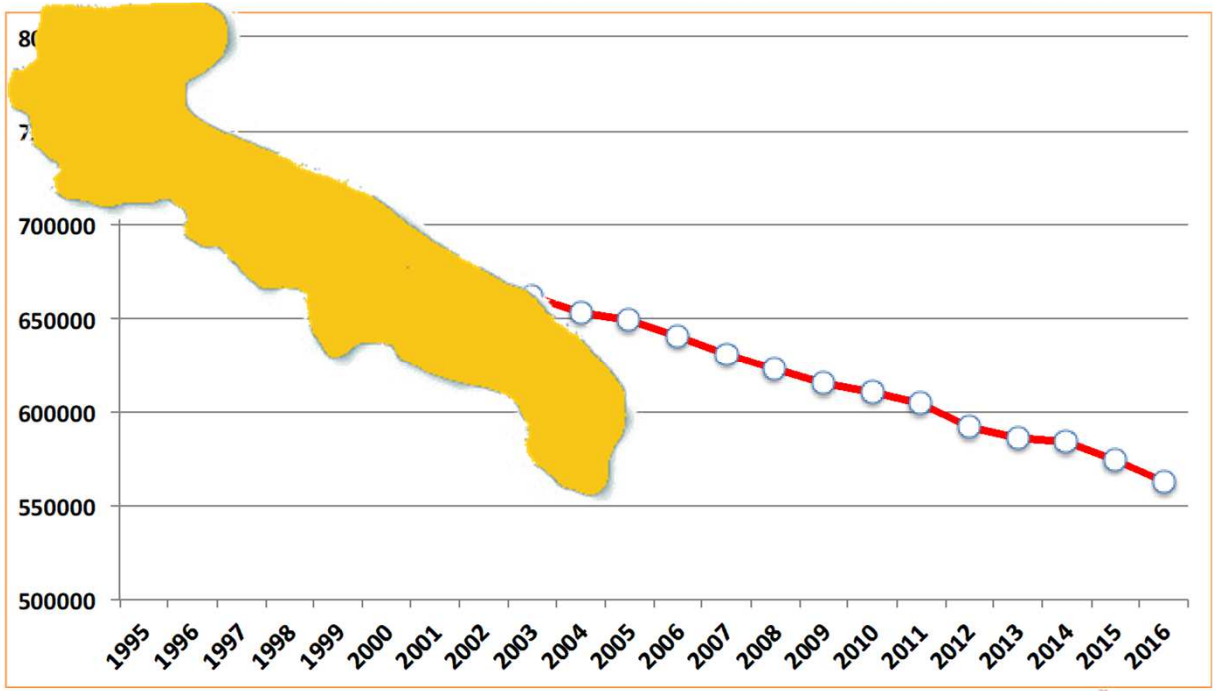
*È possibile e **URGENTE** fare PREVENZIONE PRIMARIA !*

C’è soltanto una guerra che può permettersi il genere umano: la guerra contro la propria estinzione.
(Isaac Asimov)

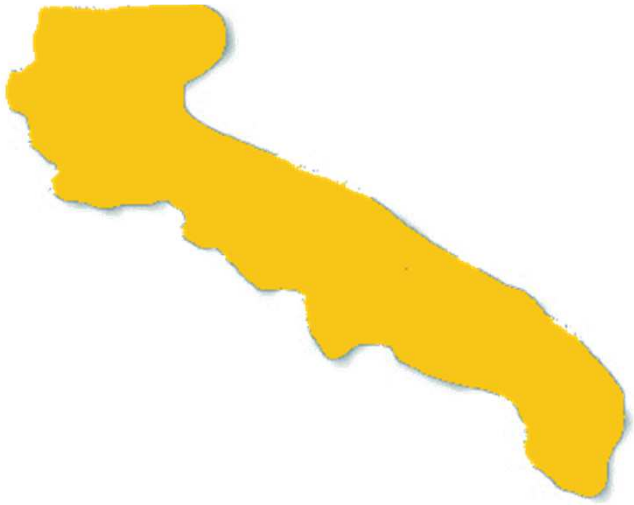
Grazie per l'attenzione

Contatti:

- www.ISDE.it
- www.ISDE.org
- agostinodiciaula@tiscali.it



Regione Puglia
n. bambini 0–14 anni
1995-2016

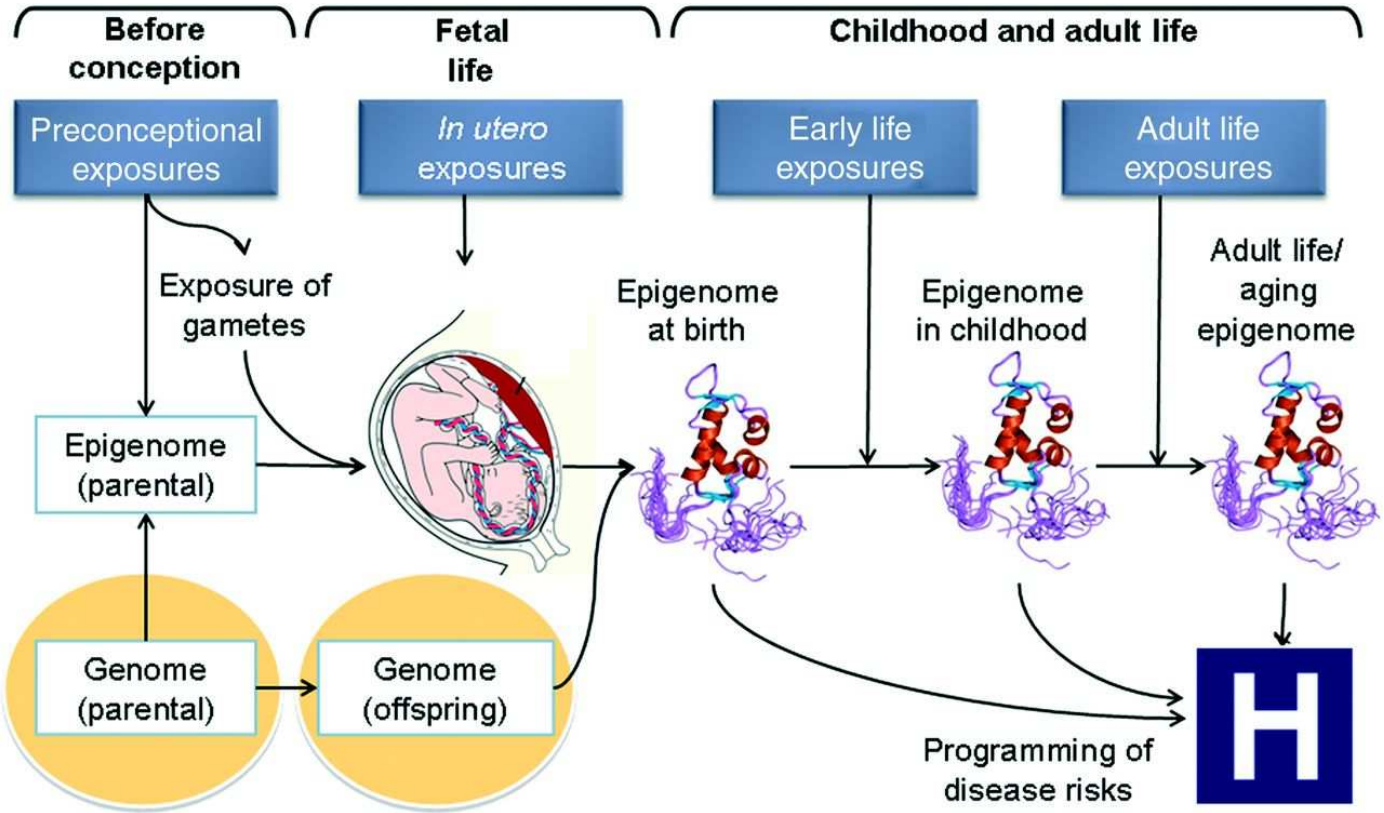


752.264
nel **1995**

562.777
nel **2016**

-25 %
- 9.023 (- 1.3 %) all'anno

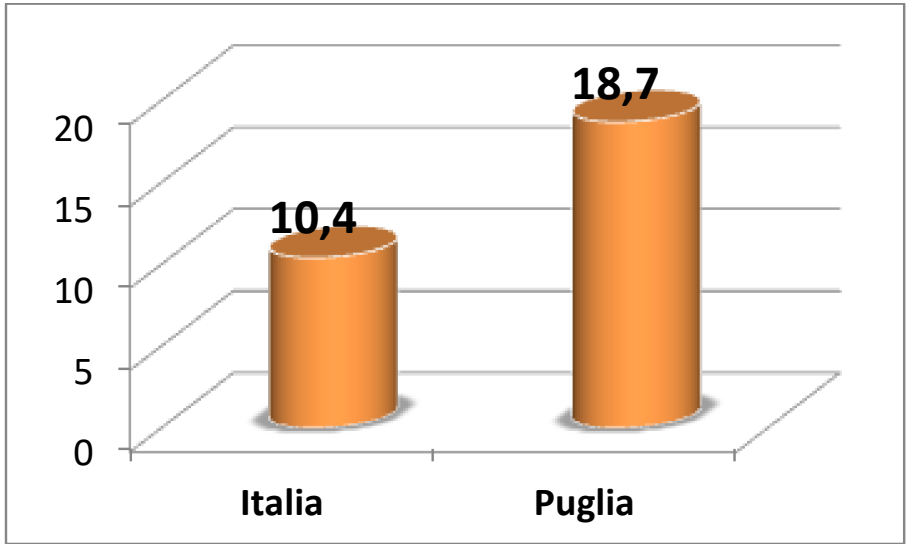
Bambini 0-14 anni


Before conception
Fetal life
Childhood and adult life
Preconceptional exposures
In utero exposures
Early life exposures
Adult life exposures
Exposure of gametes
Epigenome at birth
Epigenome in childhood
Adult life/ aging epigenome
Epigenome (parental)
Genome (parental)
Genome (offspring)
Programming of disease risks

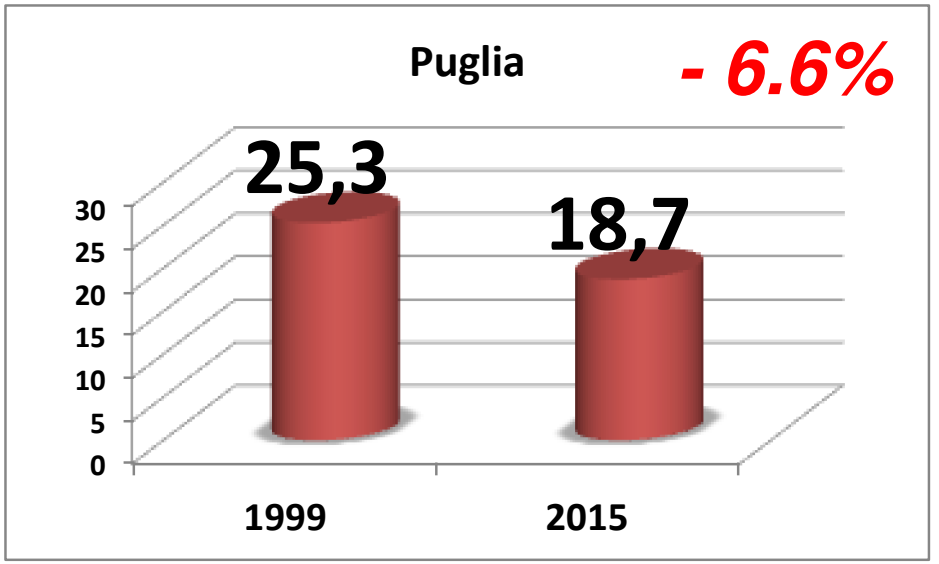
Cause maschili

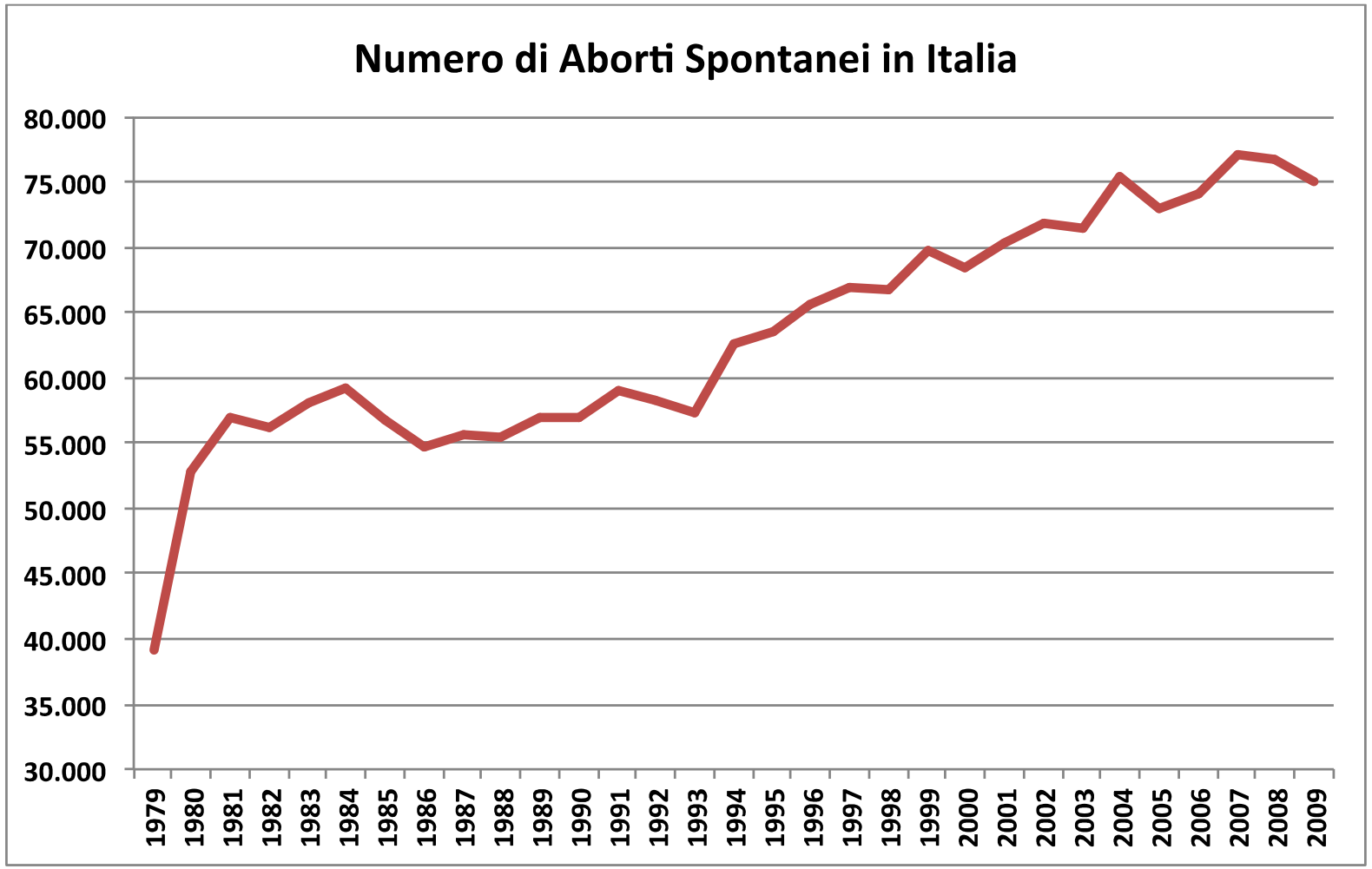
Spermatozoi
Ipospadia
Prostata (BPA)

Incidenza di povertà relativa (%)
Anno 2015



Incidenza di povertà relativa (%)
Anni 1999- 2015




Numero di Aborti Spontanei in Italia
80.000
75.000
70.000
65.000
60.000
55.000
50.000
45.000
40.000
35.000
30.000
1979
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
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1991
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(Fonte: ISTAT)