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Prevention and Therapy of Preterm Birth. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry Number 015/025, February 2019) - Part 2 with Recommendations on the Tertiary Prevention of Preterm Birth and the Management of Preterm Premature Rupture of Membranes

Prevention and therapy of premature birth. Guideline of the DGGG, OEGGG and SGGG (S2k level, AWMF register number 015/025, February 2019) - Part 2 with recommendations on tertiary prevention of premature birth and management of early premature rupture of the bladder

Richard Berger , Harald Abele , Franz Bahlmann , Ivonne Bedei , Klaus Doubek , Ursula Felderhoff-Müser , Herbert Fluhr , Yves Garnier , Susanne Grylka-Baeschlin , Hanns Helmer , Egbert Herting , Markus Hoopmann , Irene Hösli , Udo Hoyme , Alexandra Jendreizeck , Harald Krentel , Ruben Kuon , Wolf Luetje , Silke Mader , Holger Maul , Werner Mendling , Barbara Mitschdörfer , Tatjana Nicin , Monika Nothacker , Dirk Olbertz , Werner Rath , Claudia Roll , Dietmar Schlembach , Ekkehard Schleussner , Florian Schütz , Vanadin Seifert-Klauss , Susanne Steppat ,and Daniel Surbek

[1] Women's Clinic, Marienhaus Klinikum Neuwied, Neuwied, Germany
[2] Women's Clinic, University Hospital Tübingen, Tübingen, Germany
[3] Women's Clinic, Bürgerhospital Frankfurt, Frankfurt am Main, Germany
[4] Women's Clinic, Frankfurt Höchst Clinic, Frankfurt am Main, Germany
[5] gynecological practice, Wiesbaden, Germany
[6] Clinic for Pediatrics I / Perinatal Center, University Hospital Essen, University of Duisburg-Essen, Essen, Germany
[7] Women's Clinic, Heidelberg University Hospital, Heidelberg, Germany
[8] Women's Clinic, Osnabrück Clinic, Osnabrück, Germany
[9] Zurich University of Applied Sciences, Institute for Midwives, Zurich, Switzerland
[10] University Clinic for Gynecology, Medical University of Vienna, Vienna, Austria
[11] Clinic for Pediatric and Adolescent Medicine, University Medical Center Schleswig-Holstein, Lübeck Campus, Lübeck, Germany
[12] Women's Clinic, University Hospital Basel, Basel, Switzerland
[13] Women's Clinic, Ilm-Kreis-Kliniken, Arnstadt, Germany
[14] Federal Association for Premature Children, Germany
[15] Women's Clinic, Annahospital Herne, Elisabeth Group Catholic Clinics Rhein Ruhr, Herne, Germany
[16] Gynecological Clinic, Heidelberg University Hospital, Heidelberg, Germany
[17] Women's Clinic, Evangelical Amalie Sieveking Hospital Hamburg, Hamburg, Germany
[18] European Foundation for the Care of the Newborn Infants
[19] Women's Clinic, Asklepios Kliniken Hamburg, Hamburg, Germany
[20] German Center for Infections in Gynecology and Obstetrics at the Women's Clinic, Helios University Hospital Wuppertal, Wuppertal, Germany
[21] Women's Clinic, Hanau Clinic, Hanau, Germany
[22] Working Group of Scientific Medical Societies, Berlin, Germany
[23] Department of Neonatology and Neonatal Intensive Care Medicine, Klinikum Südstadt Rostock, Rostock, Germany
[24] Emeritus, Aachen University Hospital, Aachen, Germany
[25] Vestische Kinder- und Jugendklinik Datteln, University of Witten / Herdecke, Datteln, Germany
[26] Clinic for Obstetrics, Klinikum Neukölln / Berlin Vivantes Network for Health, Berlin, Germany
[27] Department of Obstetrics, Jena University Hospital, Jena, Germany
[28] Frauenklinik, Universitätsklinikum rechts der Isar Munich, Munich, Germany
[29] German Midwives Association, Germany

[30] University Women's Clinic, Inselspital, University of Bern, Bern, Switzerland

Correspondence / Correspondence address Prof. Dr. med. Richard Berger Marienhaus St. Elisabeth Clinic, Academic Teaching Hospital of the Universities of Mainz and Maastricht, Clinic for Gynecology and Obstetrics, Friedrich-Ebert-Strasse 59, 56564 NeuwiedGermany, richard.berger@marienhaus.de

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Abstract

Aims This is an official guideline of the German Society for Gynecology and Obstetrics (DGGG), the Austrian Society for Gynecology and Obstetrics (ÖGGG) and the Swiss Society for Gynecology and Obstetrics (SGGG). The aim of this guideline is to improve the prediction, prevention and management of preterm birth based on evidence obtained from recently published scientific literature, the experience of the members of the guideline commission and the views of self-help groups.

Methods The members of the participating medical societies and organizations developed Recommendations and Statements based on the international literature. The Recommendations and Statements were adopted following a formal consensus process (structured consensus conference with neutral moderation, voting done in writing using the Delphi method to achieve consensus).

Recommendations Part 2 of this short version of the guideline presents Statements and Recommendations on the tertiary prevention of preterm birth and the management of preterm premature rupture of membranes.

Key words: preterm birth, preterm labor, cervical insufficiency, preterm premature rupture of membranes

I Guideline Information

Guidelines program

For information on the guidelines program, please refer to the end of the guideline.

Citation format

Prevention and Therapy of Preterm Birth. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry Number 015/025, February 2019) - Part 2 with Recommendations on the Tertiary Prevention of Preterm Birth and the Management of Preterm Premature Rupture of Membranes. Obstetric Frauenheilk 2019; 79: 813-833

Guideline documents

The complete long version, a slide version of this guideline, a list of the conflicts of interest of all authors, and a guideline report on the methodological approach used, including the management of conflicts of interest, are available in German on the homepage of the AWMF: http://www.awmf.org/leitlinien/detail/ll/015-025.html

Guideline authors (Table 1)

Abbreviations

AFP alpha-fetoprotein
AUC area under the curve
CI confidence interval
COX cyclooxygenase
CPAP continuous positive airway pressure
CRP C-reactive protein
CTG cardiotocography
fFN fetal fibronectin
FIRS fetal inflammatory response syndrome
GBS group B streptococcus
GW week of gestation
IGFBP-1 insulin-like growth factor-binding protein-1

IL-6 interleukin-6
NEC necrotizing enterocolitis
NICU neonatal intensive care unit
NNH number needed to harm
NNT number needed to treat
OR odds ratio
17-OHPC 17α-hydroxyprogesterone caproate
PAMG-1 placental alpha microgobulin-1
phIGFBP-1 phosphorylated insulin-like growth factor-binding protein-1
PIVH periventricular / intraventricular hemorrhage
PPROM preterm premature rupture of membranes
PVL periventricular leukomalacia
RDS respiratory distress syndrome
RR relative risk
s / p status post
TCO total cervical occlusion
TNF-α tumor necrosis factor alpha
Triple I. intrauterine inflammation or infection or both

II Guideline Application

Purpose and objectives

This guideline aims to improve both the outpatient and the inpatient care of patients at imminent risk of preterm birth in order to reduce the rate of preterm births. If preterm birth cannot be prevented, the aim is to reduce perinatal and neonatal morbidity and mortality. This should lead to improvements in the psychomotor and cognitive development of children born preterm.

Targeted areas of patient care

Outpatient and / or inpatient care

Target user groups / target audience

The recommendations of this guideline are aimed at gynecologists in private practice, gynecologists in hospitals, pediatricians in hospitals, midwives in private practice and midwives in hospitals. Other target user groups include advocacy groups for affected women and children, nursing staff (obstetrics / postnatal care, pediatric intensive care), medical and scientific societies and professional associations, institutions for quality assurance (eg IQTIG), healthcare policy institutions and decision-makers at the federal and state level, funding agencies and payers.

Adoption and period of validity

The validity of this guideline was confirmed by the executive boards of the participating medical societies, working groups, organizations and associations as well as by the executive boards of the DGGG, the SGGG and the OEGGG and the DGGG / OEGGG / SGGG guidelines commission in February 2019 and was thus confirmed in its entirety. This guideline is valid from 1 February 2019 through to 31 January 2022. Because of the contents of this guideline, this period of validity is only an estimate. The guideline may need to be updated earlier in urgent cases. If the guideline continues to mirror current knowledge, its period of validity may also be extended.

III method

Basic principle

The method used to prepare this guideline was determined by the class to which this guideline was assigned. The AWMF Guidance Manual (version 1.0) has set out the respective rules and requirements for different classes of guidelines. Guidelines are differentiated into lowest (S1), intermediate (S2) and highest (S3) class. The lowest class is defined as a set of recommendations for action compiled by a non-representative group of experts. In 2004, the S2 class was divided into two subclasses: a systematic evidence-based subclass (S2e) and a structural consensus-based subclass (S2k). The highest S3 class combines both approaches. This guideline is classified as: **S2k**

Grading of recommendations

Grading of evidence and grading of recommendations is not envisaged for S2k-level guidelines. The individual Statements and Recommendations are differentiated by syntax, not by symbols (Table 2).

In addition to the level of evidence, the above listed classification of "Recommendations" also takes account of the clinical relevance of the underlying studies and the various measures / factors which were not included in the grading of evidence, such as the choice of patient cohort , intention-to-treat or per-protocol outcome analyzes, medical and ethical practice when dealing with patients, country-specific applicability, etc.

Statements

Scientific statements given in this guideline which do not consist of any direct recommendations for action but are simple statements of fact are referred to as "Statements". It is *not* possible to provide any information about the grading of evidence for these statements.

Achieving consensus and strength of consensus

As part of the structured process to achieve consensus (S2k / S3 level), authorized participants attending the session vote on draft statements and recommendations. This can lead to significant changes in the wording, etc. Finally, the extent of consensus is determined based on the number of participants (Table 3).

Expert consensus

As the name already implies, this term refers to consensus decisions taken with regard to specific Recommendations / Statements made without a prior systematic search of the literature (S2k) or for which evidence is lacking (S2e / S3). The term "expert consensus" (EC) used here is synonymous with terms used in other guidelines such as "good clinical practice" (GCP) or "clinical consensus point" (CCP). The strength of the recommendation is graded as previously described in the chapter "Grading of recommendations", ie, purely semantically ("must" / "must not" or "should" / "should not" or "may" / "may not") without the use of symbols.

Addendum of the OEGGG

To 6.9.1 Mode of delivery depending on fetal presentation and position The Austrian Society of Gynecology and Obstetrics (OEGGG) is of the opinion that there is no clinical or scientific basis for the Recommendation that cesarean section should be the preferred mode of delivery based on an assumed lower risk of perinatal cerebral hemorrhage. The OEGGG is of the opinion that the mode of delivery of infants at the limit of viability (GW 22 + 0 to 24 + 6) must be adapted to take the individual maternal and fetal clinical situation into account. For singletons at the limit of viability and in cephalic presentation, the OEGGG recommends an individualized management of delivery, which takes the maternal and fetal clinical situation into account and where the clinical decision process also includes the option of vaginal delivery as the mode of delivery 1 .

To 6.6.5 Application of antenatal steroids before late preterm delivery Based on the results of the ALPS trial 2 and the recommendations of the Society for Maternal Fetal Medicine (SMFM), the OEGGG is of the opinion that the administration of antenatal steroids in GW 34 + 0 to GW 36 + 6 may be considered, in accordance with the specifications of the SMFM.

Addendum of the SGGG

To 6.6. Administration of antenatal steroids The opinion of the SGGG on the issues in this chapter is presented in SGGG Expert Letter No. 56, which discusses the indications for glucocorticoid therapy to promote antenatal lung maturation and the appropriate doses when preterm birth is imminent. *Reasoning:* The evidence-based recommendations in Switzerland differ slightly from those given in this guideline, particularly with regard to the administration of antenatal glucocorticoids in gestational weeks 34 + 0 to 36 + 0 3 .

To 1. Definition and Epidemiology (and various other chapters: 6.9.1., 6.9.6., 6.9.7., 8.8., 8.9.) As regards care at the limits of viability, please refer to the recommendations for Switzerland which were developed together with neonatologists. *Reasoning:* The recommendations for Switzerland diverge in many points from the recommendations for Germany. They are currently being revised 4 .

To 6.2. Tocolysis With regard to tocolytic drugs, the use of beta-mimetics for tocolysis has been approved in Switzerland and they can be used as the tocolytic drug of first choice; see also SGGG Expert Letter No. 41 on tocolysis for preterm labor (only available in German: "Tokolyse in case of premature labor"). *Reasoning:* The recommendations for Switzerland differ

in many points from the recommendations for Germany 5 .

To 8.8 Clinical management before GW 22 The option of terminating the pregnancy should be mentioned to patients with a poor prognosis. *Reasoning:* The option of terminating the pregnancy by inducing the birth in cases where there is a serious physical or psychological risk to the mother is not mentioned in the guideline, even though it is clinically important.

IV guideline

6 tertiary prevention

6.1 Bed rest

6.2 Tocolysis

6.2.1 Indications

6.2.2 Drugs Of all the tocolytic drugs, beta sympathomimetics have the greatest rate of maternal (up to 80% cardiovascular) and fetal side effects as well as requiring the most monitoring 12 . There is also the additional problem of lung edema which occurs in around 1/350 applications 13 . They should therefore no longer be used for tocolysis 14 .

The data on the use of magnesium sulfate as a tocolytic drug is controversial. Meta-analyzes 11 , 12 showed that magnesium sulfate was an effective tocolytic in terms of prolonging the pregnancy by 48 hours compared to placebo (OR 2.46; 95% CI: 1.58 - 4.94); however, this flies in the face of the results and statements of the 2014 Cochrane Review 15 , which were generated using 37 studies with 3571 pregnant women. According to the Cochrane Review, magnesium sulfate was not more effective than placebo or even no therapy at prolonging pregnancy for more than 48 hours and does not reduce the rate of preterm births. However, the tocolytic efficacy of magnesium sulfate depends in the dose, which in turn has an impact on the incidence of maternal side effects. International guidelines no longer recommend using magnesium sulfate for tocolysis 16 , 17 , 18 .

6.2.3 Combining several tocolytics

6.2.4 Tocolysis for extremely preterm birth, multiple pregnancy and intrauterine growth restriction

6.2.5 Long-term tocolysis

6.3 Progesterone for maintenance tocolysis A meta-analysis carried out in 2017 which selectively included high-quality studies on this issue found that the use of progesterone for maintenance tocolysis did not significantly reduce the rate of preterm births before the 37th week of gestation (OR 1.23, 95% CI: 0.91 - 1.67) 26 .

6.4 Cervical pessary for shortened cervical length after premature labor Pratcorona et al. recently published a prospective randomized study which included 357 patients between GW 24 + 0 and GW 33 + 6 27 . If patients had a shortened cervical length (≤ 25 mm between GW 24 + 0 and GW 29 + 6; ≤ 15 mm between GW 30 + 0 and GW 33 + 6) 48 hours after being treated for premature labor, they were managed either by placing a cervical pessary or by standard protocol. The primary study outcome, in this case, the preterm birth rate before the 34th week of gestation, did not differ significantly between groups (10.7 vs. 13.7%; RR 0.78 [95% CI: 0.45-1.38]). However, the preterm birth rate before the 37th week of gestation was significantly lower after placement of a cervical pessary (14.7 vs. 25.1%; RR 0.58 [95% CI: 0.38-0.90]) as was the number of patients readmitted to hospital after previously being treated for premature labor (4.5 vs. 20.0%; RR 0.23 [95% CI: 0.11 - 0.47]). However, these results could not be confirmed in the APOSTLE VI trial 28 .

6.5 Administration of antibiotics for premature labor Meta-analyzes found that the administration of antibiotics to cases with premature labor and no rupture of membranes had no effect on the duration of the pregnancy, the preterm birth rate, respiratory distress syndrome or neonatal sepsis 29 , 30 . Given these findings, the potential risks of administering antibiotics when their administration is not indicated need to be discussed.

6.6 Administration of antenatal steroids

6.6.1 Administration and dosage

6.6.2 Starting in which week of gestation? A recently published meta-analysis found 8 non-randomized studies on this issue 32 . The impact on neonatal mortality and morbidity of a single dose of corticosteroids administered in the period GW 22 + 0 to GW 23 + 6 is shown in Tables 4 other 5 .

While neonatal mortality was significantly reduced after a single dose of corticosteroids, it apparently had no effect on morbidity. Given the rapid recent progress in the field of neonatal intensive care, prospective randomized studies on this issue are urgently required.

6.6.3 Repeat administration of antenatal steroids Zephyrin and colleagues used a Markov model to investigate how to achieve the right balance between risks and benefits with repeat administration of antenatal steroids 33 . The improved neonatal outcomes after multiple glucocorticoid administrations were set against the risk of fetal growth restriction. After 29

+ 0 weeks of gestation, a repeat administration of antenatal steroids was associated with increasing risks for the infant (Fig. 1). Any repeat administration of antenatal steroids should therefore be limited to cases with a very low gestational age (<GW 29 + 0).

6.6.4 Timing of antenatal steroid administration There are now a number of cohort studies which show that perinatal morbidity and mortality depend significantly on the timing of lung maturity 34 , 35 , 36 . An example of this is shown in Fig. 2 , which depicts the neonatal survival of infants born preterm at ≤ 26 weeks of gestation 36 .

6.6.5 Administration of antenatal steroids and late preterm birth The ALPS trial found a significant reduction in neonatal respiratory distress in children born in late preterm at GW 34 + 0 to GW 36 + 5, whose mothers were given 2 × 12 mg betamethasone IM antenatally 2 . The ASTECS trial, which studied pregnant women who underwent elective cesarean section at term, also reported a significant reduction in RDS in children born to mothers who received 2 × 12 mg betamethasone antenatally 40 . However, at a school assessment carried out by teachers 10 years later, it was found that significantly more children from the intervention group were in the lower performance quartile and fewer children were in the top performance quartile 41 . No follow-up examinations of the children in the ALPS trial have been carried out to date. Because of this, no antenatal corticoids should be administered to this group of patients for the time being.

6.7 Emergency cerclage A meta-analysis published in 2015 (n = 772 women from 11 studies, n = 496 underwent emergency cerclage placement, n = 276 were managed expectantly) found a significant prolongation of pregnancy and reduction of perinatal mortality after placement of an emergency cerclage for cervical dilation (duration of pregnancy: plus 5.4 weeks, perinatal mortality reduced from 58.5% to 29.1%) 42 . The administration of indomethacin and cefazolin increased the percentage of women who did not give birth within the following 4 weeks (92.3 vs. 62.5%) 43 .

6.8 Neuroprotection

6.8.1 Magnesium Treatment should be started with a bolus of 4 - 6 g administered over 30 min, followed by a maintenance dose of 1 - 2 g for 12 h. The aim is to double the magnesium levels in maternal serum. If the birth does not occur within 12 h, magnesium may be administered again later on when preterm birth is once again imminent.

6.8.2 Delayed cord clamping

6.9 Delivery

6.9.1 Delivery depends on fetal presentation

6.9.2 Longitudinal uterine incision for cesarean section

6.9.3 Vaginal operative delivery

6.9.4 Fetal blood gas analysis

6.9.5 Antibiotic prophylaxis for group B streptococcus

6.9.6 Cooperation with the Neonatology Department The treating pediatrician must be given all information about the pregnant woman which may be important for the initial medical treatment and therapy of the preterm infant. Such information includes any medication taken, HBsAg status, blood group, CMV antibody status (up to the 32nd week of gestation), findings from any prenatal diagnostic workups, and results of microbiological screening of the pregnant woman at imminent risk of preterm birth for GBS , MRSA, MRGN as well as the results of any repeat screenings if pregnancy is prolonged.

6.9.7 Terminal care

7 Special Aspects Relating to Twin and Multiple Pregnancies

7.1 Epidemiology and etiology

7.2 Prevention

7.2.1 Progesterone An individual patient data meta-analysis (IPDMA) of six studies 79 , 80 , 81 , 82 , 83 , 84 carried out by Romero et al. in 2017, which compared the application of vaginal progesterone with placebo or no treatment in 303 asymptomatic women with twin pregnancy and a cervical length of ≤ 25 mm in the second trimester, found a significant reduction in preterm births before the 33rd week of gestation (31.4 vs. 43.1%; RR 0.69 [95% CI: 0.51-0.93]) and improved neonatal outcomes (eg, lower neonatal mortality rate [RR 0.53; 95% CI 0.35-0.81], lower incidence of respiratory distress syndrome [RR 0.70; 95% CI: 0.56 - 0.89], fewer neonates with a birthweight <1500 g [RR 0.53; 95% CI: 0.35 - 0.80]) 85 .

7.2.2 Cerclage The first meta-analysis of three prospective randomized studies found a significantly higher preterm birth rate before the 35th week of gestation for women carrying a twin pregnancy after placement of a primary or secondary cerclage (76 vs. 36%; RR 2.15, 95% CI : 1.15 - 4.01) 86 , 87 , 88 , 89 . Another meta-analysis has since been carried out which additionally took individual patient data into account 90 . This meta-analysis found that placement of a cerclage had no negative effect on the preterm birth rate or perinatal morbidity, at least for patients with a short cervix, before the 24th week of gestation.

7.2.3 Cervical pessary for shortened cervical length

Given the fact that prospective randomized studies have reported both positive 91 , 92 , 93 and negative 94 , 95 data, the decision whether or not to carry out this procedure must be made on a case-by-case basis.

7.2.4 Cervical pessary after preterm labor and shortened cervical length In a prospective randomized study which included 132 women with twin pregnancy between GW 24 + 0 and GW 33 + 6 96 , patients who were found to have a shortened cervical length (≤ 20 mm between GW 24 + 0 and GW 29 + 6; ≤ 10 mm between GW 30 + 0 and GW 33 + 6) 48 h after treatment for preterm labor either underwent placement of a cervical pessary or received the usual standard care. The primary study outcome - ie, the preterm rate before the 34th week of gestation - was significantly lower in the intervention group (16.4 vs. 32.3%; RR 0.51 [95% CI: 0.27-0.97]) as was the number of readmitted patients after treatment for preterm labor (5.6 vs. 21.5%; RR 0.28 [95% CI: 0.10 - 0.80]). Moreover, placement of a cervical pessary significantly reduced the prevalence of necrotizing enterocolitis (0 vs. 4.6%) and of neonatal sepsis (0 vs. 6.2%).

7.2.5 Emergency cerclage As has already been established for women with singleton pregnancies, cohort studies have shown that a twin pregnancy can also be prolonged if an emergency cerclage is placed in women with an opened cervix before GW 24 + 0 97 , 98 , 99 , 100 .

8 Preterm Premature Rupture of Membranes (PPROM)

8.1 Prevalence and Etiology
8.2 Risk factors
8.3 Diagnostic workup When examining patients with PPROM, a digital examination must be avoided where possible, because digital examinations increase the risk of ascending infection and significantly reduce the latency period to delivery 106 , 107 .

8.4 Latency period
8.5 Maternal and fetal risks
8.6 Triple I (Table 6)
8.7 Maternal and fetal risks associated with Triple I
8.8 Clinical management of PPROM before GW 22 As almost all studies on antibiotic therapy in cases with rupture of membranes only recruited patients after the 24 + 0 week of gestation, there are no reliable data on the administration of antibiotics before the fetus has achieved viability. But the risk that the patient may develop sepsis due to ascending infection suggests that antibiotic therapy is advisable 128 . The same regimen as the one described for PPROM between (GW 22 + 0) GW 24 + 0 and GW 33 + 6 GW can be used.

8.9 Clinical management of PPROM between (GW 22 + 0) GW 24 + 0 and GW 33 + 6
8.9.1 Expectant management If PPROM occurs between GW 24 + 0 and GW 33 + 6 or between GW 22 + 0 and GW 23 + 6 if maximum therapy is requested, the risks of ascending infection must be weighed against the neonatal risks which can result from preterm birth (Table 7). An ascending infection with chorioamnionitis, preterm placental abruption, pathological CTG, or umbilical cord prolapse are indications for immediate delivery of the fetus. Otherwise expectant management is currently the international standard of care 129 .

8.9.2 Administration of antenatal steroids
8.9.3 Administration of antibiotics
8.9.4 Tocolysis
8.9.5 Neuroprotection See 6.8.1.

8.9.6 Maternal and fetal monitoring Pregnant women with preterm premature rupture of membranes should be routinely examined for signs of infection. In addition to the above-mentioned clinical parameters, such signs also include symptoms such as painful uterus, uterine contractions, maternal blood pressure and heart rate 116 . Blood count and CRP must additionally be monitored at least once a day. However, the benefit of daily laboratory tests is disputed 133 . Kunze et al. reported to AUC of just 0.66 for a combination of maternal fever, CRP and leukocytes to predict FIRS 134 . Musilova et al. reported a sensitivity of 47%, specificity of 96%, positive predictive value of 42% and negative predictive value of 96% for a CRP value of 17.5 mg / l in maternal serum to predict intraamniotic infection or inflammation 135 .

Daily CTG monitoring of patients with PPROM is standard clinical practice. But currently there is no fetal monitoring method which can reliably detect intrauterine inflammation or infection. Neither CTG nor the use of a biophysical profile (CTG plus fetal breathing movements and other fetal movements, fetal tone and amniotic fluid volume assessment) are suitable predictors for intrauterine infection (CTG: sensitivity 39%; biophysical profile: 25%) 115 .

Regular monitoring of amniotic fluid volumes is similarly of little benefit. While a reduction in amniotic fluid volume increases the risk of umbilical cord compression and demonstrably reduces the time to the start of labor, its predictive value for a negative outcome is low 136 . The use of Doppler sonography has no proven benefits for premature rupture of

membranes 137 .

8.9.7 Amniotic infusion

8.9.8 Antibiotic prophylaxis for Group B streptococcus See the recommendations on GBS prophylaxis.

8.9.9 Delivery

8.10 Clinical Management of PPROM between GW 34 + 0 and GW 36 + 6 A total of 1839 women between GW 34 + 0 and GW 36 + 6 who had preterm premature rupture of membranes (PPROM) were recruited into the PPROMT trial between 2004 and 2013 141 . Immediate induction of labor was compared with expectant management. In the study group, 21% of infants were born after the 37th week of gestation to women managed expectantly compared to only 3% in the control group. The prevalence of neonatal sepsis was the same for both groups, however respiratory distress syndrome (RDS) occurred significantly less often after expectant management. In this group, the birthweight of the children was also significantly higher and the stay in the neonatal intensive care unit or in hospital was shorter. However, as expected, uterine bleeding before or during birth occurred more often in the mothers of these children as did peripartum fever. The c-section rate was significantly lower compared to the group who had induction of labor 141 .

The results of the PPROMT trial were supported by the findings of the PPROMEXIL and PPROMEXIL-2 trials 142 , 143 . But if Group B streptococcus colonization was diagnosed, the prevalence of early onset sepsis was significantly higher among affected neonates (15.2 vs. 1.8%; p = 0.04) 144 .

According to a meta-analysis of this issue which included 12 studies, expectant management was still not found to be associated with an increased prevalence of neonatal sepsis. Following immediate induction of labor, the rates for RDS, neonatal mortality, required ventilation, endomyometritis and cesarean section were significantly higher while the incidence of chorioamnionitis was lower 130 . A patient-level meta-analysis came to similar conclusions 145 .

9 Psychosomatic Care and Supportive Therapy

In addition to worries about the health consequences of a preterm birth (which are difficult to estimate), therapeutic measures, which can include immobilization, medication to stop contractions and the administration of corticosteroids, may be experienced as stressful. If there are additional stresses (a previous experience of loss, prior mental health problems, partnership difficulties, etc.), then the incidence of anxiety and depression is higher 146 , 147 , 148 . Particularly for large families, admission of the mother to hospital represents substantial organizational pressures for the family.

There are a number of psychometric tests which are used to detect psychological and social stress factors, such as HADS, the Babylotse Plus screening questionnaires, etc. 149 .

Affected couples should be offered acute psychological crisis intervention, followed by offers of supportive talks and psychotherapy where necessary. This also supports parent-child bonding.

The support offered by self-help groups such as the German federal association “Das Frühgeborene Kind” [The Preterm Infant] 150 can help affected parents, and parents should be informed about such options.

Affected families should be actively offered options in the context of the Early Help network. This is a German network that creates local and regional support systems offering coordinated services to parents and children, which aims to improve familial and social development opportunities for children and parents, both in the early stages and over the long term 151 .

The “Babylotse” program, which arranges the transfer of families from the regular healthcare system to the Frühhilfe network and other social care systems has proven to be particularly useful. The core aspect of this program is the role it plays in guiding parents to find and use the most suitable options from among the numerous local choices available.

All of these measures are services which provide compassionate support to the patient and her family and which are offered in addition to the care provided by the attending midwife.

Footnotes

Conflict of Interest The conflict of interest statements of all the authors are available in the long version of the guideline./ You can find the declarations of conflicts of interest of all authors in the long version of the guideline.

Guideline Program

Editors

Leading Professional Medical Associations

German Society of Gynecology and Obstetrics (German Society for Gynecology and Obstetrics eV [DGGG])

Head Office of DGGG and Professional Societies Hausvogteiplatz 12, DE-10117 Berlin info@dggg.de http://www.dggg.de/

President of DGGG

Prof. Dr. med. Anton Scharl Director of the St. Marien Amberg Women's Clinic Mariahilfbergweg 7, DE-92224 Amberg Kliniken Nordoberpfalz AG Söllnerstraße 16, DE-92637 Weiden

DGGG Guidelines Representatives

Prof. Dr. med. Matthias W. Beckmann University Hospital Erlangen, Gynecological Clinic Universitätsstrasse 21-23, DE-91054 Erlangen

Prof. Dr. med. Erich-Franz Solomayer University Hospital of Saarland Obstetrics and Reproductive Medicine Kirrberger Straße, Building 9, DE-66421 Homburg

Guidelines coordination

Dr. med. Paul Gaß, Dr. med. Gregor Olmes, Christina Meixner Universitätsklinikum Erlangen, Frauenklinik Universitätsstrasse 21 - 23, DE-91054 Erlangen fk-dggg-leitlinien@uk-erlangen.de http://www.dggg.de/leitlinienstellunghaben

Austrian Society of Gynecology and Obstetrics (Austrian Society for Gynecology and Obstetrics [OEGGG]) Frankgasse 8, AT-1090 Vienna stephanie.leutgeb@oeggg.at http://www.oeggg.at

President of OEGGG

Prof. Dr. med. Petra Kohlberger University Clinic for Gynecology Vienna Währinger Gürtel 18–20, AT-1090 Vienna

OEGGG Guidelines Representatives

Prof. Dr. med. Karl Tamussino University Clinic for Gynecology and Obstetrics Graz Auenbruggerplatz 14, AT-8036 Graz

Prof. Dr. med. Hanns Helmer University Clinic for Gynecology Vienna Währinger Gürtel 18–20, AT-1090 Vienna

Swiss Society of Gynecology and Obstetrics (Swiss Society for Gynecology and Obstetrics [SGGG])

Gynécologie Suisse SGGG Altenbergstrasse 29, Postfach 6, CH-3000 Bern 8 sekretariat@sggg.ch http://www.sggg.ch/

President in SGGG

Dr. med. Irène Dingeldein Längmatt 32, CH-3280 Murten

SGGG Guidelines Representatives

Prof. Dr. med. Daniel Surbek University Clinic for Obstetrics and Feto-Maternal Medicine, Inselspital Bern, Effingerstraße 102, CH-3010 Bern

Prof. Dr. med. René Hornung Kantonsspital St. Gallen, Frauenklinik Rorschacher Straße 95, CH-9007 St. Gallen

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Figures and tables

Table 1 The following medical societies / working groups / organizations / associations were interested in participating in the compilation of the text of the guideline and in the consensus conference, and they nominated representatives to attend the consensus conference.

Author mandate holder	DGGG working group (AG) / AWMF / non-AWMF medical society / organization / association
Prof. Dr. Harald Abele	DGGG - Working Group for Obstetrics and Prenatal Medicine (AGG) - Premature Birth Section
Prof. Dr. Franz Bahlmann	German Society for Ultrasound in Medicine V. (DEGUM)
Dr. Ivonne Bedei	DGGG - Arbeitsgemeinschaft Kinder- und Jugendgynäkologie e. V. (AGKJ)
Prof. Dr. Richard Berger	German Society for Gynecology and Obstetrics (DGGG)
Dr. Klaus Doubek	Professional Association of Gynecologists V. (BVF)
Prof. Dr. Ursula Felderhoff-Müser	Society for Neonatal and Pediatric Intensive Care Medicine (GNPI)
Prof. Dr. Herbert Fluhr	DGGG - Working Group for Immunology in Gynecology and Obstetrics (AGIM)
PD Dr. Dr. Yves Garnier	DGGG - Working Group for Obstetrics and Prenatal Medicine (AGG) - Premature Birth Section
Dr. Susanne Grylka-Baeschlin	German Society for Midwifery Studies (DGHWi)
Prof. Dr. Hanns Helmer	Austrian Society for Gynecology and Obstetrics (OEGGG)
Prof. Dr. Egbert Herting	German Society for Child and Adolescent Medicine (DGKJ)
Prof. Dr. Markus Hoopmann	DGGG - Working Group for Ultrasound Diagnostics in Gynecology and Obstetrics (ARGUS)
Prof. Dr. Irene Hösli	Swiss Society for Gynecology and Obstetrics (SGGG)
Prof. Dr. Dr. H. c. Udo Hoyme	DGGG - Working Group for Infections and Infection Immunology (AGII)
Alexandra Jendreizeck	Federal Association “The preterm Child”]
Dr. Harald Krentel	DGGG - Working Group for Women's Health in Development Cooperation (FIDE)
PD Dr. Ruben Kuon	German Society for Gynecology and Obstetrics (DGGG)
Dr. Wolf Luetje	DGGG - German Society for Psychosomatic Gynecology and Obstetrics V. (DGPFG)
Silke Mader	European Foundation for the Care of the Newborn Infants (EFCNI)
PD Dr. Holger Maul	Deutsche Gesellschaft für Perinatale Medizin (DGPM)
Prof. Dr. Werner Mendling	DGGG – Arbeitsgemeinschaft für Infektionen und Infektionsimmunologie (AGII)
Barbara Mitschdörfer	Bundesverband “Das frühgeborene Kind” [Federal Association “The preterm Child”]
Tatjana Nicin	Deutscher Hebammenverband (DHV)
Dr. Dirk Olbertz	Gesellschaft für neonatale und pädiatrische Intensivmedizin (GNPI)
Prof. Dr. Werner Rath	Deutsche Gesellschaft für Pränatal- und Geburtsmedizin (DGPGM)
Prof. Dr. Claudia Roll	Deutsche Gesellschaft für Perinatale Medizin (DGPM)
PD Dr. Dietmar Schlembach	DGGG – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Präeklampsie
Prof. Dr. Ekkehard Schleußner	DGGG – Deutsche Gesellschaft für psychosomatische Frauenheilkunde und Geburtshilfe e. V. (DGPFG)
Prof. Dr. Florian Schütz	DGGG – Arbeitsgemeinschaft für Immunologie in Gynäkologie und Geburtshilfe (AGIM)
Prof. Dr. Vanadin Seifert-Klauss	DGGG - German Society for Gynecological Endocrinology and Reproductive Medicine e. V. (DGGEF)

Open in a separate window

Table 2 Grading of recommendations.

Level of recommendation	syntax
Strong recommendation, highly binding	must / must not
Simple recommendation, moderately binding	should / should not
Open recommendation, not binding	may / may not

Table 3 Grading of strength of consensus.

symbol	Strength of consensus	Extent of agreement in percent
+++	Strong consensus	> 95% of participants agree
++	Consensus	> 75 - 95% of participants agree
+	Majority agreement	> 50 - 75% of participants agree
-	No consensus	<51% of participants agree

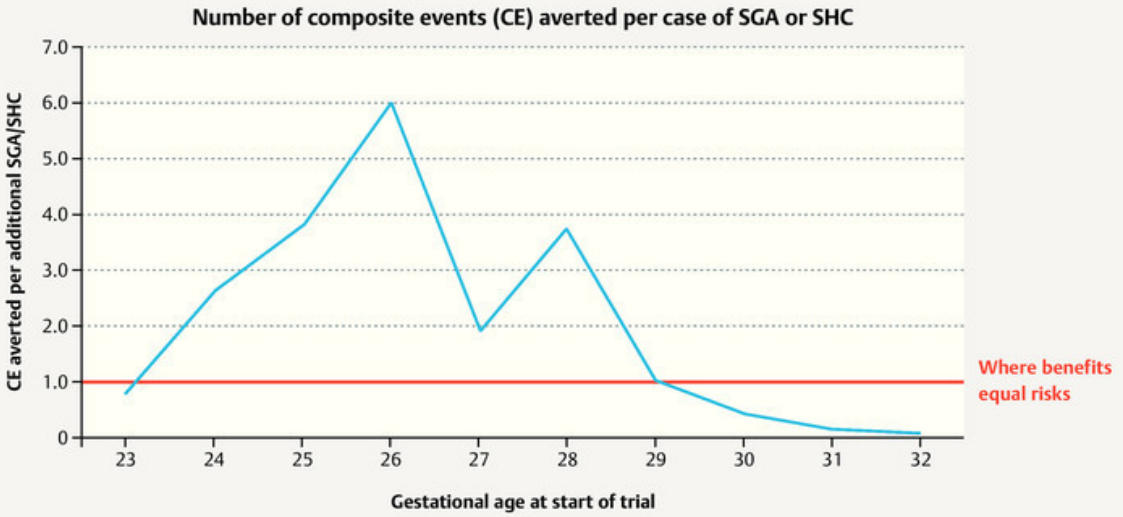
Table 4 Effects of antenatal steroids on the outcome of infants between GW 22 + 0 and GW 22 + 6 [32] .

GW 22 + 0 - GW 22 + 6	OR	95% CI
Neonatal mortality	0.58	0.38-0.89
Intraventricular cerebral hemorrhage (grade III - IV) or periventricular leukomalacia	1.03	0.55 - 1.93
Chronic pulmonary disease	1.19	0.52 - 2.73
Necrotizing enterocolitis (> stage II)	0.59	0.03 - 12.03

Table 5 Effects of antenatal steroids on the outcome of infants between GW 23 + 0 and GW 23 + 6 32 .

GW 23 + 0 - GW 23 + 6	OR	95% CI
Neonatal mortality	0.50	0.42-0.58
Intraventricular cerebral hemorrhage (grade III - IV) or periventricular leukomalacia	0.75	0.55 - 1.03
Chronic pulmonary disease	0.94	0.59 - 1.51
Necrotizing enterocolitis (> stage II)	0.93	0.66 - 1.32

Fig. 1

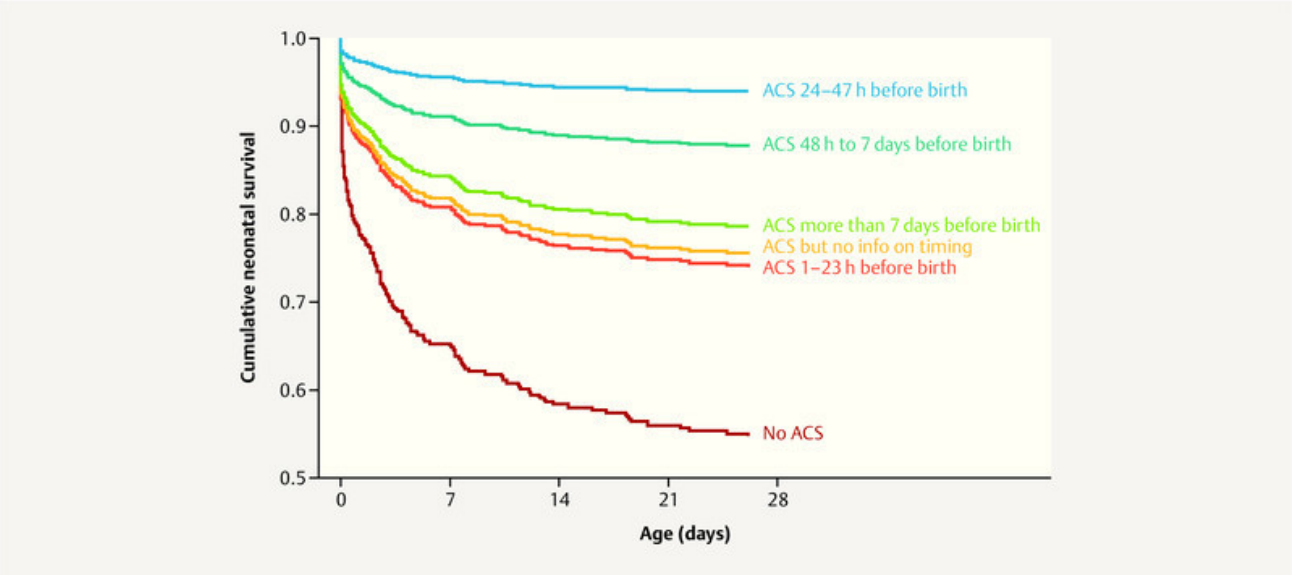


The *x-axis* shows the gestational age at entry; the *y-axis* shows the number of composite events that were averted per case of SGA/SHC. A gestational age risk benefit threshold is seen at 29 weeks' gestation, when the risk equals the benefits.

SGA: small for gestational age; SHC: small head circumference; CE: RDS, chronic lung disease (CLD), severe PIVH, PVL, bronchopulmonary dysplasia (BPD), or stillbirth

Benefits of administering antenatal steroids according to gestational age [33]

Fig. 2



Survival of very immature infants (<26th week of gestation) according to the timing of antenatal steroid administration 36 .

Table 6 Classification of maternal fever and Triple I *.

	definition
Maternal fever	Maternal fever is present when the orally measured temperature exceeds 39.0 ° C. If the orally measured temperature is between 38.0 and 38.9 ° C, the temperature should be measured again after 30 minutes. If the temperature again exceeds 38.0 ° C, then maternal fever is present.
Suspicious for Triple I.	Maternal fever of unclear origin together with at least one of the following criteria: • fetal tachycardia of more than 160 beats / min for> 10 min • maternal leukocytes> 15,000 µl without the administration of corticosteroids • purulent discharge from the cervix
Confirmed Triple I.	Suspicion of Triple I and objective findings of infection, such as: positive gram staining of amniotic fluid **, low glucose concentrations (<14 mg / dl), increased number of leukocytes (> 30 cells / mm^3), positive bacterial culture or histopathological findings *** of inflammation or infection of both of the placenta, the amniotic membranes or the umbilical cord (funisitis)

* Triple I: inflammation or infection or both; ** amniotic fluid obtained by amniocentesis; *** postpartum histopathology of the placenta 116 .

Table 7 Planned delivery vs. expectant management of PPROM between the 24th and the 37th week of gestation.

Planned delivery vs. expectant management	RR	95% CI
Neonatal sepsis	0.93	0.66 - 1.30
Neonatal infection (positive blood culture)	1.24	0.70 - 2.21
RDS	1.26	1.05 - 1.53
Cesarean section	1.26	1.11 - 1.44
Perinatal mortality	1.76	0.89 - 3.50
Intrauterine fetal death	0.45	0.13 - 1.57
Neonatal mortality	2.55	1.17 - 5.56
Mechanical ventilation required	1.27	1.02 - 1.58
Transfer to neonatal intensive care unit	1.16	1.08 - 1.24
Chorioamnionitis	0.50	0.26 - 0.95
Endomyometritis	1.61	1.00 - 2.59
Induction of labor	2.18	2.01 - 2.36

130

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Prevention and therapy of premature birth. Guideline of the DGGG, OEGGG and SGGG (S2k level, AWMF register number 015/025, February 2019) - Part 2 with recommendations on tertiary prevention of premature birth and management of early premature rupture of the bladder

Summary

Objective Official guideline of the German Society for Gynecology and Obstetrics (DGGG), the Austrian Society for Gynecology and Obstetrics (ÖGGG) and the Swiss Society for Gynecology and Obstetrics (SGGG). The aim of the guideline is to improve the prediction, prevention and management of premature birth on the basis of the current literature, the experience of the members of the guideline commission including the self-help perspective.

Methods Based on the international literature, the members of the participating professional societies and organizations developed recommendations and statements. These were adopted in a formal process (structured consensus conferences with neutral moderation, written Delphi vote).

Recommendations Part 2 of this short version of the guideline shows statements and recommendations on tertiary prevention of premature birth and the management of premature rupture of the membranes.

Keywords: premature birth, premature labor, cervical insufficiency, early premature rupture of the bladder

I guideline information

Guideline program

Information on this can be found at the end of the guideline.

How to quote

Prevention and Therapy of Preterm Birth. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry Number 015/025, February 2019) - Part 2 with Recommendations on the Tertiary Prevention of Preterm Birth and the Management of Preterm Premature Rupture of Membranes. Obstetric Frauenheilk 2019; 79: 813-833

Guidance documents

The complete long version and a DIA version of this guideline as well as a list of the conflicts of interest of all authors and a guideline report on the methodological approach including conflict of interest management can be found on the AWMF homepage: http://www.awmf.org/leitlinien/detail/ll /015-025.html

Guideline group (Tab. 1)

used abbreviations

AFP Alpha fetoprotein
AUC Area under the curve
COX Cyclooxygenase
CPAP Continuous positive airway pressure
CRP C-reactive protein
CTG Cardiotocography
fFN Fibronectin
FIRS Fetal inflammatory response syndrome
GBS Serological group B streptococci
IGFBP-1 Insulin-like growth factor-binding protein-1
IL-6 Interleukin-6
AI Confidence interval
NEC necrotizing enterocolitis
NICU Neonatal Intensive Care Unit
NNH Number needed to harm
NNT Number needed to treat
OR Odds ratio
17-OHPC 17 α-hydroxyprogesterone caproate
PAMG-1 Placenta alpha microgobulin-1
phIGFBP-1 Phosphorylated insulin-like growth factor-binding protein-1
PIVH peri- / intraventricular cerebral hemorrhage
PPROM early premature rupture of the bladder
PVL periventricular leucomalacia
RDS Respiratory Distress Syndrome
RR relative risk
SSW Week of pregnancy
TMMV total cervical occlusion
TNF-α Tumor necrosis factor alpha
Triple I. Intrauterine inflammation or infection or both
Z. n. State after

II Use of guidelines

Question and goals

The aim of the guideline is to optimize the care of patients with a threatened premature birth in the outpatient and inpatient care sector in order to reduce the premature birth rate. If the premature birth can no longer be stopped, the aim is to reduce perinatal or neonatal morbidity and mortality. This is also intended to improve the psychomotor and cognitive development of premature children.

Supply area

Outpatient and / or inpatient care area

User target group / addressees

The recommendations of the guideline are aimed at gynecologists in the branch, gynecologists employed in clinics, paediatricians employed in clinics, midwives in branch offices and midwives employed in clinics. Other addressees are interest groups for the women and children concerned, nursing staff (obstetrics / postnatal care, children's intensive care unit), medical-scientific specialist societies and professional associations, quality assurance institutions (e.g. IQTIG), health policy institutions and decision-makers at federal and state level, cost bearers.

Adoption and period of validity

The validity of this guideline was confirmed by the board members / responsible persons of the participating medical societies, working groups, organizations and associations as well as by the board of directors of the DGGG, SGGG, OEGGG and the DGGG / OEGGG / SGGG guideline commission in February 2019 and thus approved in its entire content . This guideline is valid from 02/01/2019 to 01/31/2022. This duration is estimated due to the contextual context. A guideline can be updated earlier if there is an urgent need;

III methodology

Basics

The methodology for creating this guideline is specified by assigning the level classification. The AWMF set of rules (version 1.0) provides corresponding regulations. A distinction is made between the lowest level (S1), the medium level (S2) and the highest level (S3). The lowest class is defined by a compilation of recommendations for action drawn up by a non-representative group of experts. In 2004, level S2 was subdivided into the systematic evidence research-based (S2e) or structural consensus-based lower level (S2k). Both processes are combined in the highest level S3. This guideline corresponds to the level: **S2k**

Recommendation grading

The evidence grading and recommendation grading of a guideline at S2k level is not intended. The individual statements and recommendations are only differentiated linguistically - not symbolically (Tab. 2).

The classification of "recommendations" listed above corresponds to the evaluation of the evidence as well as the clinical relevance of the underlying studies and their measures / factors not listed in the grading of the evidence, such as the choice of the patient collective, intention-to-treat or per- Protocol outcome analyzes, medical or ethical behavior towards the patient, country-specific applicability, etc.

Statements

If technical statements are not part of this guideline as recommendations for action, but rather as a simple presentation, these are referred to as "statements". It is not possible to specify levels of evidence for these statements.

Finding consensus and strength of consensus

As part of a structural consensus finding (S2k / S3 level), the authorized participants in the meeting agree on the statements and recommendations that have been formulated. Significant changes to formulations etc. can occur here. Finally, depending on the number of participants, the strength of the consensus is determined (Tab. 3).

Expert consensus

As the name already suggests, consensus decisions are meant here specifically for recommendations / statements without prior systemic literature research (S2k) or due to lack of evidence (S2e / S3). The expert consensus to be used (EK) is synonymous with the terms from other guidelines such as “Good Clinical Practice” (GCP) or “Clinical Consensus Point” (KKP). The strength of the recommendation is graded in the same way as already described in the chapter on recommendation grading without the use of the symbols shown, but purely semantically ("should" / "should not" or "should" / "should not" or "can" / "cannot") .

Addendum OEGGG

Re 6.9.1 mode of delivery depending on the child's position

The Austrian Society for Gynecology and Obstetrics (OEGGG) is of the opinion that there is no clinical and scientific basis for the recommendation to prefer a caesarean section as the delivery mode due to a supposedly lower perinatal cerebral hemorrhage risk, and that the delivery mode in the area of early preterm birth (SSW 22 + 0 to 24 + 6) must be adapted to the individual maternal and fetal clinical situation. The OEGGG recommends an individual delivery management in the area of early premature birth in the case of singles in the skull position, which takes into account the maternal and fetal clinical situation and also includes vaginal birth as a mode of delivery in the clinical decision-making process 1 .

to 6.6.5 Application of antenatal steroids in late premature birth

Based on the results of the ALPS Trial 2 and the recommendations of the Society for Maternal Fetal Medicine (SMFM), the OEGGG is of the opinion that the application of antenatal steroids in weeks 34 + 0 to 36 + 6 according to the specifications of the SMFM can be considered.

Addendum SGGG

to 6.6. Application of antenatal steroids

With regard to this chapter, reference is made to the SGGG expert letter no. 56 "Glucocorticoid therapy for antenatal lung maturation in the case of threatened premature birth: indications and dosage". *Reason:* The evidence-based recommendations in Switzerland differ slightly from these guidelines, especially with regard to the administration of antenatal glucocorticoids 34 + 0 to 36 + 0 weeks 3 .

to 1. Definition and epidemiology (and various other chapters: 6.9.1., 6.9.6., 6.9.7., 8.8., 8.9.)

With regard to care at the limit of viability, reference is made to the recommendation made by Switzerland together with neonatologists. *Reason:* The recommendations in Switzerland diverge in several aspects from the recommendations in Germany. They are currently in revision 4 .

to 6.2. Tocolysis

With regard to tocolytic drugs, betamimetics for tocolysis are approved in Switzerland and can be used as the first choice tocolytic, see also SGGG Expert Letter No. 41 “Tokolysis in Premature Labor”. *Reason:* The recommendations and practice in Switzerland diverge from those in Germany 5 .

to 8.8 clinical management in <22 weeks of gestation

If the prognosis is poor, the option of an abortion should be mentioned. *Reason:* The option of termination of pregnancy by induction in the event of severe maternal physical or psychological risk is not mentioned in the guidelines, although it is clinically important.

IV guideline

6 Tertiary prevention

6.1 bed rest

6.2 Tokolysis

6.3 Progesterone as maintenance tocolysis

A meta-analysis from 2017 with selective inclusion of the high-quality studies on this topic shows that the use of progesterone for maintenance tocolysis does not significantly reduce the rate of premature birth <37 weeks gestation (OR 1.23, 95% CI 0.91 - 1, 67) 26 .

6.4 Cervical pessary after premature labor and shortened cervical length

Recently Pratcorona et al. a prospective randomized study in which 357 patients between 24 + 0 and 33 + 6 weeks of gestation were included 27 . If the patients had a shortened cervical length 48 hours after treated premature labor (≤ 25 mm between 24 + 0 and 29 + 6 weeks; ≤ 15 mm between 30 + 0 and 33 + 6 weeks), they received either a cervical pessary or the usual standard management. The primary study objective, the premature birth rate <34 weeks of gestation, was not significantly different between the groups (10.7 vs. 13.7%; RR 0.78 [95% CI 0.45-1.38]). However, the premature birth rate

before 37 weeks of gestation was significantly lower after the cervical pessary (14.7 vs. 25.1%; RR 0.58 [95% CI 0.38-0.90]) and the number of patients re-admitted after premature treatment Labor activity (4.5 vs. 20.0%; RR 0.23 [95% CI 0.11-0.47]). However, these results could not be confirmed in the APOSTEL VI trial 28 .

6.5 Administration of antibiotics in the event of premature labor

Meta-analyzes show no effect of antibiotic administration in pregnant women with premature labor without rupture of the bladder on the length of pregnancy, the premature birth rate, respiratory distress syndrome or neonatal sepsis 29 , 30 . Against this background, the potential dangers of non-indicated antibiotic use must also be discussed.

6.6 Application of antenatal steroids

6.7 Emergency lawsuit

A meta-analysis published in 2015 (n = 772 women from 11 studies, n = 496 received an emergency dislocation, n = 276 prospective approach) showed a significant increase in the duration of pregnancy and a reduction in perinatal mortality after an emergency dislocation was created with an open cervix (pregnancy duration plus 5.4 Weeks, reduction in perinatal mortality from 58.5 to 29.1%) 42 . The application of indomethacin and cephazolin increases the proportion of women who do not give birth within the next 4 weeks (92.3 vs. 62.5%) 43 .

6.8 Neuroprotection

6.9 childbirth

7 peculiarities of Gemini and higher grade multiples

7.1 Epidemiology and Etiology

7.2 Prevention

8 early premature rupture of the bladder (PPROM)

8.1 Prevalence and Etiology

8.2 Risk Factors

8.3 Diagnostics

In patients with PPROM, digital diagnosis should be avoided as far as possible, since this increases the risk of ascending infection and significantly shortens the latency period up to birth 106 , 107 .

8.4 Latency

8.5 Maternal and fetal risks

8.6 Triple I (Tab. 6)

8.7 Maternal and fetal risks with Triple I.

8.8 Clinical management in PPROM <22 weeks

Since almost all studies on antibiotic therapy for ruptured membranes have only recruited patients after 24 + 0 weeks of gestation, no reliable data are available on application before viability is reached. But the mere danger for the patient of getting sepsis as a result of an ascending infection makes antibiosis advisable 128 . The same regime that is described for the PPROM procedure between (22 + 0) 24 + 0 - 33 + 6 weeks of gestation can be used.

8.9 Clinical management for PPROM between (22 + 0) 24 + 0 - 33 + 6 weeks of gestation

8.10 Clinical management for PPROM between 34 + 0 - 36 + 6 weeks

As part of the PPROMT trial between 2004 and 2013, 1,839 women between 34 + 0 and 36 + 6 weeks of gestation were recruited who had premature rupture of the bladder (PPROM) 141 . Immediate labor induction was compared with a wait-and-see (prospective) approach. In the study group, 21% of the children were born after 37 weeks of gestation after the prospective approach, in the control group only 3%. The prevalence of neonatal sepsis was the same in both groups, but respiratory distress syndrome (RDS) occurred significantly less after a wait-and-see approach. In this group, the birth weight of the children was also significantly increased and the length of stay in the neonatal intensive care unit or in the hospital was shorter. In contrast, as expected, the mothers of these children experienced more uterine bleeding before or during childbirth as well as fever during childbirth. The rate of caesarean section was significantly lower compared to induction 141 .

The results of the PPROMT trial are supported by the PPROMEXIL and PPROMEXIL-2 trials 142 , 143 . However, if colonization with B streptococci was diagnosed, the prevalence of “early onset sepsis” was significantly increased in the affected neonates (15.2 vs. 1.8%; p = 0.04) 144 .

In a meta-analysis on this topic, which includes 12 studies, no increased prevalence of neonatal sepsis can be observed with an expansive approach. After immediate induction of labor, the rate of IBS, neonatal mortality, the need for ventilation, endomyometritis and caesarean section was significantly increased, while the incidence of chorioamnionitis was decreased 130 . A patient-level meta-analysis also comes to similar results 145 .

9 Psychosomatic accompaniment and supportive therapy offers

In addition to worrying about z. The health consequences of a premature birth, some of which are difficult to assess, are also stressful when the therapeutic measures with immobilization, contractions and cortisone administration are experienced. In the case of additional stress (previous experience of loss, previous psychological illnesses, relationship problems, etc.), fears and depression are often found 146 , 147 , 148 . Especially with large families, hospitalization of the mother puts the family system under great organizational pressure.

Various psychometric test methods can be used to record psychological as well as social stress factors. B. HADS, Babylotse Plus screening sheet etc. 149 .

The couples concerned should be offered acute psychological crisis intervention and subsequent supportive discussions and, if necessary, psychotherapy. This also supports the development of the parent-child bond.

Accompaniment by self-help groups such as the federal association “Das Frühgeborene Kind” 150 can help those affected, so that these possibilities should be pointed out.

The families concerned should be actively offered opportunities within the framework of early aid, which form local and regional support systems with coordinated offers of help for parents and children and aim to improve development opportunities for children and parents in families and society at an early stage and sustainably 151 .

The Babylotse program has proven to be particularly helpful, as it systematises the transfer of families from the health system to the network of early aid and other social security systems. The core is the pilot function for finding and using the right facilities from the multitude of offers on site.

All of these measures are an additional offer for caring support for the patient and her relatives by the supervising midwife.

Guideline program

editor

Leading professional societies

German Society for Gynecology and Obstetrics V. (DGGG) Representation of the DGGG and professional associations Hausvogteiplatz 12, DE-10117 Berlin info@dggg.de http://www.dggg.de/

President of the DGGG

Prof. Dr. med. Anton Scharl Director of the St. Marien Amberg Women's Clinic Mariahilfbergweg 7, DE-92224 Amberg Kliniken Nordoberpfalz AG Söllnerstraße 16, DE-92637 Weiden

DGGG guideline officer

Prof. Dr. med. Matthias W. Beckmann University Hospital Erlangen, Gynecological Clinic Universitätsstrasse 21-23, DE-91054 Erlangen

Prof. Dr. med. Erich-Franz Solomayer University Hospital of Saarland Obstetrics and Reproductive Medicine Kirrberger Straße, Building 9, DE-66421 Homburg

Guideline coordination

Dr. med. Paul Gaß, Dr. med. Gregor Olmes, Christina Meixner Universitätsklinikum Erlangen, Frauenklinik Universitätsstrasse 21 - 23, DE-91054 Erlangen fk-dggg-leitlinien@uk-erlangen.de http://www.dggg.de/leitlinienstellunghaben

Austrian Society for Gynecology and Obstetrics (OEGGG) Frankgasse 8, AT-1090 Vienna stephanie.leutgeb@oeggg.at http://www.oeggg.at

President of the OEGGG

Prof. Dr. med. Petra Kohlberger University Clinic for Gynecology Vienna Währinger Gürtel 18–20, AT-1090 Vienna

OEGGG guideline officer

Prof. Dr. med. Karl Tamussino University Clinic for Gynecology and Obstetrics Graz Auenbruggerplatz 14, AT-8036 Graz

Prof. Dr. med. Hanns Helmer University Clinic for Gynecology Vienna Währinger Gürtel 18–20, AT-1090 Vienna

Swiss Society for Gynecology and Obstetrics (SGGG) Gynécologie Suisse SGGG Altenbergstraße 29, Postfach 6, CH-3000 Bern 8 sekretariat@sggg.ch http://www.sggg.ch/

President of the SGGG

Dr. med. Irène Dingeldein Längmatt 32, CH-3280 Murten

SGGG guideline officer

Prof. Dr. med. Daniel Surbek University Clinic for Obstetrics and Feto-Maternal Medicine, Inselspital Bern, Effingerstraße 102, CH-3010 Bern

Prof. Dr. med. René Hornung Kantonsspital St. Gallen, Frauenklinik Rorschacher Straße 95 CH-9007 St. Gallen

Figures and tables

Tab. 1 The following professional societies / working groups / organizations / associations have expressed an interest in participating in the creation of the guideline text and participation in the consensus conference and have named representatives for the consensus conference.

Author mandate holder	DGGG working group (AG) / AWMF / non-AWMF specialist society / organization / association
Prof. Dr. Harald Abele	DGGG - Working Group for Obstetrics and Prenatal Medicine (AGG) - Premature Birth Section
Prof. Dr. Franz Bahlmann	German Society for Ultrasound in Medicine V. (DEGUM)
Dr. Ivonne Bedei	DGGG - Arbeitsgemeinschaft Kinder- und Jugendgynäkologie e. V. (AGKJ)
Prof. Dr. Richard Berger	German Society for Gynecology and Obstetrics (DGGG)
Dr. Klaus Doubek	Professional Association of Gynecologists V. (BVF)
Prof. Dr. Ursula Felderhoff-Müser	Society for Neonatal and Pediatric Intensive Care Medicine (GNPI)
Prof. Dr. Herbert Fluhr	DGGG - Working Group for Immunology in Gynecology and Obstetrics (AGIM)
PD Dr. Dr. Yves Garnier	DGGG - Working Group for Obstetrics and Prenatal Medicine (AGG) - Premature Birth Section
Dr. Susanne Grylka-Baeschlin	German Society for Midwifery Studies (DGHWi)
Prof. Dr. Hanns Helmer	Austrian Society for Gynecology and Obstetrics (OEGGG)
Prof. Dr. Egbert Herting	German Society for Child and Adolescent Medicine (DGKJ)
Prof. Dr. Markus Hoopmann	DGGG - Working Group for Ultrasound Diagnostics in Gynecology and Obstetrics (ARGUS)
Prof. Dr. Irene Hösli	Swiss Society for Gynecology and Obstetrics (SGGG)
Prof. Dr. Dr. H. c. Udo Hoyme	DGGG - Working Group for Infections and Infection Immunology (AGII)
Alexandra Jendreizeck	Federal Association "The Premature Child"
Dr. Harald Krentel	DGGG - Working Group for Women's Health in Development Cooperation (FIDE)
PD Dr. Ruben Kuon	German Society for Gynecology and Obstetrics (DGGG)
Dr. Wolf Luetje	DGGG - German Society for Psychosomatic Gynecology and Obstetrics V. (DGPFG)
Silke Mader	European Foundation for the Care of the Newborn Infants (EFCNI)
PD Dr. Holger Maul	Deutsche Gesellschaft für Perinatale Medizin (DGPM)
Prof. Dr. Werner Mendling	DGGG – Arbeitsgemeinschaft für Infektionen und Infektionsimmunologie (AGII)
Barbara Mitschdörfer	Bundesverband „Das frühgeborene Kind“
Tatjana Nicin	Deutscher Hebammenverband (DHV)
Dr. Dirk Olbertz	Gesellschaft für neonatale und pädiatrische Intensivmedizin (GNPI)
Prof. Dr. Werner Rath	Deutsche Gesellschaft für Pränatal- und Geburtsmedizin (DGPGM)
Prof. Dr. Claudia Roll	Deutsche Gesellschaft für Perinatale Medizin (DGPM)
PD Dr. Dietmar Schlembach	DGGG – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Präeklampsie
Prof. Dr. Ekkehard Schleußner	DGGG – Deutsche Gesellschaft für psychosomatische Frauenheilkunde und Geburtshilfe e. V. (DGPFG)
Prof. Dr. Florian Schütz	DGGG – Arbeitsgemeinschaft für Immunologie in Gynäkologie und Geburtshilfe (AGIM)
Prof. Dr. Vanadin Seifert-Klauss	DGGG - German Society for Gynecological Endocrinology and Reproductive Medicine e. V. (DGGEF)

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Tab. 2 Graduation of recommendations.

Description of liability	Expression
strong recommendation with high commitment	should / shouldn't
simple recommendation with medium binding force	should should not
open recommendation with little commitment	can / can not

Tab. 3 Classification for approval of consensus formation.

symbolism	Strength of consensus	percentage agreement
+++	strong consensus	Approval from> 95% of participants
++	consensus	Approval from> 75 - 95% of the participants
+	majority approval	Approval by> 50 - 75% of the participants
-	no consensus	Agreement of <51% of the participants

Tab. 6 Classification for maternal fever and triple I *.

	definition
maternal fever	If the orally measured temperature is above 39.0 ° C, there is a maternal fever. If the temperature measured orally is between 38.0 and 38.9 ° C, it is repeated after 30 minutes.If the temperature is again above 38.0 ° C, there is maternal fever.
V. a. Triple I.	maternal fever of unknown origin and any of the following: • fetal tachycardia over 160 beats / min for> 10 min • maternal leukocytes> 15,000 µl without administration of corticosteroids • purulent fluorine from the cervix
confirmed triple I.	V. a. Triple I and objective findings of an infection, such as: amniotic fluid ** with positive Gram stain, low glucose concentration (<14 mg / dl), increased leukocyte count (> 30 cells / mm^3), positive bacterial culture or histopathological findings *** of an inflammation or Infection or both of the placenta, the membranes, or the umbilical cord (funisitis)

* Triple I: inflammation or infection or both; ** Amniotic fluid obtained by amniocentesis; *** Postpartum histopathology on placenta [116] .