

**Molto grazie  
a Prof. Chiara Benedetto  
and her team**

**European Union started in Italy**



**Foundation of Rome (753 A.C.)**



**Treaty of Rome (1957) „Oggi fanno l'Europa“**

**Rome (1999) Recognition of subspecialties by EBCOG**



**Molto grazie a Prof. Tullia Todros , for charing & sharing**

**TRIAL**  
**R**ANDOMIZING  
**U**MBILICAL and  
**F**ETAL  
**FL**OW in  
**E**UROPE



**Turino 2001**



**Muniqu 2004**



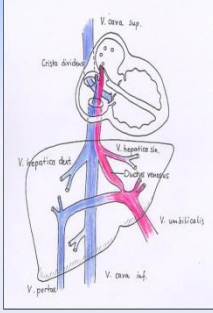
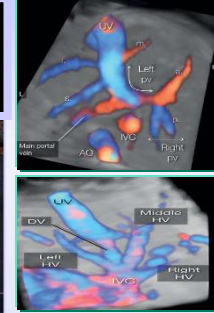
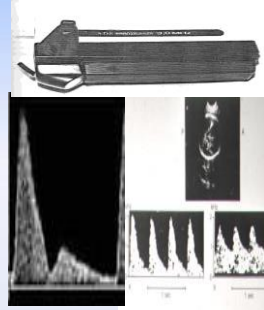
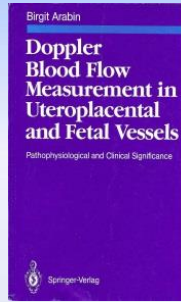
**Amsterdam 2009**

# From Fascination of Detection to Reflection

Big? Normal? Small?

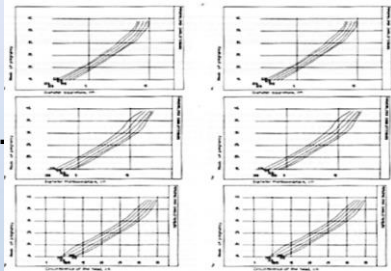
Perfusion? Diffusion?

Long-term outcome ?

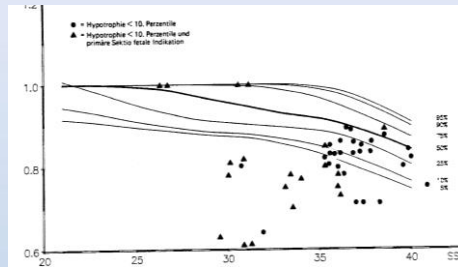


1978

Fetal growth diagnosis by sonographic somatography. Arch Gyneol. 228.1,166



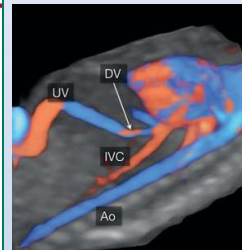
1988



2000 - 2016

2 year neurodevelopmental and intermediate perinatal outcomes in infants with very preterm fetal growth restriction (TRUFFLE): a randomised trial

Christoph C Lees, Neil Marlow, Aleid van Wassenaer-Leemhuis, Birgit Arabin, Caterina M Blando, Christoph Brezinka, Sandra Calvert, Jan B Dieks, Anke Diemert, Johannes Dovekat, Emira Fomazi, Tatiana Frasca, Wessel Garretzort, Kurt Hecher, Pasquale Martinieli, Eva Ostermayer, Ains T Papageorgiou, Dietmar Schlembach, KT M Schneider, Beckiran Thilagathan, Tullia Todros, Adriana Valamonica, Gerard HA Visser, Hans Wolff (for the TRUFFLE study group)

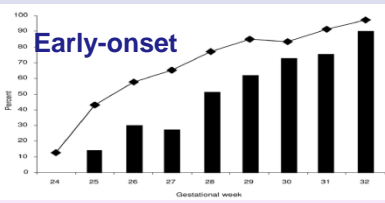


## Cross-cultural differences of outcome / „imbedded values“

Malpractice/ Profit / Ethics?



Death or CP & Blindness?

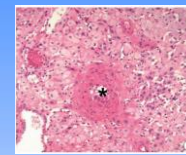
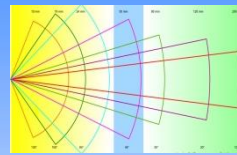


Baschat et al. Obstet Gynecol 2007; 109:223

Suffering? Common costs?



# ***Our Responsibilities***



***Placenta: „From womb to tomb?“ (scientific responsibility)***

***Outcome (parents wishes - responsibility society & policy makers)***

•What short- or long-term outcome do we care about?



•***Tertiary prevention (direct responsibility - MFM specialists)***

•When/where to deliver infants with early FGR (periviability)?

•When (how) to deliver infants with late FGR?

•When (how) to deliver infants with macrosomia?

***Secondary prevention (direct responsibility- MFM specialists)***

•Interventions in ongoing risk pregnancies (FGR / Macrosomia)?

***Primary prevention (indirect responsibility – physicians & society)***

•Pregnancy as a window for future health (Barker/ reverse Barker)

•How to prevent FGR /macrosomia preconceptionally & worldwide?

# Outcome Variations: a) Euronic Study

Differences to Start Neonatal Treatment @ the border of viability  
Consider Information of Parents/Management Decisions

(24 weeks, 560 g, poor start) Start

“When parents refuse”

Italy	96%	90%
Spain	90%	68%
France	82%	62%
Germany	98%	77%
Great Britain	96%	66%
Sweden	95%	79%
Netherlands	32%	0%



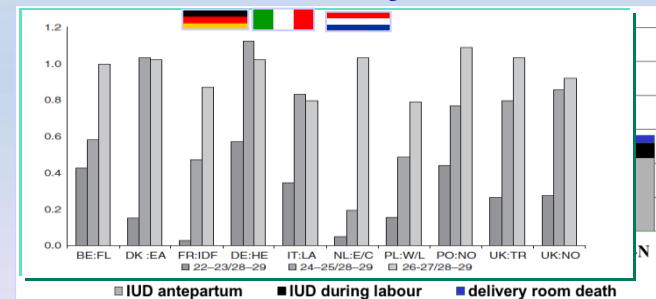
*De Leenw, et al. J Pediatr 2000 137:608-16*



# b) Mosaic Study

Different Death Rates/Interventions 22-32 wks  
LBW associated with poor outcomes (death/BPD)

*Kolle' et al. BMJ 2009; 116:1481*



Only 20% of long-term outcome in preterm FGRs attributable to data of fetal monitoring!  
Abnormal neurodevelopmental outcome at 2 years predicted by LBW, UA pH < 7.00 & placental villitis.  
Social Class/Genetics/Parental love & ambition *Torrance et al. UOG 2010; 36:171 Marlow 2010*

# Specification of Outcome Parameters

## Individual consent with parents

- Train your knowledge, vision and communicative skills!

## Delphi Procedure for prospective studies / meta-analyses

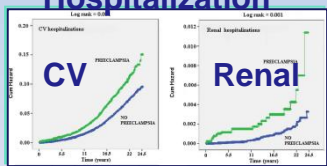
- Method for gathering data from experts
- Group communication process to achieve a consensus
- Series of questionnaires using multiple iterations to collect data
- Expert panel asked with progressive preciseness.
- Rounds follow each other with about a month's interval.
- Each participant's vote is weighed equally and grouped.
- *Ahmet.Baschat@gmail.com for FGR*



## Long-time Vision and new parameters

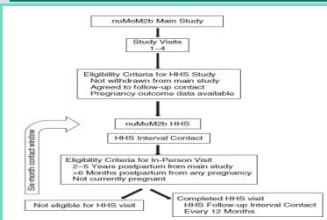
### -nuMoM26 Heart Health Study

### -look at BFJ and fetal heart



- Following NP women with FGR/PE by
- History
  - Subsequent CVD-rel.conditions (HBP,CAD,stroke, DM, thrombosis)
  - Lab(Urine:albumine/creatinine ratio, Nar peptidB, CRP, LDL-cholesterol, glucose) Metabolic syndrome

Parietal x visceral fat (mm)/ height (cm)  
BFI > 0.5 & OR GDM: OR 6.24 (1.9 - 20.9)



# Tertiary Prevention Early FGR: Immediate/Late Outcome

Obstetricians deliver in time to prevent mortality, too early to prevent long-term handicap

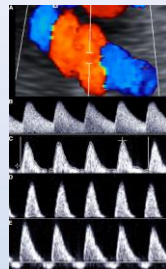
## 2 RCTs

Grit Study Based on umbilical Doppler Thornton et al. Lancet 2004; 364: 513

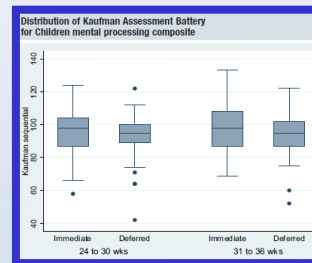
**Immediate**      **Prolongation**

Fetal death	3%	9%
Neonatal death	26%	18%
Mortality until discharge	10%	9%
Death or sev.handicap	19%	16%
CP / Griffith Score < 70	<b>10%</b>	<b>0% / 4%</b>

> 30 weeks no difference



Follow-up 6 years



**Obstetrician (no) impact on long-term outcome ?!**

Walker et al. AJOG 2011

## Truffle Study Based on DV Doppler/cCTG & safety net



Lees et al. Lancet 2015; 30;385(9983):2162-

Randomized Management Early FGR

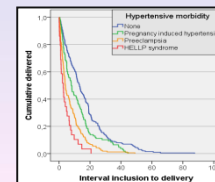
Early ductus venosus	Late ductus venosus	Computerized CTG



The proportion of infants surviving without neuroimpairment was non-significantly different, timing of delivery based on late changes in the DV improved developmental outcomes at 2 years.

131 (84%) 140 (92%) 131 (86%) Normal neurodevelopment among survivors

Sec. Analysis: CPR no impact on long-term outcome



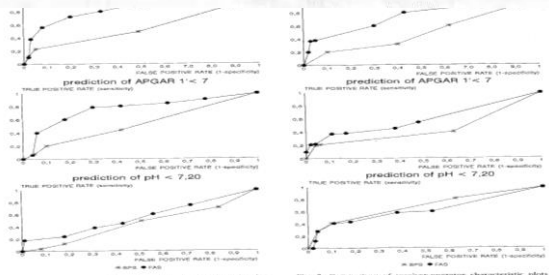
# Tertiary Prevention Late FGR: Immediate & Late Outcome

## Recognition of risks RCT – what to do?

Evaluation of the fetal assessment score in pregnancies at risk for intrauterine hypoxia

Birgi, Arabin, MD, Rosalind Snijders, MSc, Axel Mohrhaapt, BS, Volker Ragoosch, MD, and Kypros Nicolaides, MD  
Berlin, Germany and London, England

**AJOG 1993;169:549**



Results of CCA/UA & NST more predictive of later FD during labour, compared to CST and VAST (p < 0.001)

Predictiveness of antenatal umbilical artery Doppler for adverse pregnancy outcome in small-for-gestational-age babies according to customised birthweight centiles: population-based study

*Figueras et al. BJOG 2008 ;115:590*

Many instances of adverse outcome associated with FGR were attributable to the group with normal Doppler than to the group with abnormal Doppler.

**BMJ**

*Boers et al BMJ 2010;341:7087*

**RESEARCH**

Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT)

**No differences in Outcome**

Induction:€7106/ Exp. Monitoring:€6995

**Costs lowest in induction @ 38 wks.**

*Vilgen et al. Eur J Obstet Gynecol Repro Biol 2013;170: 358*

European Journal of Obstetrics & Gynecology and Reproductive Biology xxx (2013) xxx-xxx



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journal homepage: [www.elsevier.com/locate/ejogrb](http://www.elsevier.com/locate/ejogrb)

*Tajik et al. Eur J Obstet Gynecol Reprod Biol.2014 Jan;172:20-5*

Which intrauterine growth restricted fetuses at term benefit from early labour induction? A secondary analysis of the DIGITAT randomised trial

In late preterm / term pregnancies with FGR most markers seem unlikely to be helpful in identifying women who benefit from induction, **except for maternal pre-pregnancy BMI.**

**FGR & mat. BMI > 25: IUD OR 75** (95% CI: 14-350)

*Froen et al. Acta Obstet Gynecol Scand 2004; 83:801*

# Tertiary Prevention Macrosomia/Immediate Outcome

## Decision analytic Model

For each plexus injury prevented by the 4500-g or 4000-g policy, 3695 resp. 2345 additional Cesareans, additional cost of \$8.7 million vs. \$4.9 million.

In diabetic mothers with the 4500-g or 4000-g policy 443 or 489 Cesareans/ \$930 000 resp. \$880 000.

**For 97% of non diabetic women, a policy of elective Cesarean for macrosomia<sup>SON</sup> is medically and economically unsound.**

*Rouse et al. Jama 1996;13;276:1480.*

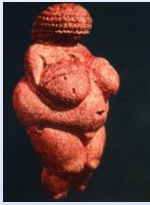
## Systematic Review

Women with spont. onset of labor higher rates of vaginal delivery (OR 2.07, 95% CI 1.34, 3,19).

Based on observational studies, labor induction for fetal macrosomia results in an increased CD rate without improving perinatal outcomes.

*Sanchez-Ramos et al. Obstet Gynecol 2002;100:997*

Induction of labour versus expectant management for large-for-date fetuses: a randomised controlled trial



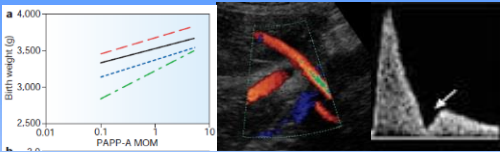
## Most recent RCT

*Boulevard et al. Lancet 2015; 385:2660*

	Induction n=407	Expectant n=411	RR (95%CI)
Est. FW (g, sonography)	3964 (229)	3971 (238)	36.0-39.0 wks ns
BMI b. pregnancy (kg/m <sup>2</sup> )	26.1 (5.7)	25.6 (5.4)	ns
Mean BW	3831 g (SD 324)	4118 g (SD 392)	
<b>Shoulder dystocia</b>	1%	4%	0.32 (0.12–0.85)
<b>Spont. vag. delivery</b>	59%	52%	1.14 (1.1-1.29)
<b>Comp. Outcome</b>	2%	6%	0.32 (0.2–0.7)
Hosp.stay b.delivery (h)	16.2 (8-131.4)	7.6 (4.6–11.)	p<0.0001
Hyperbilirubinemia >250	9%	3%	p<0.0004



# Secondary Prevention FGR



First trimester plasma levels of pregnancy-associated plasma protein-A (PAPP-A) associated with placental nutrient transfer and highly correlate with BW. *Smith et al. Nature 2002; 417:916*

## Risk Group by History

Low-dose aspirin < 16 wks

34 RCTs 11 348 women

PE: RR: 0.47, 95% CI 0.34-0.65,

Prevalence: 9.3% vs. 21%

FGR: RR: 0.44, 95% CI 0.30-0.65,

Prevalence: 7% vs. 16.3%

*Bujold et al. Obstet Gynecol. 2010, 116:402-14*

Up to 1/3 women resistant to 75–80 mg. Additional LMWH might work then.

## FRUIT STUDY

Prevalences	LMWH+A	A	P
Repetative PE< 34 W.	0	8.7%)	0.012
FGR	(18%)	(28%)	0.165

*de Vries et al. The FRUIT RCT. J Thromb Haemost 2012;10: 64–72*

No evidence to support any benefit of adding LMWH to ASA alone in women with inherited thrombophilia.

*Areia et al. Arch Gynecol Obstet 2016;293:81*

## Algorithm for detection FGR & PE @11-13 wks

Characteristics: Ut art.PI , Mean a. RR, PAPP+ PGF 1426 (2%) PE, 3168 (5%) FGR, 57458 no PE/SGA.

If FPR 10.9%

95.3 & 45.6% for PE / 55.5 & 44.3% for FGR

*Poon et al. Diagn Ther. 2013;33:16*

Intervention?

*Waiting for ASPJRE results*

## Modifiable Risks for FGR

	OR	95%CI
Smoking	2.1	1.3-3.5
WG < 5 kg	2.6	1.4-5
WG > 15 kg	2.3	1.1-4.4
N controls	69/81%	p<0.001

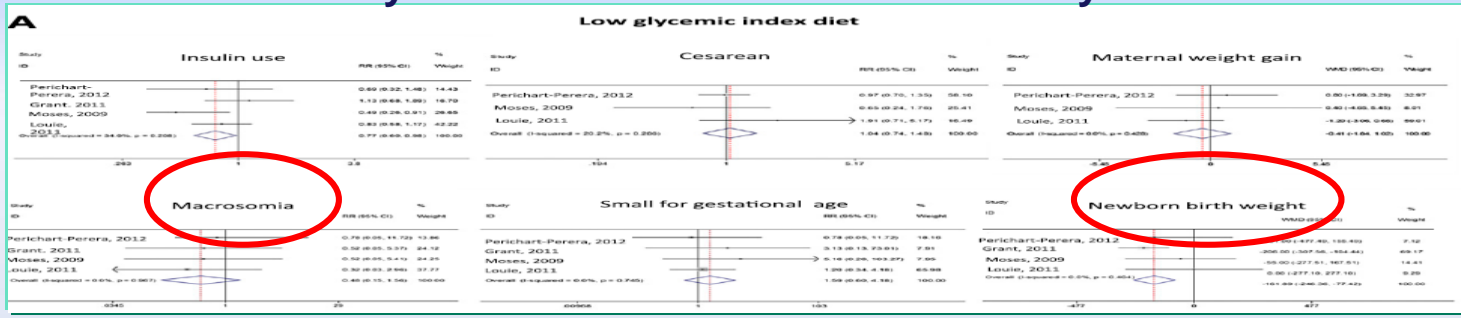
*Da Fonseca et al. BMC 2012; 23:60*

# Secondary Prevention Macrosgomia in GDM/Obesity

Maternal W, gestational WG, and maternal glucose homeostasis influence BW **BFI instead of BMI**  
 How to blunt mid & late pregnancy increase in insulin resistance to reach normal mat. WG & BW ?

## Low Glycemic index diet/ low CH or calory diet in GDM

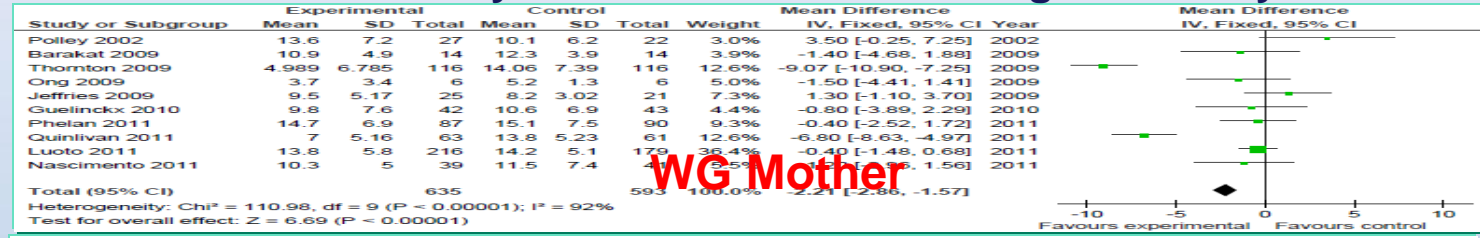
## DIET



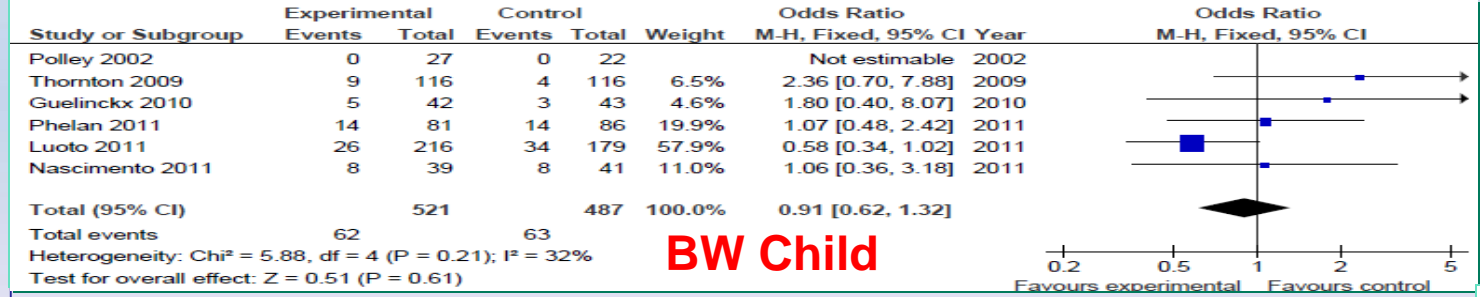
Dietary Intervention in Patients With Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis of Randomized Clinical Trials on Maternal and Newborn Outcomes  
 Luciana Verzosa Viana, Jorge Luis Grossi and Mirella Jobim Azevedo  
 Diabetes Care 2014;37:3345-3351 | DOI: 10.2337/141250

**Vercoca et al. Diabetes Care 2014;37:3345**  
**MOVE**

## Lifestyle intervention in overweight / obesity



**WG Mother**



**BW Child**

	Metformin (202)	Placebo (195)	
Median <b>WG mother</b> (IQR/kg)	4.6 (1.3 to 7.2)	6.3 (2.9 to 9.2)	p<0.001
<b>GDM</b> (n,%)	25/202 (12.4%)	22/195 (11.3%)	OR:1.11 (0.60 to 2.04)
<b>Preeclampsia</b> (n,%)	6/202 (3.0%)	22/195 (11.3%)	OR:0.24 (0.10 to 0.61)
Median <b>BW child</b> (IQR, centile)	51.8 (23.9 to 82.1)	56.6 (26.8 to 81.4)	p= 0.66

RESEARCH ARTICLE Open Access  
 Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis

**Oteng-Ntim et al. BMC Medicine 2012; 10:47**

## PILLS

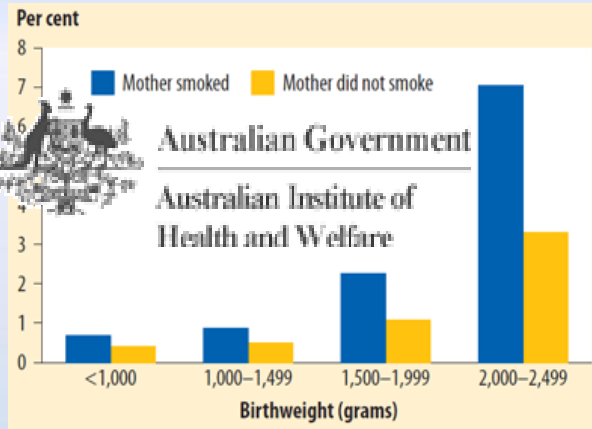
ORIGINAL ARTICLE  
 Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus  
**Sygelaki et al. NEJM 2016; 374:434**

# Primary Prevention FGR Create smoke-free environments

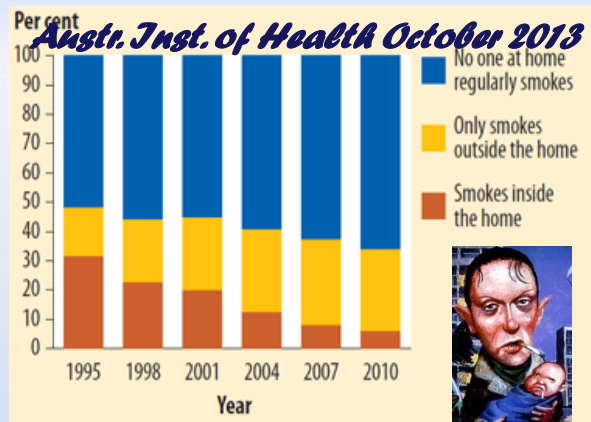
1939 Müller published on lung cancer in smokers *Z Krebsforsch* 1939;49:57

1952 Sir Doll showed connections between smoking & lung cancer

## Distribution BW



## Effect



**By 2030, if current trends continue, 8/10 deaths will be in the developing world !**

Effect of smoke-free legislation on perinatal and child health: a systematic review and meta-analysis

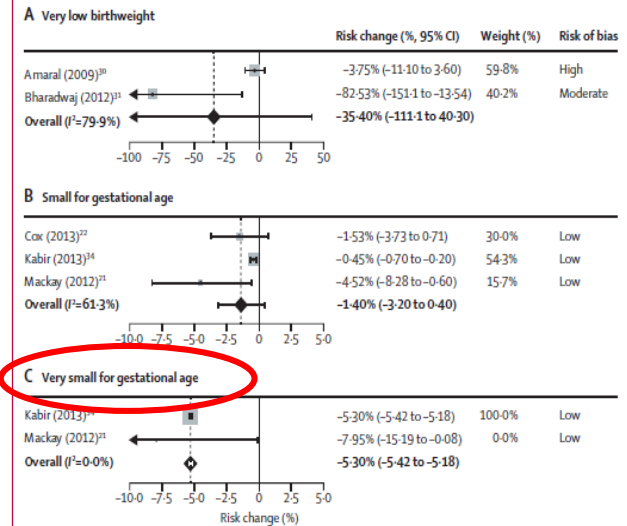
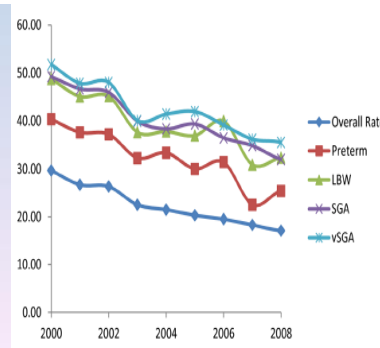
**Been et al. Lancet 2014; 383: 1549**

Jasper V Been, Ulugbek B Nurmatov, Bianca Cox, Tim S Nawrot, Constant P van Schayck, Aziz Sheikh

## Intervention : Smoking Ban

Smoking Ban and Small-For-Gestational Age Births in Ireland **Kabir et al. PLUS ONE 2013;8; e57441**

Significant decline in vSGA & SGA rates immediately after the ban: 25.3 & 20.2%;) 95% CI 25.43 - 25.17%, p,0.0001 & 20.7 to 20.19%, p,0.0007. Significant gradual effects continued: 20.6/ 20% (p,0.0001).

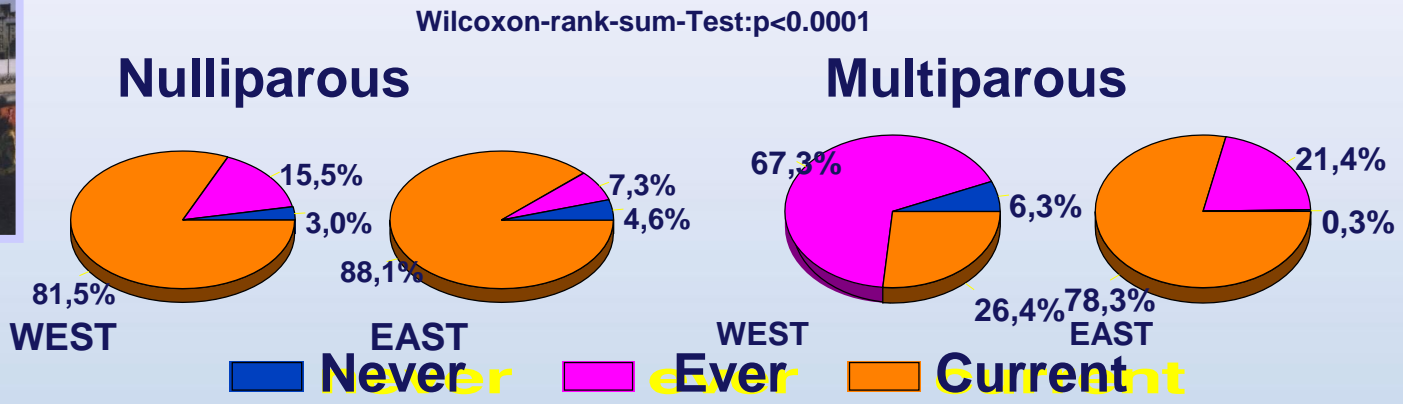
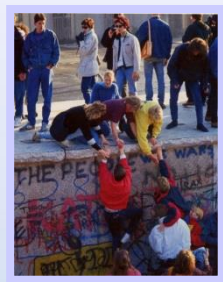


# Primary Prevention FGR *Care for friendly environment*

## Risk for FGR < 5th centile Germany 1989/90

Adjusted for smoking, BMI, parity, age, social class, education

Multivariate analysis, 7892 primiparous women, 48 items of working conditions



### East Germany

1 Child and ...

„Night work, shifts, etc.“

### West-Germany

1 Child and ...

„Unfriendly work environment, No recognition, competition“

OR = 2,3; 95 %-CI: 1,20 – 4,25

OR = 2,2; 95 % CI: 1,05 – 4,64

# Primary Prevention GDM, Macrosomia

It is likely that in high-income countries reductions in perinatal mortality/complications would justify additional services



Moss et al. *BMC Preg Child* 2007; 28:7

## Preconceptional Care

Hypertensive disorders of pregnancy less common amongst women who had attended preconception care, trend of decreased incidence of GDM, FGR.

Beckmann et al. *Aust N Z J Obstet Gynaecol* 2014;54:510

## Diet

Low glycaemic index diet in pregnancy to prevent macrosomia (ROLO study): randomised control trial

OPEN ACCESS Walsh et al. *BMJ* 2012; 30:345:e5605.

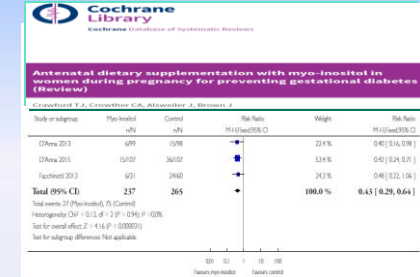
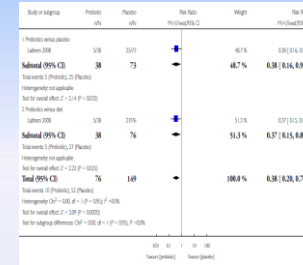
Outcome	Intervention n=372	Control group n=387	P
BW (g)	4034 (510)	4006 (497)	0.449
BW centile	70.5 (25.6)	72.8 (25.6)	0.409
WG @34 (kg)	10.1 (3.7)	10.9 (3.9)	0.012
WG @40 (kg)	12.2 (4.4)	13.7 (4.9)	0.017

### RESEARCH Open Access

Maternal low glycaemic index diet, fat intake and postprandial glucose influences neonatal adiposity – secondary analysis from the ROLO study Horan et al. *Nutri J* 2014;13:78.

Neonatal central adiposity (waist: length ratio) associated with low GI diet, maternal fat intake and postprandial glucose.

## Probiotics (GDM), Myo-Inositol



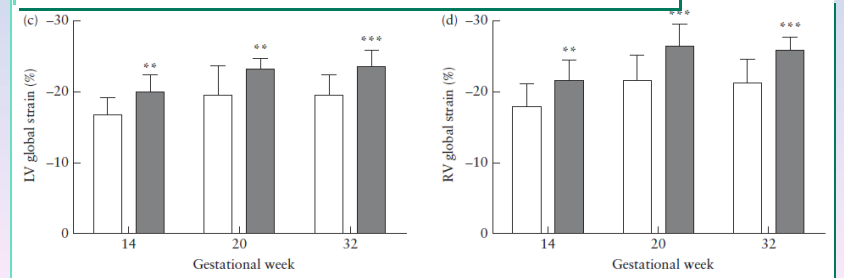
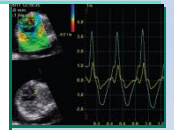
Barrett et al. *Cochrane Database Syst Rev* 2014 27;2:CD009951

## Lifestyle

Modifiable determinants of fetal macrosomia: role of lifestyle-related factors Voldner et al. *A Gyn Scand* 2008;87:423

BMI, WG, plasma glucose and GA independent determinants of macrosomia. Adding low level **pre-gestational physical activity**, showed a significant macrosomia determinant OR=2.9 (95% CI: 1.9, 7.3).  
"Targets for intervention"?

Maternal obesity affects fetal myocardial function as early as in the first trimester Jung et al. *UOG* 2016;47:433



# Primary Prevention HBW/Morbidity in Later Life

Interventions to prevent adverse fetal programming due to maternal obesity during pregnancy **DIET AND EXERCISE**

Peter W Nathanielsz, Stephen P Ford, Nathan M Long, Claudia C Vega, Luis A Reyes-Castro, and Elena Zambrano

**3x 15 minutes, 5 / 7 days running,**



**To avoid obese kids successful intervention should be implemented**

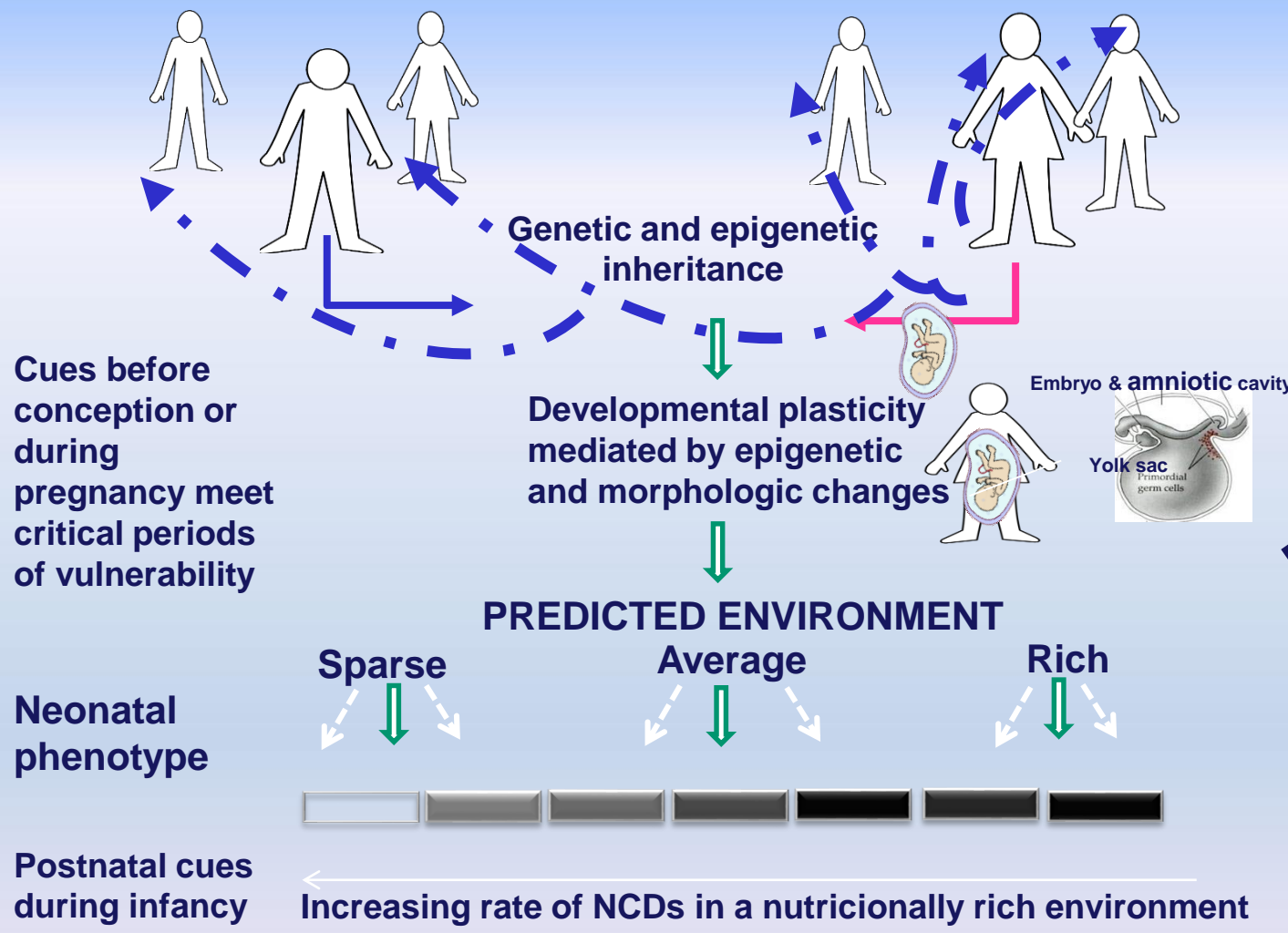
*Nathanielsz et al. Nutr Rev. 2013 ;71(0 1): S78*

*Meijer & Robbers. Proc. R Soc 2014; 8 281*

Wheel running in the wild



# Transmission of Early Nutrition to Subsequent Generations (Barker and reverse Barker phenomena)



F0

Intergenerational nongenetic effects

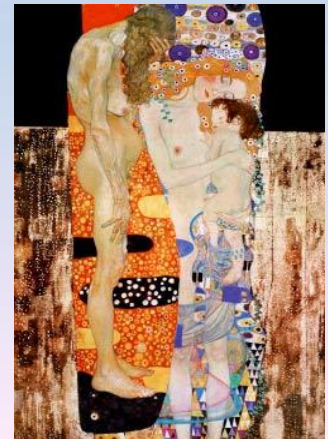
Gametes

F1

Via primordial germ cells, genomic imprinting or placental-fetal programming

Gametes → F2, F3

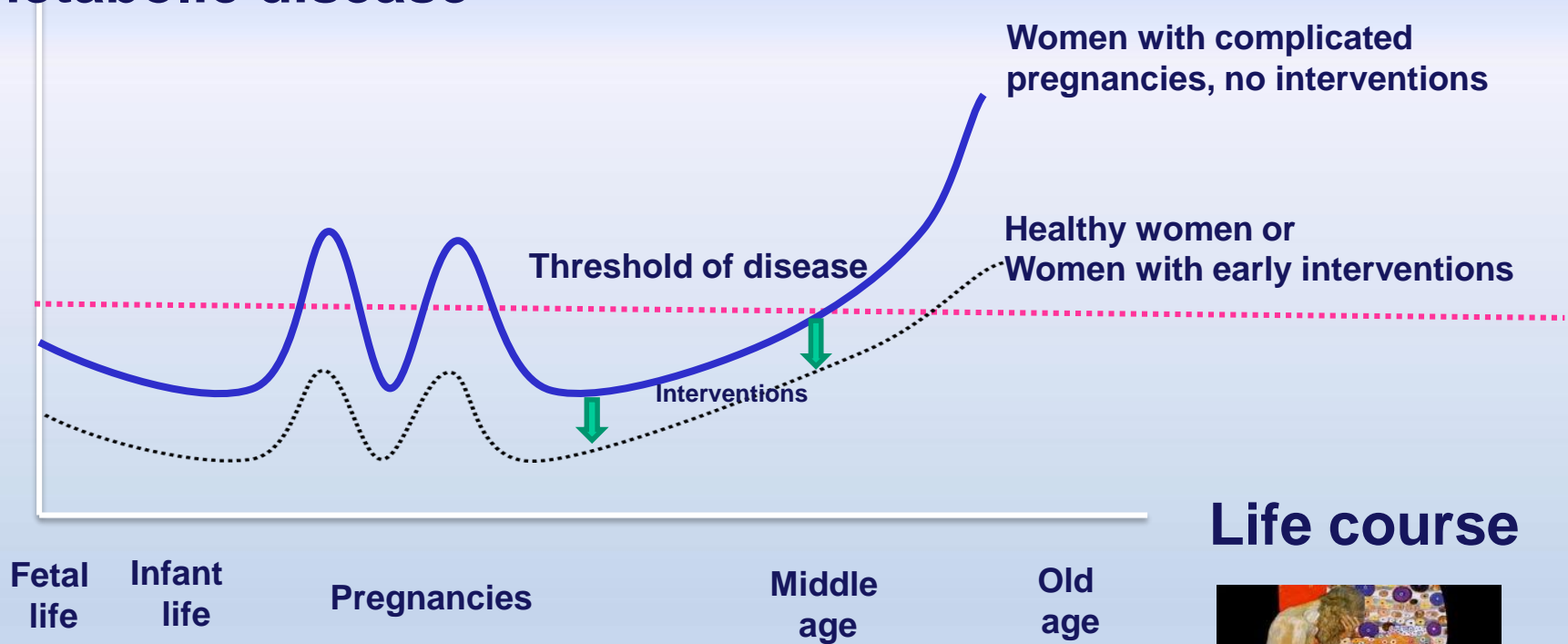
Transgenerational phenotype



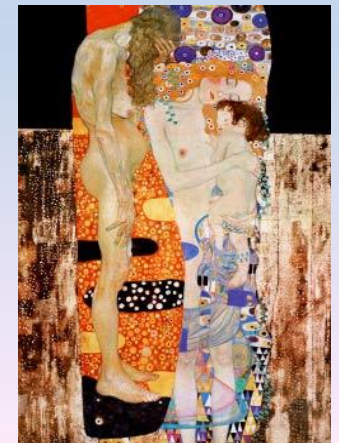
Modified acc. to  
 Gluckman et al. NEJM 2008 ; 359:61  
 Gabory et al., Biology of Sex Differences 2013 ; 4:5

# Effect of Developmental Environment on Later Phenotype

## Risk of vascular or metabolic disease



## Life course





# *LBW may Impose CVD, Metabolic and Psychiatric Disease (future generations)*

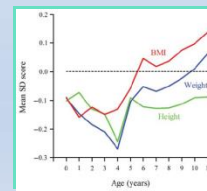
## *Cohort Studies associating Famine during Pregnancy with BW/Health of Offspring*

**There are individual differences in susceptibility towards hunger/ stress**

1977	Forsdhal et al. (N)	Poor, later rich provinces	Myocardial infarction
1986	Barker et al. (GB)	Birthplace/ LBW/hunger	CVD / Mortality from MI
1992-97	Barker et al.	LBW (“thrifty phenotype”)	Impaired glucose tolerance/ CVD
1997	Kannisto (FL)	Maternal malnutrition	HD, type-2 DM (1.-2. tr), HD, LDL (3.tr)
1990	Razzaque (BD)		Early, but not late mortality
1997	Lumey (NL)	Famine 3 <sup>rd</sup> , nor 1 <sup>st</sup> tr. Ass. with LBW	Reversal of BW 2 <sup>nd</sup> generation 1tr.exp
2011	Roseboom (NL)	Independent of BW	Schizophrenia, depression, stress res.
			Impaired glucose tolerance/ CVD
1997	Stanner (RUS)	Low BW, hunger remained	No adverse effects

## *Cohort studies associating Placental disease with BW & Health of Offspring*

**The “gateway” modifies gene expression with sex-specific placental function**



Small “minor axis” of placenta

2010 Barker et al. Low plac. surface /LW @ 2y, HW @11y Chronic heart failure , T2DM

2010 Hippisley-Cox et al. LBW & HD

40% increase of CVD as young adults

# LBW reflects familial aggregation of CVD, metab. disease

(previous generations, reverse Barker)

Women @ CVD risk may not be able to mount adequate hemodynamic responses.  
Familial aggregation of FGR/CVD: Single nucleotide polymorphisms showed an association between gene variation for cholesterol metabolism & decreased BW.

*Steffen et al. J Perinat 2007, 27:672*

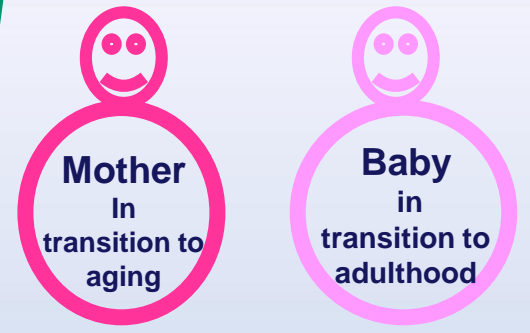
Investigated Pregnancies	Disease	Adjustment	Risk	95%CI	Author
923.586	Death/CVD	+ FGR <sub>late</sub>	HR 1.4	(1.22- 1.58)	<i>Bonamy et al. 2011</i>
			HR 3.4	(2.26 - 5.11)	
783 814	Mortality M	+ BW	HR 0.7	(0.56 - 0.99)	<i>Manor et al. 2010</i>
	Mortality <sub>mGP</sub>	+ BW	HR 0.7	(0.56 - 0.99)	
	Mortality <sub>pGP</sub>	+ BW	HR 1.1	(1.01 - 1.09)	
120317	IHD <sub>mGP</sub>	+ BW	HR 0.9	(0.85 - 1)	<i>Smith et al. 2010</i>
	CVD <sub>mGP</sub>	+ BW	HR 0.86	(0.83-0.89)	
			HR 0.82	(0.77-0.87)	

**U shaped**

For each 1-kg increase in BW the grandparental risk of IHD declined by 14% and the risk for CVD by 18%  
(*Smith et al. Am J Epid 2010; 171:736*)

# Direct Responsibility towards both our Patients

Arabin & Baschat, *Frontiers in Pharmacology*, section *Prenatal Beginnings for Better Health*, in press



## Cardiovascular Risk Profile

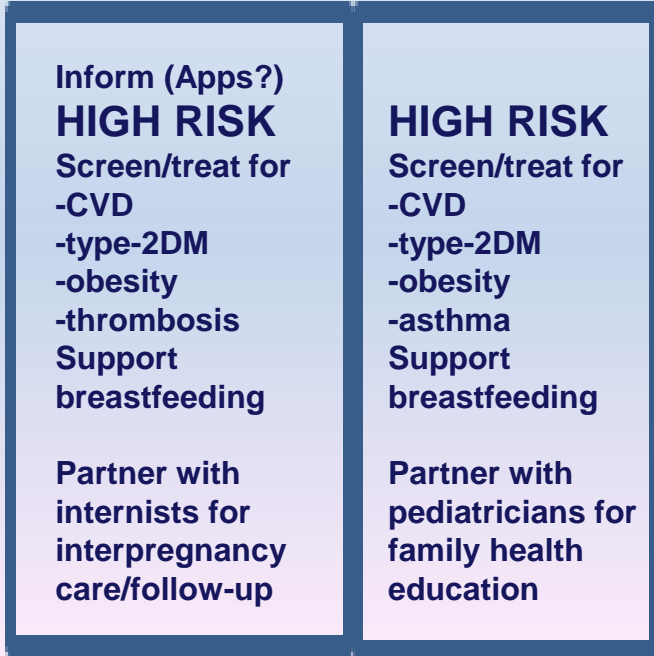
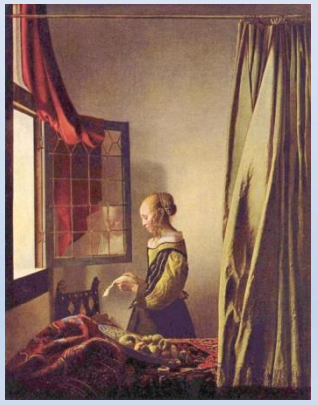
- Miscarriage
- FGR "only"
- PE
- SPB

## Metabolic Risk Profile

- (No) Breastfeeding
- Obesity
- Excessive WG
- GDM/ Macrosomia
- Subfertility

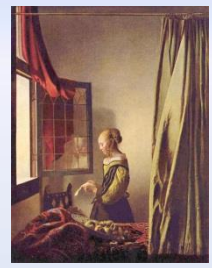
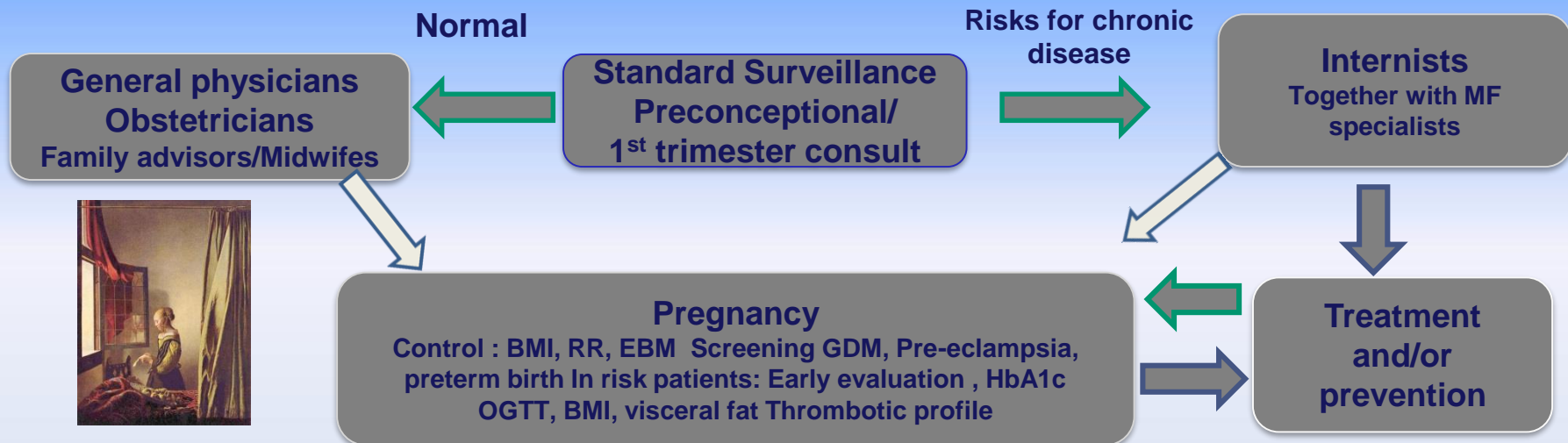
## Thrombotic Risk Profile

- Thrombophilia
- SLE
- Antiphospholipid Syndrome



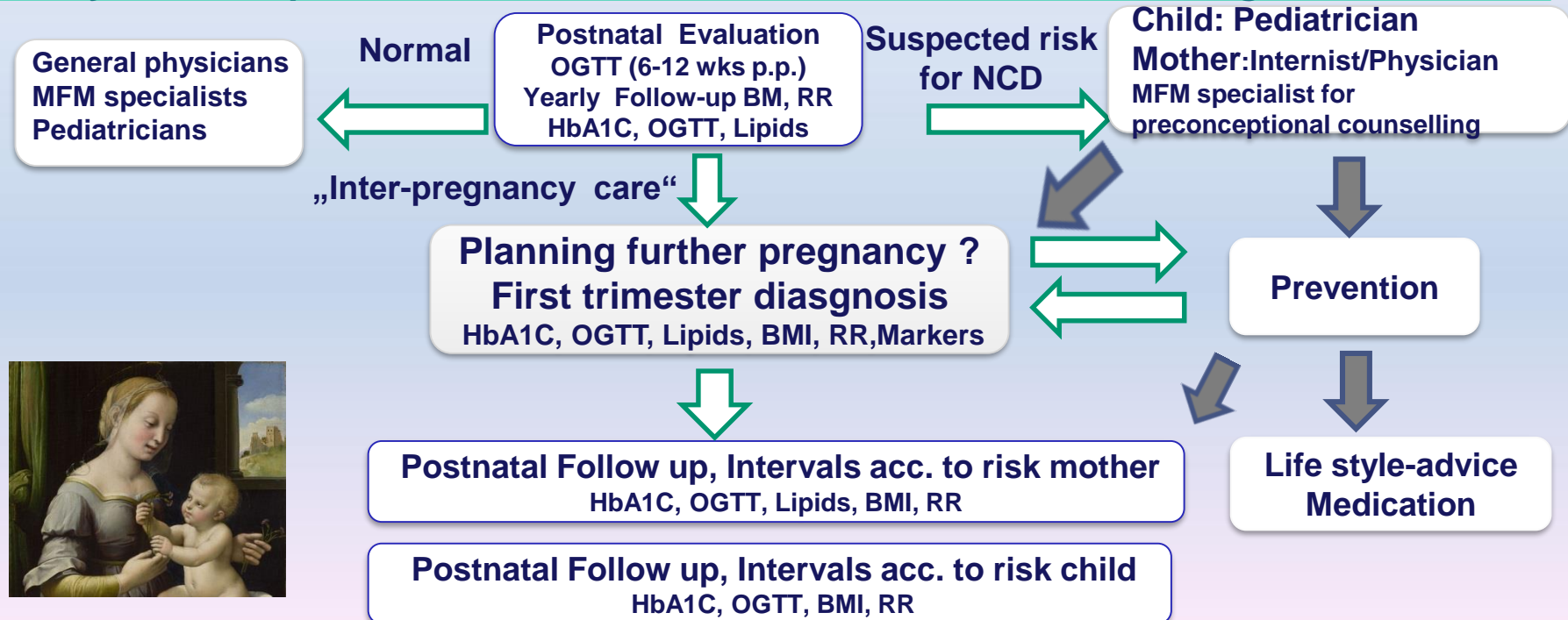
# Indirect Responsibility towards Both our patients

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## Ideally Preconceptional and First-trimester and Postnatal Visits aiming at Prevention

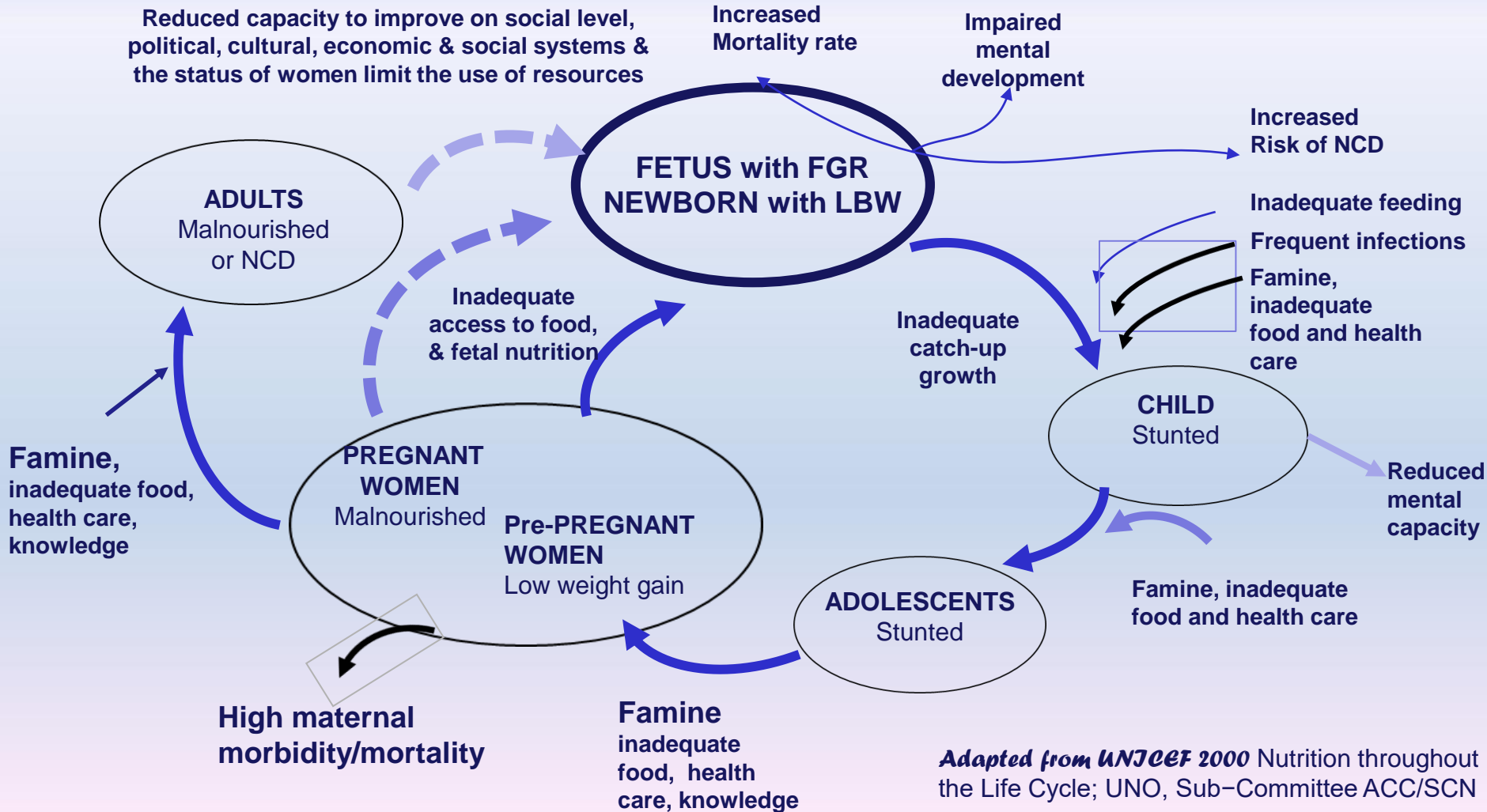
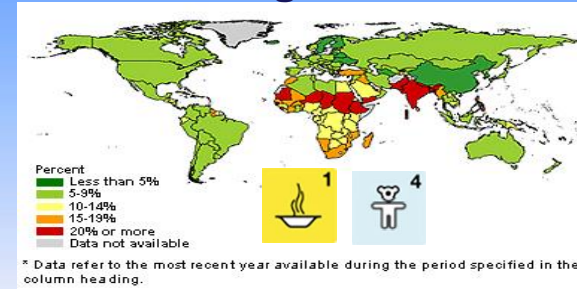
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# The vicious circle 1

The post-MDG era has started in 2016, to eradicate hunger/ poverty was the first MDG, to reduce maternal and child undernutrition is gaining high priority both as a marker and maker of development.

BW < 2500g 2003-2008

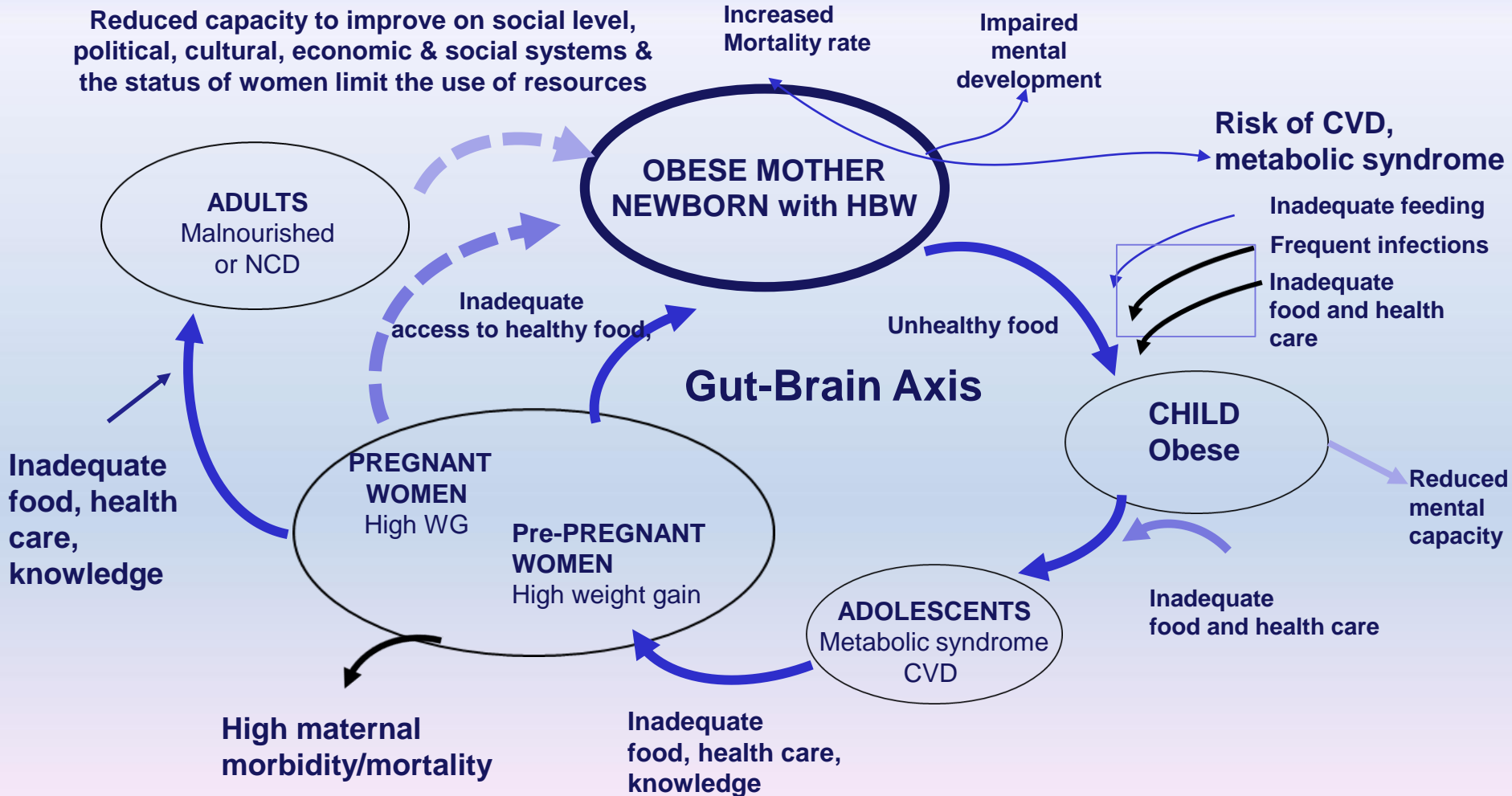
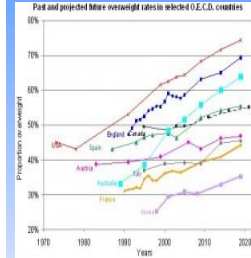
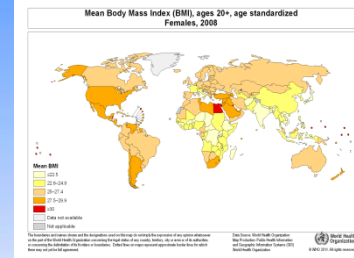


Adapted from UNICEF 2000 Nutrition throughout the Life Cycle; UNO, Sub-Committee ACC/SCN

# The vicious circle 2

Effect of maternal obesity on neonatal death in sub-Saharan Africa: multivariable analysis of 27 national datasets

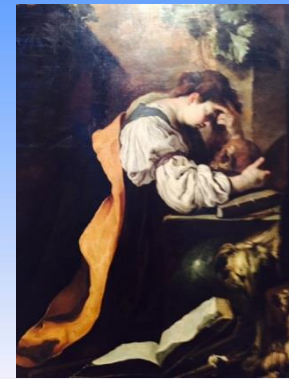
Jenny A Cresswell, Oona M R Campbell, Mary J De Silva, Véronique Filippi



# Take-home Message

## From Detection to Reflection

### What are our Responsibilities?



Quality improvement

Evidence-based medicine



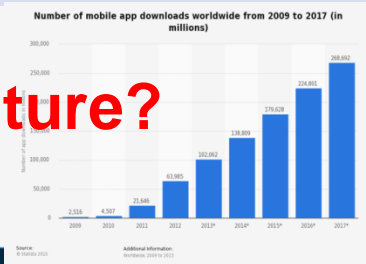
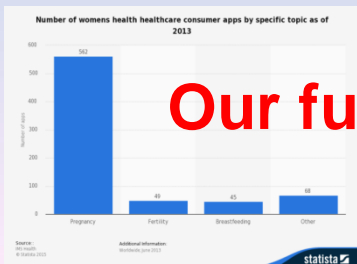
Evidence-based economics

*Duřkovic et al. Pediatrics 2016; 137:1*



FROM EXECUTIVE PRODUCER RICKI LAKE AND FROM DIRECTOR ABBY EPSTEIN  
**THE BUSINESS OF BEING BORN**  
 WWW.THEBUSINESSOFBEINGBORN.COM  
 You will never look at giving birth the same way.

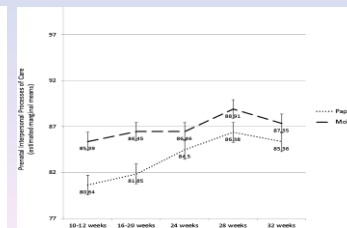
**Business with food, cigarettes or even business with the disease itself may not be more profitable than health protection of mothers and their offspring. Otherwise we hurt the professional integrity apart from our focus.**



**Our future?**

Mobile application as a prenatal education and engagement tool: A randomized controlled pilot<sup>☆</sup>

Christy J.W. Ledford<sup>a,\*</sup>, Mollie Rose Canzona<sup>b</sup>, Lauren A. Cafferty<sup>c</sup>, Joshua A. Hodge<sup>d</sup>





# *Take-home Message*

## *From Detection to Reflection*

### *What are our Responsibilities?*



- Learn how to detect risks for FGR & macrosomia (ongoing pregnancies)
- Study basic research & epidemiologic data/ implement in patient care
- Consider RCTs for immediate management to avoid poor outcome
- Consider RCTs to improve the outcome in ongoing pregnancies
- Convince policy makers for concepts of primary prevention, communicate with internists, general physicians and pediatricians
- Reflect when and where to focus and look beyond the horizon to improve family long-term health across generations/continents
- The dignity and political will for health-care concepts dealing with preconceptional, pregnancy and newborn care will be vital in the future.





**Thanks for sharing your  
time & responsibility (?)**

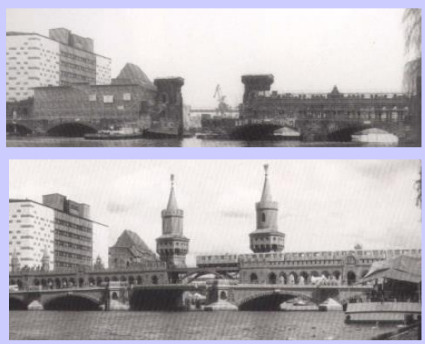


**EBCOG 2018, Paris**

~~**Liberté, Égalité, Fraternité**~~

**Communauté par Diversité pour Maternité**

**Can we re-build bridges between  
individual pregnancy care and  
long-term interests of societies?**



**In case of questions or comments: [bine.clara.angela@gmail.com](mailto:bine.clara.angela@gmail.com)  
The presentations can be seen on [www.clara-angela.info](http://www.clara-angela.info)**