Thieme

Prevention and Therapy of Preterm Birth. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry Number 015/025, February 2019) – Part 1 with Recommendations on the Epidemiology, Etiology, Prediction, Primary and Secondary Prevention of Preterm Birth

Prävention und Therapie der Frühgeburt. Leitlinie der DGGG, OEGGG und SGGG (S2k-Niveau, AWMF-Registernummer 015/025, Februar 2019) – Teil 1 mit Empfehlungen zur Epidemiologie, Ätiologie, Prädiktion, primären und sekundären Prävention der Frühgeburt

Authors

Richard Berger[1], Harald Abele[2], Franz Bahlmann[3], Ivonne Bedei[4], Klaus Doubek[5], Ursula Felderhoff-Müser[6], Herbert Fluhr[7], Yves Garnier[8], Susanne Grylka-Baeschlin[9], Hanns Helmer[10], Egbert Herting[11], Markus Hoopmann[2], Irene Hösli[12], Udo Hoyme[13], Alexandra Jendreizeck[14], Harald Krentel[15], Ruben Kuon[16], Wolf Lütje[17], Silke Mader[18], Holger Maul[19], Werner Mendling[20], Barbara Mitschdörfer[14], Tatjana Nicin[21], Monika Nothacker[22], Dirk Olbertz[23], Werner Rath[24], Claudia Roll[25], Dietmar Schlembach[26], Ekkehard Schleußner[27], Florian Schütz[16], Vanadin Seifert-Klauss[28], Susanne Steppat[29], Daniel Surbek[30]

Affiliations

1 Frauenklinik, Marienhaus Klinikum Neuwied, Neuwied, Germany
2 Frauenklinik, Universitätsklinikum Tübingen, Tübingen, Germany
3 Frauenklinik, Bürgerhospital Frankfurt, Frankfurt am Main, Germany
4 Frauenklinik, Klinikum Frankfurt Höchst, Frankfurt am Main, Germany
5 Frauenarztpraxis, Wiesbaden, Germany
6 Klinik für Kinderheilkunde I/Perinatalzentrum, Universitätsklinikum Essen, Universität Duisburg-Essen, Essen, Germany
7 Frauenklinik, Universitätsklinikum Heidelberg, Heidelberg, Germany
8 Frauenklinik, Klinikum Osnabrück, Osnabrück, Germany
9 Zürcher Hochschule für angewandte Wissenschaften, Institut für Hebammen, Zürich, Switzerland
10 Universitätsklinik für Frauenheilkunde, Medizinische Universität Wien, Wien, Austria
11 Klinik für Kinder- und Jugendmedizin, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Lübeck, Germany
12 Frauenklinik, Universitätsspital Basel, Basel, Switzerland
13 Frauenklinik, Ilm-Kreis-Kliniken, Arnstadt, Germany
14 Bundesverband das frühgeborene Kind, Germany
15 Frauenklinik, Annahospital Herne, Elisabethgruppe Katholische Kliniken Rhein Ruhr, Herne, Germany
16 Frauenklinik, Universitätsklinikum Heidelberg, Heidelberg, Germany
17 Frauenklinik, Evangelisches Amalie Sieveking-Krankenhaus Hamburg, Hamburg, Germany
18 European Foundation for the Care of the Newborn Infant
19 Frauenklinik, Asklepios Kliniken Hamburg, Hamburg, Germany
20 Deutsches Zentrum für Infektionen in Gynäkologie und Geburtshilfe an der Frauenklinik, Helios Universitätsklinikum Wuppertal, Wuppertal, Germany
21 Frauenklinik, Klinikum Hanau, Hanau, Germany
22 Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, Berlin, Germany
23 Abteilung Neonatologie und neonatologische Intensivmedizin, Klinikum Südstadt Rostock, Rostock, Germany
24 Emeritus, Universitätsklinikum Aachen, Aachen, Germany
25 Vestische Kinder- und Jugendklinik Datteln, Universität Witten/Herdecke, Datteln, Germany
26 Klinik für Geburtsmedizin, Klinikum Neukölln/Berlin Vivantes Netzwerk für Gesundheit, Berlin, Germany
27 Klinik für Geburtsmedizin, Universitätsklinikum Jena, Jena, Germany
28 Frauenklinik, Universitätsklinikum rechts der Isar München, München, Germany
29 Deutscher Hebammenverband, Germany
30 Universitäts-Frauenklinik, Inselspital, Universität Bern, Bern, Switzerland

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

Schlüsselwörter
Frühgeburt, vorzeitige Wehentätigkeit, Zervixinsuffizienz, früher vorzeitiger Blasensprung

received 30.4.2019
accepted 30.4.2019

Bibliography
DOI https://doi.org/10.1055/a-0903-2671
Geburtsh Frauenheilk 2019; 79: 800–812 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0016-5751

Correspondence
Prof. Dr. med. Richard Berger
Marienhaus Klinikum St. Elisabeth, Akademisches Lehrkrankenhaus der Universitäten Mainz und Maastricht, Klinik für Gynäkologie und Geburtshilfe
Friedrich-Ebert-Straße 59, 56564 Neuwied, Germany
richard.berger@marienhaus.de

Deutsche Version unter:
https://doi.org/10.1055/a-0903-2671

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 recent scientific literature, the experience of the members of the guideline commission and the views of self-help groups.
Methods Based on the international literature, the members of the participating medical societies and organizations developed Recommendations and Statements. These were adopted following a formal process (structured consensus conference with neutral moderation, voting was done in writing using the Delphi method to achieve consensus).
Recommendations Part I of this short version of the guideline lists Statements and Recommendations on the epidemiology, etiology, prediction and primary and secondary prevention of preterm birth.

ZUSAMMENFASSUNG

Ziel Offizielle Leitlinie der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (DGGG), der Österreichischen Gesellschaft für Gynäkologie und Geburtshilfe (ÖGGG) und der Schweizerischen Gesellschaft für Gynäkologie und Geburtshilfe (SGGG). Ziel der Leitlinie ist es, die Prädiktion, die Prävention und das Management der Frühgeburt anhand der aktuellen Literatur, der Erfahrung der Mitglieder der Leitlinienkommission einschließlich der Sicht der Selbsthilfe evidenzbasiert zu verbessern.
Methoden Anhand der internationalen Literatur entwickelten die Mitglieder der beteiligten Fachgesellschaften und Organisationen Empfehlungen und Statements. Diese wurden in einem formalen Prozess (strukturierte Konsensuskonferenzen mit neutraler Moderation, schriftliche Delphi-Abstimmung) verabschiedet.
Empfehlungen Der Teil I dieser Kurzversion der Leitlinie zeigt Statements und Empfehlungen zur Epidemiologie, Ätiologie, der Prädiktion sowie der primären und sekundären Prävention der Frühgeburt.

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 1 with Recommendations on the Epidemiology, Etiology, Prediction, Primary and Secondary Prevention of Preterm Birth. Geburtsh Frauenheilk 2019; 79: 800–812

Guideline documents

The complete long version, a slide version of this guideline 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)

▸ **Table 1** The following medical societies/working groups/organizations/associations were interested in participating in the compilation of the guideline text and in the consensus conference and nominated representatives who attended the consensus conference.

Author Mandate holder	DGGG working group (AG)/AWMF/ non-AWMF medical society/organization/association
Prof. Dr. Harald Abele	DGGG – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Frühgeburt
Prof. Dr. Franz Bahlmann	Deutsche Gesellschaft für Ultraschall in der Medizin e. V. (DEGUM)
Dr. Ivonne Bedei	DGGG – Arbeitsgemeinschaft Kinder- und Jugendgynäkologie e. V. (AGKJ)
Prof. Dr. Richard Berger	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Dr. Klaus Doubek	Berufsverband der Frauenärzte e. V. (BVF)
Prof. Dr. Ursula Felderhoff-Müser	Gesellschaft für neonatale und pädiatrische Intensivmedizin (GNPI)
Prof. Dr. Herbert Fluhr	DGGG – Arbeitsgemeinschaft für Immunologie in Gynäkologie und Geburtshilfe (AGIM)
PD Dr. Dr. Yves Garnier	DGGG – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Frühgeburt
Dr. Susanne Grylka-Baeschlin	Deutsche Gesellschaft für Hebammenwissenschaften (DGHWi)
Prof. Dr. Hanns Helmer	Österreichische Gesellschaft für Gynäkologie und Geburtshilfe (OEGGG)
Prof. Dr. Egbert Herting	Deutsche Gesellschaft für Kinder- und Jugendmedizin (DGKJ)
Prof. Dr. Markus Hoopmann	DGGG – Arbeitsgemeinschaft für Ultraschalldiagnostik in Gynäkologie und Geburtshilfe (ARGUS)
Prof. Dr. Irene Hösli	Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)
Prof. Dr. Dr. h. c. Udo Hoyme	DGGG – Arbeitsgemeinschaft für Infektionen und Infektionsimmunologie (AGII)
Alexandra Jendreizeck	Bundesverband “Das frühgeborene Kind” [Federal Association “The preterm Infant”]
Dr. Harald Krentel	DGGG – Arbeitsgemeinschaft für Frauengesundheit in der Entwicklungszusammenarbeit (FIDE)
PD Dr. Ruben Kuon	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Dr. Wolf Lütje	DGGG – Deutsche Gesellschaft für psychosomatische Frauenheilkunde und Geburtshilfe e. 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 Infant”]
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 – Deutsche Gesellschaft für Gynäkologische Endokrinologie und Fortpflanzungsmedizin e. V. (DGGEF)
Susanne Steppat	Deutscher Hebammenverband (DHV)
Prof. Dr. Daniel Surbek	Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)

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	peri-/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

The purpose of this guideline is to improve both the outpatient and the inpatient care of patients at risk of imminent 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 the 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 (e.g. 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 by 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 if urgently required. If the guideline continues to mirror current knowledge, its period of validity may also be extended.

III Method

Basic principles

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

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

▶ **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

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 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 analyses, medical and ethical practice in 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 und 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**).

▶ **Table 3** Grading of strength of consenus.

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

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", i.e., purely semantically ("must"/"must not" or "should"/"should not" or "may"/"may not") without the use of symbols.

Addendum by the SGGG

To 1. Definition and epidemiology (and a number of 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 [1].

To 3.2.3 Indications for measuring cervical length

In individual cases, an examination can also be carried out in asymptomatic women. This is described in the chapter "Asymptomatic patients" below as follows: "Measurement of cervical length using transvaginal sonography may be carried out in asymptomatic pregnant women with no risk factors for spontaneous preterm birth." *Reasoning:* Emphasizing this circumstance is important in Switzerland, because in many places in Switzerland, transvaginal sonographic measurement is done as part of standard second trimester screening.

IV Guideline

1 Definition

Consensus-based Statement 1.S1	
Expert consensus	**Strength of consensus +++**
Preterm birth is defined as delivery prior to GW 37 + 0. It has a significant effect on perinatal morbidity and mortality.	

Preterm birth is defined as a birth which occurs before the end of the 37th week of gestation. The consensus about what constitutes the limit of viability varies according to country and culture. For Germany, please refer to the German-language guideline "Frühgeborene an der Grenze der Lebensfähigkeit 024-019" [Preterm infants at the limits of viability]. Preterm birth has a significant effect on perinatal morbidity and mortality. Every year, approximately 965 000 preterm infants die worldwide in the neonatal period, and a further 125 000 children die in the first 5 years of life from the effects of preterm birth. Preterm birth is one of the main risk factors for disability-adjusted life years (lost years due to illness, disability or early death) [2].

Consensus-based Statement 1.S2	
Expert consensus	**Strength of consensus +++**
In 2017, the rate of preterm births in Germany was 8.36 %. This means that Germany ranks quite low compared to other European countries.	

The preterm birth rate for infants born before 37 weeks is more than 8 % and has remained approximately the same in Germany since 2008 [3]. This means that Germany ranks quite low compared to other European countries [4]. The rate of preterm births occurring before the 37th week of gestation was 7.9 % in Austria in 2016 [5] and 7.0 % in Switzerland in 2017 [6]. The highest rate of preterm births in Europe is reported for Cyprus where it stands at 10.4 %; the lowest rate of preterm births is in Iceland with a rate of 5.3 % [4].

The reasons for these differences are ultimately still not clear. As already mentioned, the lower limit of viability for extremely preterm infants is defined and recorded very differently in different countries. It is possible that different standards of medical care also play a role. In Portugal, for example, a structural reform carried out in 1989 during which all departments with fewer than 1500 births were closed down led to a significant decrease in the mortality of preterm infants. However, the rate of preterm births increased in subsequent years. It cannot be excluded that the improvement in healthcare led to the survival of more children, who were then recorded in the register of preterm births and who would otherwise not have been recorded in that way [4].

2 Etiology

Consensus-based Statement 2.S3	
Expert consensus	**Strength of consensus +++**
Around two thirds of all preterm births occur due to premature labor with or without premature rupture of membranes (spontaneous preterm births).	

Consensus-based Statement 2.S4	
Expert consensus	**Strength of consensus +++**
The etiology of preterm birth is multifactorial. Different pathophysiological mechanisms activate a common pathway which manifests clinically as premature labor and cervical dilation.	

Consensus-based Statement 2.S5	
Expert consensus	**Strength of consensus +++**
Preterm birth may be associated with bacterial inflammation, decidual bleeding, vascular disease, decidual senescence, impaired maternofetal immune tolerance, "functional" progesterone withdrawal or overstretching of the myometrium.	
[7]	

3 Prediction

3.1 Risk factors (▶ **Table 4**)

Consensus-based Recommendation 3.E1	
Expert consensus	**Strength of consensus +++**
Potential risk factors must be determined prior to conception or at the start of prenatal care at the latest. The particular focus must be on risk factors which can be controlled. The intervals between examinations must be adjusted to take account of the individual risk of preterm birth to implement preventive strategies.	

▶ **Table 4** Risk factors for preterm birth.

Risk factor	OR	95% CI
s/p spontaneous preterm birth	3.6	3.2–4.0
s/p medically indicated preterm birth	1.6	1.3–2.1
s/p conization	1.7	1.24–2.35
Interval between pregnancies is < 12 months	4.2	3.0–6.0
Pregnant woman is younger < 18 years	1.7	1.02–3.08
Poor socioeconomic living conditions	1.75	1.65–1.86
Single mother	1.61	1.26–2.07
Bacterial vaginosis	1.4	1.1–1.8
Asymptomatic bacteriuria	1.5	1.2–1.9
Vaginal bleeding in early pregnancy	2.0	1.7–2.3
Vaginal bleeding in late pregnancy	5.9	5.1–6.9
Twin pregnancy	ca. 6	
Smoking	1.7	1.3–2.2
Periodontitis	2.0	1.2–3.2
Anemia	1.5	1.1–2.2

[3, 8 – 13]

3.2 Cervical length

3.2.1 Measurement technique

Consensus-based Recommendation 3.E2	
Expert consensus	**Strength of consensus +++**
When using transvaginal sonography to measure cervical length to predict preterm birth, the measurement technique must be precisely adhered to.	

The approach used to standardize the measurement technique as far as possible has been described previously in detail by Kagan and Sonek [14].

3.2.2 Normal and shortened uterine cervix

Consensus-based Statement 3.S6	
Expert consensus	**Strength of consensus +++**
In singleton pregnancies, the median cervical length prior to the 22nd week of gestation (GW) as measured by transvaginal sonography is > 40 mm; between GW 22 and 32 it is 40 mm, and after GW 32 it is approximately 35 mm.	
[15]	

Consensus-based Statement 3.S7	
Expert consensus	**Strength of consensus +++**
A cervical length of ≤ 25 mm as measured by transvaginal sonography before GW 34 + 0 is considered to be shortened.	
[16]	

3.2.3 Indications for measuring cervical length

Consensus-based Recommendation 3.E3	
Expert consensus	**Strength of consensus +++**
A general screening with transvaginal sonography to investigate for shortened cervical length should not be carried out in asymptomatic pregnant women with no risk factors for spontaneous preterm birth.	

According to a single large cohort study, universal screening of singleton pregnancies in women without a previous history of preterm birth is associated with a small but significant decrease in the rates of preterm births before 37 weeks, before 34 weeks and before 32 weeks (preterm birth < GW 37: 6.7 vs. 6.0%; adjusted odds ratio [AOR] 0.82 [95% CI: 0.76–0.88]; preterm birth < GW 34: 1.9 vs. 1.7%; AOR 0.74 [95% CI: 0.64–0.85]; preterm birth < GW 32: 1.1 vs. 1.0%; AOR 0.74 [95% CI: 0.62–0.90]) [17]. Whether this study will result in any changes to the Cochrane review done in 2013 which concluded that routine screening to determine cervical length in all (asymptomatic and even symptomatic) pregnant women should not be recommended because knowledge of the cervical length only resulted in a non-significant reduction in the rate of preterm births before 37 weeks [18] remains to be seen, but it is highly unlikely. The fact is that there are no data available which can confirm the impact of measuring cervical length on the parameters considered in the perinatology literature to have a significant impact on perinatal mortality. At all events, insofar as there were any data available, the Cochrane review of 2013 was unable to find any differences with respect to the parameters 'perinatal mortality', 'preterm birth before the 34th or 28th week of gestation', 'birth weight < 2500 g', 'maternal hospitalization', 'tocolytics', 'antenatal steroid administration' [18].

Consensus-based Recommendation 3.E4	
Expert consensus	**Strength of consensus +++**
Measurement of cervical length using transvaginal sonography should be included in the therapeutic concept of symptomatic pregnant women (regular spontaneous premature contractions) and/or in pregnant women with risk factors for spontaneous preterm birth.	

Consensus-based Statement 3.S8	
Expert consensus	**Strength of consensus ++**
The benefit of carrying out serial measurements of cervical length using transvaginal sonography has not been sufficiently proven for either asymptomatic or symptomatic pregnant women.	
[19 – 23]	

Asymptomatic patients

Consensus-based Recommendation 3.E5	
Expert consensus	**Strength of consensus ++**
Measurement of cervical length using transvaginal sonography may be carried out in asymptomatic pregnant women with no risk factors for spontaneous preterm birth.	

Consensus-based Recommendation 3.E6	
Expert consensus	**Strength of consensus ++**
Measurement of cervical length using transvaginal sonography should be carried out from GW 16 in asymptomatic pregnant women with a singleton pregnancy and a prior history of spontaneous preterm birth.	
[24, 25]	

Consensus-based Recommendation 3.E7	
Expert consensus	**Strength of consensus +++**
Measurement of cervical length using transvaginal sonography may be carried out from GW 16 in asymptomatic pregnant women with a twin pregnancy.	
[26 – 29]	

Symptomatic patients

Consensus-based Recommendation 3.E8	
Expert consensus	**Strength of consensus +++**
Measurement of cervical length using transvaginal sonography must be carried out in symptomatic women (contractions, start of cervical shortening or opening of the cervix based on palpatory findings).	
[30 – 33]	

3.3 Biomarkers

Consensus-based Statement 3.S9	
Expert consensus	**Strength of consensus +++**
None of the currently available biomarkers are suitable to predict the risk of preterm birth in asymptomatic pregnant women with no cervical shortening as determined by the measurement of cervical length using transvaginal ultrasonography.	
[34]	

Consensus-based Statement 3.S10	
Expert consensus	**Strength of consensus +++**
In addition to using vaginal sonography to measure cervical length, the negative predictive value* of biomarkers obtained from cervico-vaginal secretions may be used in symptomatic pregnant women with a cervical length of between 15 and 30 mm to evaluate the risk of preterm birth occurring in the next 7 days.	
* negative predictive value [35 – 40]	

Consensus-based Recommendation 3.E9	
Expert consensus	**Strength of consensus +++**
Biomarkers should not be used to evaluate the risk of preterm birth in asymptomatic pregnant women with risk factors for preterm birth.	
[41]	

Consensus-based Recommendation 3.E10	
Expert consensus	**Strength of consensus +++**
Biomarkers must not be used to evaluate the risk of preterm birth in asymptomatic pregnant women with no risk factors for preterm birth.	
[42]	

4 Primary Prevention

4.1 Progesterone

Consensus-based Recommendation 4.E11	
Expert consensus	**Strength of consensus ++**
Progesterone may be administered to women with a singleton pregnancy and a history of previous spontaneous preterm birth, starting in GW 16 + 0 and continuing up until GW 36 + 0.	
[43 – 47]	

Dosage: 17-OHPC (17 α-hydroxyprogesterone caproate) with a weekly dose of 250 mg [43]. In the studies, progesterone was administered either orally (200–400 mg daily) or vaginally (90 mg gel, 100–200 mg capsule daily) [44, 45, 48 – 50].

4.2 Cerclage/total cervical occlusion

Consensus-based Recommendation 4.E12	
Expert consensus	**Strength of consensus +++**
Primary (prophylactic) cerclage may be considered for women with a singleton pregnancy and a history of previous spontaneous preterm birth or late miscarriage(s). The procedure should be carried out from early in the 2nd trimester of pregnancy.	

There is no longer any doubt that secondary cerclage in women who are s/p preterm birth and have a shortened cervical length of ≤ 25 mm before GW 24 + 0 is beneficial. When counseling patients who are s/p preterm birth, patients often also ask whether early placement of cerclage before the start of cervical shortening could be effective. No disadvantages have been reported for this approach compared to secondary cerclage in terms of either the prevalence of preterm birth or perinatal mortality [51]. However, a wait-and-see approach can reduce the number of surgical procedures by 58 %.

Consensus-based Statement 4.S11	
Expert consensus	**Strength of consensus +++**
There is some evidence that total cervical occlusion (TCO) may reduce the rate of preterm births in women with a singleton pregnancy and a history of previous spontaneous preterm birth or late miscarriage(s). The procedure should be carried out early in the 2nd trimester of pregnancy.	

An article published in 1996 discussed outcomes after TCO as reported by 11 German hospitals [52]. These retrospective studies found a significant prolongation of pregnancy after TCO for women who were s/p preterm birth. To date, there are no randomized, prospective studies which confirm the benefit of TCO in women with cervical shortening and a cervical length of less than 15 mm. The surgical technique used for TCO differs quite considerably in the various international centers, making it difficult to compare outcomes.

4.3 Bacterial vaginosis

Consensus-based Statement 4.S12	
Expert consensus	**Strength of consensus +++**
A vaginal flora with normal pH values and dominated by Lactobacillus species has a protective effect on the course of pregnancy in terms of preterm birth or late miscarriage.	

Consensus-based Recommendation 4.E13	
Expert consensus	**Strength of consensus +++**
Pregnant women with symptomatic bacterial vaginosis should be treated with antibiotics to deal with their symptoms.	

Consensus-based Statement 4.S13	
Expert consensus	**Strength of consensus ++**
A diagnostic workup (which includes investigation of surrogate parameters such as vaginal pH values) to detect asymptomatic and symptomatic bacterial vaginosis followed by treatment of bacterial vaginosis does not generally reduce the rate of preterm births.	

Consensus-based Statement 4.S14	
Expert consensus	**Strength of consensus +++**
There is some evidence that the diagnosis and treatment of asymptomatic and symptomatic bacterial vaginosis prior to GW 23 + 0 GW reduces the rate of preterm births which occur before GW 37 + 0.	

Numerous meta-analyses of case control and cohort studies have proven that there is an association between infections of the genital tract and the occurrence of preterm births [53, 54]. However, there is still no clear evidence that treatment of an infection, particularly if it is still subclinical, reduces the preterm birth rate [53, 55]. To date, there is only a single study [56] in which pregnant women were screened by Gram stain for bacterial vaginosis at the beginning of their 2nd trimester of pregnancy. The women were randomized into an intervention group and a control group, with the test results either communicated to the woman's clinician (in the intervention group) or not revealed. The women in the intervention group were subsequently treated (with clindamycin if the test results revealed bacterial vaginosis). In the intervention arm of the study, the preterm birth rate before 37 weeks was 3.0 % compared to 5.3 % in the control arm; the difference between the two groups was thus significantly different. This study is currently the only one which was included in the Cochrane review of this highly relevant topic, and its findings therefore affect the outcome of the review. The revision of the review published in 2015 [57] states: "There is evidence from one trial that infection screening and treatment programs for pregnant women before 20 weeks' gestation reduce preterm birth and preterm low birthweight."

The results of the PREMEVA trial were recently published [58]. More than 84 000 pregnant women were screened for bacterial vaginosis before the end of their 14th week of gestation. Bacterial vaginosis, defined as a Nugent Score of 7–10, was detected in 5360 pregnant women. Pregnant women with bacterial vaginosis but a low risk of preterm birth were then randomized 2 : 1 into 3 groups as follows: single course (n = 943) or three courses (n = 968) of 300 mg clindamycin administered 2 × daily for 4 days or placebo (n = 958). Women with a high risk of preterm birth were randomized separately 1 : 1 into 2 groups: single course (n = 122) or three courses (n = 114) of 300 mg clindamycin 2 × daily. The primary outcome was late miscarriage, defined as occurring between the 16th and the 21st week of gestation, or very early preterm birth, defined occurring as between the 22nd and the 32nd week of gestation.

In the group of 2869 pregnant women with a low risk of preterm birth, 22 women (1.2 %) in the clindamycin group and 10 women (1.0 %) in the placebo group had a late miscarriage or

a very early preterm birth (RR 1.10, 95% CI: 0.53–2.32; p = 0.82). In the group of 236 pregnant with a high risk of preterm birth, 5 women (4.4%) in the group treated with 3 courses of clindamycin and 8 women (6.0%) in the group treated with one course of clindamycin had a late miscarriage or a very early preterm birth (RR 0.67, 95% CI: 0.23–2.00; p = 0.47). Side effects were noted significantly more often in the group of pregnant women with a low risk of preterm birth in the clindamycin groups compared to the placebo group (58/1904 [3.0%] compared to 12/956 [1.3%]; p = 0.0035). The most common side effects were diarrhea and abdominal pain.

The authors concluded from their results that screening for bacterial vaginosis and treatment with clindamycin, when required, does not reduce the risk of late miscarriage or very early preterm birth in patients with a low risk of preterm birth.

4.4 Prevention programs

Consensus-based Statement 4.S15	
Expert consensus	**Strength of consensus +++**
The efficacy of multimodal prevention programs and risk scoring systems has not been sufficiently proven.	
[59]	

4.5 Cessation of smoking

Consensus-based Statement 4.S16	
Expert consensus	**Strength of consensus +++**
Stopping smoking reduces the preterm birth rate.	
[60, 61]	

4.6 Asymptomatic bacteriuria

Consensus-based Statement 4.S17	
Expert consensus	**Strength of consensus +++**
Asymptomatic bacteriuria is a significant risk factor for preterm birth. Because of the lack of data, screening for the sole purpose of reducing the preterm birth rate is not currently recommended.	

Consensus-based Recommendation 4.E14	
Expert consensus	**Strength of consensus +++**
Because of the lack of data, it is not possible to issue a recommendation that antibiotic treatment of asymptomatic bacteriuria reduces the rate of preterm births.	

In its final report on screening for asymptomatic bacteriuria published in 2015, the IQWIG came to the following conclusion [62]: The patient-relevant medical benefit or harm of screening for asymptomatic bacteriuria in pregnant women is not clear due to a lack of studies. There is no evidence that antibiotic treatment of pregnant women for asymptomatic bacteriuria has any patient-relevant medical benefit or harm, as the existing data is unsuitable with regard to the current standard of care for pregnant women.

4.7 Supplementation with omega-3 polyunsaturated fatty acids

Consensus-based Statement 4.S18	
Expert consensus	**Strength of consensus +++**
The data from studies on reducing preterm birth rates through dietary supplementation with omega-3 polyunsaturated fatty acids (omega-3 PUFA) is inconsistent. Supplementation with omega-3 PUFA may be considered for women with a history of spontaneous preterm birth.	

A Cochrane Review carried out in 2006 showed that pregnant women whose diet included higher levels of marine oil had a mean gestation that was 2.6 days longer compared to pregnant women without marine oil supplementation and women given placebo, and that women with marine oil supplementation had a significantly lower risk of preterm birth before 34 + 0 weeks of gestation (RR 0.69, 95% CI: 0.49–0.99) [63]. These findings were confirmed in a recently published update [64].

5 Secondary Prevention

5.1 Progesterone

Consensus-based Recommendation 5.E15	
Expert consensus	**Strength of consensus +++**
Women with a singleton pregnancy and a sonographically measured cervical length before 24 + 0 weeks of ≤ 25 mm must be treated with daily intravaginal administration of progesterone up until 36 + 6 weeks of gestation (200 mg capsule/day or 90 mg gel/day).	

An individual patient data meta-analysis (IPDMA) carried out in 2018, which included data from the OPPTIMUM trial [44], found that intravaginal administration of progesterone resulted in a significant reduction in the rate of preterm births and improved neonatal outcomes for pregnant women with asymptomatic cervical shortening (≤ 25 mm) before 24 + 0 weeks of gestation [65].

5.2 Cerclage

Consensus-based Recommendation 5.E16	
Expert consensus	**Strength of consensus +++**
Women with a singleton pregnancy following a previous spontaneous preterm birth or late miscarriage and whose sonographically measured cervical length before 24 + 0 weeks of gestation is ≤ 25 mm, should be treated with cerclage.	

A meta-analysis of the 5 prospective randomized studies on this topic showed that the preterm birth rate of patients who had had a previous preterm birth and had an incompetent cervix measuring less than 25 mm before 24 weeks of gestation was significantly reduced by the placement of a cerclage. Moreover – and

this is particularly clinically relevant – placement of the cerclage also significantly reduced perinatal mortality and morbidity [66].

5.3 Cervical pessary

Consensus-based Recommendation 5.E17	
Expert consensus	**Strength of consensus ++**
Women with a singleton pregnancy whose sonographically measured cervical length before 24 + 0 weeks of gestation is ≤ 25 mm may benefit from placement of a cervical pessary.	

A number of prospective randomized studies have been carried out to evaluate the benefit of cervical pessary placement in women with singleton pregnancies whose cervical length before 24 + 0 weeks of gestation was less than 25 mm as measured by transvaginal sonography. The results of these prospective studies have differed considerably. Some studies reported a significant reduction in the rate of preterm births following placement of a cervical pessary [67 – 69], other studies did not [70 – 73]. Cervical pessary placement is a procedure with an extremely low rate of complications. Increased vaginal discharge following the procedure is quite common, but this has no pathological significance. In view of the above, placement of a cervical pessary may be considered in individual cases for women with singleton pregnancies whose cervical length before 24 + 0 weeks of gestation is ≤ 25 mm.

5.4 Workload and physical activity

Consensus-based Statement 5.S19	
Expert consensus	**Strength of consensus +++**
Prolonged working hours, shift work, standing every day for more than 6 hours, heavy lifting and heavy physical labor done by working pregnant women are associated with little, if any, significant adverse effects on preterm birth. Employers must evaluate the individual risk for the pregnant woman according to the respective situation and must consider whether the activities she carries out as part of her workload constitute an unjustifiable risk. An additional individual medical consultation which takes account of other risk factors and obstetric complications would be useful.	
[74]	

Consensus-based Statement 5.S20	
Expert consensus	**Strength of consensus +++**
The data on whether pregnant women at risk for preterm birth and pregnant women not at risk for preterm birth should avoid strenuous physical activities at home is insufficient to draw reliable conclusions.	

Conflict of Interest

The conflict of interest statements of all the authors are available in the long version of the guideline.

References

[1] Swiss-Paediatrics. Perinatale Betreuung an der Grenze der Lebensfähigkeit zwischen 22 und 26 vollendeten Schwangerschaftswochen. Online: http://www.swiss-paediatrics.org/sites/default/files/paediatrica/vol23/n1/pdf/10-12_0.pdf; last access: 28.04.2019

[2] Murray CJ, Vos T, Lozano R et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2197–2223

[3] IQTIG. Bundesauswertung zum Erfassungsjahr 2017 – Geburtshilfe Qualitätsindikatoren. Online: https://iqtig.org/downloads/auswertung/2017/16n1gebh/QSKH_16n1-GEBH_2017_BUAW_V02_2018-08-01.pdf; last access: 28.04.2019

[4] Zeitlin J, Mohangoo A, Delnord M, report editors. The European Health Report 2010. Online: http://www.europeristat.com/reports/european-perinatal-health-report-2010.html; last access: 28.04.2019

[5] Institut für klinische Epidemiologie der Tirol Kliniken GmbH. Bericht Geburtenregister Östereich, Geburtsjahr 2016. Online: https://www.iet.at/data.cfm?vpath=publikationen210/groe/groe-jahresbericht-2016; last access: 28.04.2019

[6] Bundesamt für Statistik. Gesundheit der Neugeborenen. Online: https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/gesundheitszustand/gesundheit-neugeborenen.html; last access: 28.04.2019

[7] Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. Science 2014; 345: 760–765

[8] Hillier SL, Nugent RP, Eschenbach DA et al. Association between bacterial vaginosis and preterm delivery of a low-birth-weight infant. The Vaginal Infections and Prematurity Study Group. N Engl J Med 1995; 333: 1737–1742

[9] Meis PJ, Michielutte R, Peters TJ et al. Factors associated with preterm birth in Cardiff, Wales. II. Indicated and spontaneous preterm birth. Am J Obstet Gynecol 1995; 173: 597–602

[10] Murphy DJ. Epidemiology and environmental factors in preterm labour. Best Pract Res Clin Obstet Gynaecol 2007; 21: 773–789

[11] Yi SW, Han YJ, Ohrr H. Anemia before pregnancy and risk of preterm birth, low birth weight and small-for-gestational-age birth in Korean women. Eur J Clin Nutr 2013; 67: 337–342

[12] Schummers L, Hutcheon JA, Hernandez-Diaz S et al. Association of Short Interpregnancy Interval With Pregnancy Outcomes According to Maternal Age. JAMA Intern Med 2018; 178: 1661–1670

[13] Wetzka S, Gallwas J, Hasbargen U et al. Einfluss von Konisation auf die Frühgeburtenrate und das perinatale Outcome: Eine retrospektive Analyse der Daten zur externen stationären Qualitätssicherung für die Erfassungsjahre 2009–2014. Geburtsh Frauenheilk 2018. doi:10.1055/s-0038-1671476

[14] Kagan KO, Sonek J. How to measure cervical length. Ultrasound Obstet Gynecol 2015; 45: 358–362

[15] Salomon LJ, Diaz-Garcia C, Bernard JP et al. Reference range for cervical length throughout pregnancy: non-parametric LMS-based model applied to a large sample. Ultrasound Obstet Gynecol 2009; 33: 459–464

[16] Iams JD, Goldenberg RL, Meis PJ et al. The length of the cervix and the risk of spontaneous premature delivery. National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. N Engl J Med 1996; 334: 567–572

[17] Son M, Grobman WA, Ayala NK et al. A universal mid-trimester transvaginal cervical length screening program and its associated reduced preterm birth rate. Am J Obstet Gynecol 2016; 214: 365.e1–365.e5

[18] Berghella V, Baxter JK, Hendrix NW. Cervical assessment by ultrasound for preventing preterm delivery. Cochrane Database Syst Rev 2013; (1): CD007235

[19] Berghella V, Talucci M, Desai A. Does transvaginal sonographic measurement of cervical length before 14 weeks predict preterm delivery in high-risk pregnancies? Ultrasound Obstet Gynecol 2003; 21: 140–144

[20] Owen J, Yost N, Berghella V et al. Can shortened midtrimester cervical length predict very early spontaneous preterm birth? Am J Obstet Gynecol 2004; 191: 298–303

[21] Fox NS, Jean-Pierre C, Predanic M et al. Short cervix: is a follow-up measurement useful? Ultrasound Obstet Gynecol 2007; 29: 44–46

[22] Dilek TU, Yazici G, Gurbuz A et al. Progressive cervical length changes versus single cervical length measurement by transvaginal ultrasound for prediction of preterm delivery. Gynecol Obstet Invest 2007; 64: 175–179

[23] Crane JM, Hutchens D. Follow-up cervical length in asymptomatic high-risk women and the risk of spontaneous preterm birth. J Perinatol 2011; 31: 318–323

[24] Owen J, Yost N, Berghella V et al. Mid-trimester endovaginal sonography in women at high risk for spontaneous preterm birth. JAMA 2001; 286: 1340–1348

[25] Owen J, Hankins G, Iams JD et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol 2009; 201: 375.e1–375.e8

[26] Conde-Agudelo A, Romero R, Hassan SS et al. Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and metaanalysis. Am J Obstet Gynecol 2010; 203: 128.e1–128.e12

[27] Lim AC, Hegeman MA, Huis In 'T Veld MA et al. Cervical length measurement for the prediction of preterm birth in multiple pregnancies: a systematic review and bivariate meta-analysis. Ultrasound Obstet Gynecol 2011; 38: 10–17

[28] Romero R, Conde-Agudelo A, El-Refaie W et al. Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data. Ultrasound Obstet Gynecol 2017; 49: 303–314

[29] van 't Hooft J, van der Lee JH, Opmeer BC et al. Pessary for prevention of preterm birth in twin pregnancy with short cervix: 3-year follow-up study. Ultrasound Obstet Gynecol 2018; 51: 621–628

[30] Berghella V, Palacio M, Ness A et al. Cervical length screening for prevention of preterm birth in singleton pregnancy with threatened preterm labor: systematic review and meta-analysis of randomized controlled trials using individual patient-level data. Ultrasound Obstet Gynecol 2017; 49: 322–329

[31] Ness A, Visintine J, Ricci E et al. Does knowledge of cervical length and fetal fibronectin affect management of women with threatened preterm labor? A randomized trial. Am J Obstet Gynecol 2007; 197: 426.e1–426.e7

[32] Palacio M, Sánchez M, Cobo T et al. Cervical length measurement to reduce length of stay in patients admitted because of pretermlabor. Prospective and randomized trial. Final results. Ultrasound Obstet Gynecol 2006; 28: 485

[33] Alfirevic Z, Allen-Coward H, Molina F et al. Targeted therapy for threatened preterm labor based on sonographic measurement of the cervical length: a randomized controlled trial. Ultrasound Obstet Gynecol 2007; 29: 47–50

[34] Conde-Agudelo A, Papageorghiou AT, Kennedy SH et al. Novel biomarkers for the prediction of the spontaneous preterm birth phenotype: a systematic review and meta-analysis. BJOG 2011; 118: 1042–1054

[35] Melchor JC, Khalil A, Wing D et al. Prediction of preterm delivery in symptomatic women using PAMG-1, fetal fibronectin and phIGFBP-1 tests: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2018; 52: 442–451

[36] Deshpande SN, van Asselt AD, Tomini F et al. Rapid fetal fibronectin testing to predict preterm birth in women with symptoms of premature labour: a systematic review and cost analysis. Health Technol Assess 2013; 17: 1–138

[37] Abbott DS, Radford SK, Seed PT et al. Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. Am J Obstet Gynecol 2013; 208: 122.e1–122.e6

[38] Kuhrt K, Unwin C, Hezelgrave N et al. Endocervical and high vaginal quantitative fetal fibronectin in predicting preterm birth. J Matern Fetal Neonatal Med 2014; 27: 1576–1579

[39] Kuhrt K, Hezelgrave N, Foster C et al. Development and validation of a tool incorporating quantitative fetal fibronectin to predict spontaneous preterm birth in symptomatic women. Ultrasound Obstet Gynecol 2016; 47: 210–216

[40] Bruijn MM, Kamphuis EI, Hoesli IM et al. The predictive value of quantitative fibronectin testing in combination with cervical length measurement in symptomatic women. Am J Obstet Gynecol 2016; 215: 793.e1–793.e8

[41] Hezelgrave NL, Abbott DS, Radford SK et al. Quantitative Fetal Fibronectin at 18 Weeks of Gestation to Predict Preterm Birth in Asymptomatic High-Risk Women. Obstet Gynecol 2016; 127: 255–263

[42] Esplin MS, Elovitz MA, Iams JD et al. Predictive Accuracy of Serial Transvaginal Cervical Lengths and Quantitative Vaginal Fetal Fibronectin Levels for Spontaneous Preterm Birth Among Nulliparous Women. JAMA 2017; 317: 1047–1056

[43] Meis PJ, Klebanoff M, Thom E et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003; 348: 2379–2385

[44] Norman JE, Marlow N, Messow CM et al. Vaginal progesterone prophylaxis for preterm birth (the OPPTIMUM study): a multicentre, randomised, double-blind trial. Lancet 2016; 387: 2106–2116

[45] Ashoush S, ElKady O, AlHawwary G et al. The value of oral micronized progesterone in the prevention of recurrent spontaneous preterm birth: a randomized controlled trial. Acta Obstet Gynecol Scand 2017; 96: 1460–1466

[46] Dodd JM, Grivell RM, OBrien CM et al. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. Cochrane Database Syst Rev 2017; (10): CD012024

[47] Crowther CA, Ashwood P, McPhee AJ et al. Vaginal progesterone pessaries for pregnant women with a previous preterm birth to prevent neonatal respiratory distress syndrome (the PROGRESS Study): A multicentre, randomised, placebo-controlled trial. PLoS Med 2017; 14: e1002390

[48] O'Brien JM, Adair CD, Lewis DF et al. Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2007; 30: 687–696

[49] Rai P, Rajaram S, Goel N et al. Oral micronized progesterone for prevention of preterm birth. Int J Gynaecol Obstet 2009; 104: 40–43

[50] da Fonseca EB, Bittar RE, Carvalho MHB et al. Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study. Am J Obstet Gynecol 2003; 188: 419–424

[51] Berghella V, MacKeen AD. Cervical length screening with ultrasound-indicated cerclage compared with history-indicated cerclage for prevention of preterm birth: A meta-analysis. Obstet Gynecol 2011; 118: 148–155

[52] Saling E, Schumacher E. Total surgical cervical occlusion. Conclusions from data of several clinica, which use total surgical cervical occlusion. Z Geburtshilfe Neonatol 1996; 200: 82–87

[53] Leitich H, Bodner-Adler B, Brunbauer M et al. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. Am J Obstet Gynecol 2003; 189: 139–147

[54] Flynn CA, Helwig AL, Meurer LN. Bacterial vaginosis in pregnancy and the risk of prematurity: a meta-analysis. J Fam Pract 1999; 48: 885–892

[55] Lamont RF. Advances in the Prevention of Infection-Related Preterm Birth. Front Immunol 2015; 6: 566

[56] Kiss H, Petricevic L, Husslein P. Prospective randomised controlled trial of an infection screening programme to reduce the rate of preterm delivery. BMJ 2004; 329: 371

[57] Sangkomkamhang US, Lumbiganon P, Prasertcharoensuk W et al. Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery. Cochrane Database Syst Rev 2015; (2): CD006178

[58] Subtil D, Brabant G, Tilloy E et al. Early clindamycin for bacterial vaginosis in pregnancy (PREMEVA): a multicentre, double-blind, randomised controlled trial. Lancet 2018; 392: 2171–2179

[59] Hollowell J, Oakley L, Kurinczuk JJ et al. The effectiveness of antenatal care programmes to reduce infant mortality and preterm birth in socially disadvantaged and vulnerable women in high-income countries: a systematic review. BMC Pregnancy Childbirth 2011; 11: 13

[60] Moore E, Blatt K, Chen A et al. Relationship of trimester-specific smoking patterns and risk of preterm birth. Am J Obstet Gynecol 2016; 215: 109.e106

[61] Polakowski LL, Akinbami LJ, Mendola P. Prenatal smoking cessation and the risk of delivering preterm and small-for-gestational-age newborns. Obstet Gynecol 2009; 114: 318–325

[62] IQWIG 2015: Abschlußbericht S13-02 Bakteriuriescreening bei Schwangeren. Online: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwj08cDHp6HfAhVKaBoKHfVACFwQFjAAegQIBxAC&url=https%3A%2F%2Fwww.iqwig.de%2Fdownload%2FS13-02_Abschlussbericht_Bakteriuriescreening-bei-Schwangeren.pdf&usg=AOvVaw37Fv32kK5I7_Zma_9FO6n0; last access: 28.04.2019

[63] Makrides M, Duley L, Olsen SF. Marine oil, and other prostaglandin precursor, supplementation for pregnancy uncomplicated by pre-eclampsia or intrauterine growth restriction. Cochrane Database Syst Rev 2006; (3): CD003402

[64] Middleton P, Gomersall JC, Gould JF et al. Omega-3 fatty acid addition during pregnancy. Cochrane Database Syst Rev 2018; (11): CD003402

[65] Romero R, Nicolaides KH, Conde-Agudelo A et al. Vaginal progesterone decreases preterm birth </= 34 weeks of gestation in women with a singleton pregnancy and a short cervix: an updated meta-analysis including data from the OPPTIMUM study. Ultrasound Obstet Gynecol 2016; 48: 308–317

[66] Berghella V, Odibo AO, To MS et al. Cerclage for short cervix on ultrasonography: Meta-analysis of trials using individual patient-level data. Obstet Gynecol 2005; 106: 181–189

[67] Goya M, Pratcorona L, Merced C et al. Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial. Lancet 2012; 379: 1800–1806

[68] Saccone G, Maruotti GM, Giudicepietro A et al. Effect of Cervical Pessary on Spontaneous Preterm Birth in Women With Singleton Pregnancies and Short Cervical Length: A Randomized Clinical Trial. JAMA 2017; 318: 2317–2324

[69] Cruz-Melguizo S, San-Frutos L, Martinez-Payo C et al. Cervical Pessary Compared With Vaginal Progesterone for Preventing Early Preterm Birth: A Randomized Controlled Trial. Obstet Gynecol 2018; 132: 907–915

[70] Hui SY, Chor CM, Lau TK et al. Cerclage pessary for preventing preterm birth in women with a singleton pregnancy and a short cervix at 20 to 24 weeks: a randomized controlled trial. Am J Perinatol 2013; 30: 283–288

[71] Nicolaides KH, Syngelaki A, Poon LC et al. A Randomized Trial of a Cervical Pessary to Prevent Preterm Singleton Birth. N Engl J Med 2016; 374: 1044–1052

[72] Karbasian N, Sheikh M, Pirjani R et al. Combined treatment with cervical pessary and vaginal progesterone for the prevention of preterm birth: A randomized clinical trial. J Obstet Gynaecol Res 2016; 42: 1673–1679

[73] Dugoff L, Berghella V, Sehdev H et al. Prevention of preterm birth with pessary in singletons (PoPPS): randomized controlled trial. Ultrasound Obstet Gynecol 2018; 51: 573–579

[74] Palmer KT, Bonzini M, Bonde JP et al. Pregnancy: occupational aspects of management: concise guidance. Clin Med 2013; 13: 75–79

Guideline Program

Editors

Leading Professional Medical Associations

German Society of Gynecology and Obstetrics (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e. V. [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
Direktor der Frauenkliniken
Klinikum St. Marien Amberg
Mariahilfbergweg 7, DE-92224 Amberg
Kliniken Nordoberpfalz AG
Söllnerstraße 16, DE-92637 Weiden

DGGG Guidelines Representatives

Prof. Dr. med. Matthias W. Beckmann
Universitätsklinikum Erlangen, Frauenklinik
Universitätsstraße 21–23, DE-91054 Erlangen

Prof. Dr. med. Erich-Franz Solomayer
Universitätsklinikum des Saarlandes
Geburtshilfe und Reproduktionsmedizin
Kirrberger Straße, Gebäude 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/leitlinienstellungnahmen

Austrian Society of Gynecology and Obstetrics (Österreichische Gesellschaft für Gynäkologie und Geburtshilfe [OEGGG])
Frankgasse 8, AT-1090 Wien
stephanie.leutgeb@oeggg.at
http://www.oeggg.at

President of OEGGG

Prof. Dr. med. Petra Kohlberger
Universitätsklinik für Frauenheilkunde Wien
Währinger Gürtel 18–20, AT-1090 Wien

OEGGG Guidelines Representatives

Prof. Dr. med. Karl Tamussino
Universitätsklinik für Frauenheilkunde und Geburtshilfe Graz
Auenbruggerplatz 14, AT-8036 Graz

Prof. Dr. med. Hanns Helmer
Universitätsklinik für Frauenheilkunde Wien
Währinger Gürtel 18–20, AT-1090 Wien

Swiss Society of Gynecology and Obstetrics (Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe [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
Universitätsklinik für Frauenheilkunde
Geburtshilfe und feto-maternale Medizin
Inselspital Bern
Effingerstraße 102, CH-3010 Bern

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

Thieme

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

Prävention und Therapie der Frühgeburt. Leitlinie der DGGG, OEGGG und SGGG (S2k-Niveau, AWMF-Registernummer 015/025, Februar 2019) – Teil 2 mit Empfehlungen zur tertiären Prävention der Frühgeburt und zum Management des frühen vorzeitigen Blasensprungs

Authors

Richard Berger[1], Harald Abele[2], Franz Bahlmann[3], Ivonne Bedei[4], Klaus Doubek[5], Ursula Felderhoff-Müser[6], Herbert Fluhr[7], Yves Garnier[8], Susanne Grylka-Baeschlin[9], Hanns Helmer[10], Egbert Herting[11], Markus Hoopmann[2], Irene Hösli[12], Udo Hoyme[13], Alexandra Jendreizeck[14], Harald Krentel[15], Ruben Kuon[16], Wolf Lütje[17], Silke Mader[18], Holger Maul[19], Werner Mendling[20], Barbara Mitschdörfer[14], Tatjana Nicin[21], Monika Nothacker[22], Dirk Olbertz[23], Werner Rath[24], Claudia Roll[25], Dietmar Schlembach[26], Ekkehard Schleußner[27], Florian Schütz[16], Vanadin Seifert-Klauss[28], Susanne Steppat[29], Daniel Surbek[30]

Affiliations

1 Frauenklinik, Marienhaus Klinikum Neuwied, Neuwied, Germany
2 Frauenklinik, Universitätsklinikum Tübingen, Tübingen, Germany
3 Frauenklinik, Bürgerhospital Frankfurt, Frankfurt am Main, Germany
4 Frauenklinik, Klinikum Frankfurt Höchst, Frankfurt am Main, Germany
5 Frauenarztpraxis, Wiesbaden, Germany
6 Klinik für Kinderheilkunde I/Perinatalzentrum, Universitätsklinikum Essen, Universität Duisburg-Essen, Essen, Germany
7 Frauenklinik, Universitätsklinikum Heidelberg, Heidelberg, Germany
8 Frauenklinik, Klinikum Osnabrück, Osnabrück, Germany
9 Zürcher Hochschule für angewandte Wissenschaften, Institut für Hebammen, Zürich, Switzerland
10 Universitätsklinik für Frauenheilkunde, Medizinische Universität Wien, Wien, Austria
11 Klinik für Kinder- und Jugendmedizin, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Lübeck, Germany
12 Frauenklinik, Universitätsspital Basel, Basel, Switzerland
13 Frauenklinik, Ilm-Kreis-Kliniken, Arnstadt, Germany
14 Bundesverband das frühgeborene Kind, Germany
15 Frauenklinik, Annahospital Herne, Elisabethgruppe Katholische Kliniken Rhein Ruhr, Herne, Germany
16 Frauenklinik, Universitätsklinikum Heidelberg, Heidelberg, Germany
17 Frauenklinik, Evangelisches Amalie Sieveking-Krankenhaus Hamburg, Hamburg, Germany
18 European Foundation for the Care of the Newborn Infants
19 Frauenklinik, Asklepios Kliniken Hamburg, Hamburg, Germany
20 Deutsches Zentrum für Infektionen in Gynäkologie und Geburtshilfe an der Frauenklinik, Helios Universitätsklinikum Wuppertal, Wuppertal, Germany
21 Frauenklinik, Klinikum Hanau, Hanau, Germany
22 Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, Berlin, Germany
23 Abteilung Neonatologie und neonatologische Intensivmedizin, Klinikum Südstadt Rostock, Rostock, Germany
24 Emeritus, Universitätsklinikum Aachen, Aachen, Germany
25 Vestische Kinder- und Jugendklinik Datteln, Universität Witten/Herdecke, Datteln, Germany
26 Klinik für Geburtsmedizin, Klinikum Neukölln/Berlin Vivantes Netzwerk für Gesundheit, Berlin, Germany
27 Klinik für Geburtsmedizin, Universitätsklinikum Jena, Jena, Germany
28 Frauenklinik, Universitätsklinikum rechts der Isar München, München, Germany
29 Deutscher Hebammenverband, Germany
30 Universitäts-Frauenklinik, Inselspital, Universität Bern, Bern, Switzerland

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

Schlüsselwörter
Frühgeburt, vorzeitige Wehentätigkeit, Zervixinsuffizienz, früher vorzeitiger Blasensprung

received 30.4.2019
accepted 30.4.2019

Bibliography
DOI https://doi.org/10.1055/a-0903-2735
Geburtsh Frauenheilk 2019; 79: 813–833 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0016-5751

Correspondence
Prof. Dr. med. Richard Berger
Marienhaus Klinikum St. Elisabeth, Akademisches Lehrkrankenhaus der Universitäten Mainz und Maastricht, Klinik für Gynäkologie und Geburtshilfe
Friedrich-Ebert-Straße 59, 56564 Neuwied, Germany
richard.berger@marienhaus.de

Deutsche Version unter:
https://doi.org/10.1055/a-0903-2735

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.

ZUSAMMENFASSUNG

Ziel Offizielle Leitlinie der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (DGGG), der Österreichischen Gesellschaft für Gynäkologie und Geburtshilfe (ÖGGG) und der Schweizerischen Gesellschaft für Gynäkologie und Geburtshilfe (SGGG). Ziel der Leitlinie ist es, die Prädiktion, die Prävention und das Management der Frühgeburt anhand der aktuellen Literatur, der Erfahrung der Mitglieder der Leitlinienkommission einschließlich der Sicht der Selbsthilfe evidenzbasiert zu verbessern.
Methoden Anhand der internationalen Literatur entwickelten die Mitglieder der beteiligten Fachgesellschaften und Organisationen Empfehlungen und Statements. Diese wurden in einem formalen Prozess (strukturierte Konsensuskonferenzen mit neutraler Moderation, schriftliche Delphi-Abstimmung) verabschiedet.
Empfehlungen Der Teil 2 dieser Kurzversion der Leitlinie zeigt Statements und Empfehlungen zur tertiären Prävention der Frühgeburt sowie zum Management des frühen vorzeitigen Blasensprungs.

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. Geburtsh 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)

▸ **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 – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Frühgeburt
Prof. Dr. Franz Bahlmann	Deutsche Gesellschaft für Ultraschall in der Medizin e. V. (DEGUM)
Dr. Ivonne Bedei	DGGG – Arbeitsgemeinschaft Kinder- und Jugendgynäkologie e. V. (AGKJ)
Prof. Dr. Richard Berger	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Dr. Klaus Doubek	Berufsverband der Frauenärzte e. V. (BVF)
Prof. Dr. Ursula Felderhoff-Müser	Gesellschaft für neonatale und pädiatrische Intensivmedizin (GNPI)
Prof. Dr. Herbert Fluhr	DGGG – Arbeitsgemeinschaft für Immunologie in Gynäkologie und Geburtshilfe (AGIM)
PD Dr. Dr. Yves Garnier	DGGG – Arbeitsgemeinschaft für Geburtshilfe und Pränatalmedizin (AGG) – Sektion Frühgeburt
Dr. Susanne Grylka-Baeschlin	Deutsche Gesellschaft für Hebammenwissenschaften (DGHWi)
Prof. Dr. Hanns Helmer	Österreichische Gesellschaft für Gynäkologie und Geburtshilfe (OEGGG)
Prof. Dr. Egbert Herting	Deutsche Gesellschaft für Kinder- und Jugendmedizin (DGKJ)
Prof. Dr. Markus Hoopmann	DGGG – Arbeitsgemeinschaft für Ultraschalldiagnostik in Gynäkologie und Geburtshilfe (ARGUS)
Prof. Dr. Irene Hösli	Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)
Prof. Dr. Dr. h. c. Udo Hoyme	DGGG – Arbeitsgemeinschaft für Infektionen und Infektionsimmunologie (AGII)
Alexandra Jendreizeck	Bundesverband “Das frühgeborene Kind” [Federal Association “The preterm Child”]
Dr. Harald Krentel	DGGG – Arbeitsgemeinschaft für Frauengesundheit in der Entwicklungszusammenarbeit (FIDE)
PD Dr. Ruben Kuon	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG)
Dr. Wolf Lütje	DGGG – Deutsche Gesellschaft für psychosomatische Frauenheilkunde und Geburtshilfe e. 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 – Deutsche Gesellschaft für Gynäkologische Endokrinologie und Fortpflanzungsmedizin e. V. (DGGEF)
Susanne Steppat	Deutscher Hebammenverband (DHV)
Prof. Dr. Daniel Surbek	Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG)

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 (e.g. 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**).

▶ **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

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 analyses, 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**).

▶ **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

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", i.e., 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 bis 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 (only available in German: "Glucocorticoidtherapie zur antenatalen Lungenreifung bei drohender Frühgeburt: Indikationen und Dosierung"). *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 bei vorzeitiger Wehentätigkeit"). *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

Consensus-based Statement 6.S21	
Expert consensus	**Strength of consensus ++**
There is currently no data which can confirm that bed rest reduces the rate of preterm births. However, bed rest does increase the maternal risk of thrombosis and contributes to the development of muscular atrophy and osteoporosis.	
[6 – 10]	

6.2 Tocolysis

Consensus-based Recommendation 6.E18	
Expert consensus	**Strength of consensus +++**
The aim of tocolysis must be to prolong the pregnancy by at least 48 hours. This additional period would make it possible to administer antenatal steroids and carry out an in-utero transfer to a perinatal center with a neonatal intensive care unit.	

6.2.1 Indications

Consensus-based Recommendation 6.E19	
Expert consensus	**Strength of consensus +++**
Tocolytic therapy should be administered if the patient has spontaneous, regular, preterm contractions of ≥ 4/20 min with shortening of the functional cervical length (transvaginal measurement) and/or opening of the cervix.	

Consensus-based Statement 6.S22	
Expert consensus	**Strength of consensus +++**
If the indications are present and contra-indications have been excluded, tocolysis is indicated in the period between GW 22 + 0 and GW 33 + 6.	

Consensus-based Statement 6.S23	
Expert consensus	**Strength of consensus +++**
In cases of premature labor with cervical dilation, tocolytic therapy (beta sympathomimetics, atosiban, nifedipine, indomethacin, NO donors) can delay the birth by 48 h in 75–93 % of cases and by 7 days in 62–78 % of cases.	
[11, 12]	

6.2.2 Drugs

Consensus-based Recommendation 6.E20	
Expert consensus	**Strength of consensus ++**
Because of the significantly higher rate of maternal side effects (beta sympathomimetics) compared to other tocolytic drugs and the lack of evidence confirming its tocolytic efficacy (magnesium sulfate), beta sympathomimetics and magnesium sulfate should no longer be used for tocolysis.	

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-analyses [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 – 18].

Consensus-based Recommendation 6.E21	
Expert consensus	**Strength of consensus ++**
After considering their efficacy and side effects profile, calcium antagonists (nifedipine), oxytocin-receptor antagonists (atosiban) and COX inhibitors (indomethacin) should be used preferentially for tocolysis, even though some have not yet been approved for use.	
[11, 12]	

6.2.3 Combining several tocolytics

Consensus-based Recommendation 6.E22	
Expert consensus	**Strength of consensus +++**
Based on current data, combining different tocolytics is associated with significantly increased rates of maternal side effects compared to administering a single tocolytic, and as there are no data confirming any increase in efficacy, combining different tocolytics should be avoided.	
[13, 19]	

Consensus-based Recommendation 6.E23	
Expert consensus	**Strength of consensus +++**
Tocolytics should not be administered in combination with oral/vaginal progesterone (“adjunctive tocolysis”), because data on this issue is still insufficient.	
[20]	

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

Consensus-based Statement 6.S24	
Expert consensus	**Strength of consensus +++**
Evidence from randomized controlled studies on the benefits of tocolytics for extremely preterm birth, multiple pregnancy and intrauterine growth restriction is lacking. The decision whether to administer tocolytics in such cases must be made on a case-by-case basis.	
[21]	

6.2.5 Long-term tocolysis

Consensus-based Recommendation 6.E24	
Expert consensus	**Strength of consensus +++**
According to the information currently available, long-term or maintenance tocolysis (generally defined as tocolysis for more than 48 h) should not be used to reduce the rate of preterm births or neonatal morbidity and mortality rates.	
[22 – 25]	

6.3 Progesterone for maintenance tocolysis

Consensus-based Recommendation 6.E25	
Expert consensus	**Strength of consensus +++**
After tocolysis, pregnant women with a singleton pregnancy should not be given progesterone to maintain the pregnancy and prevent preterm birth.	

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

Consensus-based Statement 6.S25	
Expert consensus	**Strength of consensus +++**
There is some evidence from a prospective randomized study that placement of a cervical pessary in pregnant women previously treated for premature labor who have a shortened cervical length as measured by transvaginal ultrasound (< 25 mm between GW 24 + 0 and GW 29 + 6; < 15 mm between GW 30 + 0 and GW 33 + 6) may reduce the rate of preterm births.	

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 APOSTEL VI trial [28].

6.5 Administration of antibiotics for premature labor

Consensus-based Recommendation 6.E26	
Expert consensus	**Strength of consensus +++**
Cases of premature labor without rupture of membranes must not be treated with antibiotics with the goal of prolonging the pregnancy or reducing neonatal morbidity.	

Meta-analyses 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

Consensus-based Recommendation 6.E27	
Expert consensus	**Strength of consensus +++**
Antenatal steroids must be administered to women at imminent risk of preterm birth before GW 34 + 0, with treatment consisting of 2 × 12 mg betamethasone administered IM at an interval of 24 h (alternatively: dexamethasone, 4 × 6 mg every 12 h).	
[31]	

6.6.2 Starting in which week of gestation?

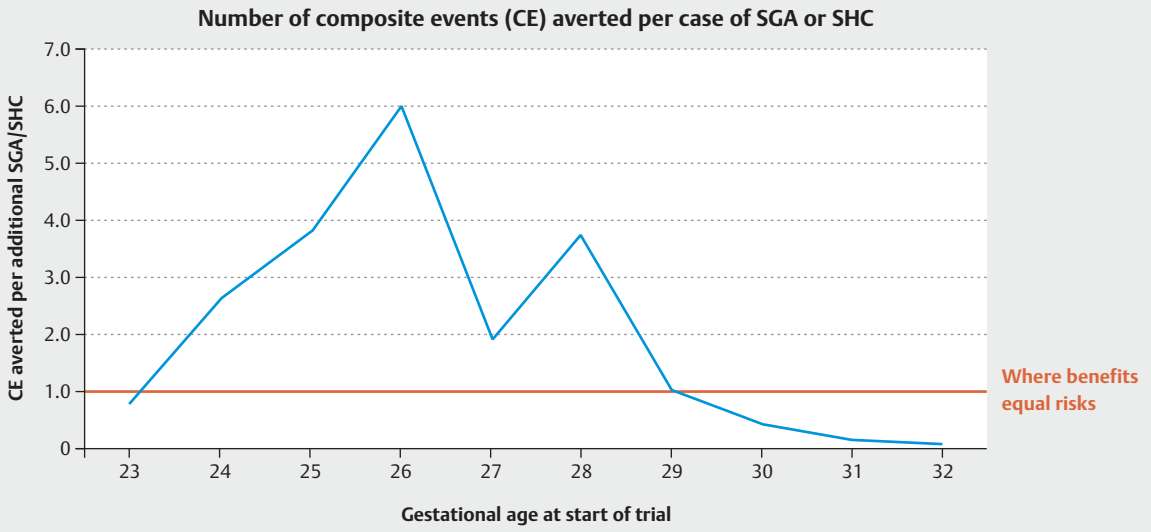
Consensus-based Recommendation 6.E28	
Expert consensus	**Strength of consensus +++**
Antenatal steroids should also be administered in cases at imminent risk of preterm birth < GW 24 + 0 if maximum therapy in a neonatal intensive care unit is planned.	

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** and **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.

▶ **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



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

▶ **Fig. 1** Benefits of administering antenatal steroids according to gestational age [33]

▶ **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

6.6.3 Repeat administration of antenatal steroids

Consensus-based Recommendation 6.E29	
Expert consensus	**Strength of consensus +++**
If steroids are administered to women before the 29 + 0 week of gestation because of an imminent risk of preterm birth and steroids were administered more than 7 days previously, a further dose of steroids may be administered after the patient has been re-assessed if the imminent risk of preterm birth is increasing.	

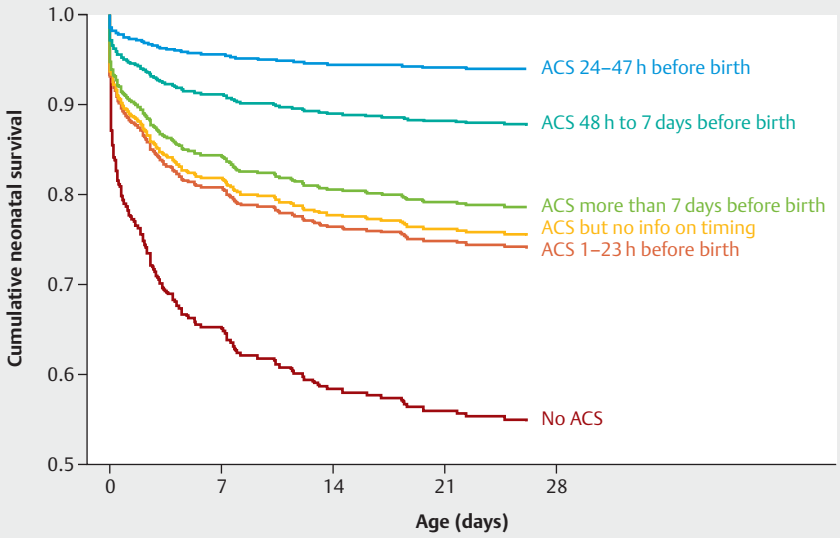
Zephyrin and colleagues used a Markov model to investigate how to achieve the right balance between risks and benefits with repeat administration of antenatal steroids [33]. The improved neonatal outcomes after multiple glucocorticoid administrations were set against the risk of fetal growth restriction.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

Consensus-based Statement 6.S26	
Expert consensus	**Strength of consensus +++**
The timing of and indication for administering antenatal steroids must be carefully weighed up, as neonatal morbidity and mortality can only be reduced in the period between 24 h and 7 days after the first administration. There is some evidence that administering antenatal steroids already has an effect before 24 h.	

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

Consensus-based Recommendation 6.E30	
Expert consensus	**Strength of consensus +++**
Patients with premature contractions and a cervical length of > 30 mm or 15–30 mm as measured by transvaginal ultrasound and who additionally test negative for fibronectin, phIGFBP-1 and PAMG-1 should not be given antenatal steroids just because of the contractions, as the risk of preterm birth in the next 7 days is low (< 5 %).	
[37, 38]	



▶ **Fig. 2** Survival of very immature infants (< 26th week of gestation) according to the timing of antenatal steroid administration [36].

Consensus-based Recommendation 6.E31	
Expert consensus	**Strength of consensus +++**
So-called rapid maturation, consisting of the administration of a second dose of betamethasone after just 12 h rather than after 24 h, should be avoided as this significantly increases the risk of necrotizing enterocolitis.	
[39]	

6.6.5 Administration of antenatal steroids and late preterm birth

Consensus-based Recommendation 6.E32	
Expert consensus	**Strength of consensus ++**
Administering antenatal steroids to patients between GW 34 + 0 and GW 36 + 5 with an imminent risk of preterm birth should currently be avoided as there are still no studies on the impact this can have on the children's psychomotor development later on.	

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

Consensus-based Recommendation 6.E33	
Expert consensus	**Strength of consensus +++**
An emergency cerclage may be placed in women with a singleton pregnancy and cervical dilation of more than 1 cm before GW 24 + 0 with the goal of significantly prolonging the pregnancy.	

Consensus-based Recommendation 6.E34	
Expert consensus	**Strength of consensus +++**
Women treated with emergency cerclage should receive indomethacin and antibiotics perioperatively.	

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

Consensus-based Statement 6.S27	
Expert consensus	**Strength of consensus +++**
Periventricular/intraventricular hemorrhage (PIVH) and periventricular leukomalacia (PVL)/diffuse cerebral white matter injury are typical forms of brain injury found in survivors of preterm birth.	
[44]	

6.8.1 Magnesium

Consensus-based Recommendation 6.E35	
Expert consensus	**Strength of consensus +++**
Magnesium may be administered intravenously for fetal neuroprotection to patients < GW 32 at imminent risk of preterm birth.	
[45, 46]	

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

Consensus-based Recommendation 6.E36	
Expert consensus	**Strength of consensus +++**
Cord clamping of infants born preterm should be delayed or umbilical cord milking should be carried out.	
[47 – 49]	

6.9 Delivery

6.9.1 Delivery depends on fetal presentation

Consensus-based Recommendation 6.E37	
Expert consensus	**Strength of consensus ++**
Delivery by cesarean section may be considered after carefully weighing up the risk/benefits in each individual case if the fetus is aged < GW 30 + 0 and in cephalic presentation.	
[50 – 63]	

Consensus-based Recommendation 6.E38	
Expert consensus	**Strength of consensus ++**
Depending on the sonographically estimated fetal weight and other factors, delivery by cesarean section should be considered to reduce neonatal morbidity and mortality if the fetus is aged < GW 36 + 0 and in breech presentation.	
[64]	

6.9.2 Longitudinal uterine incision for cesarean section

Consensus-based Recommendation 6.E39	
Expert consensus	**Strength of consensus +++**
Particularly in cases of extremely preterm birth, longitudinal uterine section may be appropriate in individual cases as it may be the most beneficial form of delivery for the infant.	

Consensus-based Recommendation 6.E40	
Expert consensus	**Strength of consensus +++**
Because of the increased risk of uterine rupture, women who have had a previous longitudinal c-section must be delivered by primary repeat c-section in all subsequent births.	
[65, 66]	

6.9.3 Vaginal operative delivery

Consensus-based Recommendation 6.E41	
Expert consensus	**Strength of consensus ++**
Because of the increased risk of intraventricular hemorrhage, fetuses under the age of 34 + 0 weeks of gestation should not be delivered by vacuum extraction.	
[67]	

6.9.4 Fetal blood gas analysis

Consensus-based Recommendation 6.E42	
Expert consensus	**Strength of consensus +++**
Fetal blood gas analysis should not be carried out for fetuses under the age of 34 + 0 weeks of gestation because of the potential risk of injury.	

6.9.5 Antibiotic prophylaxis for group B streptococcus

Consensus-based Recommendation 6.E43	
Expert consensus	**Strength of consensus +++**
If the GBS status of a case of preterm birth is positive or unknown, antibiotic prophylaxis must be administered during delivery.	
[68]	

6.9.6 Cooperation with the Neonatology Department

Consensus-based Recommendation 6.E44	
Expert consensus	**Strength of consensus ++**
A pediatrician/neonatologist must be involved early on in the treatment and counselling of women with an imminent risk of preterm birth.	
[69 – 71]	

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.

Consensus-based Recommendation 6.E45	
Expert consensus	**Strength of consensus ++**
When an infant is born preterm (< GW 35 + 0), a physician with experience in neonatology must be present to directly oversee the care of the newborn infant. If there is an imminent risk of preterm birth before GW 32 + 0 and/or the estimated weight/birthweight is < 1500 g, a specialist physician with a subspecialization in neonatology must be on call.	
[72]	

6.9.7 Terminal care

Consensus-based Recommendation 6.E46	
Expert consensus	**Strength of consensus +++**
Specially trained staff must be called in to offer palliative and terminal care to deceased or dying newborns and their family in the perinatal phase. Terminal care is included in perinatology training. According to the tenets of the German Medical Association, offering terminal care with dignity is a key medical duty for physicians which they cannot delegate.	
[73 – 75]	

7 Special Aspects Relating to Twin and Multiple Pregnancies

7.1 Epidemiology and etiology

Consensus-based Statement 7.S28	
Expert consensus	**Strength of consensus +++**
Women carrying a multiple pregnancy have a significantly higher risk of preterm birth.	
[76, 77]	

7.2 Prevention

7.2.1 Progesterone

Consensus-based Recommendation 7.E47	
Expert consensus	**Strength of consensus +++**
Women must not be given progesterone to prevent preterm birth only because they are carrying twins.	
[78, 79]	

Consensus-based Recommendation 7.E48	
Expert consensus	**Strength of consensus +++**
Women carrying a twin pregnancy who have a cervical length of ≤ 25 mm before GW 24 + 0 as measured by transvaginal ultrasound should receive a daily dose of 200–400 mg progesterone applied intravaginally until GW 36 + 6.	

An individual patient data meta-analysis (IPDMA) of six studies [79 – 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 (e.g., 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

Consensus-based Recommendation 7.E49	
Expert consensus	**Strength of consensus +++**
Primary or secondary cerclage should not be placed in women with twin pregnancies.	

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 – 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

Consensus-based Recommendation 7.E50	
Expert consensus	**Strength of consensus +++**
A cervical pessary can be placed in individual cases with twin pregnancy and a cervical length of ≤ 25 mm before GW 24 + 0 as measured by transvaginal sonography.	

Given the fact that prospective randomized studies have reported both positive [91 – 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

Consensus-based Statement 7.S29	
Expert consensus	**Strength of consensus +++**
There is some evidence from a prospective randomized study that placement of a cervical pessary in cases with twin pregnancy previously treated for preterm labor and with a shortened cervical length as measured by transvaginal ultrasound (< 20 mm between GW 24 + 0 and GW 29 + 6; < 10 mm between GW 30 + 0 and GW 33 + 6) can reduce the rate of preterm births.	

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 – i.e., the preterm rate before the 34th week of gestation – was significantly lower in the intervention goup (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

Consensus-based Recommendation 7.E51	
Expert consensus	**Strength of consensus +++**
If the cervix has opened more than 1 cm before GW 24 + 0, emergency cerclage may be carried out even in women with a twin pregnancy with the aim of significantly prolonging the pregnancy.	

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 – 100].

8 Preterm Premature Rupture of Membranes (PPROM)

8.1 Prevalence and Etiology

Consensus-based Statement 8.S30	
Expert consensus	**Strength of consensus +++**
Around 3 % of all pregnant women are affected by preterm premature rupture of membranes (rupture of membranes before GW 37 + 0): 0.5 % before the 27th week of gestation, 1 % between 27 and 34 weeks of gestation and 1 % between the 34th and the 37th week of gestation.	
[101]	

8.2 Risk factors

Consensus-based Statement 8.S31	
Expert consensus	**Strength of consensus +++**
A previous history of PPROM is a significant risk factor for preterm premature rupture of membranes. The additional risk factors are similar to those for spontaneous preterm birth.	
[102, 103]	

8.3 Diagnostic workup

Consensus-based Recommendation 8.E52	
Expert consensus	**Strength of consensus +++**
In most cases, PPROM can be diagnosed by speculum examination. If there is still some uncertainty, then biochemical tests must be carried out.	
[104, 105]	

Consensus-based Recommendation 8.E53	
Expert consensus	**Strength of consensus +++**
A digital examination must be avoided in patients with PPROM.	

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

Consensus-based Statement 8.S32	
Expert consensus	**Strength of consensus +++**
More than 50 % of all patients with PPROM are delivered within one week.	
[108, 109]	

8.5 Maternal and fetal risks

Consensus-based Statement 8.S33	
Expert consensus	**Strength of consensus +++**
Patients with PPROM have a risk of clinical infection. Additional risks include placental abruption and umbilical cord prolapse.	
[110 – 115]	

8.6 Triple I (▶ **Table 6**)

Consensus-based Statement 8.S34	
Expert consensus	**Strength of consensus +++**
Internationally, the term "Triple I" has superseded the term chorioamnionitis to differentiate maternal fever from infection or inflammation or both.	

▶ **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/mm³), 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].

8.7 Maternal and fetal risks associated with Triple I

Consensus-based Statement 8.S35	
Expert consensus	**Strength of consensus +++**
In addition to sepsis, maternal risks associated with Triple I include uterine dysfunction with the risk of failure to progress in labor and uterine atony post partum. In cases where delivery was by cesarean section, risks include wound infection, endomyometritis, thrombophlebitis and pelvic abscess formation.	
[117 – 122]	

Consensus-based Statement 8.S36	
Expert consensus	**Strength of consensus +++**
The fetus may develop inflammatory response syndrome as part of Triple I. Affected infants have a higher risk of sepsis post partum.	
[123, 124]	

8.8 Clinical management of PPROM before GW 22

Consensus-based Recommendation 8.E54	
Expert consensus	**Strength of consensus +++**
If PPROM occurs before the fetus has achieved viability, the risk of maternal sepsis, fetal pulmonary hypoplasia and fetal skeletal deformities must be discussed with the future parents.	
[125 – 127]	

Consensus-based Recommendation 8.E55	
Expert consensus	**Strength of consensus +++**
Antibiotic therapy may be considered in patients with PPROM before the fetus has achieved viability.	

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.

Consensus-based Recommendation 8.E56	
Expert consensus	**Strength of consensus +++**
Antenatal steroid administration, tocolysis and neuroprotection with magnesium must not be carried out in cases with PPROM before the fetus has achieved viability.	

8.9 Clinical management of PPROM between (GW 22 + 0) GW 24 + 0 and GW 33 + 6

Consensus-based Recommendation 8.E57	
Expert consensus	**Strength of consensus +++**
Recommendation: Between GW 22 + 0 and GW 23 + 6 the further course of action should be agreed upon with the parents in accordance with the German-language guideline "Frühgeborene an der Grenze der Lebensfähigkeit 024–019" [Preterm infants at the limits of viability].	

8.9.1 Expectant management

Consensus-based Recommendation 8.E58	
Expert consensus	**Strength of consensus ++**
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, expectant management must be considered first if there is no immediate risk to mother or child.	

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].

▶ **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]

8.9.2 Administration of antenatal steroids

Consensus-based Recommendation 8.E59	
Expert consensus	**Strength of consensus +++**
Patients with PPROM between GW 24 + 0 and GW 33 + 6 or between GW 22 and GW 23 + 6, if maximum therapy is requested, must be given antenatal steroids consisting of 2 × 12 mg betamethasone administered IM at an interval of 24 h (alternatively dexamethasone, 4 × 6 mg every 12 h).	

8.9.3 Administration of antibiotics

Consensus-based Recommendation 8.E60	
Expert consensus	**Strength of consensus ++**
Patients with PPROM between GW 24 + 0 and GW 33 + 6 or between GW 22 and GW 23 + 6, if maximum therapy is requested, must be given antibiotic therapy.	
[131]	

Consensus-based Recommendation 8.E61	
Expert consensus	**Strength of consensus +++**
The data are not sufficient to permit any recommendations to be made about specific therapy regimens. One option is IV administration of ampicillin over 2 days followed by 5 days of oral amoxicillin and a single oral dose of azithromycin at the start. Amoxicillin must not be combined with clavulanic acid.	
[108, 129, 131]	

8.9.4 Tocolysis

Consensus-based Statement 8.S37	
Expert consensus	**Strength of consensus +++**
Tocolysis is not associated with any significant improvement in perinatal morbidity and mortality rates in cases with PPROM.	
[132]	

8.9.5 Neuroprotection

See 6.8.1.

8.9.6 Maternal and fetal monitoring

Consensus-based Recommendation 8.E62	
Expert consensus	**Strength of consensus +++**
Patients with PPROM must be carefully monitored for Triple I. Clinical signs include maternal fever plus one of the following: fetal tachycardia (> 160 beats/min) or leukocytes > 15 000/µl or purulent discharge from the cervix.	

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 an 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].

Consensus-based Statement 8.S38	
Expert consensus	**Strength of consensus ++**
The use of amniocentesis to diagnose Triple I is only useful in exceptional cases, e.g. when the source of maternal infection is not clear.	
[138]	

Consensus-based Statement 8.S39	
Expert consensus	**Strength of consensus +++**
The prediction of Triple I based on biochemical parameters measured in vaginal secretions is not useful according to current knowledge.	
[134, 139]	

8.9.7 Amniotic infusion

Consensus-based Statement 8.S40	
Expert consensus	**Strength of consensus +++**
The value of amniotic infusion in cases of PPROM cannot be sufficiently evaluated based on the data currently available.	
[140]	

8.9.8 Antibiotic prophylaxis for Group B streptococcus

See the recommendations on GBS prophylaxis.

8.9.9 Delivery

Consensus-based Recommendation 8.E63	
Expert consensus	**Strength of consensus +++**
Patients with PPROM between GW 24 + 0 and GW 33 + 6 or between GW 22 and GW 23 + 6, if maximum therapy is requested, can be delivered from GW 34 + 0 onwards. Indications for immediate delivery are Triple I (suspicion of Triple I or confirmed), premature placental abruption, pathological CTG or high risk, or umbilical cord prolapse.	
[129, 130]	

Consensus-based Recommendation 8.E64	
Expert consensus	**Strength of consensus +++**
Patients with Triple I (suspicion or confirmed) must be given antibiotics and their infant must be delivered.	

8.10 Clinical Management of PPROM between GW 34 + 0 and GW 36 + 6

Consensus-based Recommendation 6.E65	
Expert consensus	**Strength of consensus +++**
If preterm premature rupture of membranes occurs between GW 34 + 0 and GW 36 + 6, expectant management may be considered as an alternative to prompt delivery, with the aim of prolonging the pregnancy until GW 37 + 0. This does not apply if Group B streptococcus is detected in vaginal secretions.	

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].

Consensus-based Recommendation 8.E66	
Expert consensus	**Strength of consensus +++**
Clinical monitoring and antibiotic therapy in cases with PPROM between GW 34 + 0 and GW 36 + 6 must follow the recommendations for (GW 22 + 0) GW 24 + 0 – GW 33 + 6. Antenatal steroids, tocolysis or neuroprotection with magnesium must not be administered.	

9 Psychosomatic Care and Supportive Therapy

Consensus-based Recommendation 9.E67	
Expert consensus	**Strength of consensus ++**
Pregnant women admitted to hospital for premature labor and women who had a preterm birth should be offered 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 – 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 Frühe Hilfe 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 Frühe Hilfe 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.

Conflict of Interest

The conflict of interest statements of all the authors are available in the long version of the guideline.

References

[1] Fischer T, Mörtl M, Reif P et al. Statement by the OEGGG with Review of the Literature on the Mode of Delivery of Premature Infants at the Limit of Viability. Geburtsh Frauenheilk 2018; 78: 1212–1216

[2] Gyamfi-Bannerman C, Thom EA, Blackwell SC et al.; NICHD Maternal–Fetal Medicine Units Network. Antenatal betamethasone for women at risk for late preterm delivery. N Engl J Med 2016; 374: 1311–1320

[3] SGGG. Lungenreifungsinduktion bei drohender Frühgeburt. Online: https://www.sggg.ch/fileadmin/user_upload/56_Lungenreifungsinduktion_bei_drohender_Fruehgeburt.pdf; last access: 28.04.2019

[4] Swiss-Paediatrics. Perinatale Betreuung an der Grenze der Lebensfähigkeit zwischen 22 und 26 vollendeten Schwangerschaftswochen. Online: http://www.swiss-paediatrics.org/sites/default/files/paediatrica/vol23/n1/pdf/10-12_0.pdf; last access: 28.04.2019

[5] SGGG. Expertenbrief Tokolyse. Online: https://www.sggg.ch/fileadmin/user_upload/Dokumente/3_Fachinformationen/1_Expertenbriefe/De/41_Tokolyse_2013.pdf; last access: 28.04.2019

[6] Sosa CG, Althabe F, Belizán JM et al. Bed rest in singleton pregnancies for preventing preterm birth. Cochrane Database Syst Rev 2015; (3): CD003581

[7] Hobel CJ, Ross MG, Bemis RL et al. The West Los Angeles Preterm Birth Prevention Project. I. Program impact on high-risk women. Am J Obstet Gynecol 1994; 170: 54–62

[8] Elliott JP, Miller HS, Coleman S et al. A randomized multicenter study to determine the efficacy of activity restriction for preterm labor management in patients testing negative for fetal fibronectin. J Perinatol 2005; 25: 626–630

[9] Bigelow CA, Factor SH, Miller M et al. Pilot Randomized Controlled Trial to Evaluate the Impact of Bed Rest on Maternal and Fetal Outcomes in Women with Preterm Premature Rupture of the Membranes. Am J Perinatol 2016; 33: 356–363

[10] da Silva Lopes K, Takemoto Y, Ota E et al. Bed rest with and without hospitalisation in multiple pregnancy for improving perinatal outcomes. Cochrane Database Syst Rev 2017; (3): CD012031

[11] Haas DM, Imperiale TF, Kirkpatrick PR et al. Tocolytic therapy: A meta-analysis and decision analysis. Obstet Gynecol 2009; 113: 585–594

[12] Haas DM, Caldwell DM, Kirkpatrick P et al. Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. BMJ 2012; 345: e6226

[13] de Heus R, Mol BW, Erwich JJ et al. Adverse drug reactions to tocolytic treatment for preterm labour: prospective cohort study. BMJ 2009; 338: b744

[14] Vogel JP, Oladapo OT, Manu A et al. New WHO recommendations to improve the outcomes of preterm birth. Lancet Glob Health 2015; 3: e589–e590

[15] Crowther CA, Brown J, McKinlay CJ et al. Magnesium sulphate for preventing preterm birth in threatened preterm labour. Cochrane Database Syst Rev 2014; (8): CD001060

[16] [Anonymous]. Practice Bulletin No. 171: Management of Preterm Labor. Obstet Gynecol 2016; 128: e155–e164

[17] Sentilhes L, Senat MV, Ancel PY et al. Prevention of spontaneous preterm birth: Guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol 2017; 210: 217–224

[18] Di Renzo GC, Cabero Roura L, Facchinetti F et al. Preterm Labor and Birth Management: Recommendations from the European Association of Perinatal Medicine. J Matern Fetal Neonatal Med 2017; 30: 2011–2030

[19] Vogel JP, Nardin JM, Dowswell T et al. Combination of tocolytic agents for inhibiting preterm labour. Cochrane Database Syst Rev 2014; (7): CD006169

[20] Martinez de Tejada B, Karolinski A, Ocampo MC et al. Prevention of preterm delivery with vaginal progesterone in women with preterm labour (4P): randomised double-blind placebo-controlled trial. BJOG 2015; 122: 80–91

[21] Miyazaki C, Moreno Garcia R, Ota E et al. Tocolysis for inhibiting preterm birth in extremely preterm birth, multiple gestations and in growth-restricted fetuses: a systematic review and meta-analysis. Reprod Health 2016; 13: 4

[22] Dodd JM, Crowther CA, Middleton P. Oral betamimetics for maintenance therapy after threatened preterm labour. Cochrane Database Syst Rev 2012; (12): CD003927

[23] Naik Gaunekar N, Raman P, Bain E et al. Maintenance therapy with calcium channel blockers for preventing preterm birth after threatened preterm labour. Cochrane Database Syst Rev 2013; (10): CD004071

[24] van Vliet E, Dijkema GH, Schuit E et al. Nifedipine maintenance tocolysis and perinatal outcome: an individual participant data meta-analysis. BJOG 2016; 123: 1753–1760

[25] Han S, Crowther CA, Moore V. Magnesium maintenance therapy for preventing preterm birth after threatened preterm labour. Cochrane Database Syst Rev 2013; (5): CD000940

[26] Wood S, Rabi Y, Tang S et al. Progesterone in women with arrested premature labor, a report of a randomised clinical trial and updated meta-analysis. BMC Pregnancy Childbirth 2017; 17: 258

[27] Pratcorona L, Goya M, Merced C et al. Cervical pessary to reduce preterm birth < 34 weeks of gestation after an episode of preterm labor and a short cervix: a randomized controlled trial. Am J Obstet Gynecol 2018; 219: 99.e16

[28] Hermans FJR, Schuit E, Bekker MN et al. Cervical Pessary After Arrested Preterm Labor: A Randomized Controlled Trial. Obstet Gynecol 2018; 132: 741–749

[29] King J, Flenady V. Prophylactic antibiotics for inhibiting preterm labour with intact membranes. Cochrane Database Syst Rev 2002; (4): CD000246

[30] Simcox R, Sin WT, Seed PT et al. Prophylactic antibiotics for the prevention of preterm birth in women at risk: a meta-analysis. Aust N Z J Obstet Gynaecol 2007; 47: 368–377

[31] Roberts D, Brown J, Medley N et al. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017; 3: CD004454

[32] Deshmukh M, Patole S. Antenatal corticosteroids for neonates born before 25 Weeks-A systematic review and meta-analysis. PLoS One 2017; 12: e0176090

[33] Zephyrin LC, Hong KN, Wapner RJ et al. Gestational age-specific risks vs. benefits of multicourse antenatal corticosteroids for preterm labor. Am J Obstet Gynecol 2013; 209: 330.e337

[34] Norman M, Piedvache A, Borch K et al. Association of Short Antenatal Corticosteroid Administration-to-Birth Intervals With Survival and Morbidity Among Very Preterm Infants: Results from the EPICE Cohort. JAMA Pediatr 2017; 171: 678–686

[35] Liebowitz M, Clyman RI. Antenatal Betamethasone: A Prolonged Time Interval from Administration to Delivery Is Associated with an Increased Incidence of Severe Intraventricular Hemorrhage in Infants Born before 28 Weeks Gestation. J Pediatr 2016; 177: 114–120.e1

[36] Norberg H, Kowalski J, Marsal K et al. Timing of antenatal corticosteroid administration and survival in extremely preterm infants: a national population-based cohort study. BJOG 2017; 124: 1567–1574

[37] van Baaren GJ, Vis JY, Wilms FF et al. Predictive value of cervical length measurement and fibronectin testing in threatened preterm labor. Obstet Gynecol 2014; 123: 1185–1192

[38] Melchor JC, Khalil A, Wing D et al. Prediction of preterm delivery in symptomatic women using PAMG-1, fetal fibronectin and phIGFBP-1 tests: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2018; 52: 442–451

[39] Khandelwal M, Chang E, Hansen C et al. Betamethasone dosing interval: 12 or 24 hours apart? A randomized, noninferiority open trial. Am J Obstet Gynecol 2012; 206: 201.e1–201.e11

[40] Stutchfield P, Whitaker R, Russell I. Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomised trial. BMJ 2005; 331: 662

[41] Stutchfield PR, Whitaker R, Gliddon AE et al. Behavioural, educational and respiratory outcomes of antenatal betamethasone for term caesarean section (ASTECS trial). Arch Dis Child Fetal Neonatal Ed 2013; 98: F195–F200

[42] Ehsanipoor RM, Seligman NS, Saccone G et al. Physical Examination-Indicated Cerclage. Obstet Gynecol 2015; 126: 125–135

[43] Miller ES, Grobman WA, Fonseca L et al. Indomethacin and antibiotics in examination-indicated cerclage: a randomized controlled trial. Obstet Gynecol 2014; 123: 1311–1316

[44] Volpe J. Neurology of the Newborn. Philadelphia: W.B. Saunders Company; 1995

[45] Doyle LW, Crowther CA, Middleton P et al. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev 2009; (1): CD004661

[46] Crowther CA, Middleton PF, Voysey M et al. Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis. PLoS Med 2017; 14: e1002398

[47] Backes CH, Rivera BK, Haque U et al. Placental transfusion strategies in very preterm neonates: A systematic review and meta-analysis. Obstet Gynecol 2014; 124: 47–56

[48] Tarnow-Mordi W, Morris J, Kirby A et al. Delayed versus Immediate Cord Clamping in Preterm Infants. N Engl J Med 2017; 377: 2445–2455

[49] Fogarty M, Osborn DA, Askie L et al. Delayed vs. early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. Am J Obstet Gynecol 2018; 218: 1–18

[50] Jonas HA, Khalid N, Schwartz SM. The relationship between Caesarean section and neonatal mortality in very-low-birthweight infants born in Washington State, USA. Paediatr Perinat Epidemiol 1999; 13: 170–189

[51] Lee HC, Gould JB. Survival rates and mode of delivery for vertex preterm neonates according to small- or appropriate-for-gestational-age status. Pediatrics 2006; 118: e1844

[52] Muhuri PK, Macdorman MF, Menacker F. Method of delivery and neonatal mortality among very low birth weight infants in the United States. Matern Child Health J 2006; 10: 47–53

[53] Malloy MH. Impact of cesarean section on neonatal mortality rates among very preterm infants in the United States, 2000–2003. Pediatrics 2008; 122: 285–292

[54] Jonas HA, Lumley JM. The effect of mode of delivery on neonatal mortality in very low birthweight infants born in Victoria, Australia: Caesarean section is associated with increased survival in breech-presenting, but not vertex-presenting, infants. Paediatr Perinat Epidemiol 1997; 11: 181–199

[55] Riskin A, Riskin-Mashiah S, Lusky A et al. The relationship between delivery mode and mortality in very low birthweight singleton vertex-presenting infants. BJOG 2004; 111: 1365–1371

[56] Wylie BJ, Davidson LL, Batra M et al. Method of delivery and neonatal outcome in very low-birthweight vertex-presenting fetuses. Am J Obstet Gynecol 2008; 198: 4

[57] Ghi T, Maroni E, Arcangeli T et al. Mode of delivery in the preterm gestation and maternal and neonatal outcome. J Matern Fetal Neonatal Med 2010; 23: 1424–1428

[58] Durie DE, Sciscione AC, Hoffman MK et al. Mode of delivery and outcomes in very low-birth-weight infants in the vertex presentation. Am J Perinatol 2011; 28: 195–200

[59] Reddy UM, Zhang J, Sun L et al. Neonatal mortality by attempted route of delivery in early preterm birth. Am J Obstet Gynecol 2012; 207: 117.e1–117.e8

[60] Barzilay E, Gadot Y, Koren G. Safety of vaginal delivery in very low birthweight vertex singletons: a meta-analysis. J Matern Fetal Neonatal Med 2016; 29: 3724–3729

[61] Humberg A, Hartel C, Paul P et al. Delivery mode and intraventricular hemorrhage risk in very-low-birth-weight infants: Observational data of the German Neonatal Network. Eur J Obstet Gynecol Reprod Biol 2017; 212: 144–149

[62] Holzer I, Lehner R, Ristl R et al. Effect of delivery mode on neonatal outcome among preterm infants: an observational study. Wien Klin Wochenschr 2017; 129: 612–617

[63] Racusin DA, Antony KM, Haase J et al. Mode of Delivery in Premature Neonates: Does It Matter? AJP Rep 2016; 6: e251–e259

[64] Bergenhenegouwen L, Vlemmix F, Ensing S et al. Preterm breech presentation: A comparison of intended vaginal and intended cesarean delivery. Obstet Gynecol 2015; 126: 1223–1230

[65] Landon MB, Hauth JC, Leveno KJ et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. N Engl J Med 2004; 351: 2581–2589

[66] Landon MB, Lynch CD. Optimal timing and mode of delivery after cesarean with previous classical incision or myomectomy: a review of the data. Semin Perinatol 2011; 35: 257–261

[67] Aberg K, Norman M, Ekeus C. Preterm birth by vacuum extraction and neonatal outcome: A population-based cohort study. BMC Pregnancy Childbirth 2014; 14: 42

[68] Franz A, Härtel C, Herting E für die Gesellschaft für Neonatologie und Pädiatrische Intensivmedizin (GNPI) (Federführung); Kehl S für die Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG); Gille C für die Deutsche Gesellschaft für pädiatrische Infektiologie (DGPI); Doubek K für den Berufsverband der Frauenärzte BVF e. V.; Spellerberg B für die Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM); Maier RF, Vetter K für die Deutsche Gesellschaft für Perinatale Medizin (DGPM); Eglin K für den Bundesverband „Das frühgeborene Kind“ e. V. (BVDfK). Sepsis bei Neugeborenen-frühe Form-durch Streptokokken der Gruppe B, Prophylaxe. Online: https://www.awmf.org/leitlinien/detail/ll/024-020.html; last access: 03.12.2018

[69] Simon A (Leiter der Arbeitsgruppe), Christoph J, Geffers C et al. Empfehlung zur Prävention nosokomialer Infektionen bei neonatologischen Intensivpflegepatienten mit einem Geburtsgewicht unter 1500 g. Online: https://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/Neo_Rili.pdf?__blob=publicationFile; last access: 28.04.2019

[70] Simon A (federführender Autor). Ergänzende Empfehlung (2011) zur „Prävention nosokomialer Infektionen bei neonatologischen Intensivpflegepatienten mit einem Geburtsgewicht unter 1.500 g“ (2007). Online: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2012/Ausgaben/02_12.pdf?__blob=publicationFile; last access: 28.04.2019

[71] Christoph J, Dame C, Eckmanns T et al. Praktische Umsetzung sowie krankenhaushygienische und infektionspräventive Konsequenzen des mikrobiellen Kolonisationsscreenings bei intensivmedizinisch behandelten Früh- und Neugeborenen. Online: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2013/Ausgaben/42_13.pdf?__blob=publicationFile; last access: 28.04.2019

[72] Richtlinie Qualitätssicherungs-Richtlinie Früh- und Reifgeborene, Stand: Inkrafttreten 01.01.2018 des Gemeinsamen Bundesausschusses über Maßnahmen zur Qualitätssicherung der Versorgung von Früh- und Reifgeborenen gemäß § 136 Absatz 1 Nummer 2 SGBV in Verbindung mit § 92 Abs. 1 Satz 2 Nr. 13 SGB V. Online: https://www.g-ba.de/downloads/62-492-1487/QFR-RL_2017-10-19_iK-2018-01-01.pdf; last access: 28.04.2019

[73] Destatis. Todesursachen. Online: https://www.destatis.de/DE/ZahlenFakten/GesellschaftStaat/Gesundheit/Todesursachen/Todesursachen.html; last access: 28.04.2019

[74] Bundesverband „Das frühgeborene Kind“ e.V. Leitsätze für Palliativversorgung und Trauerbegleitung in der Peri- und Neonatologie. Online: https://www.fruehgeborene.de/fuer-fachleute/palliativversorgung-und-trauerbegleitung; last access: 28.04.2019

[75] Grundsätze der Bundesärztekammer zur ärztlichen Sterbebegleitung. Deutsches Ärzteblatt: Ausgabe A, Praxis-Ausgabe: niedergelassene Ärzte 2011; 108: Heft 7: A346–A348. Online: https://www.bundesaerztekammer.de/fileadmin/user_upload/downloads/Sterbebegleitung_17022011.pdf; last access: 28.04.2019

[76] IQTIG. Bundesauswertung zum Erfassungsjahr 2017 – Geburtshilfe Qualitätsindikatoren. Online: https://iqtig.org/downloads/auswertung/2017/16n1gebh/QSKH_16n1-GEBH_2017_BUAW_V02_2018-08-01.pdf; last access: 28.04.2019

[77] AQUA-Institut. 16/1 – Geburtshilfe Qualitätsindikatoren. Online: https://sqg.de/downloads/Bundesauswertungen/2014/bu_Gesamt_16N1-GEBH_2014.pdf; last access: 28.04.2019

[78] Dodd JM, Grivell RM, OBrien CM et al. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. Cochrane Database Syst Rev 2017; (10): CD012024

[79] Serra V, Perales A, Meseguer J et al. Increased doses of vaginal progesterone for the prevention of preterm birth in twin pregnancies: a randomised controlled double-blind multicentre trial. BJOG 2013; 120: 50–57

[80] Fonseca EB, Celik E, Parra M et al. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med 2007; 357: 462–469

[81] Cetingoz E, Cam C, Sakalli M et al. Progesterone effects on preterm birth in high-risk pregnancies: A randomized placebo-controlled trial. Arch Gynecol Obstet 2011; 283: 423–429

[82] Brizot ML, Hernandez W, Liao AW et al. Vaginal progesterone for the prevention of preterm birth in twin gestations: a randomized placebo-controlled double-blind study. Am J Obstet Gynecol 2015; 213: 82.e1–82.e9

[83] Elrefaie W, Abdelhafez MS, Badawy A. Vaginal progesterone for prevention of preterm labor in asymptomatic twin pregnancies with sonographic short cervix: a randomized clinical trial of efficacy and safety. Arch Gynecol Obstet 2016; 293: 61–67

[84] Rode L, Klein K, Nicolaides KH et al. Prevention of preterm delivery in twin gestations (PREDICT): a multicenter, randomized, placebo-controlled trial on the effect of vaginal micronized progesterone. Ultrasound Obstet Gynecol 2011; 38: 272–280

[85] Romero R, Conde-Agudelo A, El-Refaie W et al. Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data. Ultrasound Obstet Gynecol 2017; 49: 303–314

[86] Berghella V, Odibo AO, To MS et al. Cerclage for short cervix on ultrasonography: Meta-analysis of trials using individual patient-level data. Obstet Gynecol 2005; 106: 181–189

[87] Rust OA, Atlas RO, Reed J et al. Revisiting the short cervix detected by transvaginal ultrasound in the second trimester: why cerclage therapy may not help. Am J Obstet Gynecol 2001; 185: 1098–1105

[88] Berghella V, Odibo AO, Tolosa JE. Cerclage for prevention of preterm birth in women with a short cervix found on transvaginal ultrasound examination: a randomized trial. Am J Obstet Gynecol 2004; 191: 1311–1317

[89] Althuisius SM, Dekker GA, Hummel P et al. Final results of the Cervical Incompetence Prevention Randomized Cerclage Trial (CIPRACT): therapeutic cerclage with bed rest versus bed rest alone. Am J Obstet Gynecol 2001; 185: 1106–1112

[90] Saccone G, Rust O, Althuisius S et al. Cerclage for short cervix in twin pregnancies: systematic review and meta-analysis of randomized trials using individual patient-level data. Acta Obstet Gynecol Scand 2015; 94: 352–358

[91] Liem S, Schuit E, Hegeman M et al. Cervical pessaries for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicentre, open-label randomised controlled trial. Lancet 2013; 382: 1341–1349

[92] Goya M, de la Calle M, Pratcorona L et al.; PECEP-Twins Trial Group. Cervical pessary to prevent preterm birth in women with twin gestation and sonographic short cervix: A multicenter randomized controlled trial (PECEP-Twins). Am J Obstet Gynecol 2016; 214: 145–152

[93] Dang VQ, Nguyen LK, He YTN et al. Cervical pessary versus vaginal progesterone for the prevention of preterm birth in women with a twin pregnancy and a cervix < 38 mm: A randomized controlled trial. Am J Obstet Gynecol 2018; 218: 603–604

[94] Nicolaides KH, Syngelaki A, Poon LC et al. Cervical pessary placement for prevention of preterm birth in unselected twin pregnancies: a randomized controlled trial. Am J Obstet Gynecol 2016; 214: 3.e1–3.e9

[95] Berghella V, Dugoff L, Ludmir J. Prevention of preterm birth with pessary in twins (PoPPT): a randomized controlled trial. Ultrasound Obstet Gynecol 2017; 49: 567–572

[96] Carreras E. Cervical pessary for preventing birth in Twin pregnancies with maternal short cervix after an episode of threatened preterm labour: randomised control trial. Abstract, 17th World Congress in Fetal Medicine, Athen 2018

[97] Rebarber A, Bender S, Silverstein M et al. Outcomes of emergency or physical examination-indicated cerclage in twin pregnancies compared to singleton pregnancies. Eur J Obstet Gynecol Reprod Biol 2014; 173: 43–47

[98] Miller ES, Rajan PV, Grobman WA. Outcomes after physical examination-indicated cerclage in twin gestations. Am J Obstet Gynecol 2014; 211: 46.e1–46.e5

[99] Roman A, Rochelson B, Fox NS et al. Efficacy of ultrasound-indicated cerclage in twin pregnancies. Am J Obstet Gynecol 2015; 212: 788.e1–788.e6

[100] Park JY, Cho SH, Jeon SJ et al. Outcomes of physical examination-indicated cerclage in twin pregnancies with acute cervical insufficiency compared to singleton pregnancies. J Perinat Med 2018; 46: 845–852

[101] van der Heyden JL. Preterm prelabor rupture of membranes: different gestational ages, different problems [Thesis]. Maastricht: Maastricht University; 2014

[102] Mercer BM, Goldenberg RL, Moawad AH et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 1999; 181: 1216–1221

[103] Asrat T, Lewis DF, Garite TJ et al. Rate of recurrence of preterm premature rupture of membranes in consecutive pregnancies. Am J Obstet Gynecol 1991; 165: 1111–1115

[104] Ramsauer B, Vidaeff AC, Hosli I et al. The diagnosis of rupture of fetal membranes (ROM): a meta-analysis. J Perinat Med 2013; 41: 233–240

[105] Palacio M, Kuhnert M, Berger R et al. Meta-analysis of studies on biochemical marker tests for the diagnosis of premature rupture of membranes: comparison of performance indexes. BMC Pregnancy Childbirth 2014; 14: 183

[106] Munson LA, Graham A, Koos BJ et al. Is there a need for digital examination in patients with spontaneous rupture of the membranes? Am J Obstet Gynecol 1985; 153: 562–563

[107] Alexander JM, Mercer BM, Miodovnik M et al. The impact of digital cervical examination on expectantly managed preterm rupture of membranes. Am J Obstet Gynecol 2000; 183: 1003–1007

[108] Mercer BM, Miodovnik M, Thurnau GR et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes. A randomized controlled trial. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. JAMA 1997; 278: 989–995

[109] Melamed N, Hadar E, Ben-Haroush A et al. Factors affecting the duration of the latency period in preterm premature rupture of membranes. J Matern Fetal Neonatal Med 2009; 22: 1051–1056

[110] Garite TJ, Freeman RK. Chorioamnionitis in the preterm gestation. Obstet Gynecol 1982; 59: 539–545

[111] Beydoun SN, Yasin SY. Premature rupture of the membranes before 28 weeks: Conservative management. Am J Obstet Gynecol 1986; 155: 471–479

[112] Major CA, de Veciana M, Lewis DF et al. Preterm premature rupture of membranes and abruptio placentae: is there an association between these pregnancy complications? Am J Obstet Gynecol 1995; 172 (2 Pt 1): 672–676

[113] Ananth CV, Oyelese Y, Srinivas N et al. Preterm premature rupture of membranes, intrauterine infection, and oligohydramnios: Risk factors for placental abruption. Obstet Gynecol 2004; 104: 71–77

[114] Soraisham AS, Singhal N, McMillan DD et al. A multicenter study on the clinical outcome of chorioamnionitis in preterm infants. Am J Obstet Gynecol 2009; 200: 372.e1–372.e6

[115] Lewis DF, Robichaux AG, Jaekle RK et al. Expectant management of preterm premature rupture of membranes and nonvertex presentation: what are the risks? Am J Obstet Gynecol 2007; 196: 6

[116] Higgins RD, Saade G, Polin RA et al. Evaluation and Management of Women and Newborns With a Maternal Diagnosis of Chorioamnionitis: Summary of a Workshop. Obstet Gynecol 2016; 127: 426–436

[117] Gibbs RS, Blanco JD, St Clair PJ et al. Quantitative bacteriology of amniotic fluid from women with clinical intraamniotic infection at term. J Infect Dis 1982; 145: 1–8

[118] Silver RK, Gibbs RS, Castillo M. Effect of amniotic fluid bacteria on the course of labor in nulliparous women at term. Obstet Gynecol 1986; 68: 587–592

[119] Blanco JD, Gibbs RS, Malherbe H et al. A controlled study of genital mycoplasmas in amniotic fluid from patients with intra-amniotic infection. J Infect Dis 1983; 147: 650–653

[120] Gibbs RS, Blanco JD, St. Clair PJ et al. Mycoplasma hominis and intrauterine infection in late pregnancy. Sex Transm Dis 1983; 10: 303–306

[121] Gibbs RS, Blanco JD, Lipscomb K et al. Asymptomatic parturient women with high-virulence bacteria in the amniotic fluid. Am J Obstet Gynecol 1985; 152 (6 Pt 1): 650–654

[122] Hauth JC, Gilstrap LC, Hankins GDV et al. Term maternal and neonatal complications of acute chorioamnionitis. Obstet Gynecol 1985; 66: 59–62

[123] Gomez R, Romero R, Ghezzi F et al. The fetal inflammatory response syndrome. Am J Obstet Gynecol 1998; 179: 194–202

[124] Hofer N, Kothari R, Morris N et al. The fetal inflammatory response syndrome is a risk factor for morbidity in preterm neonates. Am J Obstet Gynecol 2013; 209: 542.e1–542.e11

[125] Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. Am J Obstet Gynecol 2009; 201: 230–240

[126] van Teeffelen AS, van der Ham DP, Oei SG et al. The accuracy of clinical parameters in the prediction of perinatal pulmonary hypoplasia secondary to midtrimester prelabour rupture of fetal membranes: a meta-analysis. Eur J Obstet Gynecol Reprod Biol 2010; 148: 3–12

[127] Blott M, Greenough A. Neonatal outcome after prolonged rupture of the membranes starting in the second trimester. Arch Dis Child 1988; 63: 1146–1150

[128] [Anonymous]. Obstetric Care Consensus No. 6 Summary: Periviable Birth. Obstet Gynecol 2017; 130: 926–928

[129] [Anonymous]. ACOG Practice Bulletin No. 188: Prelabor Rupture of Membranes. Obstet Gynecol 2018; 131: e14

[130] Bond DM, Middleton P, Levett KM et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database Syst Rev 2017; (3): CD004735

[131] Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev 2013; (12): CD001058

[132] Mackeen AD, Seibel-Seamon J, Muhammad J et al. Tocolytics for preterm premature rupture of membranes. Cochrane Database Syst Rev 2014; (2): CD007062

[133] Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010; 37: 339–354

[134] Kunze M, Klar M, Morfeld CA et al. Cytokines in noninvasively obtained amniotic fluid as predictors of fetal inflammatory response syndrome. Am J Obstet Gynecol 2016; 215: 96.e1–96.e98

[135] Musilova I, Kacerovsky M, Stepan M et al. Maternal serum C-reactive protein concentration and intra-amniotic inflammation in women with preterm prelabor rupture of membranes. PLoS One 2017; 12: e0182731

[136] Mercer BM, Rabello YA, Thurnau GR et al. The NICHD-MFMU antibiotic treatment of preterm PROM study: impact of initial amniotic fluid volume on pregnancy outcome. Am J Obstet Gynecol 2006; 194: 438–445

[137] Abramowicz JS, Sherer DM, Warsof SL et al. Fetoplacental and uteroplacental Doppler blood flow velocity analysis in premature rupture of membranes. Am J Perinatol 1992; 9: 353–356

[138] Dudley J, Malcolm G, Ellwood D. Amniocentesis in the management of preterm premature rupture of the membranes. Aust N Z J Obstet Gynaecol 1991; 31: 331–336

[139] Musilova I, Bestvina T, Hudeckova M et al. Vaginal fluid interleukin-6 concentrations as a point-of-care test is of value in women with preterm prelabor rupture of membranes. Am J Obstet Gynecol 2016; 215: 619.e1–619.e12

[140] Hofmeyr GJ, Eke AC, Lawrie TA. Amnioinfusion for third trimester preterm premature rupture of membranes. Cochrane Database Syst Rev 2014; (3): CD000942

[141] Morris JM, Roberts CL, Bowen JR et al. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. Lancet 2016; 387: 444–452

[142] van der Ham DP, Vijgen SM, Nijhuis JG et al. Induction of labor versus expectant management in women with preterm prelabor rupture of membranes between 34 and 37 weeks: a randomized controlled trial. PLoS Med 2012; 9: e1001208

[143] van der Ham DP, van der Heyden JL, Opmeer BC et al. Management of late-preterm premature rupture of membranes: the PPROMEXIL-2 trial. Am J Obstet Gynecol 2012; 207: 276.e1–276.e10

[144] Tajik P, van der Ham DP, Zafarmand MH et al. Using vaginal Group B Streptococcus colonisation in women with preterm premature rupture of membranes to guide the decision for immediate delivery: a secondary analysis of the PPROMEXIL trials. BJOG 2014; 121: 1263–1272; discussion 1273

[145] Quist-Nelson J, de Ruigh AA, Seidler AL et al.; Preterm Premature Rupture of Membranes Meta-analysis (PPROMM) Collaboration. Immediate Delivery Compared With Expectant Management in Late Preterm Prelabor Rupture of Membranes: An Individual Participant Data Meta-analysis. Obstet Gynecol 2018; 131: 269–279

[146] Brisch KH. Prävention durch prä- und postnatale Psychotherapie. In: Brisch K-H, Hellbrügge T, Hrsg. Die Anfänge der Eltern-Kind-Bindung. Schwangerschaft, Geburt und Psychotherapie. Stuttgart: Klett-Cotta; 2007: 271–303

[147] Wehkamp KH. Psychosoziale Ätiologie und psychosomatische Betreuung bei vorzeitigen Wehen. Arch Gynecol Obstet 1987; 242: 712–713

[148] Mahler G, Grab D, Kächele H, Kreienberg R, Zimmer I. Geeignete Bewältigung bei drohender Frühgeburt – Expertenrating. In: Rohde A, Riecher-Rössler A, Hrsg. Psychische Erkrankungen bei Frauen – Psychiatrie und Psychosomatik in der Gynäkologie. Regensburg: S. Roderer Verlag; 2001: 226–232

[149] Fisch S, Klapp C, Bergmann R et al. Psychosoziales Frühwarnsystem Babylotse Plus – Untersuchung der diagnostischen Genauigkeit des Babylotse Plus Screeningbogens. Z Geburtshilfe Neonatol 2015: 219 - P201_214

[150] Frühgeborene: Für Familien. Online: https://www.fruehgeborene.de/fuer-familien; last access: 28.04.2019

[151] Frühe Hilfen. Online: https://www.fruehehilfen.de; last access: 28.04.2019

Guideline Program

Editors

Leading Professional Medical Associations

German Society of Gynecology and Obstetrics (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e. V. [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
Direktor der Frauenkliniken
Klinikum St. Marien Amberg
Mariahilfbergweg 7, DE-92224 Amberg
Kliniken Nordoberpfalz AG
Söllnerstraße 16, DE-92637 Weiden

DGGG Guidelines Representatives

Prof. Dr. med. Matthias W. Beckmann
Universitätsklinikum Erlangen, Frauenklinik
Universitätsstraße 21–23, DE-91054 Erlangen

Prof. Dr. med. Erich-Franz Solomayer
Universitätsklinikum des Saarlandes
Geburtshilfe und Reproduktionsmedizin
Kirrberger Straße, Gebäude 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/leitlinienstellungnahmen

Austrian Society of Gynecology and Obstetrics (Österreichische Gesellschaft für Gynäkologie und Geburtshilfe [OEGGG])
Frankgasse 8, AT-1090 Wien
stephanie.leutgeb@oeggg.at
http://www.oeggg.at

President of OEGGG

Prof. Dr. med. Petra Kohlberger
Universitätsklinik für Frauenheilkunde Wien
Währinger Gürtel 18–20, AT-1090 Wien

OEGGG Guidelines Representatives

Prof. Dr. med. Karl Tamussino
Universitätsklinik für Frauenheilkunde und Geburtshilfe Graz
Auenbruggerplatz 14, AT-8036 Graz

Prof. Dr. med. Hanns Helmer
Universitätsklinik für Frauenheilkunde Wien
Währinger Gürtel 18–20, AT-1090 Wien

Swiss Society of Gynecology and Obstetrics (Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe [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
Universitätsklinik für Frauenheilkunde
Geburtshilfe und feto-maternale Medizin
Inselspital Bern
Effingerstraße 102, CH-3010 Bern

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