La nascita prematura
Tavolo Tecnico Regione Lazio

Domenico Arduini
Dipartimento di Ostetricia e Ginecologia
Polo assistenziale S. Famiglia
Università Tor Vergata, Roma

Utilità della diagnosi precoce

In 2012, preterm birth affected more than **450,000 babies—that's 1 of every 9 infants born in the United States**. Preterm birth is the birth of an infant before 37 weeks of pregnancy. Preterm-related causes of death together accounted for 35% of all infant deaths in 2010, more than any other single cause. Preterm birth is also a leading cause of long-term neurological disabilities in children. **Preterm birth costs the U.S. health care system more than $26 billion in 2005.**

Rischio Parto Pretermine

Possibilità di diagnosi precoce : Ecografia

Effects of interventions

1. In symptomatic women
2. with singleton gestations
3. with signs and/or symptoms of PTL,

knowledge of TVU CL results was associated with a non-significant decrease in preterm birth at less than 37 weeks compared to no such knowledge (22.3% versus 34.7%, respectively; risk ratio (RR) 0.59, 95% confidence interval (CI) 0.26 to 1.32; 2 trials, n = 242).

THE COCHRANE LIBRARY
Independent high-quality evidence for health care decision making
from The Cochrane Collaboration

Cervical assessment by ultrasound for preventing preterm delivery (Review)
Berghella V, Baxter JK, Hendrix NW Cochrane Pregnacny and Childbirth Group
Published on line 31.01.13

Possibilità di diagnosi precoce : Ecografia

Furthermore, it is unclear which interventions are most efficacious once TVU CL results are known.

Ness suggested

Am J Obstet Gynecol. **2007** Oct;197(4):426.e1-7

- intervention with steroids for fetal lung maturity and tocolysis for women with TVU CL less than 20 mm
- use of FFN for management of women with TVU CL of 20 to 29 mm, and
- no intervention for women with CL equal to or greater than 30 mm

Implications for practice

…is insufficient evidence to recommend routine screening of asymptomatic or symptomatic pregnant women with TVU CL.

Cervical assessment by ultrasound for preventing preterm delivery (Review)
Berghella V, Baxter JK, Hendrix NW Cochrane Pregnacny and Childbirth Group
Published on line 31.01.13

Possibilità terapeutiche nella diagnosi precoce

Health Technology Assessment 2009; Vol. 13: No. 43
Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling

Our evaluation supports previous **conclusions about lack of evidence that screening for and treatment of bacterial vaginosis is likely to be a cost-effective strategy.**

Suggestions that fetal fibronectin test or cervical length measurement may be useful are supported**, more so for cervical length measurement. This is, however, only in the context of delaying delivery in symptomatic mothers**

Terbutaline was found to be a potentially cost- effective intervention in past evaluations, albeit in three studies with concerns about study quality. **This evaluation, however, provided no direct support for the superiority of terbutaline relative to other tocolytic agents.**

currently there is not sufficient evidence to recommend its use. Since this review found an association between knowledge of FFN results and a lower incidence of preterm birth before 37 weeks, further research should be encouraged.

Fetal fibronectin testing for reducing the risk of preterm birth
Vincenzo Berghella[1,*], Edward Hayes[2], John Visintine[2], Jason K Baxter[2]
Editorial Group: Cochrane Pregnancy and Childbirth Group
Published Online: 8 OCT 2008

Possibilità terapeutiche nella diagnosi precoce

Health Technology Assessment 2009; Vol. 13: No. 43
Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling

Our evaluation supports previous **conclusions about lack of evidence that screening for and treatment of bacterial vaginosis is likely to be a cost-effective strategy.**

Suggestions that fetal fibronectin test or cervical length measurement may be useful are supported**, more so for cervical length measurement. This is, however, only in the context of delaying delivery in symptomatic mothers**

Terbutaline was found to be a potentially cost- effective intervention in past evaluations, albeit in three studies with concerns about study quality. **This evaluation, however, provided no direct support for the superiority of terbutaline relative to other tocolytic agents.**

…….currently there is not sufficient evidence to recommend its use. Since this review found an association between knowledge of FFN results and a lower incidence of preterm birth before 37 weeks**, further research should be encouraged.**

Fetal fibronectin testing for reducing the risk of preterm birth
Vincenzo Berghella[1,*], Edward Hayes[2], John Visintine[2], Jason K Baxter[2]
Editorial Group: Cochrane Pregnancy and Childbirth Group
Published Online: 8 OCT 2008

THE COCHRANE LIBRARY
Independent high-quality evidence for health care decision making
from The Cochrane Collaboration

Possibilità terapeutiche nella diagnosi precoce

Health Technology Assessment 2009; Vol. 13: No. 43
Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling

There is insufficient direct evidence to support the routine use of oxytocin receptor antagonists such as atosiban.

Tocolysis should be used in women symptomatic with threatened preterm labour to prevent or delay spontaneous preterm birth.

Antenatal corticosteroids are the most favourable interventions to treat symptomatic women in terms of preventing complications of prematurity in the newborn.

Results confirm that progesterone is an efficient treatment in singleton gestation with short cervical length, and in singleton gestation with prior preterm birth with or without short cervical length. Apart from these indications, should not be used outside research protocols.

Gynecol Obstet Fertil. 2014 Feb;42(2):112-22 ***[Progesterone and preterm delivery: back to the future?].*** *Fuchs et al.*

17α-Hydroxyprogesterone caproate **has not been shown to be effective in reducing the rate of spontaneous preterm birth in women with a short cervix.**

Semin Fetal Neonatal Med. 2014 Feb;19(1):15-26
Progesterone to prevent spontaneous preterm birth.
Romero et al

Possibilità terapeutiche nella diagnosi precoce

Health Technology Assessment 2009; Vol. 13: No. 43
Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling

There is insufficient direct evidence to support the routine use of oxytocin receptor antagonists such as atosiban.

Tocolysis should be used in women symptomatic with threatened preterm labour to prevent or delay spontaneous preterm birth.

Antenatal corticosteroids are the most favourable interventions to treat symptomatic women in terms of preventing complications of prematurity in the newborn.

Results confirm that progesterone is an efficient treatment in singleton gestation with short cervical length, and in singleton gestation with prior preterm birth with or without short cervical length. Apart from these indications, should not be used outside research protocols.

Gynecol Obstet Fertil. 2014 Feb;42(2):112-22 ***[Progesterone and preterm delivery: back to the future?].*** *Fuchs et al.*

17α-Hydroxyprogesterone caproate **has not been shown to be effective in reducing the rate of spontaneous preterm birth in women with a short cervix.**

Semin Fetal Neonatal Med. 2014 Feb;19(1):15-26
Progesterone to prevent spontaneous preterm birth.
Romero et al

Possibilità terapeutiche nella diagnosi precoce

Health Technology Assessment 2009; Vol. 13: No. 43
Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling

There is insufficient direct evidence to support the routine use of oxytocin receptor antagonists such as atosiban.

Tocolysis should be used in women symptomatic with threatened preterm labour to prevent or delay spontaneous preterm birth.

Antenatal corticosteroids are the most favourable interventions to treat symptomatic women in terms of preventing complications of prematurity in the newborn.

Results confirm that progesterone is an efficient treatment in singleton gestation with short cervical length, and in singleton gestation with prior preterm birth with or without short cervical length. Apart from these indications, should not be used outside research protocols.

Gynecol Obstet Fertil. 2014 Feb;42(2):112-22 ***[Progesterone and preterm delivery: back to the future?].*** *Fuchs et al.*

17α-Hydroxyprogesterone caproate **has not been shown to be effective in reducing the rate of spontaneous preterm birth in women with a short cervix.**

Semin Fetal Neonatal Med. 2014 Feb;19(1):15-26
Progesterone to prevent spontaneous preterm birth.
Romero et al

Possibilità terapeutiche nella diagnosi precoce

For the initial tocolysis, the use of **atosiban or nifedipine** for 48 h is **recommended** based on the largest effectiveness and most favorable side effect profile. However, since **data that convincingly indicate the beneficial effect of tocolytics on neonatal outcome are lacking, it might well be that tocolytics are ineffective.**

Expert Opin Pharmacother. 2014 Apr;15(6):787-97
Preterm labor: current pharmacotherapy options for tocolysis.
van Vliet EO1, Boormans EM, de Lange TS, Mol BW, Oudijk MA.

There was very little evidence about using COX inhibitors for preventing preterm labour. There are inadequate data to make any recommendation about using COX inhibitor in practice to prevent preterm labour. Future research should include follow-up of the babies to examine the short-term and long-term effects of COX inhibitors.

Cyclo-oxygenase (COX) inhibitors for preventing preterm labour
Thirawut Khanprakob[1,*], Malinee Laopaiboon[2], Pisake Lumbiganon[3], Ussanee S Sangkomkamhang[1]
Editorial Group: Published Online: 17 OCT 2012

Possibilità terapeutiche nella diagnosi precoce

For the initial tocolysis, the use of **atosiban or nifedipine** for 48 h is **recommended** based on the largest effectiveness and most favorable side effect profile. However, since **data that convincingly indicate the beneficial effect of tocolytics on neonatal outcome are lacking, it might well be that tocolytics are ineffective.**

Expert Opin Pharmacother. 2014 Apr;15(6):787-97
Preterm labor: current pharmacotherapy options for tocolysis.
van Vliet EO1, Boormans EM, de Lange TS, Mol BW, Oudijk MA.

There was very little evidence about using COX inhibitors for preventing preterm labour. There are inadequate data to make any recommendation about using COX inhibitor in practice to prevent preterm labour. Future research should include follow-up of the babies to examine the short-term and long-term effects of COX inhibitors.

Cyclo-oxygenase (COX) inhibitors for preventing preterm labour
Thirawut Khanprakob[1,*], Malinee Laopaiboon[2], Pisake Lumbiganon[3], Ussanee S Sangkomkamhang[1]
Editorial Group: Published Online: 17 OCT 2012

Utilità della diagnosi precoce

There **is a need to develop new tools for the treatment of patients with PTL.** Research focussed on improving tocolysis, the physiology of labour and pathological processes involved in PTL would afford new approaches for the treatment of PTL, **allowing clinicians to provide integrative solutions for this multifactorial disease.**

Expert Opin Investig Drugs. 2014 Jun;23(6):759-71.
Preterm labour: association between labour physiology, tocolysis and prevention.
Illanes SI, Perez-Sepulveda A, Rice GE, Mitchell MD

A significant heterogeneity in all topics surveyed suggests **an urgent need for networking, more evidence-based guidelines** and prospective comparative audits to **ascertain the real impact of specialist PTL clinics** on the reduction in preterm birth and its sequelae.

Royal College of Obstetricians and Gynaecologists 2013

BJOG. 2014 Mar;121(4):417-21.
Provision and practice of specialist preterm labour clinics: a UK survey of practice.
Sharp AN, Alfirevic Z.

Utilità della diagnosi precoce

There **is a need to develop new tools for the treatment of patients with PTL.** Research focussed on improving tocolysis, the physiology of labour and pathological processes involved in PTL would afford new approaches for the treatment of PTL, **allowing clinicians to provide integrative solutions for this multifactorial disease.**

Expert Opin Investig Drugs. 2014 Jun;23(6):759-71.
Preterm labour: association between labour physiology, tocolysis and prevention.
Illanes SI, Perez-Sepulveda A, Rice GE, Mitchell MD

A significant heterogeneity in all topics surveyed suggests **an urgent need for networking, more evidence-based guidelines** and prospective comparative audits to **ascertain the real impact of specialist PTL clinics** on the reduction in preterm birth and its sequelae.

Royal College of Obstetricians and Gynaecologists 2013

BJOG. 2014 Mar;121(4):417-21.
Provision and practice of specialist preterm labour clinics: a UK survey of practice.
Sharp AN, Alfirevic Z.

Utilità della diagnosi precoce: il riposo a letto

There is **no evidence, either supporting or refuting the use of bed rest at home or in hospital**, to prevent preterm birth. Although bed rest in hospital or at home is widely used as the first step of treatment, there is no evidence that this practice could be beneficial. **Due to the potential adverse effects that bed rest could have on women and their families,** and the increased costs for the healthcare system, clinicians **should not routinely advise women to rest in bed** to prevent preterm birth.

Bed rest in singleton pregnancies for preventing preterm birth
Claudio Sosa[1,*], Fernando Althabe[2], José M Belizán[2], Eduardo Bergel[3]
Editorial Group: Cochrane Pregnancy and Childbirth Group
Published Online: 26 JAN 2004

THE COCHRANE LIBRARY
Independent high-quality evidence for health care decision making
from The Cochrane Collaboration

A significant heterogeneity in all topics surveyed suggests **an urgent need for networking, more evidence-based guidelines** and prospective comparative audits to **ascertain the real impact of specialist PTL clinics** on the reduction in preterm birth and its sequelae.

Royal College of Obstetricians and Gynaecologists 2013

BJOG. 2014 Mar;121(4):417-21.
Provision and practice of specialist preterm labour clinics: a UK survey of practice.
Sharp AN, Alfirevic Z.

RCTs

Pochi dati!

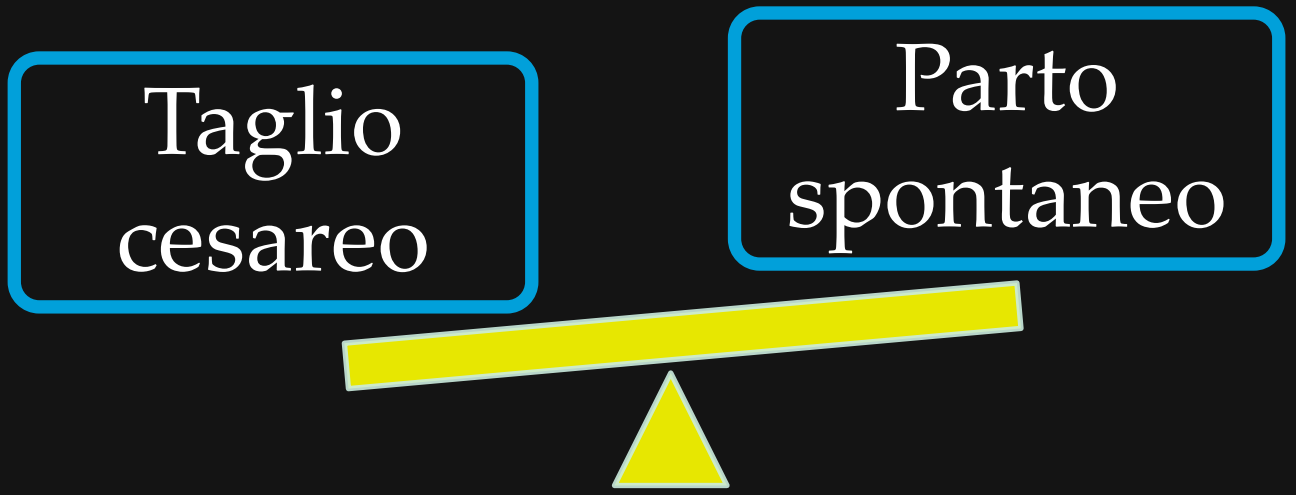
Specialmente per i parti podalici

- Esiguità degli studi randomizzati
- Difficoltà nel randomizzare sul parto vaginale
- Variabili da considerare

Drife J. *BJOG 2006*;113(Suppl. 3):81–85.

Lumley J.*BJOG 2003*, Vol. 110 (Suppl 20), pp. 88–92

Stato dell' arte



Prematurità non è indicazione al TC elettivo.

La scelta dovrebbe basarsi su indicazioni :

- ✓materne
- ✓ fetali

Drife J. *BJOG 2006*;113(Suppl. 3):81–85.

NICE guideline ,18 October 2006.

??Quesiti??

La modalità del parto può modificare:

Mortalità neonatale

Morbilità neonatale

Morbilità materna

?

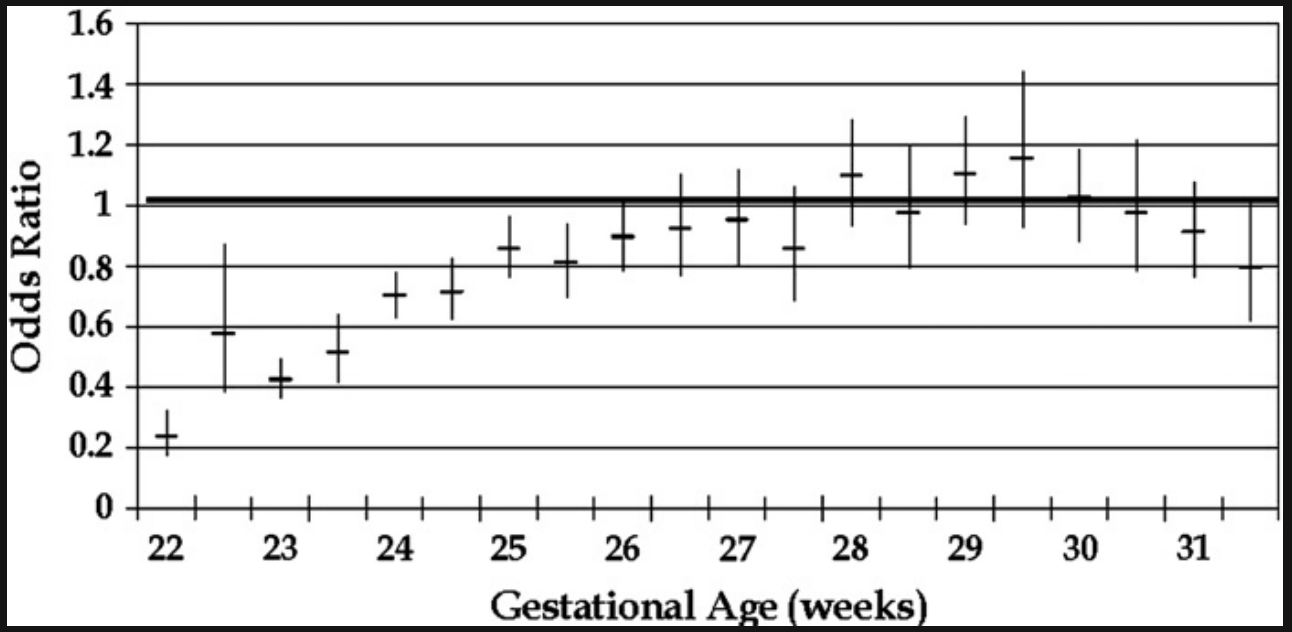
Mortalità neonatale

Fattori confondenti presenti nel 90% dei pretermine:

- SGA
- Presentazione podalica
- Anomalie congenite
- Gravidanza multipla
- Complicanze associate al travaglio

Mortalità neonatale 22-31 wks

Taglio cesareo vs Parto vaginale



Odds Ratio 22-25 wks = 0,2-0,7

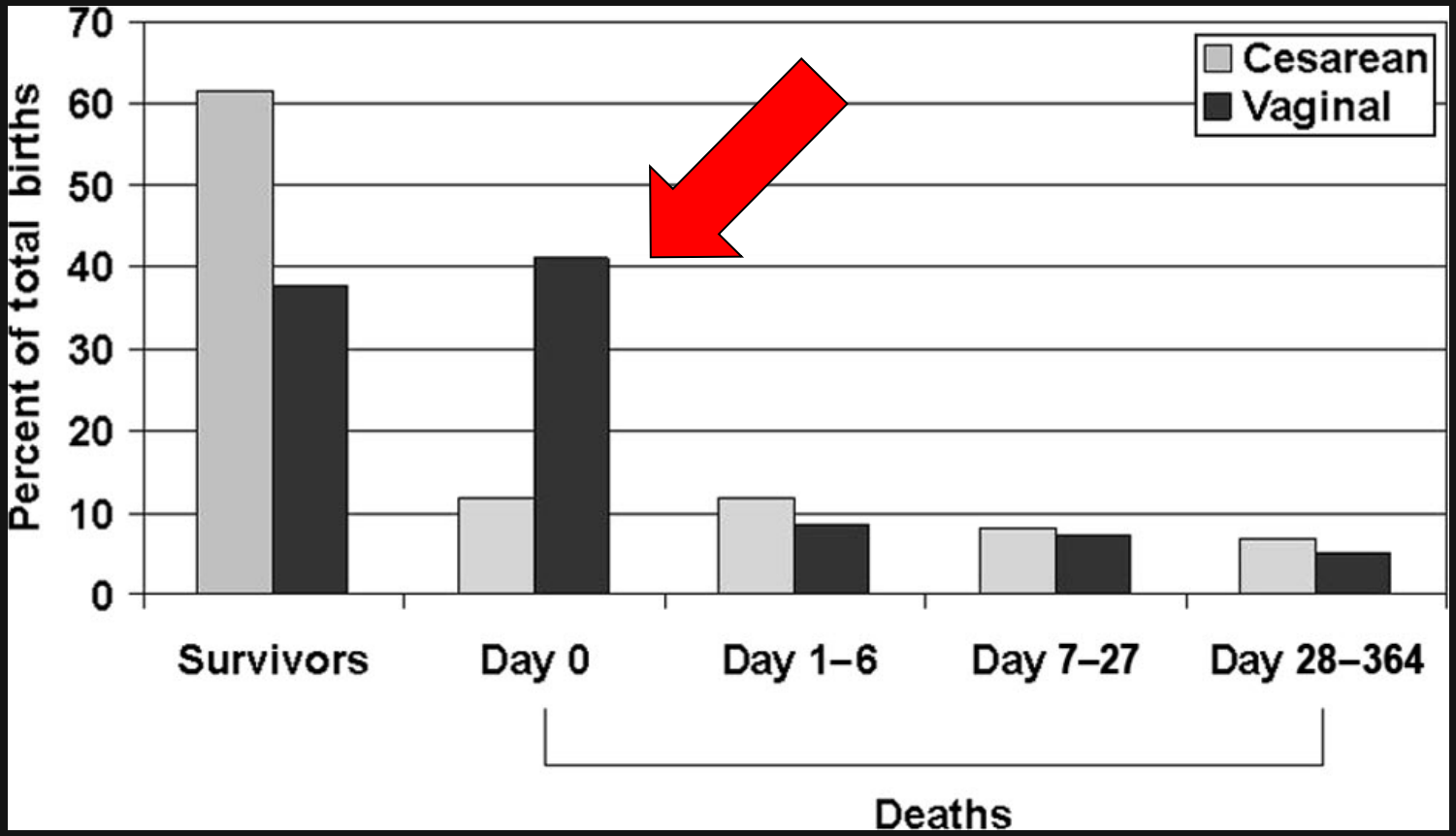
TC → ↑ sopravvivenza

26-31 wks mortalità TC/parto vaginale sovrapponibile

Malloy M. *Clin Perinatol* 35 (2008) 421–435

Mortalità neonatale

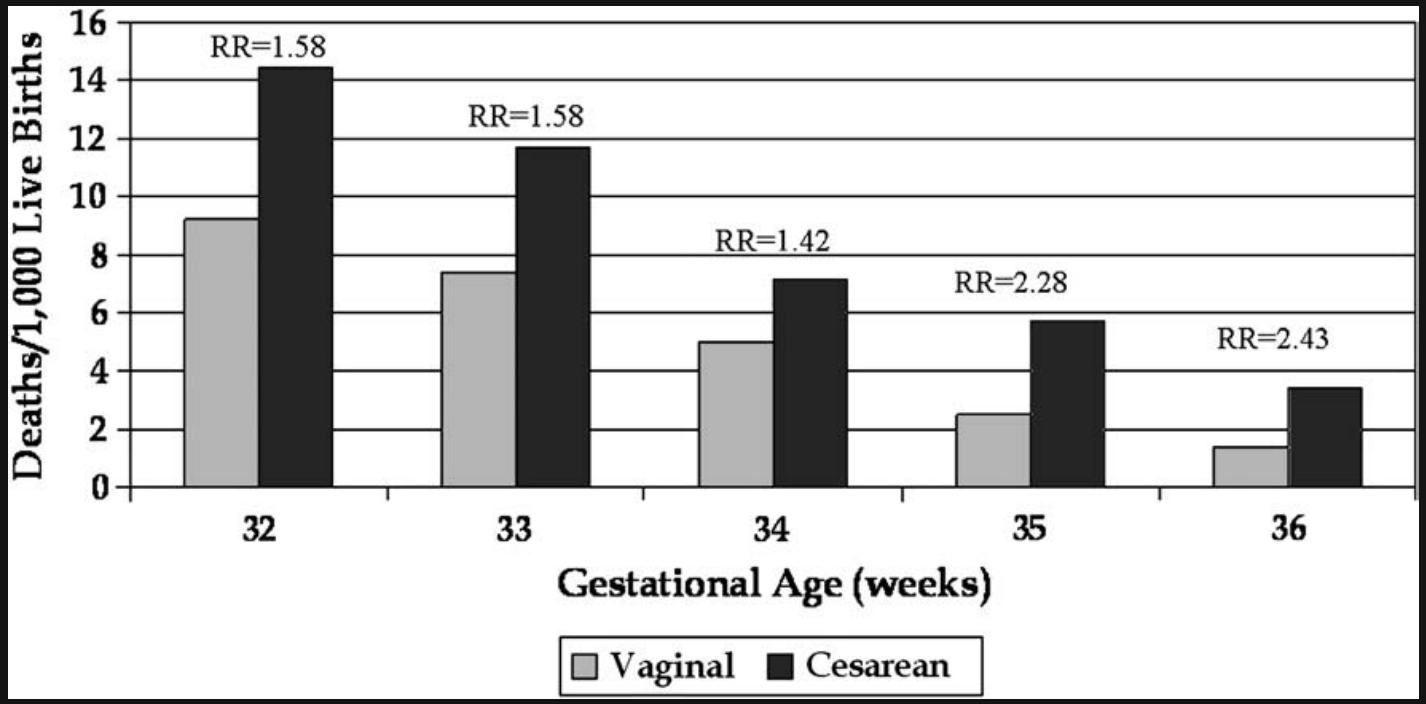
22-25 wks



Malloy M. *Pediatrics 2008;122;285-292*

Mortalità neonatale 32-36 wks

Taglio cesareo vs Parto vaginale



RR TC/Parto vaginale

32 wks → 1,58

36 wks → 2,43

Malloy M. *BIRTH* 2009;36:1

Mortalità neonatale

Fattori confondenti presenti nel 90% dei pretermine :

- SGA
- Presentazione podalica
- Anomalie congenite
- Gravidanza multipla
- Complicanze associate al travaglio

Presentazione podalica

Term Breech Trial

Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial

*Mary E Hannah, Walter J Hannah, Sheila A Hewson, Ellen D Hodnett, Saroj Saigal, Andrew R Willan, for the Term Breech Trial Collaborative Group**

TC nel podalico a termine

Tale accordo non è stato raggiunto nei confronti del pretermine **specialmente se < 26 settimane**

??Quesiti??

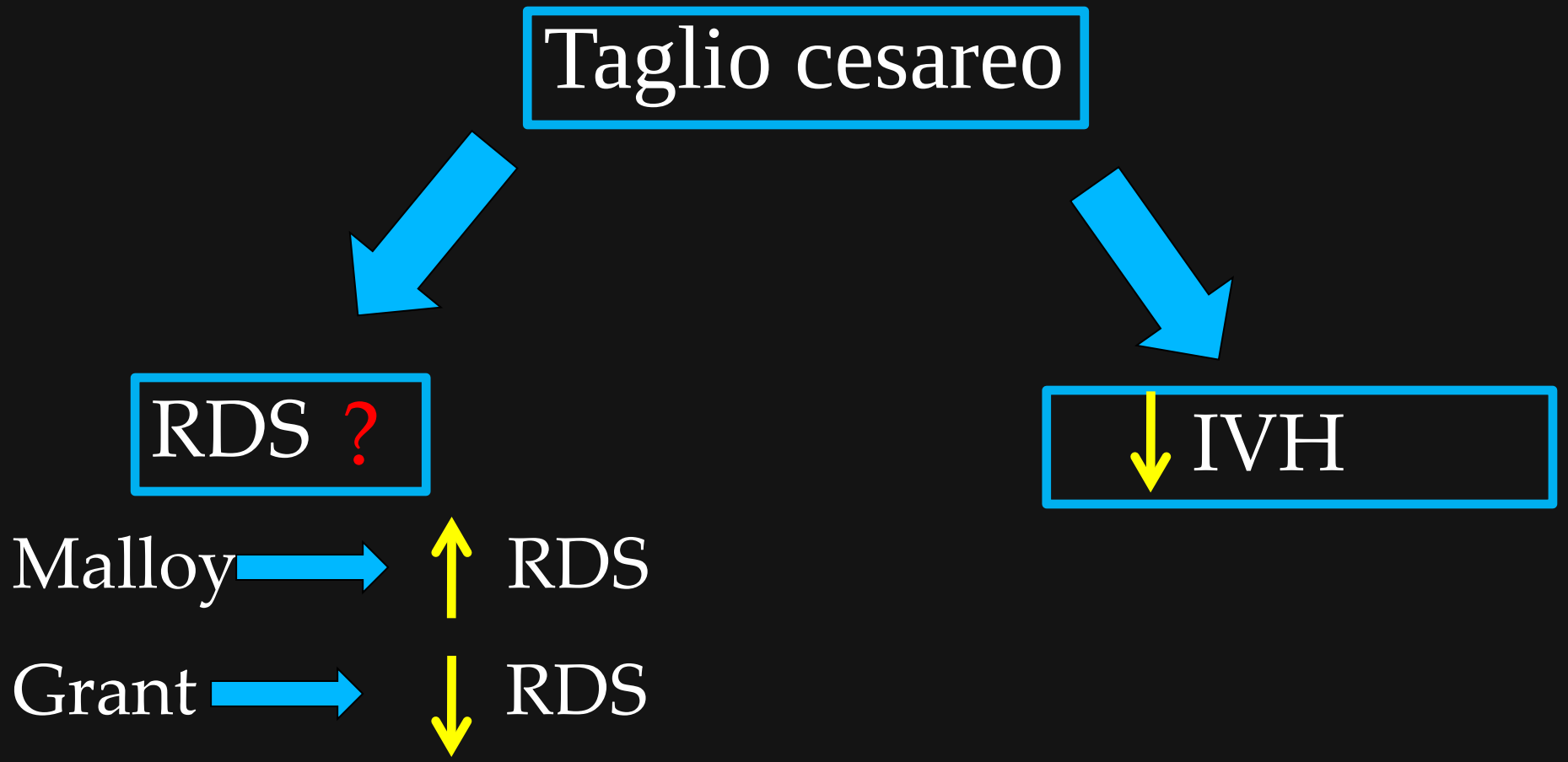
La modalità del parto può modificare:

Mortalità neonatale

Morbilità neonatale ?

Morbilità materna

Esiti a breve termine



Malloy M. *Clin Perinatol* 35 (2008) 421–435

Grant *A.* *Cochrane Database Syst Rev. 2009;*(2):CD000078. Review.

??Quesiti??

La modalità del parto può modificare:

Mortalità neonatale

Morbilità neonatale

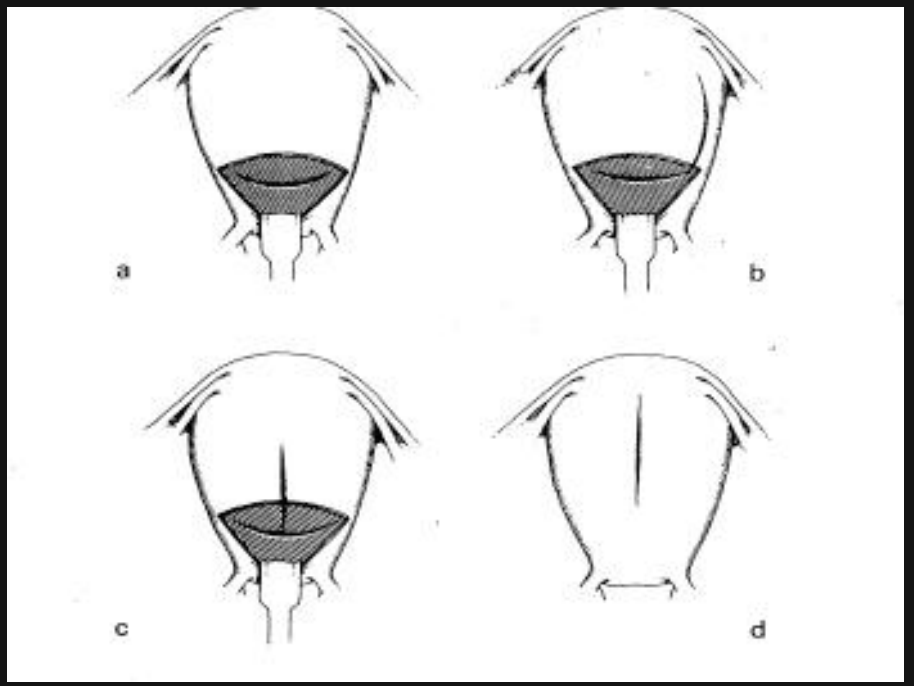
Morbilità materna ?

TC pretermine

Formazione SUI > 30 settimane.

Necessità di incisioni differenti da quella abituale:

- Longitudinale classica
- Bassa sull' istmo
- Trasversa sul corpo
- A "T invertita" o a "J"



Dodd JM .Cochrane Database of Systematic Reviews 2004

Management ostetrico

In assenza di linee guida che possano indirizzare il medico verso la "condotta perfetta"

Cosa Fare?

- Completo ed esaustivo counseling con la coppia
- Condivisione della condotta piu' consona per la situazione specifica
- Consenso informato

Counseling

Tener conto di:

- Fragilità e possibili complicanze nel pretermine
- Epoca gestazionali con relativi tassi di sopravvivenza
- Eziologia parto pre-termine
- Morbilità materna relativa alla modalità del parto
- Presentazione del feto
- Reperto cervicale al momento del travaglio

Conclusioni

Assenza linee guida

Auspicabile nuovi studi randomizzati

Prematurità non è indicazione TC

↓Mortalità neonatale dopo TC in caso di:

- Epoca gestazionale < 25 settimane
- SGA
- Presentazione podalica