Preterm birth

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General introduction and outline of this thesis

GENERAL INTRODUCTION

Preterm birth, defined by the World Health Organization as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of the last menstrual period, is one of the main problems in perinatal medicine.[1] The incidence of preterm birth is between 5 and 10% in European countries and is 11.4% in the United States.[2-5] Worldwide, in 2010, an estimated 14.9 million babies were born preterm.[5]
Preterm birth and its complications like respiratory immaturity, intracranial hemorrhages, and infections are responsible for the majority of neonatal deaths in otherwise healthy infants, accounting for one million deaths each year.[6] In addition to its significant contribution to mortality, the effects of preterm birth amongst survivors may continue throughout life, leading to impaired neuro-developmental functioning, learning impairment, visual disorders and long-term physical ill health.[6,7] The economic costs of preterm birth, both short term and long term, are considerable in terms of neonatal intensive care, ongoing long-term complex health needs, as well as lost economic productivity.[8]

Preterm birth can be classified into two broad subtypes: spontaneous preterm birth and iatrogenic preterm birth. Spontaneous preterm birth occurs after spontaneous onset of labor or following prelabor premature rupture of membranes (PPROM). In high-income countries the majority of preterm birth (60-65%) occurs spontaneously.[9] Premature rupture of membranes occurs in 2 to 3.5% of all pregnancies, but accounts for 30% to 40% of preterm deliveries and is therefore a leading clinically identifiable cause of preterm birth. [10,11]
Iatrogenic preterm birth, also known as provider initiated or indicated preterm birth, is defined as induction of labor or elective caesarean birth before 37 completed weeks of gestation for maternal or fetal indications like hypertensive disorder or fetal growth restriction.

The complete pathogenesis of preterm birth has not fully been resolved, but several risk factors have been identified.[12] These risk factors can be divided in fetal and maternal risk factors. Fetal factors include male gender of the fetus and multiple gestation. Maternal factors include young or advanced maternal age, low socio-economic-status (SES) short or long inter-pregnancy intervals, low maternal body mass index, non-White ethnicity, smoking, multiple gestation, uterine abnormalities, and a history of preterm birth. Nevertheless, a large proportion of spontaneous preterm birth occurs in women without any of these risk factors.

Some gynaecological interventions also increase the risk of preterm birth, i.e. cervical surgery or assisted reproductive technology.
Invasive treatment for cervical intraepithelial neoplasia (CIN), like a large loop excision of the transformation zone (LLETZ) is associated with an increased risk of preterm birth and subsequent poor pregnancy outcome.[13-15] More extensive forms of invasive treatment (e.g. knife cones) are even more strongly associated with preterm birth.[13] Deeper excisions significantly increase the risk of preterm birth compared with less deep excisions, and the magnitude of the effect is increased in deeper cones. A similar pattern is seen for cone volumes.[13, 16,17] This increased risk of preterm birth is not limited to the first birth after treatment.[18]
In screening programs, women with abnormal cervical smears are referred for subsequent colposcopy and possibly biopsy. If high-grade lesions (CIN II+ lesions) are diagnosed, large loop excision of the transformation zone (LLETZ) is indicated according to guidelines.[19-21] As a substantial percentage of high-grade CIN lesions show spontaneous regression, i.e. up to 40%, LLETZ may both lead to overtreatment as well as unnecessary complications, like preterm birth. Since CIN II has a higher spontaneous regression rate than CIN III, the risk on overtreatment is most profound for CIN II lesions.[22]

Assisted reproduction has been associated with a 20-fold rate of multiple pregnancies compared with spontaneous twin pregnancies.[23] This was originally due to multiple embryo transfer, but when pregnancy rates after assisted reproductive technology increased, single embryo transfer (SET) was introduced to diminish the risk of multiple pregnancies.[24,25] Worldwide in 2010, in fresh non-donor IVF and ICSI cycles, the global rate of single embryo transfer (SET) increased to 30%, but still in 49% double embryo transfer took place. [26] Thus, although some countries have mitigated the risk of multiple births by single embryo transfer, multiple transfer is still common in many parts of the world, including the United States and Asia, where multiple birth rates are 20% to 30%.[27] In 2014 in Europe the multiple pregnancy rate after ART was 17.0%, varying from 4.2% in Sweden and the Netherlands and 29.3% in Serbia. [28] These multiple pregnancies after ART are associated with maternal and perinatal complications such as preterm birth.[29,30] But even SET will never completely eradicate preterm birth after IVF, since also singletons conceived after IVF have an increased risk of preterm birth.[31-34]

BACKGROUND OF THE THESIS

Although several risk factors for preterm birth have been identified, better understanding of the complex etiologies of preterm birth would increase our ability to select women at risk of preterm birth and –possibly- to prevent preterm birth. In this thesis we focus on risk factors of -recurrent- preterm birth (part I) and preterm birth after gynaecological interventions including invasive treatment for cervical intraepithelial neoplasia and assisted reproductive technology (part II).

Recurrence and risks

The highest risk for recurrent preterm birth is a history of preterm birth. Our understanding of recurrent preterm birth risk has mainly focused on the risk of recurrent preterm birth in the next pregnancy, divided in spontaneous and iatrogenic preterm birth. How spontaneous and iatrogenic preterm birth interact and how prior preterm birth subtype modifies the risk of recurrent preterm birth in more than two consecutive pregnancies is not fully understood. Therefore, we studied the spontaneous and iatrogenic preterm birth rates in unselected women with three subsequent singleton pregnancies both on a population level and on an individual level in relation to the gestational age at delivery and type of preterm birth in previous pregnancies. Also, we analysed the impact of the outcome of the first and second pregnancy on the risk of (recurrent) preterm birth in the third pregnancy.

Another risk factor for preterm birth is either a short or a long interval between pregnancies. Both are associated with adverse perinatal outcomes, including preterm birth, low birth weight and small for gestational age.[36-38] This suggests that there would be an optimal interval between pregnancies and that spacing pregnancies appropriately could help to prevent the adverse perinatal outcomes associated with preterm birth. The World Health Organization recommends a minimum interpregnancy interval of 2 years based on the available information and evidence.[39]

Whether this association is confounded by other risk factors, including various aspects of socioeconomic status, ethnicity, demographics, and lifestyle, is unclear.[37] Several authors even propose that the relation between interpregnancy interval and perinatal outcome is entirely due to these confounders.[40-41]

If there is an independent association between both a short and a long interpregnancy interval and adverse neonatal outcome, this knowledge could be used to counsel women about birth spacing, particularly in those women with a previous preterm birth. In this thesis we therefore examined the association

more in depth and tried to rule out any unknown confounders in between mother-comparison by both conventional and conditional logistic regression analyses in a cohort of women who have had three births. We used a matched model to analyse the impact of the interpregnancy interval, in which each mother was used as her own control for risk factors, to adjust completely for persistent maternal factors.

How fetal and maternal risk factors interact or whether they are all part of the same mechanism is not fully understood. It is known that fetal gender is a factor impacting the likelihood of spontaneous preterm birth, with male fetal gender being associated with an relative risk of 1.1-1.3.[42] This could suggest that women who deliver a preterm female fetus, who is less likely to be born preterm than a male fetus, are themselves more likely to have an underlying maternal factor contributing to the preterm birth than women who deliver prematurely a male fetus at the same gestational age. This would point at separate impact of maternal and fetal factors on preterm birth. Since this maternal factor will remain present in the second pregnancy, women who delivered a female fetus preterm, would have a higher risk of recurrent preterm birth in the second pregnancy. In this thesis we tested this hypothesis by studying the effect of fetal gender in the first pregnancy on the risk of recurrent spontaneous preterm birth in the subsequent pregnancy.

Gynaecological interventions

The interventions we studied were screening and treatment for cervical intraepithelial neoplasia and IVF.

Screening and treatment of cervical intraepithelial neoplasia

Cervical cancer screening programs aim to detect precancerous changes in the cervix that can be treated before they develop into invasive disease. Early detection and treatment of cervical intraepithelial neoplasia (CIN) have considerably reduced the incidence of cervical cancer and lowered the mortality of the disease. [43,44] Around the world, screening programs vary widely with respect to start age and screening interval.[45] In Australia routine screening with Pap smears every 2 years for women between the ages of 18 and 69 years is recommended.[46] In the United Kingdom screening starts at age 25 with a 3-year interval, and changes to a 5-year interval at age 50.[47] In the Netherlands, women are invited for cytological screening from age 30 with a 5-year interval.[48] The American College of Obstetricians and Gynaecologists (ACOG) advises to start cervical cytology screening at age 21 years with 3-year intervals, while women aged 30–65 years should preferably have a

Pap test and an HPV test every 5 years, although it is acceptable to have a Pap test alone every 3 years.[49]
Since many preinvasive lesions would regress naturally without ever resulting in cancer, i.e. up to 40% of natural regression of CIN II lesions has been described, treatment of CIN is often unnecessary.[50,51] As it is not (yet) possible to differentiate between CIN lesions that will regress naturally and those that will progress to cancer, most CIN II+ lesions are treated. Thus, the diagnosing of precancerous lesions and subsequent treatment has resulted in unintended adverse effects due to preterm birth in women who became pregnant after treatment.
Previous studies comparing the cost-effectiveness of cervical screening programs, have not taken these unintended adverse effects into account. In this thesis we assessed the impact of various cytology-based screening programs on the risk of additional preterm birth and subsequent neonatal morbidity and mortality, relative to the maternal the life years gained due to prevented cervical cancer and the costs of both screening and preterm birth.

Although cervical surgery is associated with preterm birth, recent studies question whether this is related to the surgery itself or due to the cervical intraepithelial neoplasia or maybe even to an underlying communal disorder resulting both in cervical intraepithelial neoplasia and preterm birth, thus potentially confounding the association between cervical surgery and preterm birth. To address this issue, we conducted a systematic review and meta-analysis, in which we compared pregnancy outcomes between women with CIN who have been treated before pregnancy, treated during pregnancy, or not treated as well as women without CIN.

IVF

Multiple pregnancy after IVF increases the risk of preterm birth, but even singleton pregnancies after IVF have an increased risk of preterm birth. Due to increased success rates over the years, the number of embryos transferred could be reduced to one embryo and subsequent transfer of a single frozen embryo resulting in comparable pregnancy rates, for much lower multiples pregnancy rates.[52-55]
The individual risk profile for spontaneous preterm birth of women entering an IVF program has never been taken into account. This might be a missed opportunity since the individual risk of a woman for preterm birth differs based on both female characteristics and obstetric history.[56-58] Such information, rather than the risk of multiple pregnancy alone, could possibly be used in the decision to apply SET or DET. In this thesis we assessed whether the incorporation of an

individual risk profile for preterm birth could affect the decision for SET or DET in an IVF program.

Since the birth of Louise Brown, the first baby by IVF in 1978, the technique has earned its reputation as a major medical breakthrough of the 20th century. Soon the 10th million baby will be born after IVF. Although IVF has allowed many infertile couples to have a family, nowadays IVF is also offered in couples with mild male subfertility, endometriosis, and unexplained subfertility. Since IVF is associated with an increased risk of preterm birth, can the risks of IVF be justified for these more liberal applications? In this thesis we give an overview of the existing evidence underpinning the use of IVF for different types of infertility and the change in indications over the years and the adverse pregnancy and health outcomes in IVF children.

OUTLINE OF THIS THESIS

Part I: Idiopathic spontaneous (recurrent) preterm birth

Chapter 2 presents a nationwide retrospective cohort study of 52,978 women in which we compared the incidence of spontaneous and iatrogenic preterm birth in three sequential singleton pregnancies and the impact of the outcome of the first and second pregnancy on the (recurrent) preterm birth risk in the third pregnancy.

Chapter 3 presents a nationwide retrospective cohort study of 2,361 women with three sequential singleton pregnancies with a spontaneous preterm birth <37 weeks in the first pregnancy. We evaluated the impact of interpregnancy interval on the recurrent preterm birth risk in the second and third pregnancy.

Chapter 4 presents a nationwide retrospective cohort study with 15,351 women with two sequential singleton pregnancies with a spontaneous preterm birth <37 weeks in the first pregnancy. We assessed the association between fetal gender in the first pregnancy and the risk of recurrent spontaneous preterm birth.

Part II: Spontaneous preterm birth after routine interventions

Chapter 5 presents a decision and cost-effectiveness analysis to compare the impact of eight different screening programs for cervical cancer on the risk of

preterm birth and subsequent neonatal outcome relative to maternal live years gained and costs of both screening and preterm birth.

Chapter 6 presents a systematic review and meta-analysis of 20 studies with a total of 12,159,293 women. We assessed the risk of preterm birth of treated versus untreated cervical intraepithelial neoplasia (CIN).

Chapter 7 presents a decision analysis to assess the impact of the individual preterm birth risk on the ongoing pregnancy rates, multiplicity and neonatal outcome after single and double embryo transfer according to the Hunault model.

Chapter 8 presents an opinion paper in which we discuss how the indications for IVF have expanded, what the evidence is that underpins its extended remit and how the balance is between risks and benefits for certain indications.

REFERENCES

1. WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstet Gynecol Scand*. 1977;56(3):247-53.
2. Zeitlin J, Szamotulska K, et al; Euro-Peristat Preterm Study Group. Preterm birth time trends in Europe: a study of 19 countries. *BJOG* 2013 Oct;120(11):1356-1365.
3. Chang HH, Larson J, et al; Born Too Soon preterm prevention analysis group. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013; Jan 19;381(9862):223-234.
4. National Vital Statistics System, US Department of Health and Human Services, Centers for Disease, Control and Prevention, National Center for Health Statistics. http://205.207.175.93/Vitalstats/ExtractViewer/extractView.aspx?ReportId=70836 . Accessed July 6, 2015.
5. Blencowe H, Cousens S, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet*. 2012 Jun 9;379(9832):2162–2172.
6. Blencowe H, Cousens S, et al. Born Too Soon Preterm Birth Action Group. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health*. 2013;10 Suppl 1:S2.
7. Liu L, Johnson HL, et al. Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet*. 2012 Jun 9;379(9832):2151-61.
8. Petrou S, Eddama O, Mangham L. A structured review of the recent literature on the economic consequences of preterm birth. *Arch Dis Child Fetal Neonatal* Ed. 2011 May;96(3):F225-32.
9. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008 Jan 5;371(9606):75-84.
10. Mazaki-Tovi S, Romero R, et al. Recurrent preterm birth. *Semin Perinatol*. 2007 Jun;31(3):142-58.
11. van Os M, van der Ven J, et al. Individualizing the risk for preterm birth: an overview of the literature. *Expert Rev. Obstet. Gynecol.* 8(5), 435–442 (2013).
12. Romero R, Espinoza J, et al. The preterm parturition syndrome. *BJOG*. 2006 Dec;113 Suppl 3:17-42.
13. Kyrgiou M, Koliopoulos G, Martin-Hirsch P, Arbyn M, Prendiville W, Paraskevaidis E. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. *Lancet* 2006 Feb 11;367(9509):489–98.
14. M. Arbyn, M. Kyrgiou, et al. Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis. *BMJ*, 2008 Sep 18;337:a1284.

15. S.N. Conner, H.A. Frey, A.G. Cahill, G.A. Macones, G.A. Colditz, M.G. Tuuli Loop electrosurgical excision procedure and risk of preterm birth: a systematic review and meta-analysis. *Obstet Gynecol*, 2014 Apr;123(4):752-61.

16. Castanon A, Landy R, Brocklehurst P, Evans H, Peebles D, Singh N, et al. Risk of preterm delivery with increasing depth of excision for cervical intraepithelial neoplasia in England: nested case-control study. *BMJ* 2014 Nov 5;349:g6223.

17. Kyrgiou M, Athanasiou A, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ*. 2016 Jul 28;354:i3633.

18. Castanon A, Landy R, et al. Is the increased risk of preterm birth following excision for cervical intraepithelial neoplasia restricted to the first birth post treatment? *BJOG* 2015 Aug;122(9):1191–9.

19. Australian Gynaecological Cancer Foundation. Cervical Intraepithelial Neoplasia. http://www.agcf.org.au/about-gynae-cancer/cervical-cancer/cervical-intraepithelial-neoplasia-cin. Accessed December 29th, 2016.

20. National Health Service UK. Cervical screening – treatment for CIN http://www.nhs.uk/ipgmedia/National/Macmillan%20Cancer%20Support/assets/Cervicalscreening-treatmentofCINMCS8pages.pdf. Accessed December 29th, 2016.

21. Uptodate: Cervical intraepithelial neoplasia: Management of low-grade and high-grade lesions. https://cdpnlidzsrmbxfxrb7u-03di.sec.amc.nl/contents/cervical-intraepithelial-neoplasia-management-of-low-grade-and-high-grade-lesions?source=search_result&search=treatment%20CIN&selectedTitle=1~108. Accessed December 29th, 2016.

22. Holowaty P, Miller AB, Rohan T, To T. Natural history of dysplasia of the uterine cervix. J *Natl Cancer Inst* 1999 Feb 3;91(3):252-8.

23. Kresowik JD, Stegmann BJ, Sparks AE, Ryan GL, van Voorhis BJ. Five-years of a mandatory single-embryo transfer (mSET) policy dramatically reduces twinning rate without lowering pregnancy rates. *Fertil Steril* 2011 Dec;96(6):1367-9.

24. Tiitinen A, Unkila-Kallio L, Halttunen M, Hyden-Granskog C. Impact of elective single embryo transfer on the twin pregnancy rate. *Hum Reprod* 2003 Jul;18(7):1449–53.

25. Gerris J, De Neubourg D, Mangelschots K, Van Royen E, Van de Meerssche M, Valkenburg M. Prevention of twin pregnancy after in-vitro fertilization or intracytoplasmic sperm injection based on strict embryo criteria: a prospective randomized clinical trial. *Hum Reprod* 1999 Oct;14(10):2581–7.

26. Bergh C. Single embryo transfer: a mini-review. *Hum Reprod* 2005 Feb;20(2):323-7.

27. Helmerhorst FM, Perquin DAM, Donker D, Keirse MJNC. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ* 2004 Jan 31;328(7434):261.

28. The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE) ART in Europe, 2014: results generated from European registries by ESHRE, *Human Reprod* 2018 Sep 1;33(9):1586-1601.

29. Fauser BC, Devroey P, Macklon NS: Multiple birth resulting from ovarian stimulation for subfertility treatment. *Lancet* 2005 May 21-27;365(9473):1807-16.

30. Templeton A. Elective single versus double embryo transfer. *BMJ* 2010 Dec 21;341:c7083.

31. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. *Hum Reprod Update* 2012; Sept-Oct 18(5):485-503.

32. Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. *Obstet Gynecol* 2004 Mar;103(3):551-63.

33. Barnhart KT. Assisted reproductive technologies and perinatal morbidity: interrogating the association. *Fertil Steril* 2013 Feb;99(2):299-302.

34. Pinborg A, Wennerholm UB, et al. Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. *Hum ReprodUpdate* 2013 Mar-Apr;19(2):87-104.

35. Scherrer U, Rimoldi SF, et al. Systemic and pulmonary vascular dysfunction in children conceived by assisted reproductive technologies. *Circulation* 2012 April 17;125(15):1890-6.

36. Zhu BP, Rolfs RT, Nangle BE, Horan JM. Effect of the interval between pregnancies on perinatal outcomes. *N Engl J Med* 1999 Feb 25;340(8):589-594.

37. Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. *JAMA* 2006 Apr 19;295(15):1809-1823.

38. Smith GC, Pell JP, Dobbie R. Interpregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study. *BMJ* 2003 Aug 9;327(7410):313.

39. World Health Organization. Report of a WHO Technical Consultation on Birth Spacing. World Health Organization; 2005: 1-34.

40. Klebanoff MA. The interval between pregnancies and the outcome of subsequent births. *N Engl J Med* 1999 Feb 25;340(8):643-4.

41. Ball SJ, Pereira G, Jacoby P, de Klerk N, Stanley FJ. Re-evaluation of link between interpregnancy interval and adverse birth outcomes: retrospective cohort study matching two intervals per mother. *BMJ* 2014 Jul 23;349:g4333.

42. Zeitlin J, Saurel-Cubizolles MJ, et al. Fetal sex and preterm birth: are males at greater risk? *Hum Reprod*. 2002 Oct;17(10):2762–8.

43. Habbema D, De Kok IM, Brown ML. Cervical cancer screening in the United States and the Netherlands: a tale of two countries. Milbank Q. 2012 Mar;90(1): 5-37.

44. Edwards BK, Noone AM, et al., Annual Report to the Nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer*. 2014 May 1; 120(9):1290-314.

45. Anttila A, von Karsa L, et al., Cervical cancer screening policies and coverage in Europe. *Eur J Cancer.* 2009 Oct; 45(15):2649-58.

46. Australian Goverment Department of Health. National Cervical Screening Program. http://www.cancerscreening.gov.au/internet/ screening/publishing.nsf/Content/cervical-about. Accessed July 10, 2014.

47. National Health Service Cervical Screening Program. About cervical cancer screening. Sheffield, UK: National Health Service; 2011. www.cancerscreening.nhs.uk/cervical/about-cervical-screening.html. Accessed May 11, 2014.

48. Van Ballegooijen M, Hermens R. Cervical cancer screening in The Netherlands. *Eur J Cancer.* 2000 Nov;36(17):2244-6.

49. American Congress of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 109: Cervical cytology screening. *Obstet. Gynecol.*, 2009 Dec;114(6):1409-20.

50. Vesco KK, Whitlock EP, Eder M, Burda BU, Senger CA, Lutz K. Risk factors and other epidemiologic considerations for cervical cancer screening: a narrative review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2011 Nov 15;155(10):698-705, W216.

51. Castle PE, Schiffman M, Wheeler CM, Solomon D. Evidence for frequent regression of cervical intraepithelial neoplasia-grade 2. *Obstet Gynecol.* 2009 Jan;113(1):18-25.

52. McLernon DJ, Harrild K, et al. Clinical effectiveness of elective single versus double embryo transfer: meta-analysis of individual patient data from randomised trials. *BMJ* 2010 Dec 21;341:c6945.

53. Thurin A, Hausken J, et al. Elective single-embryo transfer versus double-embryo transfer in in vitro fertilization. *N Engl J Med* 2004 Dec 2;351(23):2392–402.

54. Pandian Z, Bhattacharya S, Ozturk O, Serour G, Templeton A. Number of embryos for transfer following in-vitro fertilisation or intra-cytoplasmic sperm injection. *Cochrane Database Syst Rev* 2009 Apr 15;(2):CD003416.

55. Dyer S, Chambers GM, et al. International Committee for Monitoring Assisted Reproductive Technologies world report: Assisted Reproductive Technology 2008, 2009 and 2010. *Hum Reprod.* 2016 Jul;31(7):1588-609.

56. Cnossen JS, Vollebregt KC, et al. Accuracy of mean arterial pressure and blood pressure measurements in predicting PE: systematic review and meta-analysis. *BMJ* 2008 May 17;336(7653):1117–20.

57. Mehta-Lee S, Palma A, Bernstein P, Lounsbury D, Schlect N. A preconception nomogram to predict PTB. *Am J Obstet Gynecol* 2013;208:S107–8.

58. Kazemier B, Buijs P, Mignini L, Limpens J, de Groot C, Mol B. Impact of obstetric history on the risk of spontaneous preterm birth in singleton and multiple pregnancies: a systematic review. *BJOG* 2014 Sep;121(10):1197–208.