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