Convegno

Il sistema delle sorveglianze regionali e nazionali in ambito materno infantile

Salone delle Robbiane - Villa la Quiete, *via di Boldrone 2, Firenze*

9:00 - 13:30

Giovedì 28 Marzo 2019

Progetto SPITOSS
Premesse

Federico Mecacci

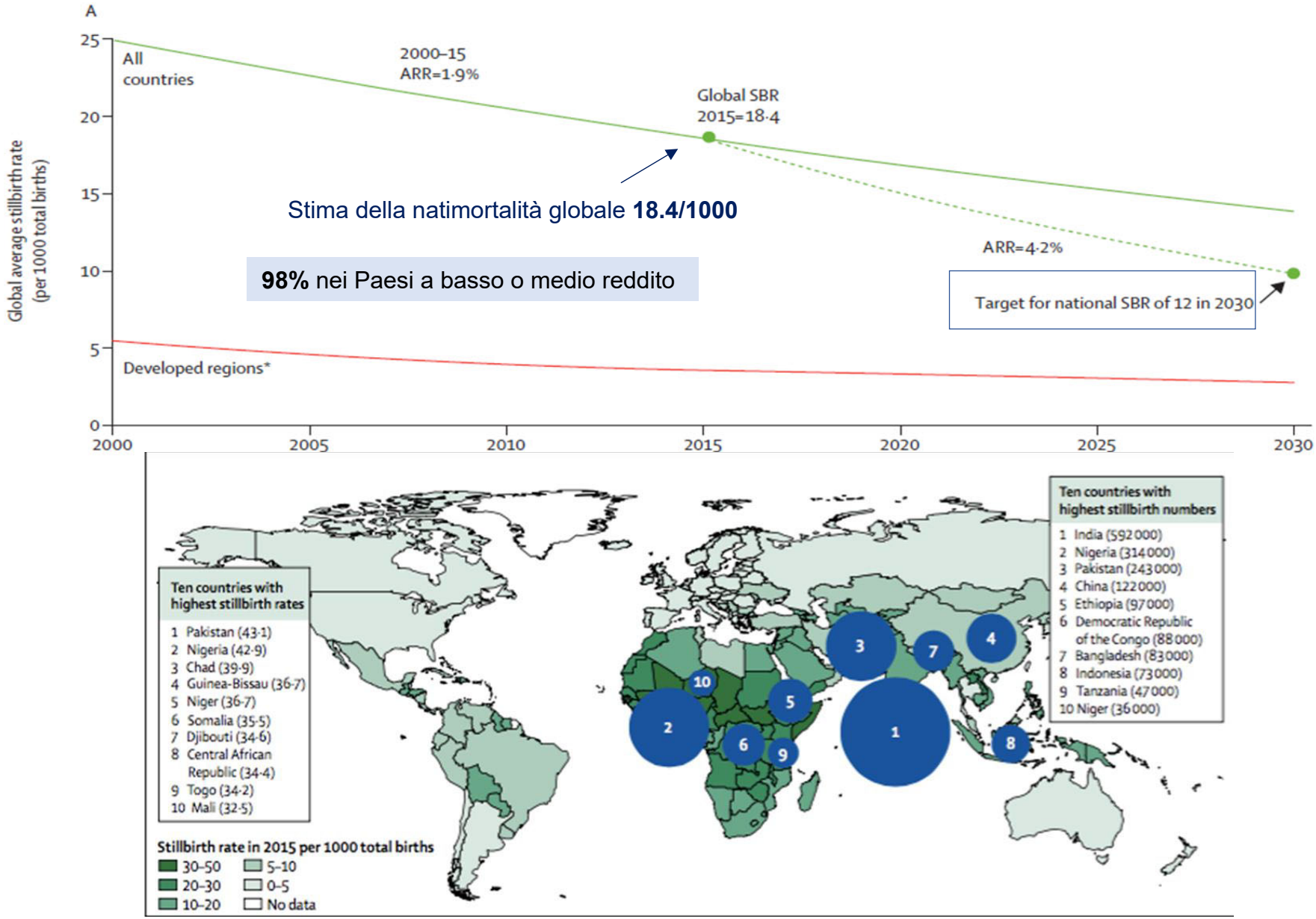
Medicina Prenatale
Centro di Riferimento Regionale Gravidanze ad Alto Rischio
Azienda Ospedaliera Universitaria Careggi

Progetto Spitoss

Implementare un modello di sorveglianza attiva per elaborare stime *population based* della mortalità perinatale e raccogliere informazioni utili a prevenire i decessi evitabili.

Istituto Superiore Sanità

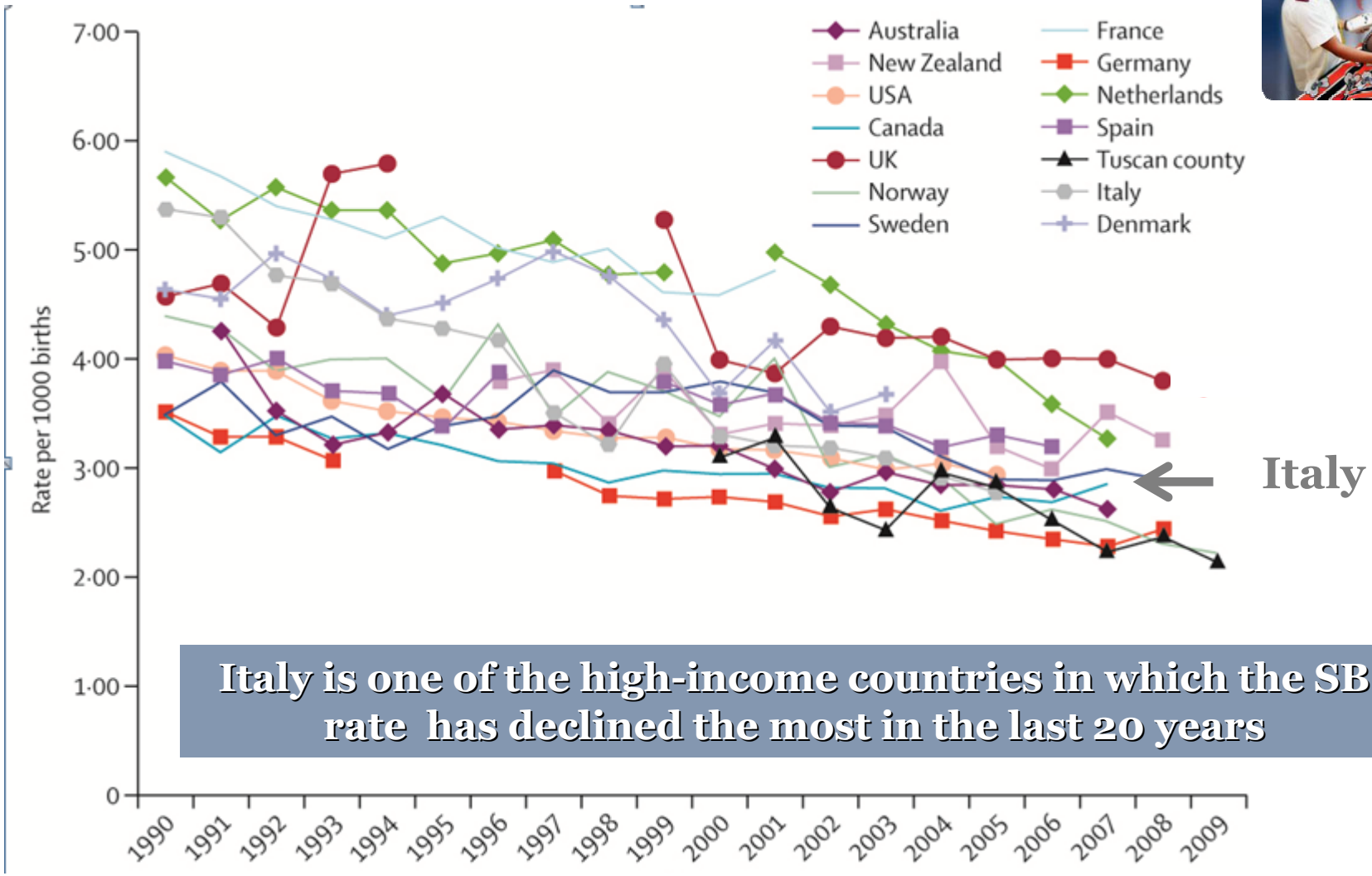
STILLBIRTH RATES REFLECT THE OVERALL LEVEL OF *MATERNITY CARE* IN VARIOUS COUNTRIES



ncet's Series 2016. Stillbirths: rates, risk factor, and acceleration towards 2030

Stillbirths in high-income countries

THE LANCET
April 14, 2011 www.thelancet.com



Italy is one of the high-income countries in which the SB rate has declined the most in the last 20 years

THE LANCE
April 14, 2011

lbirths: the vision for 2020

Goldenberg, Elizabeth M McClure, Zulfiqar A Bhutta, José M Belizán, Uma M Reddy, Craig E Rubens, Hillary Mabeya, Vicki Flenady, armstadt, for The Lancet's Stillbirths Series steering committee*

High-income countries need to *eliminate* all *preventable* stillbirth

he goal is to reduce by 2020 the SB rate to fewer than 5/100 births

- **DEMOGRAPHICS:**
  Maternal age >35 years

- **NON-COMMUNICABLE DISORDERS**:
  Overweight and obesity
  Maternal pre-existing diabetes
  Maternal pre-existing hypertension
  Pre-eclampsia/eclampsia
  Tobacco

- **FETAL DISORDERS:**
  Post-term pregnancy ≥ 42 weeks

They explain less than 20% of the variance in the incidence of S

Many fetal losses are associated with a failure in identifying risk factors

tentially Preventable Stillbirth in a Diverse S. Cohort

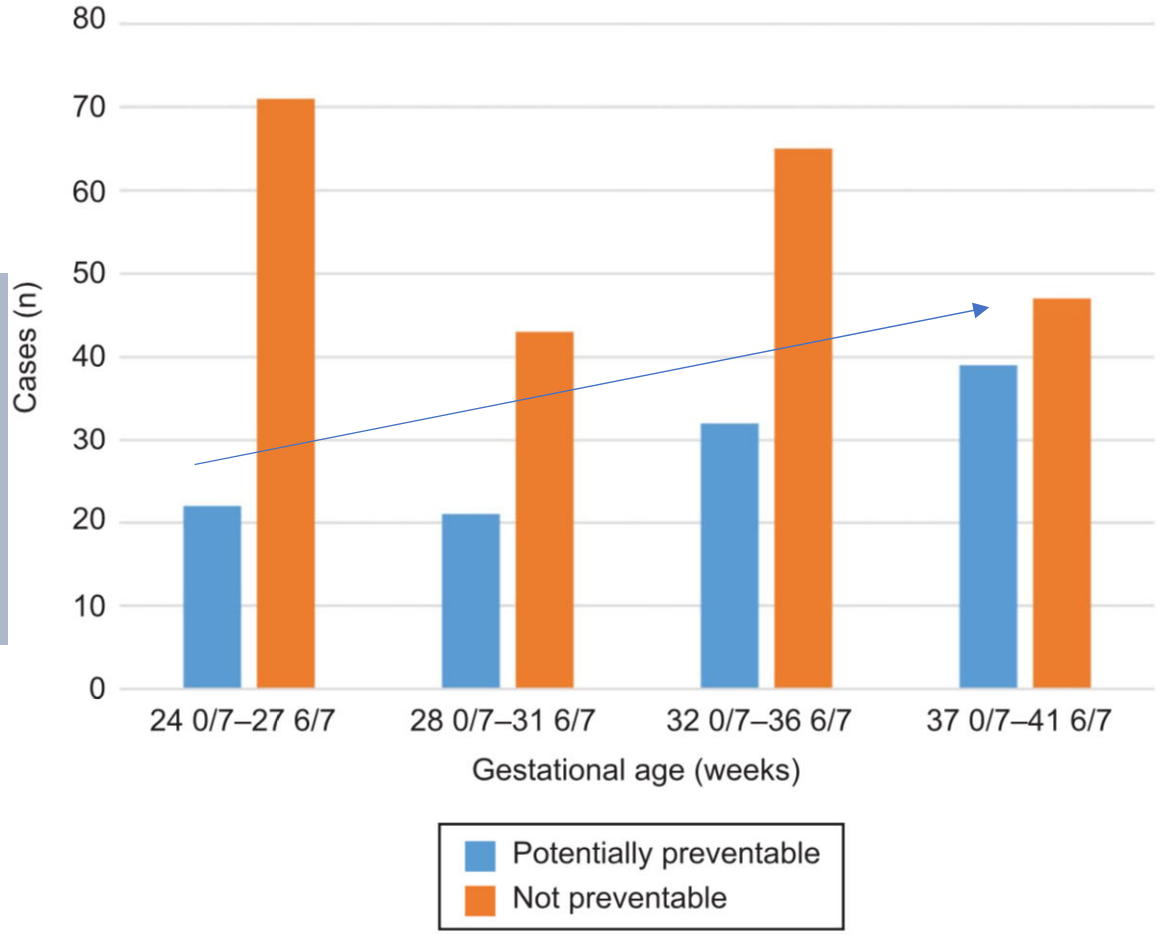
M. Page, MD, Vanessa Thorsten, MPH, Uma M. Reddy, MD, MPH, Donald J. Dudley, MD, J. Rowland Hogue, PhD, George R. Saade, MD, Halit Pinar, MD, Corette B. Parker, DrPH, ah Conway, MD, Barbara J. Stoll, MD, Donald Coustan, MD, Radek Bukowski, MD, PhD, el W. Varner, MD, Robert L. Goldenberg, MD, Karen Gibbins, MD, and Robert M. Silver, MD

stet Gynecol 2018;0:1–8)

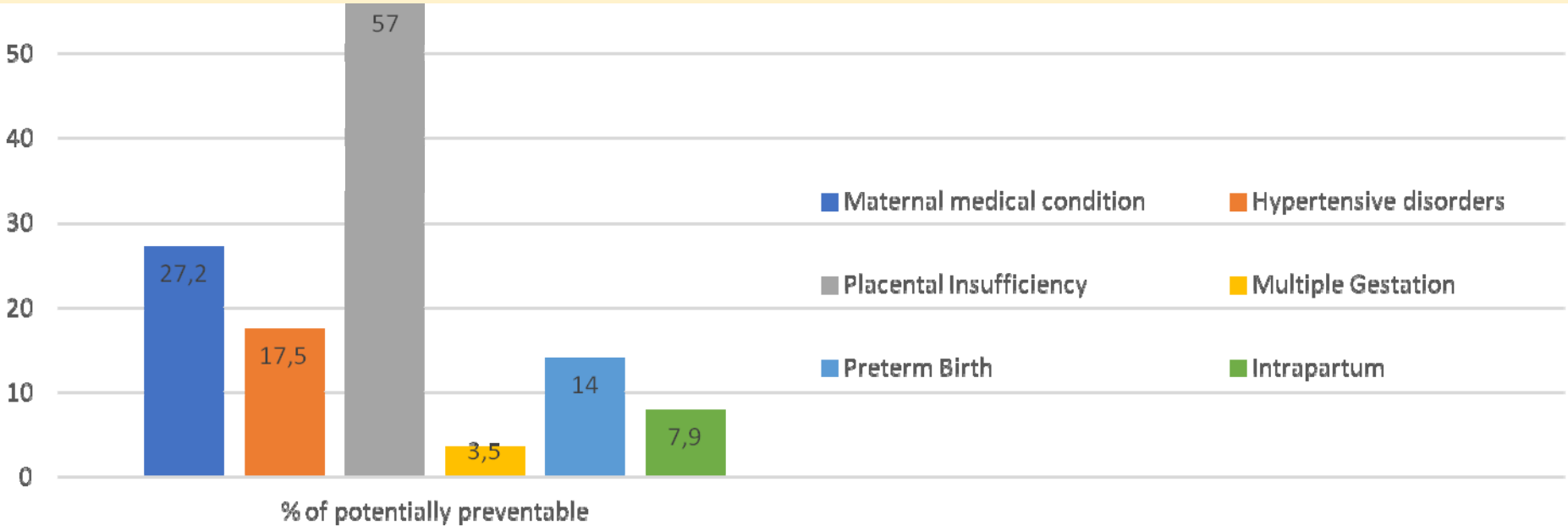
Stillbirth cases (512)
-NOT PREVENTABLE (398)
- < 24 week of gestation
- Birthweight < 500 g
- Fetal anomalies or genetic condition

-PREVENTABLE (104)

There is an increase in the proportion of potentially preventable stillbirths with increasing gestational age



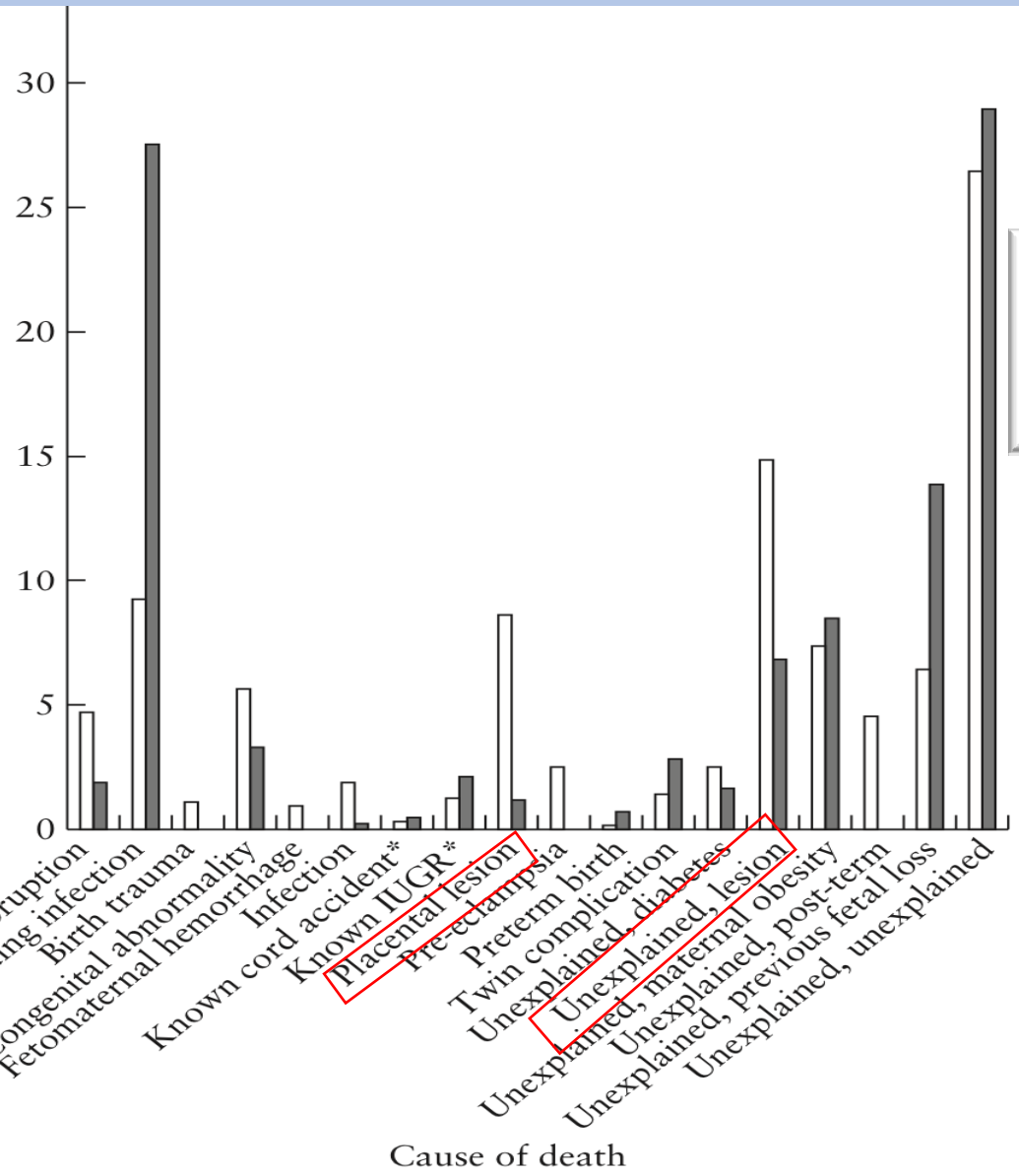
CATEGORIES OF POTENTIALLY PREVENTABLE STILLBIRTH >37 wks gestation



Category	Definition
Intrapartum	Fetal cardiac activity present on admission with stillborn fetus
Maternal medical complications	Diabetes mellitus, gestational diabetes, chronic hypertension, antiphospholipid syndrome, systemic lupus erythematosus
Hypertensive disorders of pregnancy	Gestational hypertension, preeclampsia
Placental insufficiency	Abnormal placental pathology findings (small, fibrin, infarcts, thrombotic vasculopathy), fetal growth restriction
Multiple gestation	Otherwise uncomplicated multiple gestation (excluded TTTS, TRAP, monoamniotic pregnancies)
Preterm birth	Preterm PROM, preterm labor, chorioamnionitis

TTTS, twin–twin transfusion syndrome; TRAP, twin reversed arterial perfusion syndrome; PROM, preterm prelabor rupture of membranes.

ied cause of death, based on autopsy findings, in 1064 cases of intrauterine death



An **impaired placenta** might became t
limiting element of **fetal growth**

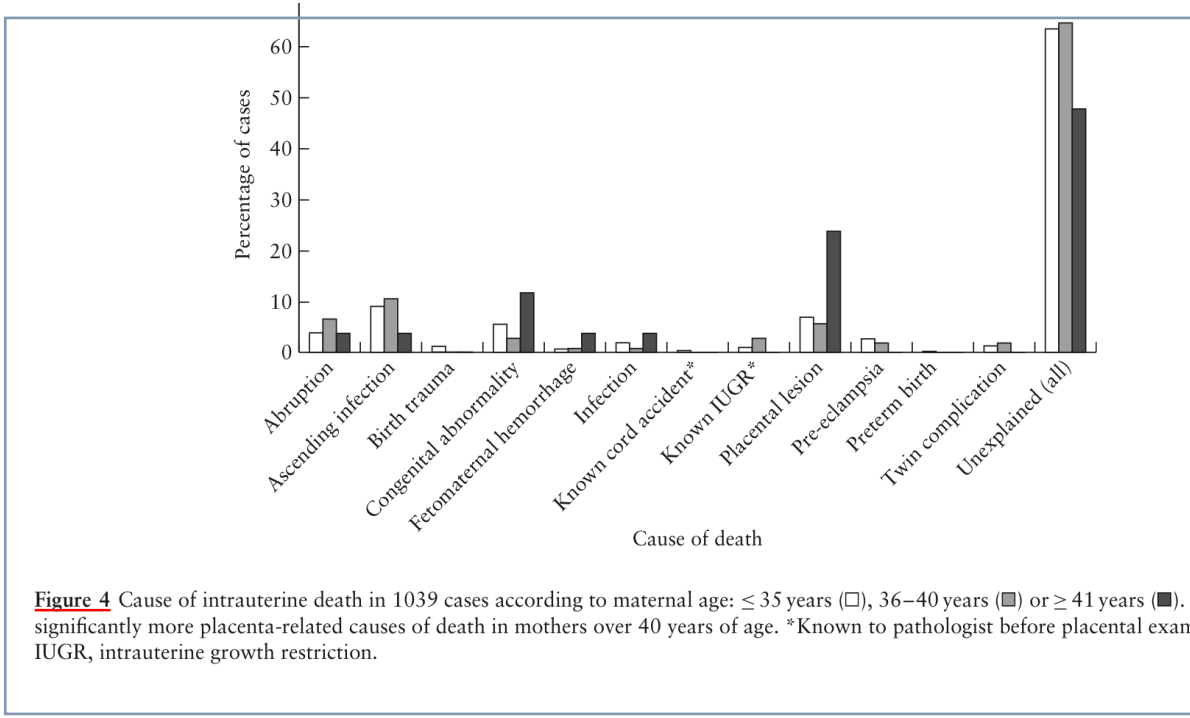
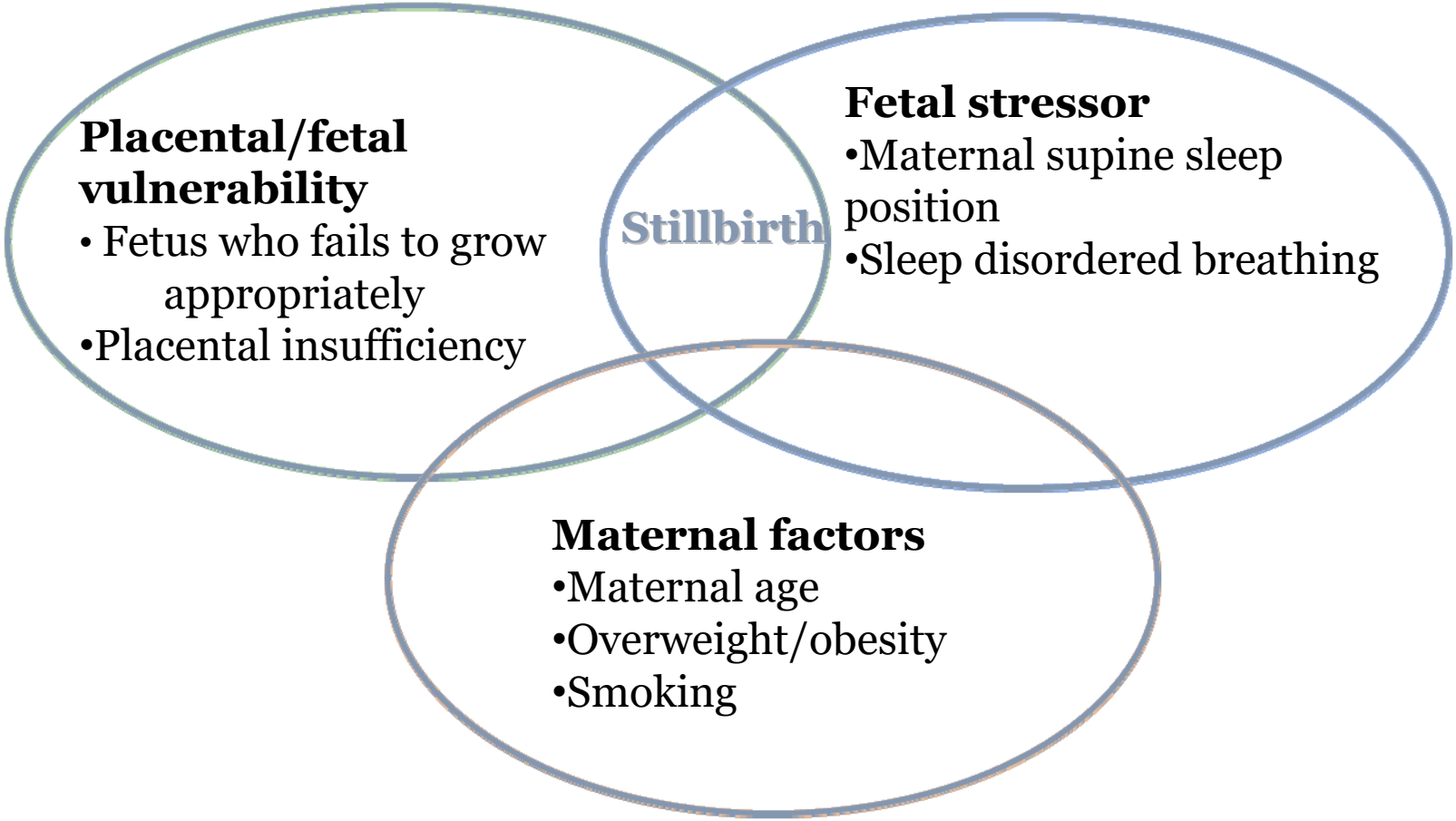


Figure 4 Cause of intrauterine death in 1039 cases according to maternal age: ≤ 35 years (□), 36–40 years (▩) or ≥ 41 years (■). significantly more placenta-related causes of death in mothers over 40 years of age. *Known to pathologist before placental exam IUGR, intrauterine growth restriction.

n et al. Stillbirth and intrauterine fetal death: factors affecting determination of cause of death at autopsy. sound Obstet Gynecol 2016

A triple risk model for unexplained late stillbirth

Warland and Mitchell *BMC Pregnancy and Childbirth* 2014



La nostra esperienza

UNIVERSITÀ DEGLI STUDI FIRENZE

575 MIF
Centro Regionale Gravidanze ad Alto Rischio
2008-2018

Approfondita anamnesi

Esami di laboratorio

Valutazione preconcezionale

Esame istologico della placenta;
Autopsia fetale;
Cariotipo fetale

Classificazione eziologica **ICD-PM**

116 MIF inspiegate

Valutazione del peso fetale alla nascita (ritardo di crescita misconosciuto?)

76 gravidanze successive

Valutazione MIF inspiegate

- RITARDO DI CRESCITA
- BMI
- EPOCA GESTAZIONALE

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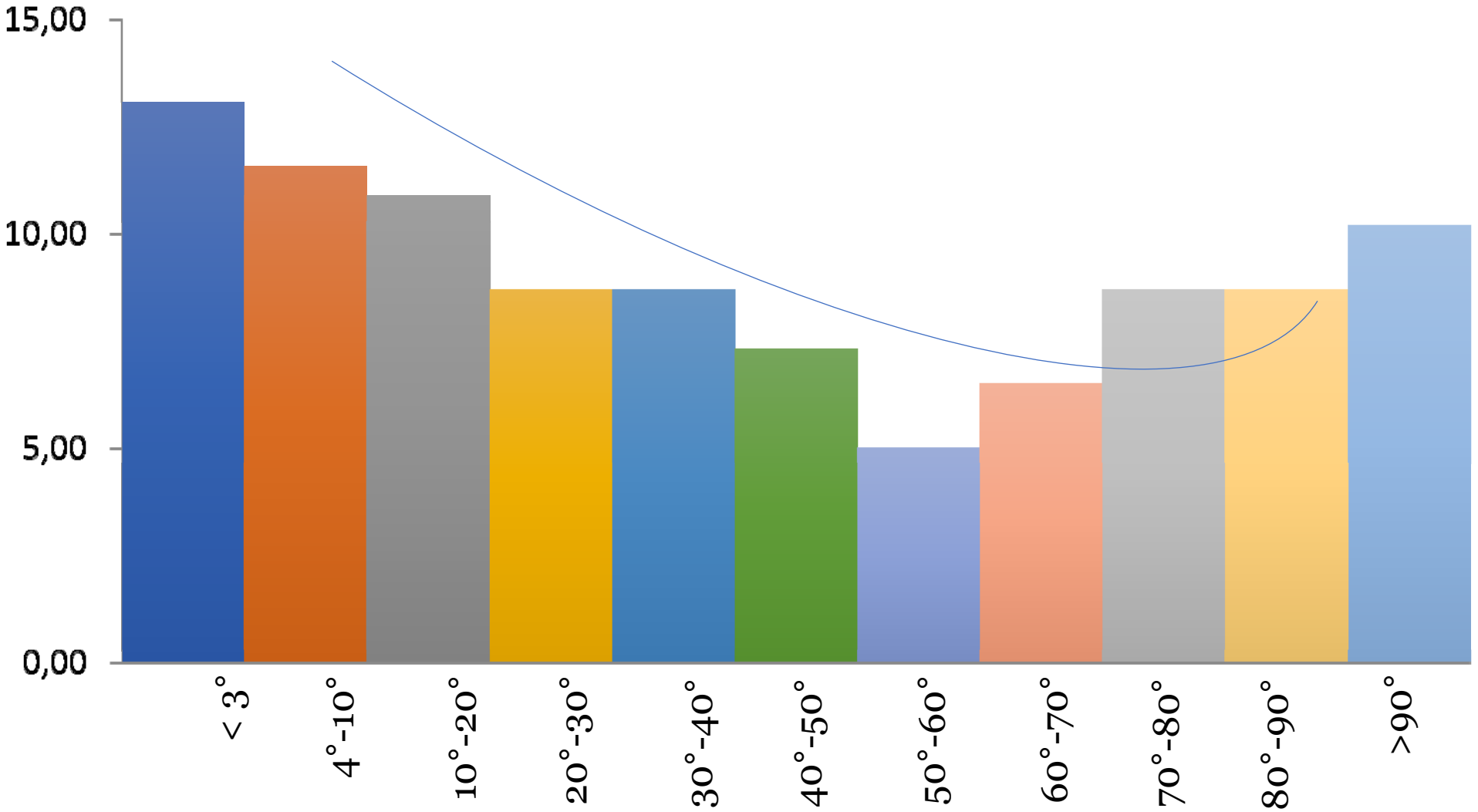
Prenatal Medicine Unit
R.R.C. Maternal Fetal Medicine
High Risk Pregnancy
Careggi University Hospital



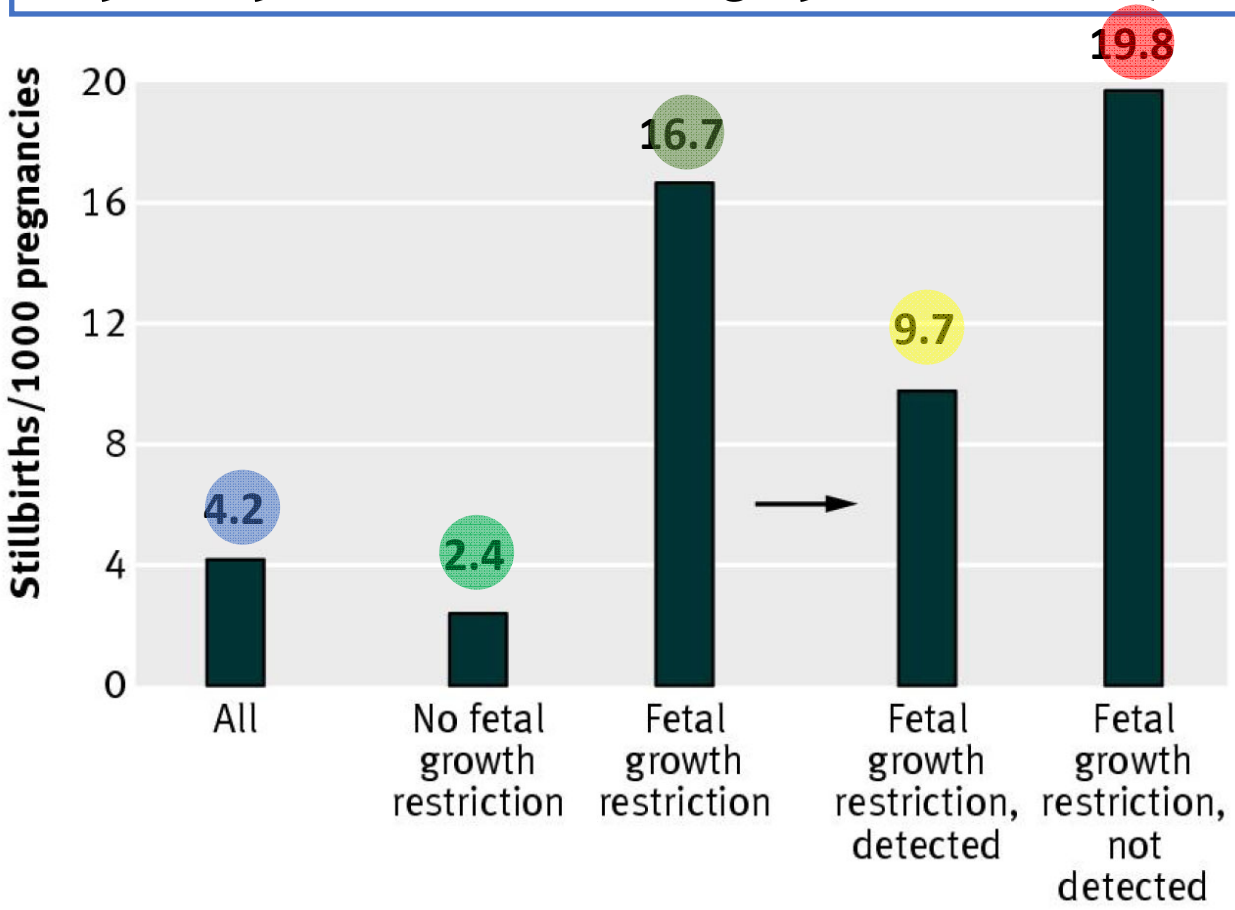
h weight percentile groups by customized curves in Stillbirth

Maternal and fetal risk factors for stillbirth: population based study

BMJ

J. Gardosi, V. Madurasinghe, M. Williams, A. Malik, A. Francis. BMJ 2013

- Cohort study, 92 218 normally formed singleton pregnancies: 91 829 live births and 389 stillbirths (after 24th weeks)



The highest risk factor identifyed was:

undetected FGR

perinatal institute
maternal and child health

The Growth Assessment Protocol: a national programme to improve patient safety in maternity care

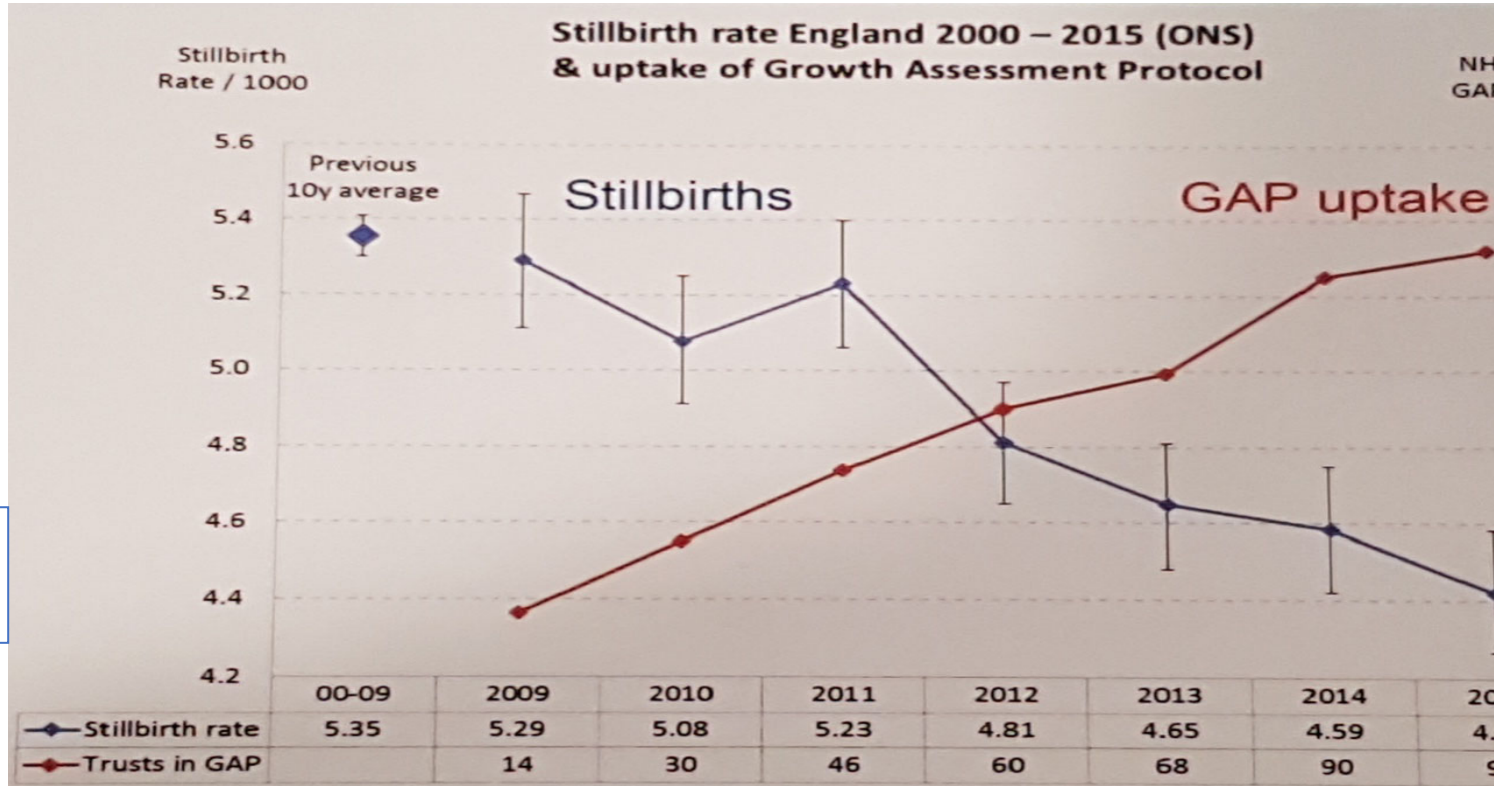
Sally Clifford, Sally Giddings, Michelle Southam, Mandy Williams, Jason Gardosi

ogramme of accreditation, training, and implementation of protocols in fetal growth assess

ndardised fundal height
asurement
tting on customised charts
otocols and referral pathways
ial scans for high risk pregnancy

A 17% reduction
mpered to the previous 10 years

Stillbirth rate have fallen again 2015



Ultrasound screening for fetal growth restriction at 36 *vs* 32 weeks' gestation: a randomized trial (ROUTE)

E. ROMA*, A. ARNAU†, R. BERDALA*, C. BERGOS*, J. MONTESINOS† and F. FIGUERAS‡

Ultras Obstet Gynecol October 2015

Table 4 Performance of ultrasound examination at 32 or 36 weeks' gestation for detection of fetal growth restriction (FGR) or severe FGR*

	32 weeks	*36 weeks*
Sensitivity (%)		
FGR	22.5 (15.7–31.1)	38.8 (31.2–47.3)
Severe FGR	32.5 (20.1–48.0)	61.4 (46.6–74.3)
Specificity (%)		
FGR	91.8 (89.8–93.5)	93.6 (91.8–95.0)
Severe FGR	91.3 (89.4–93.0)	91.5 (89.6–93.1)
PPV (%)		
FGR	25.8 (18.1–35.3)	48.2 (39.2–57.4)
Severe FGR	13.5 (8.1–21.8)	24.1 (17.1–32.8)
NPV (%)		
FGR	90.4 (88.3–92.2)	91.0 (88.9–92.6)
Severe FGR	97.0 (95.7–97.9)	98.2 (97.1–98.8)
LR+		
FGR	2.7	6.1
Severe FGR	3.7	7.2
LR–		
FGR	0.84	0.65
Severe FGR	0.74	0.40

Gravidanze a basso rischio, ecografia a 32 wks (n=1272) vs 36 wks (n=1314)

Valutazione MIF inspiegate

- RITARDO DI CRESCITA
- BMI
- EPOCA GESTAZIONALE

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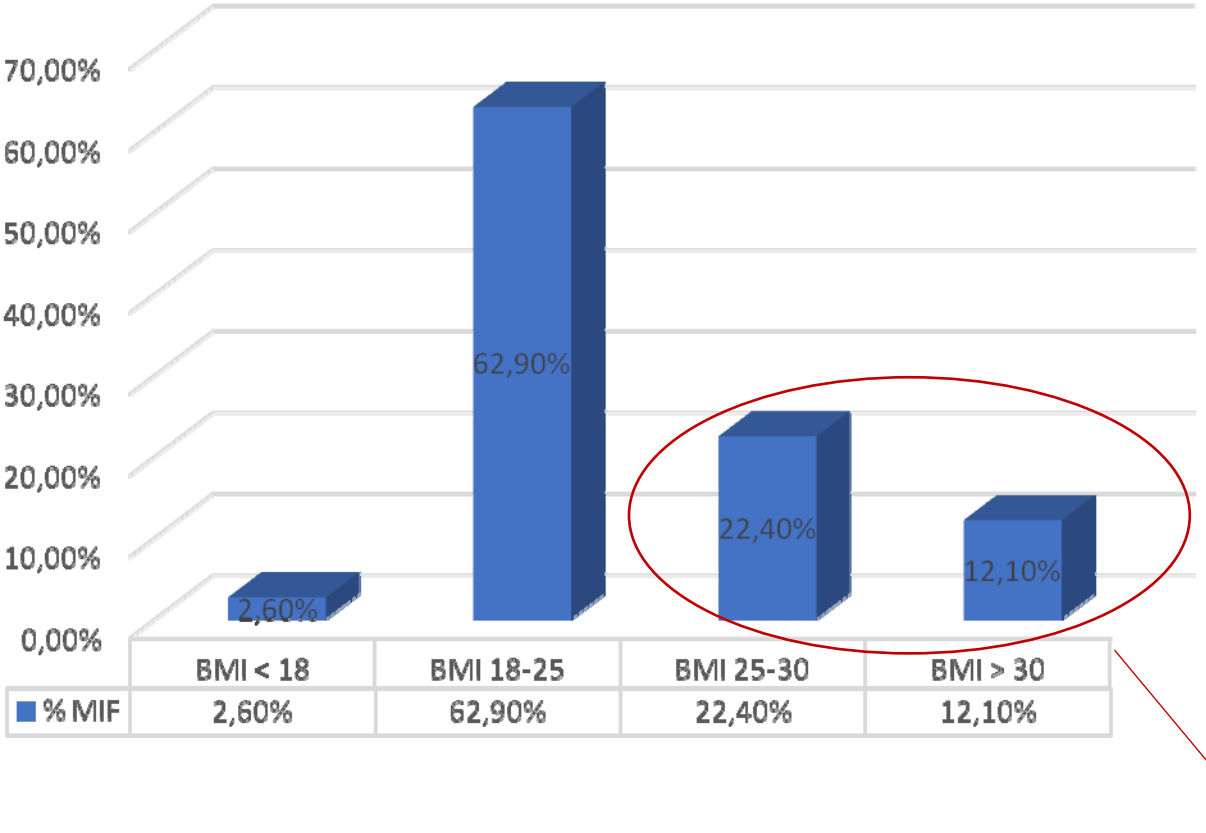
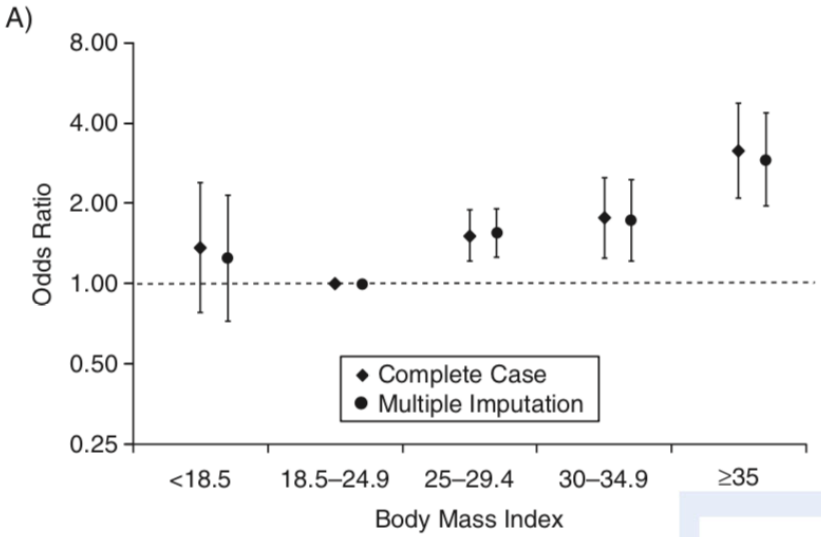
N. 116 MIF INSPIEGATE

VALUTAZIONE BMI



BMI>25 nel 34,5 delle MIF inspiega

Obesity and stillbirth



Tennant P.W.G. Am J Obstet Gynecol 2007

STILLBIRTH RISK

BMI 25-29.9 **OR 1.51** (95% CI 1.21-1.89)
BMI 30-34.9 **OR 1.77** (95% CI 1.24-2.5)
BMI > 35 **OR 3.16** (95% CI 2.10-4.76)

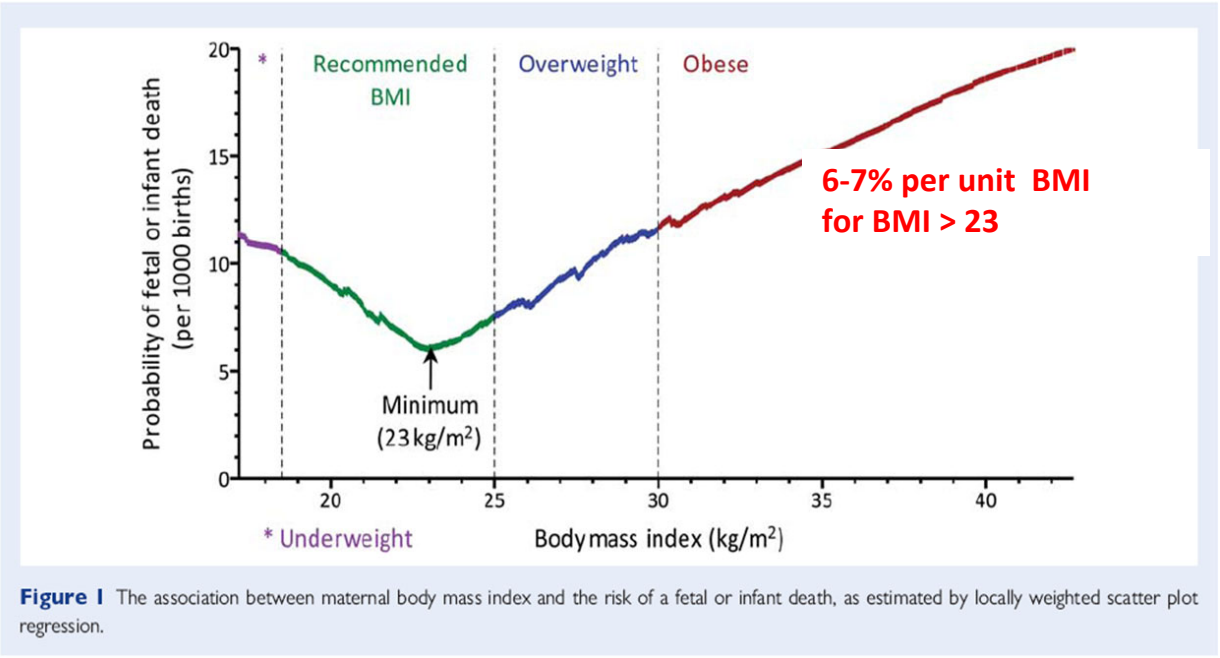


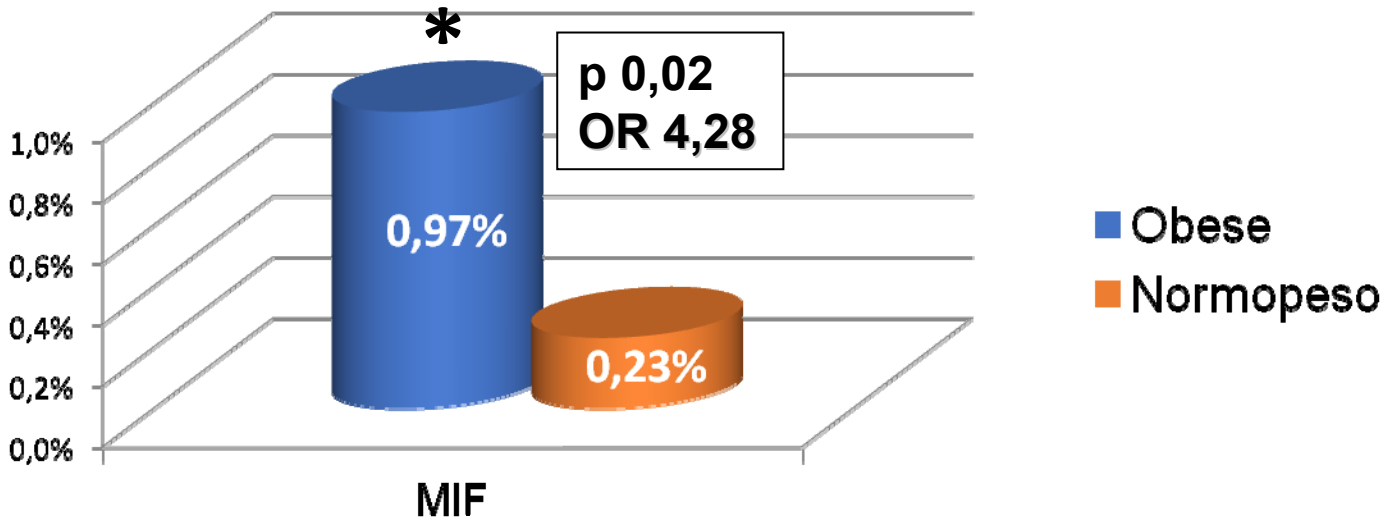
Figure 1 The association between maternal body mass index and the risk of a fetal or infant death, as estimated by locally weighted scatter plot regression.

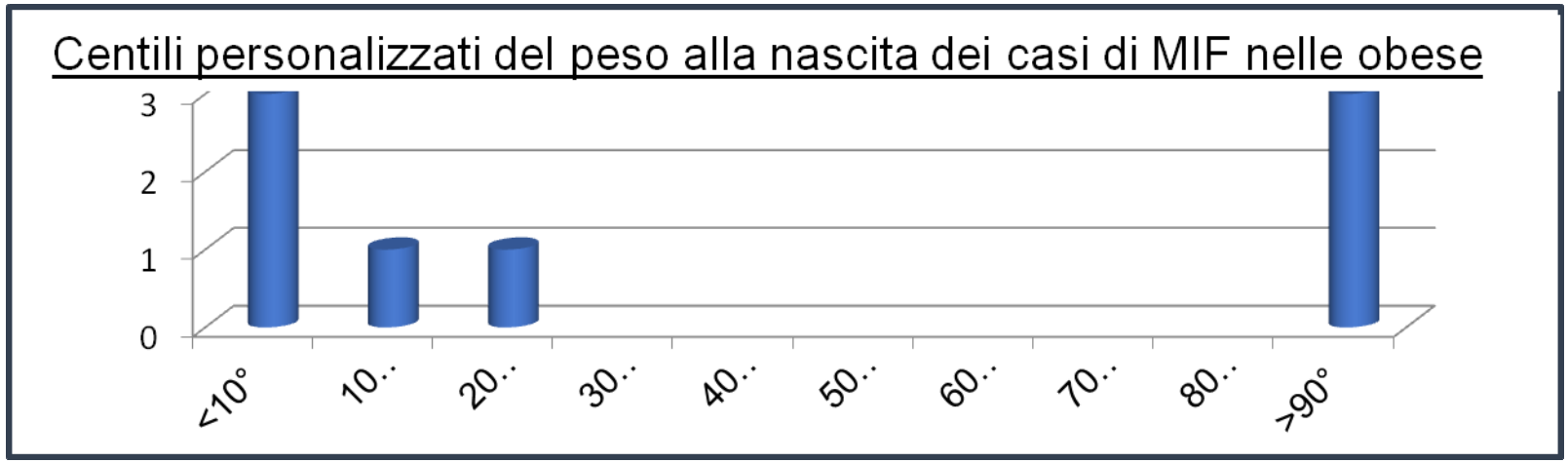
A Lindam et al. High maternal body mass index in early pregnancy and risks of stillbirth and infant mortality . A population-based Sibling study in Sweden. American Journal of Epidemiology 2016

ANTEPARTUM

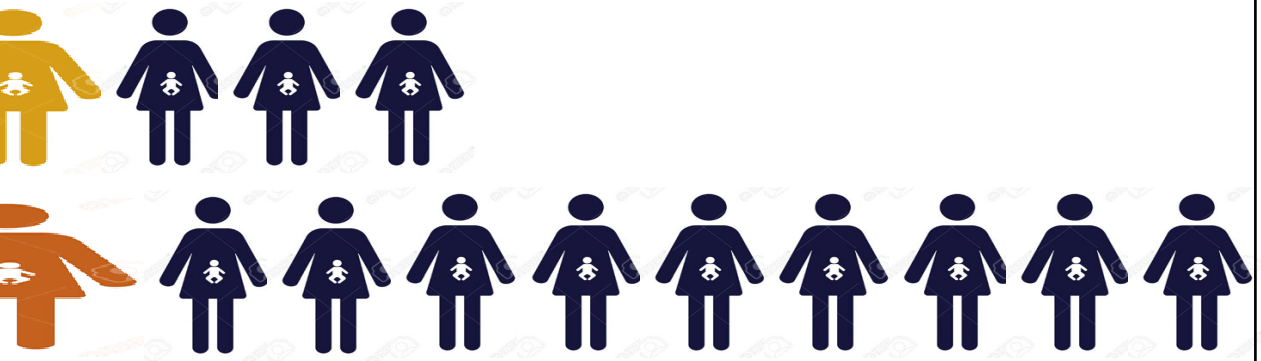
OBESITY AND INTRAUTRINE FETAL DEATH

CAREGGI UNIVERSITY HOSPITAL 2010-2015
822 obese: 16511 deliveries



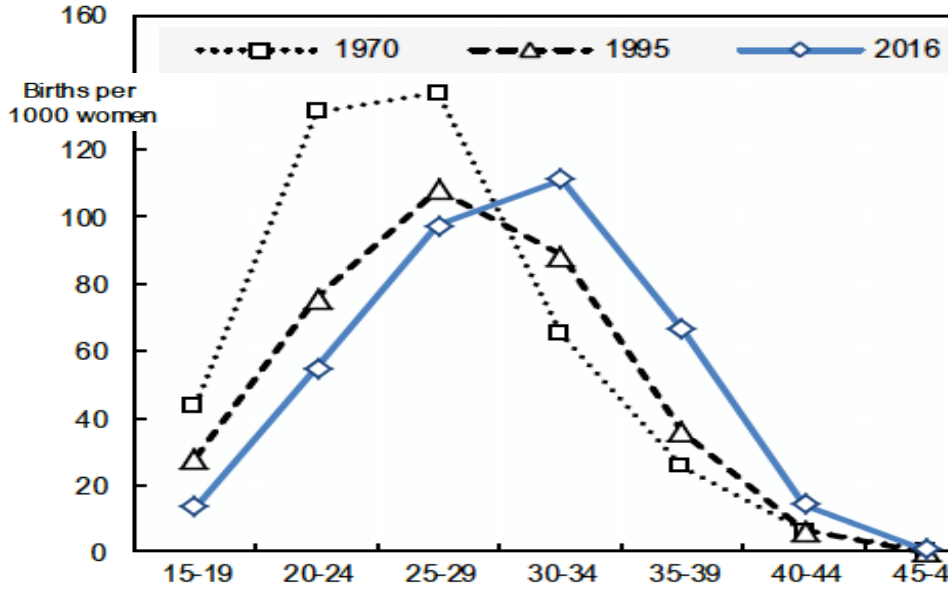


2 OBESITY EPIDEMIC



ITY AND OVERWEIGHT IS AN ESCALATING PROBLEM AMONG WOMEN EPRODUCTIVE AGE IN USA and EUROPE WITH MORE THAN 1 IN 10 NANT WOMEN BEING OBESE, AND 1 IN 4 BEING OVERWEIGHT

3 ADVANCED MATERNAL AGE



AGE AT CHILDBIRTH CONTINUES TO RISE IN EUROPE.
RISK OF GDM INCREASES BY 74% AFTER AGE 40

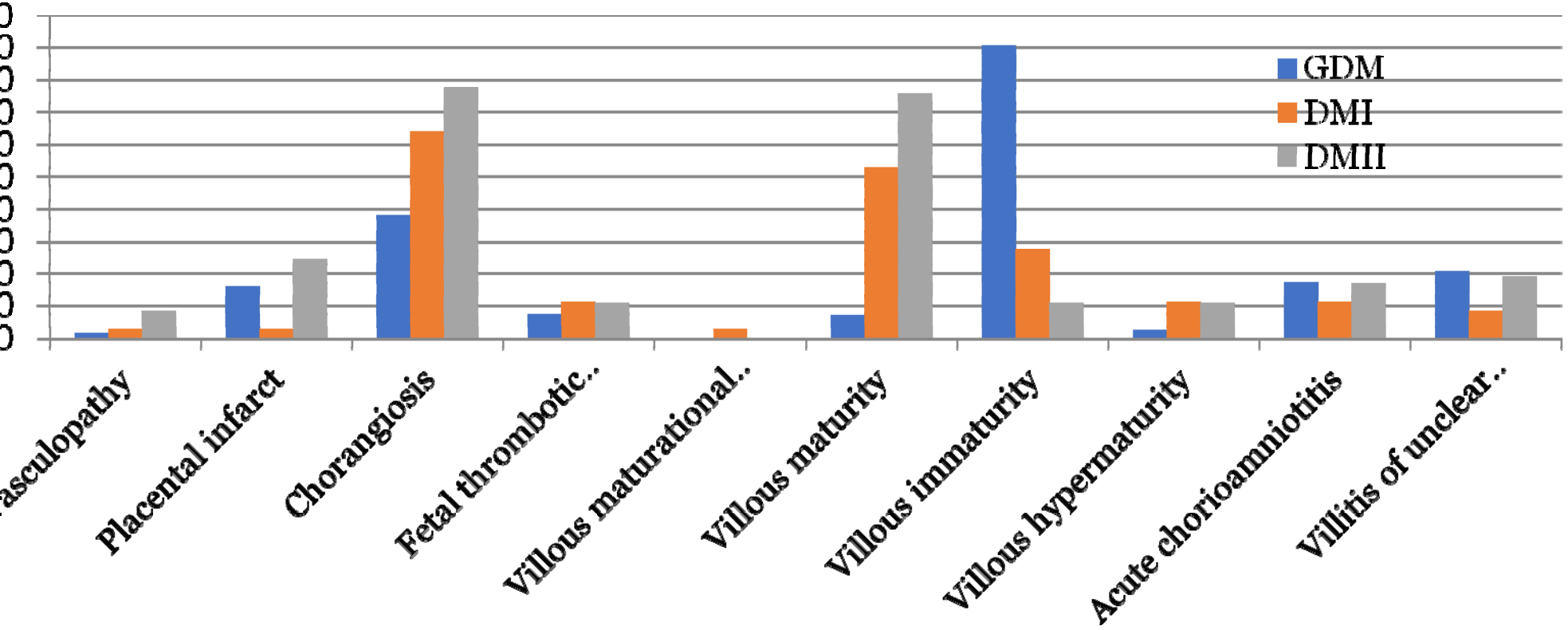
Eurostat Demographic Statistics 2017

A. Dietl et al. Geburtshilfe Frauenheilkd, 2015

GDM IS ON THE RISE GLOBALLY

HIP IS A MAJOR GLOBAL HEALTH PROBLEM

Differences in placental pathology according to diabetes types



GDM is associated with a greater rate of villous immaturity

ype 2 and Gestational Diabetes Mellitus Differentially Impact Placental Pathologic Characteristics of Uteroplacental Malperfusion. Jennifer Huynh et al. Pla

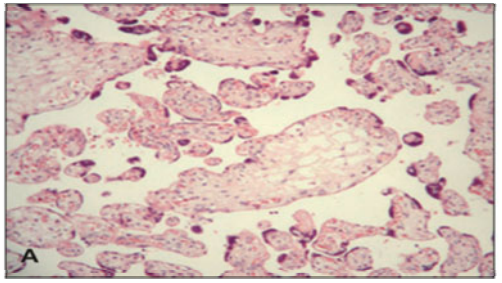
Pediatr Dev Pathol. 2011 Jul-Aug;14(4):273-9. doi: 10.2350/10-07-0872-OA.1. Epub 2011 Feb 17.

Clinical associations with a placental diagnosis of delayed villous maturation retrospective study.

Higgins M[1], McAuliffe FM, Mooney EE.

layed villous maturation (**DVM**)is associated with an increased **risk of stillbirth** in the **late** th trimester

- decreased tertiary villus formation
- reduced vasculosyncytial membrane formation
- increased large bullous villi



A retrospective study on 175 placentas with DVM vs 175 controls

Pregestational diabetes (8% vs 2.8%, $P < 0.05$; relative risk 2.8
Gestational diabetes (8.6% vs 3.4%, $P < 0.05$; relative risk 2.5
Prenatal or intrapartum intrauterine death (8.6% vs 0%, $P < 0.05$)

Valutazione MIF inspiegate

- RITARDO DI CRESCITA
- BMI
- EPOCA GESTAZIONALE

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Stillbirths occurring *near term* are more likely to be *unexplained* than stillbirths occurring earlier in gestation

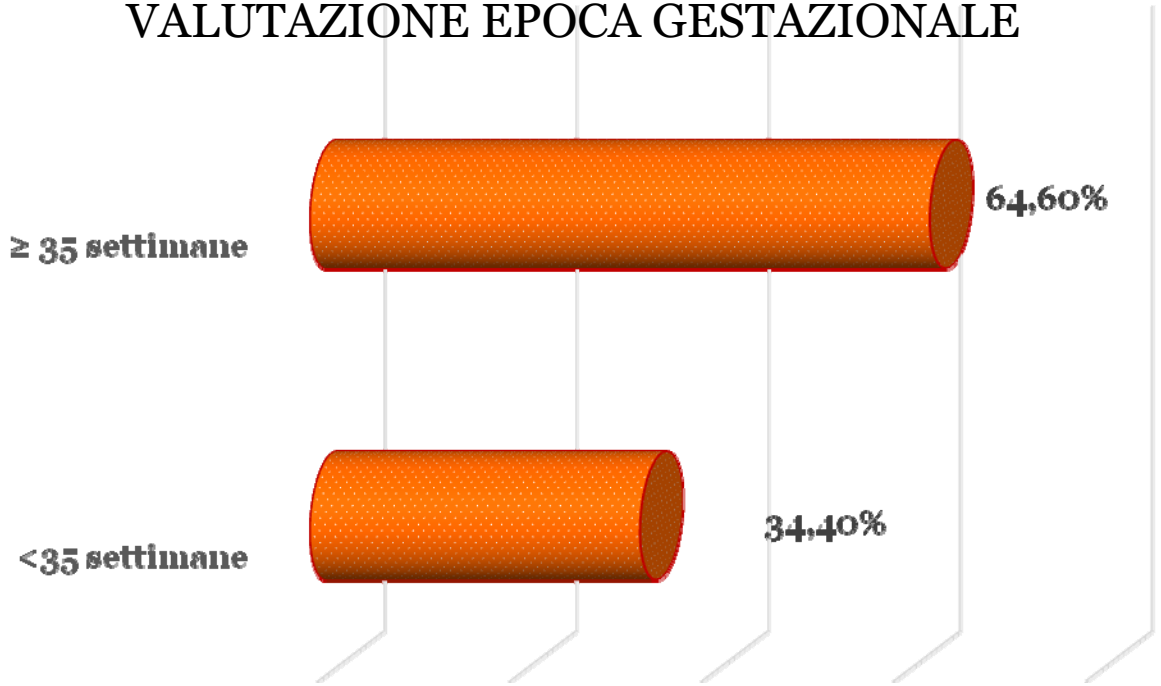
Two thirds of the unexplained fetal deaths

after 35 weeks' gestation

Yudkin PL et al.Lancet. 1987
Huang DY et al. Obstet Gynecol.

N. 116 MIF INSPIEGATE

VALUTAZIONE EPOCA GESTAZIONALE



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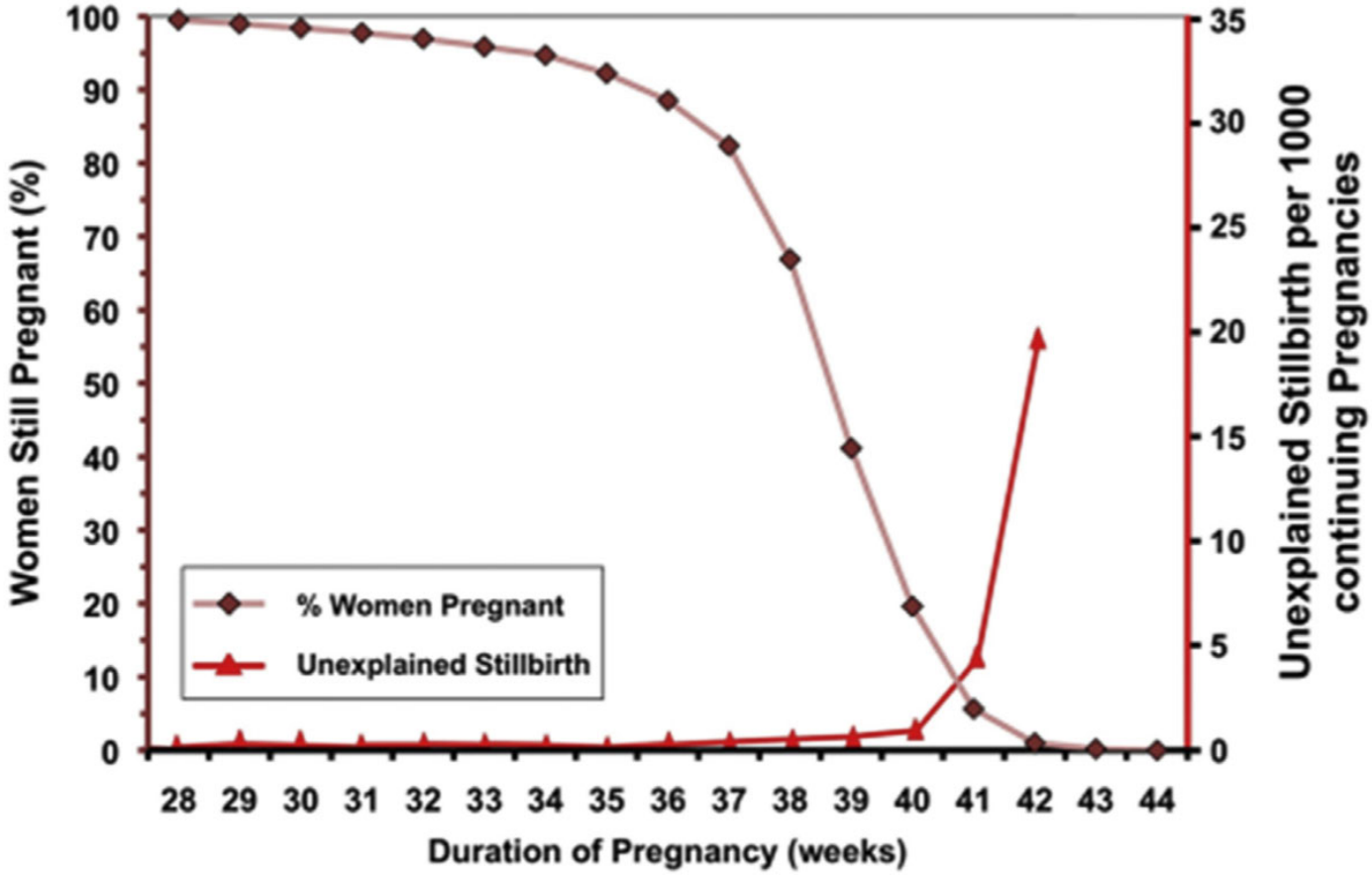
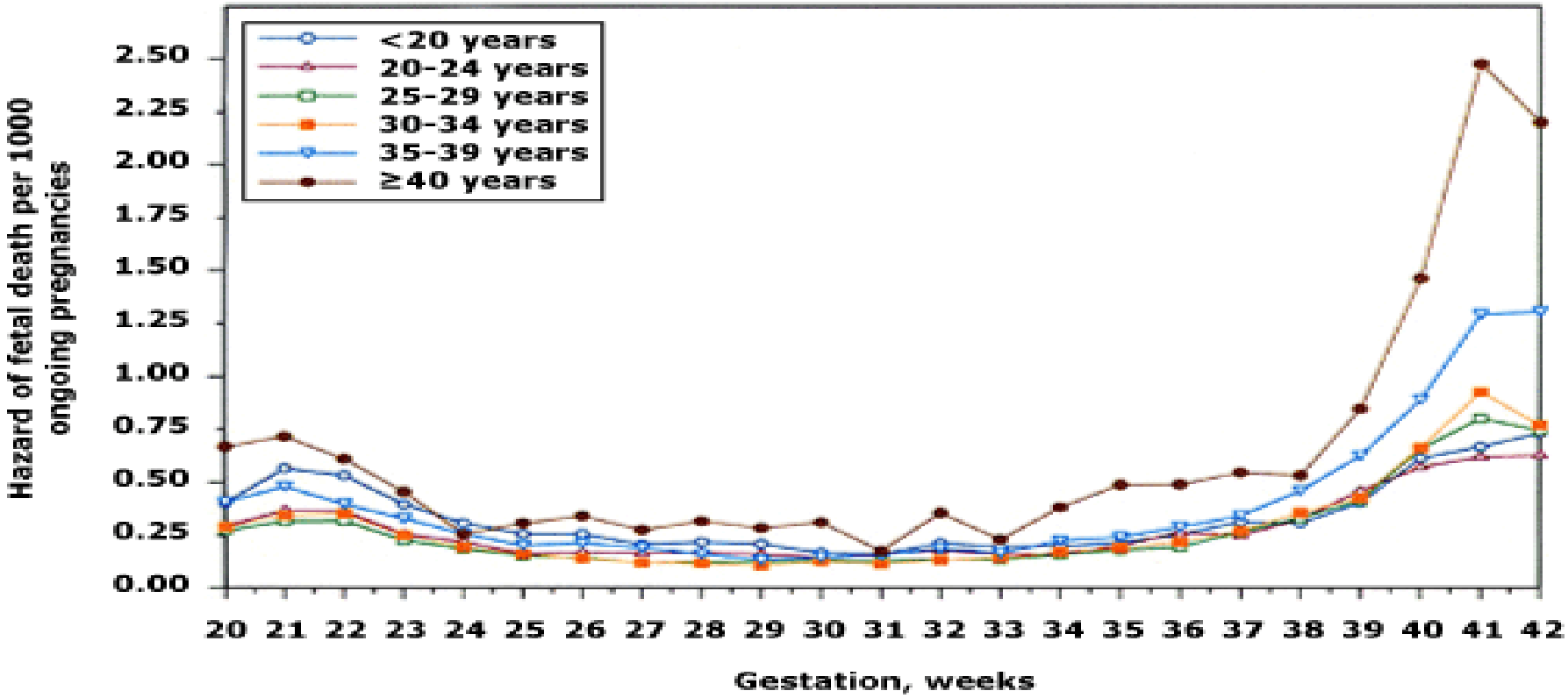
A role for aging in the etiology of stillbirth



Johnson FB et al. Molecular biology of aging. Cell 1999

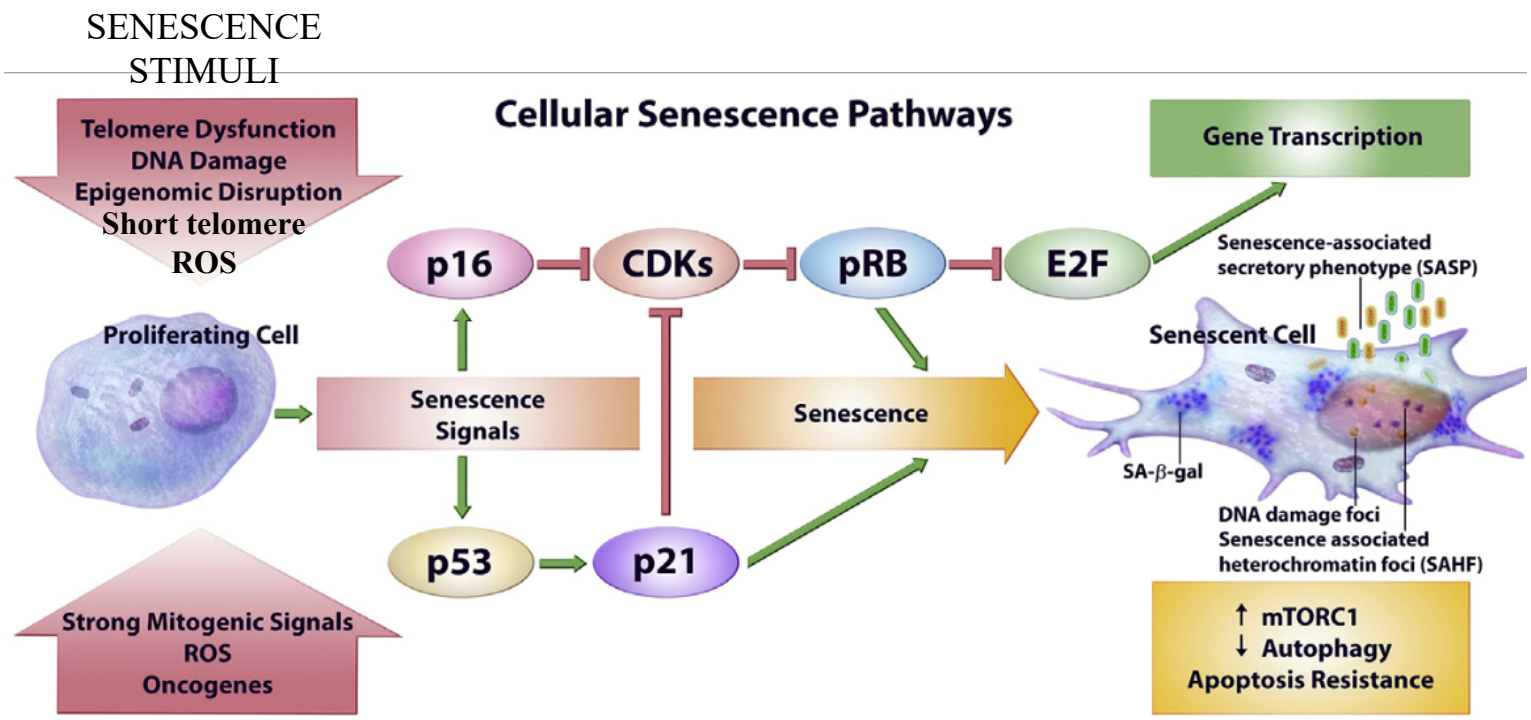
Hazard (risk) of stillbirth for singleton births without congenital anomalies by maternal age and gestational age, 2001–2002



Older women experience an increased risk of stillbirth at all gestational ages, and this risk is magnified at term.

Reproduced with permission from: Reddy, UM, Ko, CW, Willinger, M. Maternal age and the risk of stillbirth throughout pregnancy in the United States. Am J Obstet Gynecol 2006; 195:764. Copyright ©2006 Elsevier.

AN OVERVIEW OF CELLULAR SENESCENCE



SENESCENCE BIOMARKERS:

- Short and dysfunction telomeres
- ↑expression of oncogenes deteriorating mitochondrial function
- ↑ DNA damage (oxidation)
- ↑ level of proinflammatory cytokine (IL- 1b and IL-6)

Smith R. Am J Obstet Gynecol

Management of post-date pregnancies and perinatal mortality

Danish national guidelines for management of post-date pregnancies.
Danish population studied: 102.167 pts

	The national guidelines in 2010	The national guidelines in 2012
Singleton uncomplicated pregnancies	Induction ***at* GA 42^{+0}**	Induction ***between GA*** 41^{+2}-41^{+6}
Singleton pregnancies with risk factors: Maternal age > 40 years or BMI > 35 kg/m^2	Induction at **GA 42^{+0}**	Induction at **GA 41^{+0}**
Surveillance	***No*** surveillance after GA 40+0	Surveillance ***at GA*** 41^{+0} (CTG and/or ultrasound)

102,167

Induction at 41 ws	28.2%	42.6%	
Stillbirth	0.09%	0.005%	ORa 0.50
Perinatal death	0.13%	0.08%	ORa 0.62

A 50% decline in the risk of stillbirt

et al. Decline in stillbirths and perinatal mortality after implementation of a more aggressive induction policy in post
nancies: a nationwide register study. Acta Obstet Gynecol Scand. 2017

Stillbirth cannot continue to be invisible

Thank you for you attention