not updated for > 5 years, Guideline is being revised

DGPPN

German Association for Psychiatry, Psychotherapy and Psychosomatics, DGPPN

(Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V.)

(Publisher)

S3 Guideline for Schizophrenia

AWMF Register No. 038-009

Abbreviated version (english)

Date: 15.03.2019

(English translation version: 28.12.2019)

Published by the Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V. (DGPPN)

Previous versions of this guideline

- **Version 1.0** from 15 March 2019, published on the AWMF website, English translation version 1.0 from 28 December 2019

Versions of this guideline

I. Long version (German)
II. Abbreviated version (German)
III. Abbreviated version (English)
IV. Guideline report (German)

Please cite as follows

DGPPN e.V. (ed.) for the Guideline Group: S3 Guideline for Schizophrenia. Abbreviated version (English), 2019, Version 1.0, last updated on 29 December 2019, available at: https://www.awmf.org/leitlinien/detail/ll/038-009.html

Publishers

This completely updated S3 Guideline for Schizophrenia was initiated and coordinated under the leadership of the Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V. (DGPPN) and is published in collaboration with the participating organisations.

The associations and organisations listed below were involved in the consensus process:

AGNP	Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakotherapie e.V.
AkdÄ	Arzneimittelkommission der deutschen Ärzteschaft
BAG-KT	Bundesarbeitsgemeinschaft Künstlerische Therapien (BAG-KT)
BApK	Bundesverband der Angehörigen Psychisch Kranker e.V.
BAPP	Bundesinitiative Ambulante Psychiatrische Pflege e.V.
BAR	Bundesarbeitsgemeinschaft für Rehabilitation e.V.
BdB	Bundesverband der Berufsbetreuer/innen e.V.
BDK	Bundesdirektorenkonferenz
BDP	Berufsverband deutscher Psychologinnen u. Psychologen e.V.
BFLK	Bundesfachverband Leitender Krankenpflegepersonen in der Psychiatrie
BKJPP	Berufsverband für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie in Deutschland e.V.
BPE	Bundesverband Psychiatrie-Erfahrener e.V.
BPtK	Bundespsychotherapeutenkammer
BVDN	Berufsverband deutscher Nervenärzte
BVDP	Berufsverband deutscher Psychiater e.V.
BVKJ	Berufsverband der Kinder- und Jugendärzte e.V.
bvvp	Bundesverband der Vertragspsychotherapeuten e.V.
DDPP	Dachverband Deutschsprachiger Psychosen Psychotherapie e.V.
DEGAM	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V.
DFPP	Deutsche Fachgesellschaft für Psychiatrische Pflege
DGGPP	Deutsche Gesellschaft für Gerontopsychiatrie und -psychotherapie e.V.
DGKJ	Deutsche Gesellschaft für Kinder- und Jugendmedizin e.V.
DGKJP	Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie e.V.
DGPE	Deutsche Gesellschaft für Psychoedukation e.V.
DGPPN	Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde
DGPs	Deutsche Gesellschaft für Psychologie e.V.
DGPT	Deutsche Gesellschaft für Psychoanalyse, Psychotherapie, Psychosomatik und Tiefenpsychologie e.V.
DGSF	Deutsche Gesellschaft für Systemische Therapie und Familientherapie e.V.
DGSP	Deutsche Gesellschaft für Soziale Psychiatrie e.V.
DGVP	Dachverband Gemeindepsychiatrie e.V.
DGVT	Deutsche Gesellschaft für Verhaltenstherapie e.V.
DMtG	Deutsche Musiktherapeutische Gesellschaft e.V.
DPtV	Deutsche PsychotherapeutenVereinigung e.V.
DVE	Deutscher Verband der Ergotherapeuten e.V.
DVSG	Deutsche Vereinigung für Soziale Arbeit im Gesundheitswesen e.V.
GNP	Deutsche Gesellschaft für Neuropsychologie e.V.
KNS	Kompetenznetz Schizophrenie
ZVK	Deutscher Verband für Physiotherapie e.V.

Apart from the Bundesverband Psychiatrie-Erfahrener e.V., all the above-named associations and organisations approved the final version of this guideline.

Guideline report
The full methodology of the guideline revision process can be found in the guideline report.

DGPPN Steering Group
The DGPPN Steering Group was responsible for managing, coordinating and organising the whole guideline process, including preparing meetings, telephone conferences and written votes; providing the methodology; implementing evidence searches; evaluating the literature; preparing evidence tables; and writing the guideline texts.

Project management and supervision

- Prof. Dr. Wolfgang Gaebel, Department of Psychiatry and Psychotherapy, LVR-Klinikum Düsseldorf, Heinrich-Heine-University Düsseldorf, Medical Faculty (responsible)
- Prof. Dr. Alkomiet Hasan, Department of Psychiatry and Psychotherapy, Hospital of the University of Munich
- Prof. Dr. Peter Falkai, Department of Psychiatry and Psychotherapy, Hospital of the University of Munich

Project organisation and coordination, methodological preparation

- Dr. Isabell Lehmann, LVR Institute for Healthcare Research, Cologne

Additional members of the Steering Group

- Prof. Dr. Birgit Janssen, LVR Hospital Langenfeld
- Prof. Dr. Thomas Wobrock, District Hospitals Darmstadt-Dieburg and University Hospital Göttingen
- Prof. Dr. Jürgen Zielasek, LVR Institute for Healthcare Research, Cologne

Extended Steering Group
The Extended Steering Group worked with the DGPPN Steering Group on specific issues to ensure that the steering group was representative of the guideline users. The Extended Steering Group consisted of the following people:

- Prof. Dr. Thomas Becker, Department of Psychiatry and Psychotherapy II of the University of Ulm at the District Hospital Günzburg
- Prof. Dr. Andreas Bechdolf, Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Hospital Am Urban, Berlin
- Prof. Dr. Stefan Klingberg, Department of Psychiatry and Psychotherapy at the University of Tübingen
- Prof. Dr. Hans Joachim Salize, Central Institute of Mental Health, Mannheim
- Prof. Dr. Rainer Richter (until May 2015), Dr. Nikolaus Melcop (from June 2016), Bundespsychotherapeutenkammer
- Prof. Dr. Stefan Wilm, Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V.
- Prof. Dr. Tania Lincoln, Deutsche Gesellschaft für Psychologie e.V.
- Dr. Christian Raida, Berufsverband Deutscher Nervenärzte e.V.
- Dr. Sabine Köhler, Berufsverband Deutscher Psychiater e.V.
- Ruth Fricke, Bundesverband Psychiatrie Erfahrener e.V.
- Gudrun Schliebener (until August 2017), Karl-Heinz Möhrmann (from September 2017), Bundesverband der Angehörigen psychisch Kranker e.V. (BApK)
- Prof. Dr. Benno Schimmelmann (until May 2016), Prof. Dr. Christoph Correll (from June 2016), Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie

Assistance and support from the AWMF
The AWMF supported all phases of the development and revision of the guideline. Prof. Dr. Ina Kopp, Head of the AWMF Institute for Medical Knowledge Management (AWMF-IMWi), moderated all consensus conferences and provided methodological advice and assistance throughout the entire guideline revision process.

Expert group

- Prof. Dr. Thomas Becker, Department of Psychiatry and Psychotherapy II of the University of Ulm at the District Hospital Günzburg
- Prof. Dr. Andreas Bechdolf, Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Klinikum Am Urban, Berlin
- Prof. Dr. Peter Falkai, Department of Psychiatry and Psychotherapy, Hospital of the University of Munich
- Prof. Dr. Wolfgang Gaebel, Department of Psychiatry and Psychotherapy, LVR-Klinikum Düsseldorf, Heinrich-Heine-University Düsseldorf, Medical Faculty
- Prof. Dr. Hermann-Josef Gertz, Department of Psychiatry and Psychotherapy, University Hospital Leipzig (representative: Prof. Dr. Carsten Spitzer, Tiefenbrunn Specialist Hospital for Psychiatry and Psychotherapy)
- Prof. Dr. Gerhard Gründer, Central Institute of Mental Health, Mannheim
- Prof. Dr. Stefan Klingberg, Department of Psychiatry and Psychotherapy at the University of Tübingen
- PD Dr. Markus Kösters, Department of Psychiatry and Psychotherapy II, University of Ulm at the District Hospital Günzburg
- Prof. Dr. Martin Lambert, Department of Psychiatry and Psychotherapy, University of Hamburg, University Hospital Hamburg-Eppendorf
- Prof. Dr. Stefan Leucht, Department of Psychiatry and Psychotherapy at the TU Munich, Munich
- Prof. Dr. Wolfgang Maier, Department of Psychiatry and Psychotherapy, University of Bonn, University Hospital Bonn
- Prof. Dr. Eva Meisenzahl, LVR Hospital Düsseldorf – Hospitals of the Heinrich Heine University Düsseldorf
- Prof. Dr. Andreas Meyer-Lindenberg, Central Institute of Mental Health, Mannheim
- Prof. Dr. Hans-Jürgen Möller, Department of Psychiatry and Psychotherapy at the LMU Munich
- Prof. Dipl.-Psych. Wulf Rössler, Psychiatric University Hospital Zürich, Zürich (Switzerland)
- Prof. Dr. Hans Joachim Salize, Central Institute of Mental Health, Mannheim
- Prof. Dr. Wolfgang Wölwer, Department of Psychiatry and Psychotherapy, LVR Hospital Düsseldorf – Hospitals of the Heinrich Heine University Düsseldorf

Experts in the field of child and adolescent psychiatry and psychotherapy

- Prof. Dr. Christoph Correll, Department of Psychiatry, Psychosomatics and Psychotherapy in Childhood and Adolescence, Charité – Universitätsmedizin Berlin
- Prof. Dr. Frauke Schultze-Lutter, Department of Psychiatry and Psychotherapy, LVR Hospital Düsseldorf, Medical Faculty, Heinrich Heine University Düsseldorf
- Prof. Dr. Stefanie J. Schmidt, Clinical Psychology in Childhood and Adolescence, Department of Clinical Psychology and Psychotherapy, University of Bern
- Prof. Dr. Benno Schimmelmann, practising child and adolescent psychiatrist, honorary professor at the Faculty of Medicine of the University of Bern
- Dr. Reinhard Martens, practising child and adolescent psychiatrist, Pirna

Other supporting staff

- Dr. Andrea Hinsche-Böckenholt, LVR Hospital Düsseldorf – Hospitals of the Heinrich Heine University Düsseldorf
- Daniela Reich-Erkelenz, MA, Institute of Psychiatric Phenomics and Genomics, Hospital of the University of Munich
- Anja Dorothée Streb, MA, Department of Psychiatry and Psychotherapy, Hospital of the University of Munich
- Dipl.-Psych. Harald Zäske, LVR Hospital Düsseldorf – Hospitals of the Heinrich Heine University Düsseldorf

Module Working Groups

For the revision process, the guideline was arranged into topic-specific modules which were updated by experts from the Steering, Expert and Consensus Groups in topic-specific Module Working Groups (WGs). These Module WGs worked with the members of the DGPPN Steering Group to update and expand the guideline texts. The spokespeople of the Module WGs were responsible for content development, in consultation with the representatives of the DGPPN Steering Group. The latter were responsible for evaluating and summarising the literature. The members of the Module WGs were involved in writing the recommendations and background texts.

Module WG 1 General Principles	
Spokesperson	Prof. Dr. Wolfgang Gaebel
Members	• Prof. Dr. Andreas Bechdolf • Prof. Dr. Thomas Becker • Prof. Dr. Peter Falkai • Prof. Dr. Alkomiet Hasan • Prof. Dr. Birgit Janssen • Prof. Dr. Martin Lambert • Prof. Dr. Wolfgang Maier • Dr. Nikolaus Melcop • Dr. Christian Raida • Prof. Dr. Jürgen Zielasek

Representative of the DGPPN Steering Group: Prof. Dr. Jürgen Zielasek

Module WG 2 Classification, Diagnosis and Differential Diagnosis	
Spokesperson	Prof. Dr. Wolfgang Maier
Members	• Prof. Dr. Andreas Bechdolf • Prof. Dr. Wolfgang Gaebel • Prof. Dr. Alkomiet Hasan • Dr. Burkhard Lawrenz • Prof. Dr. Frauke Schultze-Lutter • Prof. Dr. Tillmann Supprian • Prof. Dr. Stefan Wilm • Prof. Dr. Jürgen Zielasek

Representative of the DGPPN Steering Group: Prof. Dr. Wolfgang Gaebel

Module WG 3 General Treatment	
Spokesperson	Prof. Dr. Peter Falkai
Members	• Prof. Dr. Andreas Bechdolf • Prof. Dr. Wolfgang Gaebel • Prof. Dr. Alkomiet Hasan • Dr. Petra Godel-Ehrhardt • Prof. Dr. Gerhard Gründer • Prof. Dr. Dorothea von Haebler/Dr. Günter Lempa • Prof. Dr. Martin Lambert • Prof. Dr. Wolfgang Maier • Dr. Nikolaus Melcop • Dr. Christian Raida • Prof. Dr. Wulf Rössler • Prof. Dr. Stefan Wilm • Prof. Dr. Thomas Wobrock • Prof. Dr. Wolfgang Wölwer

Representative of the DGPPN Steering Group: Prof. Dr. Peter Falkai

Module WG 4a Pharmacotherapy and other Medical Treatment Approaches	
Spokesperson	Prof. Dr. Gerhard Gründer
Members	• Prof. Dr. Peter Falkai • Prof. Dr. Wolfgang Gaebel • Prof. Dr. Alkomiet Hasan • Dr. Sabine Köhler • Prof. Dr. Stefan Leucht • Prof. Dr. Benno Schimmelmann/Prof. Dr. Christoph Correll • Prof. Dr. Stefan Wilm • Prof. Dr. Thomas Wobrock

Representative of the DGPPN Steering Group: Prof. Dr. Thomas Wobrock

Module WG Psychotherapeutic and Psychosocial Interventions	
Spokesperson	Prof. Dr. Stefan Klingberg
Members	• Prof. Dr. Josef Bäuml • Prof. Dr. Andreas Bechdolf • Eckhardt Böhle • Dr. Ulrike Borst • Beatrix Evers-Grewe • Petra Godel-Ehrhardt • Prof. Dr. Dorothea von Haebler/Dr. Günter Lempa • Prof. Dr. Alkomiet Hasan • Martina Knuth • Prof. Dr. Tania Lincoln • Dr. Nikolaus Melcop/Dr. Tina Wessels • Dr. Christian Raida • Prof. Dr. Stefanie J. Schmidt • Prof. Dr. Wolfgang Wölwer

Representative of the DGPPN Steering Group: Prof. Dr. Wolfgang Wölwer (not a member of the DGPPN Steering Group, but commissioned by the Steering Group to take over this function for Module 4b)

Module WG 4c Treatment in Special Circumstances	
Spokesperson	Prof. Dr. Thomas Wobrock
Members	• Dr. Beate Baumgarte • Prof. Dr. Christoph Correll • Prof. Dr. Gerhard Gründer • Prof. Dr. Dorothea von Haebler/Dr. Günter Lempa • Prof. Dr. Alkomiet Hasan • Dr. Reinhard Martens • Prof. Dr. Benno Schimmelmann • Prof. Dr. Stefanie J. Schmidt • Prof. Dr. Frauke Schultze-Lutter • Prof. Dr. Tillmann Supprian

Representative of the DGPPN Steering Group: Prof. Dr. Alkomiet Hasan

Module WG 4d Rehabilitation	
Spokesperson	Prof. Dr. Thomas Becker
Members	• Prof. Dr. Wulf Rössler • Prof. Dr. Katarina Stengler • Prof. Dr. Jürgen Zielasek

Representative of the DGPPN Steering Group: Prof. Dr. Jürgen Zielasek

Module WG 5 Care Coordination	
Spokesperson	Prof. Dr. Peter Falkai
Members	• Prof. Dr. Wolfgang Gaebel • Petra Godel-Ehrhardt • Prof. Dr. Alkomiet Hasan • Prof. Dr. Martin Lambert • Prof. Dr. Eva Meisenzahl • Dr. Nikolaus Melcop • Dr. Christian Raida • Prof. Dr. Wulf Rössler • Prof. Dr. Stefan Wilm • Prof. Dr. Thomas Wobrock

Representative of the DGPPN Steering Group: Prof. Dr. Thomas Wobrock

Module WG 6 Cost Effectiveness of Treatment	
Spokesperson	Prof. Dr. Hans Joachim Salize
Member	• Prof. Dr. Alkomiet Hasan

Representative of the DGPPN Steering Group: Prof. Dr. Alkomiet Hasan

Module WG 7 Quality Management	
Spokesperson	PD Dr. Markus Kösters
Members	• Prof. Dr. Wolfgang Gaebel • Prof. Dr. Birgit Janssen

Representative of the DGPPN Steering Group: Prof. Dr. Birgit Janssen

Methodology

The complete methods report (336 pages) of this guideline is published in German (available at https://www.awmf.org/leitlinien/detail/ll/038-009.html). The AWMF Guidance Manual and Rules for Guideline Development in English is available at https://www.awmf.org/fileadmin/user_upload/Leitlinien/AWMF-Regelwerk/AWMF-Guidance_2013.pdf. The S3 Guideline for Schizophrenia was developed in full accordance with the AWMF Guidance manual.

AWMF S-classification for medical guidelines in Germany

S3	Evidence- and consensus-based guideline	Representative committee, systematic review and synthesis of the evidence, structured consensus development
S2e	Evidence-based guideline	Systematic review and synthesis of the evidence
S2k	Consensus-based guideline	Representative committee, structured consensus development process
S1	Recommendations by expert groups	Consensus development in an informal procedure

S3 guidelines correspond to the highest degree of systematic development

Grid for grading recommendations for the S3 Guideline for Schizophrenia based on the methodology of the Scottish Intercollegiate Guidelines Network (1)

1++	High-quality meta-analyses, systematic reviews of RCTs or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews or RCTs with a low risk of bias
*1-**	Meta-analyses, systematic reviews or RCTs with a high risk of bias
2++	High-quality systematic reviews of case control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
*2-**	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

*LoE 1- or 2- publications should in general not be used to defined recommendation grades due to the high risk of possibke.

Level of Evidence	Strength of Recommendation	Syntax
1++, 1+, (1-)	A	Strong recommendation (‘we recommend/we recommend not to’)
2++, 2+, (2-) or downgrading of 1++ / 1+ / (1-) due to methodological considerations	B	Recommendation (‘we suggest/we suggest not to’)
3, 4 or downgrading of 2++ / 2+ / (2-) due to methodological considerations	0	Open recommendation (‘may/may not be considered’)
-	GCP	Clinical consensus (different strengths of recommendation possible)

Establishing the strength of consensus

Strong consensus: agreement of > 95% of the participants; Consensus: agreement of > 75 to 95% of the participants; Mayority agreement: agreement of > 50 to 75 % of the participants; No consensus: agreement of < 50 % of the participants

Special Notes

The masculine form used in this guideline in intended to include women and non-binary people. The only reason for not using all three genders is to improve the readability of the text. The text should be understood as gender neutral and unbiased.

The field of medicine is continuously developing, which means that all the information in this S3 Guideline, in particular regarding diagnostic and therapeutic approaches, can only ever reflect the state of knowledge at the time when the searches were completed and the guideline was printed. The greatest possible care was taken when making recommendations for diagnosis and treatment and the choice and dosages of medicines, psychotherapy and psychosocial procedures. Nevertheless, users who treat patients with medicines must refer to the package insert and manufacturer's information and, if in any doubt, consult a specialist. Users of this guideline remain responsible when they apply the guidelines for diagnosis and treatment. When prescribing a medicine (or other therapeutic procedure described in this guideline) for an indication for which it has not been approved, users must consider the criteria for off-label use. This point is highlighted at the respective locations as follows:

> 'This (therapeutic procedure) is an **off-label use**. "Off-label use" refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee).
>
> The following criteria must be fulfilled if substances are to be used off label in clinical practice:
>
> - Proven efficacy;
> - Favourable risk/benefit profile;
> - Lack of alternatives – treatment trial.
>
> In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared.'

Guidelines from medical associations are systematically developed to help doctors make decisions in specific situations. They are based on current scientific findings and established clinical procedures and ensure greater safety in medicine. They should also consider economic aspects. Guidelines are not legally binding for doctors and therefore cannot be a reason for doctors being held liable or for limiting their liability.

Errors and misprints in published guidelines cannot be completely ruled out, even when the utmost care is taken to avoid them. Furthermore, guidelines only consider abstract risk-benefit potentials, in particular in their recommendations on drug treatments. Therefore, doctors who follow guideline recommendations for drug treatment must always consider the risk-benefit profile of the individual patient. For this reason, the authors, Steering Group members, experts, members of the consensus group and other people involved in the guideline development process are not liable for harm arising from a wrong or missing diagnosis or treatment in individual cases.

In this guideline, registered trademarks are mostly not specifically indicated. Consequently, even if a trademark is not shown next to a product name it cannot be assumed that the name is not trademarked.

Table of Contents

1. General Principles (Module 1)

This practice guideline deals with the diagnosis and treatment of schizophrenia (ICD-10: F20; the revised version ICD-11 will be published soon). The aims are to (1) provide systematically developed guidance to practitioners who treat people with schizophrenia to help them make decisions in specific situations and (2) present and evaluate procedures relating to diagnosis, treatment, rehabilitation and care. These recommendations aim to promote the use of effective procedures and reduce both the use of procedures with little or no effect and the occurrence of side effects and consequently to improve the quality of treatment. Guidelines should also enable practitioners and service users to jointly make informed decisions about diagnosis and treatment under special consideration of the service user's individual characteristics and the available resources in individual cases.

The detailed presentation of Module 1 can be found in the background text of the long version (in German). Module 1 does not contain any recommendations.

2. Classification, Diagnosis and Differential Diagnosis (Module 2)

2.1 Clinical and psychopathological diagnosis on the basis of ICD-10, recording the medical history and screening for substances

Recommendation 1	Strength of recommendation
We recommend making a diagnosis of schizophrenia on the basis of operationalised criteria. Internationally recognised diagnostic definitions are operationalised in two diagnostic manuals, DSM-5 and ICD-10. ICD-10 must be used in medical practice in Germany. According to ICD-10, the main symptoms of schizophrenia are: 1. Thought echo, insertion, withdrawal, broadcasting. 2. Delusions of control or influence; feeling of physical movements, thoughts, actions or perceptions made by external agents; delusional perceptions. 3. Commenting or discussing voices. 4. Persistent, culturally inappropriate or completely impossible delusions (bizarre delusions). 5. Persistent hallucinations in any modality. 6. Thought blocking or interpolations in the train of thought. 7. Catatonic behaviour, such as excitement, posturing, negativism or stupor. 8. Negative symptoms, such as marked apathy, paucity of speech, blunting or incongruity of emotional responses. A diagnosis of schizophrenia requires **at least one very clear symptom** (two or more if less clear cut) from **Groups 1 – 4** or at least two symptoms from Groups 5 – 8. These symptoms must have been **clearly present for most of the time during a period of 1 month or more.** Schizophrenia should not be diagnosed **in the presence of overt brain disease or during states of drug intoxication or withdrawal**.	**GCP**

Recommendation 2	Strength of recommendation
When recording the medical history in the initial diagnostic process and over the course of the illness, we recommend including the following aspects: • Structured psychopathological evaluation • Biographical and social history • Substance use history • General health history • Family history • Previous treatments • The service user's preferences and wishes regarding possible diagnostic and therapeutic options • Desire/possibility to include family members and close confidants	**GCP**

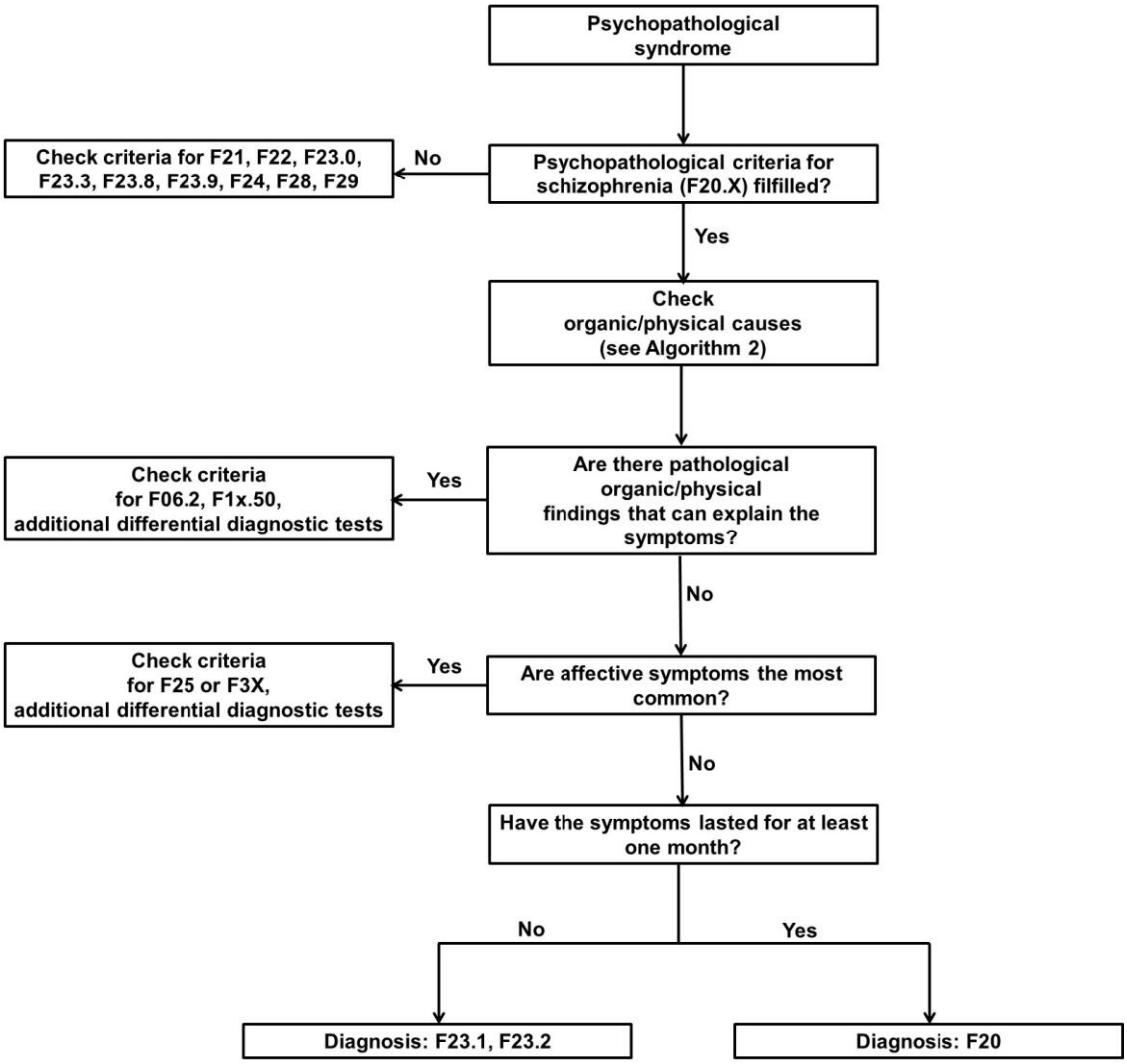

Figure 1: Algorithm 1 – Differential diagnosis of schizophrenia according to ICD-10

Recommendation 3	Strength of recommendation
In acute psychotic syndromes, we recommend performing a drug screening to exclude a substance-related cause.	**GCP**

2.2 Differential diagnosis: distinguishing from organic psychotic disorders, autoimmune encephalitis

Recommendation 4	Strength of recommendation
In every new case of psychotic symptoms, we recommend offering differential diagnostic tests for organic causes. The following factors may indicate an organic cause of the symptoms: • Early and acute onset • Focal neurological symptoms, clouded consciousness, epileptic seizures • Significant cognitive deficits*, subacute memory deficits (within 3 months) as the main symptoms that are not compatible with the known symptoms of schizophrenia • Confusion • Optical hallucinations • Psychomotor symptoms (incl. catatonia) • Fluctuating course of the illness • Early treatment resistance • Fluctuating psychopathology • Comorbid developmental delay/disorder • Fever, exsiccosis *The cognitive domains that should be evaluated and the suggested test procedures are presented later in the text (full version, in German).	**GCP**

Drug group	Examples
Drugs that affect the CNS	L-dopa and other dopaminergic drugs, anticholinergics, triptans
Cardiovascular drugs	Digoxin, clonidine, methyldopa, betablockers, ACE inhibitors, angiotensin-II receptor blockers, calcium channel blockers, diuretics, statins
Gastroenterological drugs	Metoclopramide, H2 blockers, pantoprazole
Hormone preparations	L-thyroxine, oral contraceptives, steroids
Analgesics	Non-steroidal antiphlogistics, opioids
Anti-infectives	Sulphonamides, chinolone, clarithromycin, amoxicillin, cephalexin, metronidazole, chloroquine, isoniazid, acyclovir
Immune suppressants and immune modulators	Corticosteroids, methotrexate, vincristine, ifosfamide, cyclosporine, 4-fluorouracil, cisplatin, doxorubicin, cyclophosphamide

Table 1: Examples of drugs that can induce a secondary psychotic syndrome. Adapted from (2)

The diagnostic criteria for possible autoimmune encephalitis according to **an international expert consensus** are summarised below (adapted from (3)). The diagnosis can be made when all three of the following criteria are met:

1. Subacute onset (rapid progression within <3 months) of working memory deficits, qualitative or quantitative change in level of consciousness, lethargy, personality change or other psychiatric symptoms
2. At least one of the following:
   - New focal neurological deficits (focal CNS findings)
   - New epileptic seizures (seizures not explained by a previously known seizure disorder)
   - Lymphocyte pleocytosis in CSF (>5 cells/µL)
   - MRI features suggestive of encephalitis: hyperintense MRI signal in T2 or FLAIR sequences, restricted to medial temporal lobes (limbic encephalitis) or in multifocal areas that involve grey or white matter or both.
3. Exclusion of other causes, such as infectious encephalitis (neurotropic viruses, e.g. CMV, EBV, HSV, influenza, measles, mumps, rubella, VZV; other pathogens, e.g. borrelia, chlamydia, mycoplasma, candida albicans and *Toxoplasma gondii*) or sepsis, rheumatic diseases (e.g. lupus erythematosus, sarcoidosis), metabolic and toxic encephalopathies (e.g. hepatic, renal), mitochondrial diseases, cerebrovascular diseases, tumours, Creutzfeldt-Jakob disease.

Table 2: International expert consensus on the criteria for a possible autoimmune encephalitis (adapted from (3))

‘Hard signs’	‘Soft signs’
• Lymphocytic pleocytosis in CSF with no indication of an infectious cause	• Quantitative disturbances of consciousness
• Epileptic seizures	• Motor disorder or unsteadiness when standing or unsteady gait
• Faciobrachial dystonic seizures	• Autonomic instability
MRI abnormalities (medial temporal hyperintensities, atrophy in this region)	• Focal neurological deficits, incl. aphasia or dysarthria
EEG abnormalities (slowing of basic rhythm, pattern typical for epilepsy, holocephalic extreme delta brush [beta-delta complexes, consisting of bilateral delta activity with 1-3 Hz and overlaid beta activity with 20-30 Hz]) (4) for which there is no other explanation. The extreme delta brush seems to be a common feature of NMDAR autoimmune encephalitis in people other than newborns, although its specificity is unclear **(4, 5)**	• Rapid progression of psychotic symptoms, despite treatment
	• Hyponatraemia
	• Catatonia
	• Headache of unclear aetiology
	• Other comorbid autoimmune diseases

Table 3: Clinical warning signs for a possible autoimmune encephalitis with psychotic symptoms (3, 6, 7).

Antigen	Clinical signs	Specific features	Age distribution	Tumour
NMDA receptor (NR1/GluN1 subunit)	Deficits in short-term memory, schizophreniform psychosis, epileptic seizures/perioral dyskinesias/dystonia, disturbances of consciousness, hypoventilation	Cerebral MRI often normal, usually pleocytosis in CSF, slowing in EEG	All age groups, most frequent in childhood and adolescence, 75% women	In women, often ovarian teratoma
LGI1	Deficits in short-term memory (rapidly progressing dementia), psychosis/catatonia, faciobrachial dystonic seizures	Medial temporal hyperintensity in MRI, hyponatraemia	Older adults (>40 years)	Rare
CASPR2	Neuromyotonia, Morvan syndrome (= sleeplessness, autonomic excitement, neuromyotonia + symptoms of a limbic encephalitis, e.g. psychosis, epileptic seizures)	Similar to LGI1, no hyponatraemia	Older adults	Thymoma possible
AMPA receptor	Deficits in short-term memory, psychosis, epileptic seizures	CSF usually abnormal	Adults	Rare (thymoma)
DPPX	Deficits in short-term memory, irritability/apathy, sleep disorder, psychosis/mutism, epileptic seizures	Treatment-refractory diarrhoea	Older adults	Not known
$GABA_B$ receptor	Epileptic seizures are main symptom, memory disorders	Pleocytosis, MRI changes	Adults	Primarily small-cell bronchial carcinoma
mGluR5	Personality change, emotional instability	Ophelia syndrome	Younger adults	Hodgkin's lymphoma
Glycine receptor	Cognitive deficits, hyperexcitability	Progressive encephalomyelitis with rigidity and myoclonias), stiff person syndrome	Older adults	Rare

Table 4: Important types of autoimmune encephalitis with specific antibodies against synaptic and neuronal cell surface proteins and psychotic/cognitive syndromes. Adapted and expanded from (6, 8, 9). *AMPA*: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, *GABA*: gamma-aminobutyric acid. *CASPR2*: contactin-associated protein 2, *DPPX:* dipeptidyl-peptidase-like protein-6, *LGI1:* leucine-rich glioma inactivated 1, *mGluR5:* metabotropic glutamate receptor 5*, NMDA:* N-methyl-D-aspartate

2.3 Comorbid medical illnesses and additional diagnostic tests

In principle, there are **different levels** of medical and differential diagnostic tests:

1. The recommended strategies to detect and treat medical comorbidities can be found in Recommendations 5 to 7.
2. The recommended basic diagnostic procedures for the first onset of an illness and a relapse can be found in Recommendations 8 and 9.
3. Optional tests may be needed because of a clinical suspicion or findings from the basic diagnostic procedures; these tests are described in Recommendations 8 and 9 and in detail in the text of the long version (in German).
4. Tests to monitor antipsychotic treatment and related side-effects are presented in Module 4 of the long version (in German).

Statement 1	
People with schizophrenia have a statistically significantly higher risk for metabolic and cardiovascular diseases, cancer, pulmonary disease and other medical comorbidities. Expert consensus based on Correll et al. 2017 (133), Vancampfort et al. 2015 (139), Vancampfort et al. 2016 (138), WFSBP guideline (Hasan et al. 2012)	

Recommendation 5	Strength of recommendation
Independent of the illness phase, in addition to guideline-based pharmacotherapy, psychotherapy and psychosocial therapy we recommend offering people with schizophrenia regular monitoring of their physical health to reduce the excess mortality.	**GCP**

Recommendation 6	Strength of recommendation
We recommend that practitioners treating people with schizophrenia actively enquire about clinical symptoms that indicate typical medical comorbidities in schizophrenia and, in case of clinical suspicion, evaluate and classify the symptoms. Possible causes should be taken into account during treatment.	**GCP**

Recommendation 7	Strength of recommendation
We recommend offering treatment, according to the respective recommendations, to people with schizophrenia who have high blood pressure, abnormal lipid levels, obesity, diabetes or a risk for diabetes, who smoke (see Module 4c) or who are not very physically active (see Modules 4a, 4b). Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults: prevention and management' 2014 (10).	**GCP**

Recommendation 8	Strength of recommendation
We recommend that during the course of treatment practitioners actively ask whether the tests recommended as part of the diagnostic process for the first onset of the illness were performed and, if not, offer to perform these tests.	**GCP**

Recommendation 9	Strength of recommendation

In a **first manifestation of schizophrenia**, we recommend offering the following tests:
 	
Obligatory
• Complete physical and neurological evaluation (incl. weight and height, temperature, blood pressure/pulse)
• Blood tests
  ○ Differential blood count
  ○ Fasting blood glucose and perhaps HbA1c
  ○ GPT, gamma-GT, creatinine/eGFR
  ○ Sodium, potassium, calcium
  ○ ESR/CRP
  ○ Thyroid parameters (initial TSH)
• Urine drug screening
• Structural imaging of the brain with cranial MRI (with T1, T2, FLAIR sequences; if abnormal, further evaluation with contrast MRI)
  ○ If MRI is not available or contraindicated: CCT
 	
Optional
• We recommend offering a lumbar puncture if clinical, laboratory or instrument-based diagnostic tests indicate a possible secondary physical cause for the symptoms (see background text [in German] and Recommendation 4).
• We recommend offering psychological testing in the areas attention, learning and memory, executive functions and social cognition (see Table 4) to obtain information for decisions regarding differential diagnoses and to prepare for making decisions about additional neuropsychological and psychosocial treatment and rehabilitation options.
• We recommend offering an EEG if there are clinical indications of possible epileptic events or other specific neurological illnesses (see background text [in German]).
• We recommend offering to clarify the presence of dementia in older people, and in people of other ages with suspected dementia, in accordance with the AWMF guideline ‘Dementia’.
	GCP

Optional **laboratory tests** to be performed in case the medical history and/or clinical findings and/or other sources indicate physical causes (see background text) include:

- Creatinine kinase (CK),
- Laboratory tests for rheumatic diseases,
- Iron and copper metabolism,
- Vitamins B1, B6, B12,
- Serology for relevant infectious diseases (HIV, hepatitis, lues, etc.),
- Additional laboratory tests for other differential diagnoses (see background text)

For further information on ECG, EEG and CSF tests, see the long version of this guideline (in German).

Functional area	Example test procedures
General intelligence	Subtests from a relevant normalised and standardised intelligence test (e.g. WAIS-IV)
Processing speed	Symbol search (WAIS-IV) or Trail Making Test, Part A
Attention (divided, selective)	d2 test or subtests from the TAP or VTS
Working memory (verbal/visual)	Digit span test or letter-number sequencing test from the WAIS-IV, picture completion from the WAIS-IV, subtests from the TAP or VTS
Verbal learning/memory	CVLT or VLMT
Visual learning/memory	Figural Memory Test from the VTS, visual reproduction from the WAIS-IV
Executive functions (inhibition control, planning, problem solving)	Colour-word interference test, Trail Making Test Part B, Wisconsin Card Sorting Test, Tower of London, Response inhibition subtest from VTS
Social cognition	Recognition and regulation of emotions from the MSCEIT, Theory of Mind from the VTS

Table 5: Example neuropsychological test procedures. WAIS-IV: Wechsler Adult Intelligence Scale - Fourth Edition (German version: (11)), TAP: Test of Attentional Performance, computer-based test battery (12), VTS: Vienna Test System, computer-based test battery: WMS-IV: Wechsler Memory Scale – Fourth Edition (German version: (13)), CVLT: California Verbal Learning Test (German version: (14)), VLMT: Verbal Learning and Memory Test (German version: (15)), MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test (German version (16)).

Recommendation 10	Strength of recommendation
We recommend that, in case of relapse, practitioners confirm that the recommended initial diagnostic tests were performed (Recommendation 9). If not, we recommend to offer these tests again.	**GCP**

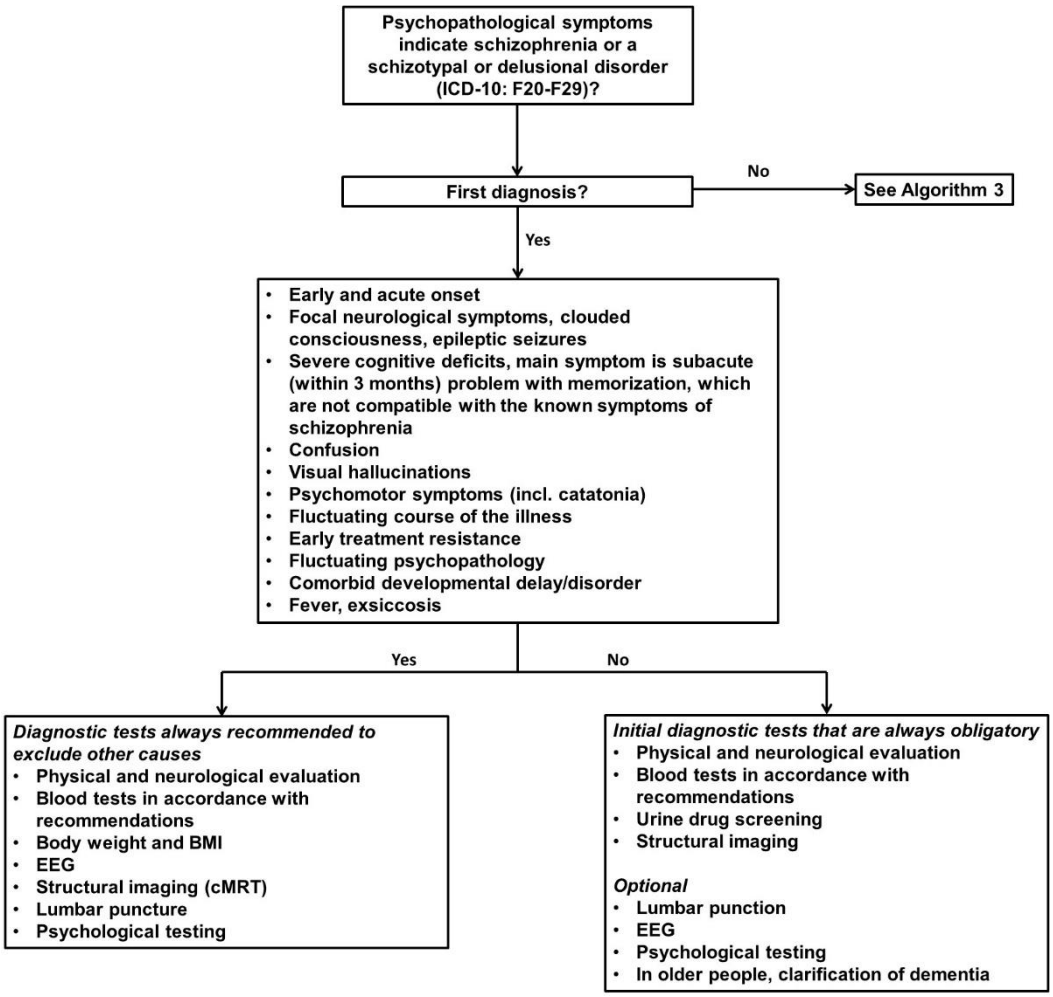

Figure 2: Algorithm 2: Tests for differential diagnosis from organic disorders in first-episode schizophrenia. See also Recommendations 4 and 9 and the background text of the long version (in German) for additional details regarding this algorithm

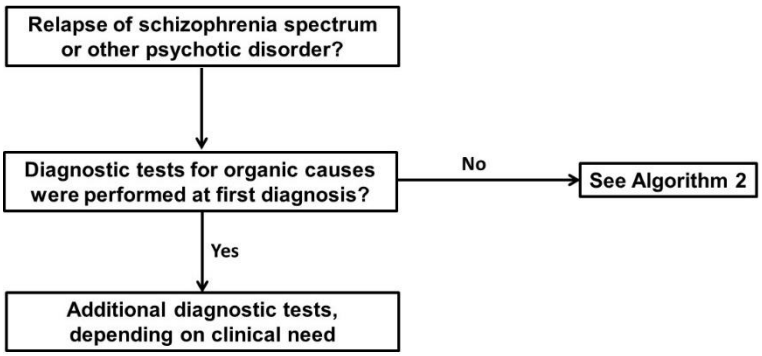

Figure 3: Algorithm 3: Tests for differential diagnosis from organic disorders in case of relapse. See also Recommendation 10 and the background text of the long version (in German) for additional details regarding this algorithm

3. General Treatment (Module 3)

3.1 General principles of treatment, continuing education and three-way discussions

Recommendation 11	Strength of recommendation
The aim of treatment is for the patient to be largely symptom free and to be able to both lead a self-determined life and evaluate therapeutic procedures while being aware of their risks and benefits. To achieve this goal, we recommend developing an overall treatment plan together with service users and everyone participating in the treatment process. We recommend establishing a collaboration with family members and close confidants, arranging for the treating institutions to coordinate and cooperate with each other and involving the non-professional support and self-help systems. We recommend integrating all treatment steps into the overall treatment plan and coordinating each treatment step and phase as part of a multiprofessional treatment that is offered as close to the service user's home as possible. We recommend facilitating the service user's access to the support system and coordinating resources in the psychiatric-psychotherapeutic and general health care systems. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 12	Strength of recommendation
People with schizophrenia have a right to be perceived with their special needs and individually different needs for assistance and should be empowered and enabled to assert their own interests, organise themselves and determine their own living conditions themselves (empowerment). Adapted and revised from the AWMF guideline 'Psychosocial Therapies in Severe Mental Illness' 2013 and 2018 (in German) (18).	**GCP**

Recommendation 13	Strength of recommendation
Quality assurance measures for the multiprofessional team (e.g. recognised continuing education, supervision, intervision, case discussions, team discussions) can improve care for people with schizophrenia and we suggest implementing these measures.	**GCP**

Recommendation 14	Strength of recommendation
We recommend offering to arrange a trialogue between service users, family members and close confidants and professionals for providing information and forming relationships throughout the help system. Such collaboration is an important prerequisite for open, trustworthy and successful cooperation between all parties involved and forms the basis for pursuing joint interests and treatment goals. The results of the trialogue are not limited to the individual therapeutic relationship but also affect the adequate presentation of patients' and family members' interests in public and political spheres, quality promotion and the further development of health care structures. Adapted and revised from the AWMF guideline 'Psychosocial Therapies in Severe Mental Illness' 2013 and 2018 (in German) (18).	**GCP**

4. Specific Treatment Procedures (Module 4)

5. Pharmacotherapy and other Medical Treatment Approaches (Module 4a)

5.1 General principles of pharmacotherapy

Recommendation 15	Strength of recommendation
We recommend embedding pharmacotherapy in a holistic treatment concept that includes general and specific psychotherapeutic and psychosocial measures and psychiatric treatment, depending on the differential indication. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 16	Strength of recommendation
We recommend telling the patient at the start of pharmacotherapy about the acute and long-term effects and adverse effects of the drugs (risk-benefit evaluation) and actively involving patients in the decision-making process (shared decision-making, see Module 3). We also recommend presenting the advantages and disadvantages of the treatment and possible alternatives in clear language and explaining technical terms. Adapted and expanded from the AWMF guidelines 'Schizophrenia' (17) and 'Unipolar depression' 2015 (in German) (19).	**GCP**

Recommendation 17	Strength of recommendation
Before starting pharmacotherapy, we recommend performing laboratory tests, as shown in Table 9, and recording an ECG. We recommend ruling out pregnancy in women of child-bearing age.	**GCP**

Recommendation 18	Strength of recommendation
We recommend that the decision about the suitable antipsychotic and route of administration is made jointly by the service user and treating doctor. We recommend considering and discussing the following: • The clinical syndrome to be treated • Previous experience of effects and side effects of one or more drugs during treatment to date • Advantages and disadvantages of the respective drug • Metabolic, motor, cardiovascular or hormonal/sexual side effects (see Table 9) • Benefits and risks of forgoing treatment with antipsychotics • The service user's preferences • Sex-specific aspects, patient's age and comorbidities We recommend taking into consideration any treatment agreements or crisis plans that the patient may have (see also Module 4c). We recommend continually reviewing the risk-benefit assessment in the course of treatment and taking appropriate measures if there are any changes. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17) and the NICE guideline 'Psychosis and schizophrenia in adults 2014' (10).	**GCP**

5.2 Routes of administration of antipsychotic substances

Recommendation 19	Strength of recommendation
There is insufficient evidence of any differences in the efficacy of oral, intramuscular and intravenous antipsychotics in the treatment of the acute illness. We recommend using parenteral administration only in very exceptional cases. We recommend choosing the oral route of administration in cooperative patients, unless the patient requests a different route, because it is the least invasive, has similarly good efficacy and best ensures patient autonomy. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17) and the NICE guideline 'Psychosis and schizophrenia in adults 2014' (10).	**GCP**

5.3 Therapeutic Drug Monitoring (TDM)

Recommendation 20	Strength of recommendation
Therapeutic drug monitoring (TDM) may be considered in case of adverse drug reactions, clinical non-response, suspected drug interactions and suspected non-compliance. We recommend basing the use and frequency of TDM on the 2017 update of the Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP) guidelines. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17), the NICE guideline 'Psychosis and schizophrenia in adults 2014' (10) and the AGNP guideline 'Consensus guidelines for therapeutic drug monitoring in neuropsychopharmacology: update 2017' (20).	**GCP**

Recommendation 21	Strength of recommendation
In case of treatment resistance, we suggest reaching a serum level of clozapine of at least 350 ng/ml, as long as there are no tolerability issues. LoE 2++ (based on 5 studies, which are summarised in the PORT guideline (21) and the WFSBP guideline (22) – although neither guideline was thoroughly and systematically searched – and on the lower value of the therapeutic reference range for clozapine (20)).	**B**

Antipsychotic	Chemical class[4]	D1	D2	D3	5-HT2	M1	α 1	H1
Amisulpride	Benzamide	0	+++	+++	0	0	0	0
Aripiprazole[1,2]	Phenylpiperazine quinoline	0	+++	+++	++	0	+	+
Cariprazine	Dichlorophenylpiperazine	+	+++	+++(+)	++	0	0	+
Clozapine[2]	Dibenzodiazepine	++	+	++	+++	+++	+	+++
Flupentixol	Thioxanthene	++	+++	+++	++	0	+	+
Fluphenazine	Phenothiazine	++	+++	+++	++	0	++	++
Haloperidol[2]	Butyrophenone	++	+++	++	+	0	++	0
Melperone	Butyrophenone	0	+	+	++	0	+	+
Lurasidone[3]	Benzisothiazol piperazine	+	++	0	++	0	0	0
Olanzapine[2]	Thienobenzodiazepine	++	+++	++	+++	++	++	+++
Paliperidone	Benzisoxazole	0	+++	+	+++	+	+	+
Perphenazine	Phenothiazine	+	+++	+++	++	0	++	++
Pipamperone	Butyrophenone	0	+	+	++	0	+	0
Quetiapine	Dibenzothiazepine	+	+	+	+	0	+	++
Risperidone[2]	Benzisoxazole	++	+++	++	+++	0	+++	+
Sertindole	Indole	++	+++	+	+++	0	++	0
Ziprasidone[2]	Benzisothiazine	+	++	++	+++	0	+	++
Zuclopenthixol	Thioxanthene	++	+++	++	0	+++	+++	+++

Table 6: Receptor physiology-related properties of various antipsychotics. This table was taken from (23) and expanded. In accordance with (23), this semiquantitative information represents in vitro receptor affinities and always represent the clinical (in vivo) effects. [1]Partial D2/D3 agonist and 5-HT1A agonist; [2]D4 antagonist; [3]5-HT7 antagonist and partial 5-HT1A agonist, [3]Lurasidone is approved in Germany for the treatment of schizophrenia, but the statutory health insurance companies do not cover the cost. [4]Translations of the German nomenclature (abbreviated in parts)

	Dosing interval[1]	Minimum effective dose[2]	Initial dose[3, 6] (mg/d)	Mean dose ranges[4, 6] (mg/d)	Recommended maximum dose[6] (mg/d)	Approved maximum dose[5] (mg/d)
Amisulpride	(1) – 2	-	100	200 – 800	1000	1200
Aripiprazole	1	10	5 – 10	7.5 – 30	30	30
Cariprazine	1	1.5	1.5	1.5 – 6	6	6
Clozapine	2 – (4)	300	12.5	150 – 500	800	900
Flupentixole	1 – (2)	-	3	5 – 12	18	60
Fluphenazine	2 – (3)	-	3	5 – 15	20	40
Haloperidol	1 – (2)	4[7]	3	2 – 10	10	20[7]
Lurasidone[8]	1	40	40	40 – 160	160	160
Melperone	1 – 2		50	25 – 100	200	400
Olanzapine	1	7.5	5	5 – 20	20	20
Paliperidone	1	3	3	3 – 9	12	12
Perphenazine	1 – 2	-	8	8 – 12	24	24
Pipamperone	1 – 3	-	20	20 – 120	120 – 260	360
Quetiapine	2	150	100	150 – 750	750	750
Risperidone	1 – (2)	2	2	2 – 6	8	16
Sertindole	1	12	4	12 – 20	20	24
Ziprasidone	2	40	40	120 – 160	160	160
Zuclopenthixole	1 – 3	-	20	20 – 60	75	75

Table 7: Recommended oral doses of various antipsychotics in acute treatment. [1]Recommended distribution of the specified total dose over a day. Once a day = 1, twice a day = 2, etc. Maximum doses may have to be spread over several administrations at different times. [2]Minimal effective doses are those that were significantly better than placebo in at least one acute phase study (updated on the basis of Leucht et al. Schizophrenia Bulletin 2014, see Appendix). The doses shown in the table are for chronic patients. An international consensus suggested that first-episode patients need about 30% lower doses and older patients about 50% lower doses (Gardner et al. Am J Psych 2010). [3]The initial doses can also be higher; the minimum initial doses are specified here, [4]Mean dose ranges that are often used in clinical practice. In general, one should aim to use the lowest possible dose in acute and maintenance treatment because the risk for side effects increases with increasing doses. [5]Highest approved dose according to the prescribing information (if no German prescribing information is available, the FDA prescribing information is used). [6]Partially modified recommendations of an international consensus (Gardner et al. Am J Psych 2010). [7]Doses of haloperidol > 20 mg/day, which were approved at an earlier point in time, are no longer to be used and are also not compatible with the EMA/BfArM provisions, which specify an approved dose of 20 mg/day but recommend a maximum dose of 10 mg/day. [8]Lurasidone is approved in Germany for the treatment of schizophrenia, but the statutory health insurance companies do not cover the cost. A table can be found in the Appendix that shows evidence-based calculations of the minimum effective dose according to Leucht et al. 2014 (24). Deviations from the approved doses (see respective prescribing information) are only permitted in very exceptional cases, taking into account the scientific evidence, and are considered to be off-label use, which must be explained to be patient separately.

	Akathisia	Parkinsonism	Tardive dyskinesia	Weight gain	Metabolic changes	Diabetes mellitus	Constipation	Hyperprolactinaemia	Dysmenorrhoea/ amenorrhoea	Sexual dysfunction	Sedation	Orthostatic dysregulation	Prolongation of the QT interval	Increased transaminases/ bilirubin	Changes in blood count	Agranulocytosis/ pancytopaenia	Epileptic seizures	MNS*	Pneumonia
Amisulpride	+	+	+	0/+	0/+	0/+	++	+++	++	++	0/+	0/+	++	0/+	0/+	0/+	0/+	?	0
Aripiprazole	++	+	+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	?
Cariprazine	++	++	+	0/+	0/+	0/+	0	0	0	0	0	0/+	0/+	++	0/+	0/+	0/+	0/+	?
Clozapine	+	0	0	+++	+++	+++	+++	0/+	0/+	+	+++	+++	+	++	+	++	++	0/+	++
Flupentixole	+++	+++	++	++	+	+	++	0/+	0/+	+	++	++	0/+	+	0/+	0/+	+	0/+	?
Fluphenazine	+++	+++	+++	0/+	0/+	0/+	+	0/+	0/+	+	++	++	+	+	+	0/+	++	0/+	?
Haloperidol	+++	+++	+++	+	0/+	0/+	+	+++	++	++	+	0	0/+	++	+	0/+	0/+	+	?
Lurasidone[1]	+/++	+/++	+	0/+	0/+	0/+	+	+	+	+	+	0/+	0/+	+	0/+	0/+	0/+	0/+	?
Melperone	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+	++	++	+	0/+	+	0/+	?	0/+	?
Olanzapine	+	0/+	0/+	+++	+++	+++	++	+	0	+	+/++	++	0/+	+	0/+	0/+	0/+	0/+	+
Paliperidone	+	++	+	++	+	+	++	+++	+++	++	0/+	+	+	++	0/+	0/+	0/+	0/+	?
Perphenazine	++	++	++	++	+	?	+	+	+	+	+	+	+	0/+	0/+	0/+	0/+	0/+	?
Pipamperone	++	+	0/+	?	?	+	?	0/+	++	++	++	++	+	+	+	0/+	0/+	0/+	?
Quetiapine	+	0/+	0/+	++	++	++	+	0/+	0/+	+	++[2]	++[2]	+	++	++	0/+	0/+	0/+	+
Risperidone	+	++	+	++	+	+	++	+++	++	++	+	+	+	+	0/+	0/+	0/+	0/+	+
Sertindole	+	0/+	+	++	+	+	+	+	+	+	0/+	+	+++	0/+	0/+	0/+	0/+	0/+	?
Ziprasidone	+/++	+	+	0/+	0/+	0/+	0/+	+	0/+	+	+	0/+	++	+	0/+	0/+	0/+	?	?
Zuclopenthixole	+++	+++	++	++	+	+	++	++	++	++	+++	++	0/+	0/+	0/+	0/+	+	0/+	?

Table 8: Side effects of antipsychotics. The table was developed on the basis of the CINP schizophrenia guidelines and the references given there (25) and the previous AWMF guideline 'Schizophrenia' (in German) (17) and adapted in an expert consensus on the basis of the prescribing information and information from recent meta-analyses (26, 27). Missing data were added from the prescribing information and by using standard German psychopharmacology textbooks (23). The information on pneumonia was extracted from a meta-analysis (28). In principle, side effects can also occur when these drugs are widely used, so that pharmacovigilance (see Table 7) is always required. [1]Lurasidone is approved in Germany for the treatment of schizophrenia, but the statutory health insurance companies do not cover the cost. 0=does not occur, (+)=rare or no significant difference to placebo, +=infrequent, ++=occasional, +++=frequent ?=insufficient data to assess frequency. Please note that these are not systematically collected quantitative frequency estimates, but qualitative estimates that are based on clinical experience and the above-mentioned sources. *MNS: malignant neuroleptic syndrome

5.4 Dose, determining the lowest possible dose, treatment frequency and discontinuation

Recommendation 22	Strength of recommendation
We recommend offering antipsychotics at a dose that is within the range recommended by the respective international consensuses and is as low as possible and as high as necessary (lowest possible dose). Particularly in first episodes of the illness, we recommend choosing the dose in the lower range because people with a first episode have a higher sensitivity for side effects and an overall better response to a lower dose. Adapted and revised from the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10), SIGN guideline 'Management of schizophrenia' (1) and meta-analysis LoE 1+ Uchida et al. 2011 (29). The strength of recommendation 'A' was assigned because many studies showed no advantage of a higher dose but did show an increase in side effects and because patients prefer lower doses.	**A**

Recommendation 23	Strength of recommendation
We suggest offering continuous antipsychotic pharmacotherapy for relapse prevention. Adapted and revised from the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10), SIGN guideline 'Management of schizophrenia' (1), meta-analysis LoE 1+ DeHert et al. 2014 (30), meta-analysis LoE 1+ Sampson et al. 2013 (31). The available data would allow a strength of recommendation 'A'; however, the strength of recommendation was decreased because these data only have adequate methodological quality up to a follow-up of six months.	**B**

Recommendation 24	Strength of recommendation
If the patient is stable and there are reasons why continuous long-term medication cannot be continued (e.g. lack of acceptance), we suggest offering stepwise dose reduction, followed by supervised intermittent treatment combined with targeted early intervention in case of prodromal symptoms of an impending relapse.	**GCP**

Recommendation 25	Strength of recommendation
After a decision has been made that the dose of antipsychotics can be reduced, we suggest offering a dose reduction, taking into account the recommended treatment duration (Recommendations 36 and 37). We suggest reducing the dose in very small steps at intervals of 6 to 12 weeks, depending on the patient's preferences. Furthermore, we suggest involving the patient's family and close confidants and taking into consideration the overall treatment plan, course of treatment to date and tolerability of the existing antipsychotic medication.	**GCP**

Recommendation 26	Strength of recommendation
A reduction and possible discontinuation of antipsychotics at any stage of the illness in terms of shared decision-making between the patient and the treating doctor may be considered, as long as sufficient stability and psychosocial support and regular, ongoing monitoring of symptoms are guaranteed and there are no indications that the patient is a danger to self or others. We recommend informing every patient about the increased risk of relapse after discontinuation. Suggestions for dose reduction and discontinuation can be found in the background text.	**GCP**

Recommendation 27	Strength of recommendation
We suggest that after discontinuing antipsychotics, signs and symptoms of a relapse should be continually monitored for at least two years as part of the overall treatment plan. Adapted and revised from the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10).	**GCP**

5.5 Definitions of response, remission, causes of non-response/non-remission and when to switch the antipsychotic medication in case of non-response

Recommendation 28	Strength of recommendation
We recommend that in cases of insufficient response to treatment despite adequate treatment duration, practitioners reassess the diagnosis, psychiatric and medical comorbidities, adherence, illegal substance use, presence of debilitating side effects, effective dosing (incl. serum level monitoring and confirmation of the indication), environmental factors (e.g. stress, high expressed emotions) and effective treatment duration. We recommend evaluating these secondary causes for insufficient treatment and, if necessary, addressing them before offering to change the medication. Adapted and expanded from AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 29	Strength of recommendation
We recommend evaluating the response status after two weeks (at the latest after four weeks) by using a suitable scale (ideal: PANSS, BPRS; easier: CGI) (A). In case of lack of response (CGI unchanged or worse [CGI < 3]) despite adequate dosing and after excluding secondary causes, we recommend offering the patient a switch to an antipsychotic with a different receptor binding profile, with the aim to achieve response (GCP). LoE 1+ (meta-analysis: Samara et al. 2015 (32)). Because the meta-analyses did not directly evaluate the effect of changing the antipsychotic on the course, a strength of recommendation 'GCP' was assigned for the second part of the recommendation.	**A/GCP**

Recommendation 30	Strength of recommendation
If response is adequate but there are tolerability issues, an early switch to a drug with a different side-effect profile may be considered.	**GCP**

5.6 Strategies for switching antipsychotics

Recommendation 31	Strength of recommendation
Every change in medication can result in a worsening of symptoms or an increase in side effects. When switching to a different antipsychotic, the cross-taper or overlap-and-taper strategy may be considered. The stop-start strategy may be considered if the antipsychotic has to be discontinued immediately because of side effects. We suggest considering equivalence doses when changing antipsychotic treatment.	**GCP**

5.7 Antipsychotics for treating psychotic symptoms in the acute phase – first episode and relapse

Recommendation 32	Strength of recommendation
We recommend offering pharmacological treatment with an antipsychotic as a monotherapy with the goal to reduce psychotic symptoms. LoE 1++, based on almost all meta-analyses identified in the research because, unless otherwise indicated, only studies with an antipsychotic monotherapy were evaluated. Also, the risk of side effects is generally lower in monotherapy than in combination therapy.	**A**

Recommendation 33	Strength of recommendation
During the acute phase, we recommend reviewing and documenting the psychopathological findings at appropriate intervals so that a danger to self and others can be recognised in a timely manner and treatment response can be evaluated. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 34	Strength of recommendation
In first-episode schizophrenia, we recommend offering antipsychotics to reduce psychotic symptoms, after considering the respective risk-benefit. The risks of the treatment can be derived from the respective side-effect profile of the antipsychotics used. Because there are few differences in the efficacy of the various drugs and the response rate is high in first-episode schizophrenia, we recommend basing the choice of antipsychotic primarily on the side-effect profile. LoE 1+: meta-analysis Zhu et al. 2017 (33); LoE 1-: meta-analysis Zhu et al. 2017 (34); LoE 1+: meta-analysis Zhang et al. 2013 (35); LoE 1+: Alvarez-Jimenez et al. 2011 (36); LoE 1++: Leucht et al. 2012 (37).	**A**

Recommendation 35	Strength of recommendation
In first-episode schizophrenia, we suggest offering antipsychotic treatment as early as possible. Depending on the psychopathology, treatment setting and patient preferences, in first-episode schizophrenia practitioners may consider waiting a few days to weeks before initiating antipsychotic pharmacotherapy as part of a psychosocial overall plan, while closely monitoring the psychopathology.	**GCP**

5.8 Antipsychotics to prevent further psychotic episodes – relapse prevention and duration of the antipsychotic treatment

Recommendation 36	Strength of recommendation
After an individual risk-benefit evaluation has been performed, we recommend offering people with schizophrenia (first episode and multiple episode) antipsychotic treatment for relapse prevention. Meta-analysis LoE 1++ Kishimoto et al. 2013 (38). Meta-analysis LoE 1++ Leucht et al. 2012 (37).	**A**

Recommendation 37	Strength of recommendation
For relapse prevention, we recommend offering the antipsychotic that has already resulted in good treatment response or remission, as long as no tolerability issues exist (A). When choosing the antipsychotic for relapse prevention, we recommend considering the service user's preferences and previous experiences, as well as the differing risks of side effects such as tardive dyskinesia, sedation and cardiac, metabolic, endocrine and other effects (GCP). Meta-analysis LoE 1++ Kishimoto et al. 2013 (38). Meta-analysis LoE 1++ Leucht et al. 2012 (37).	**A/GCP**

Statement 2	
We recommend informing people with a relapsing illness course, their family members and close confidants that the relapse risk doubles one year after discontinuing antipsychotic treatment (27% if treatment is continued, 65% if it is discontinued) and remains higher for the next 3-6 years (22% if treatment is continued, 63% if it is discontinued). Meta-analysis LoE 1++ Leucht et al. 2012 (37).	

Statement 3	
The duration of treatment is influenced by a number of variables and individual factors, such as the severity of the index episode, treatment response, adverse drug reactions, motivation of the service user, family history, illness severity, the psychosocial situation, the available psychotherapeutic and psychosocial treatment options and the overall health care situation, which should be considered in each individual situation. No LoE, expert consensus.	

5.9 Depot antipsychotics

Recommendation 38	Strength of recommendation
Like oral antipsychotics, depot antipsychotics are effective for relapse prevention and show no relevant differences in efficacy. Because of their guaranteed administration and good bioavailability, depot antipsychotics are an effective alternative to oral medication, and we suggest offering depot antipsychotics as an alternative treatment for relapse prevention. Adapted and revised from the NICE guideline ‚Psychosis and schizophrenia in adults' 2014 (10), SIGN guideline 'Management of schizophrenia' (1) and additional literature, which was not systematically searched for (see background text) .	**B**

Recommendation 39	Strength of recommendation
Because there is insufficient evidence for superior efficacy of any individual depot antipsychotic, we suggest choosing a depot antipsychotic on the basis of the side-effect profile and the desired injection interval. Before starting treatment with the depot form of an antipsychotic, we suggest ensuring its efficacy and tolerability by offering the oral form of the respective antipsychotic for at least several weeks.	**GCP**

5.10 Pharmacological treatment of negative symptoms

Recommendation 40	Strength of recommendation
In case of predominant negative symptoms, we suggest offering amisulpride (at a low dose) or olanzapine. We suggest avoiding the use of strong D2 receptor blockers by using antipsychotics with a suitable profile or avoiding high-dose treatments. Meta-analysis LoE 1++ Leucht et al. 2009 (39) and meta-analysis LoE 1+ Zhu et al. 2017 (33), as well as additional publications in the background text. The evidence for amisulpride and olanzapine in particular is based on meta-analyses of smaller studies with a higher risk for bias. For this reason, the strength of recommendation 'B' was chosen for the overall recommendation.	**B**

Recommendation 41	Strength of recommendation
In case of inadequate response to antipsychotic monotherapy, we suggest offering additional treatment with antidepressants to people with schizophrenia and predominant negative symptoms. Meta-analysis LoE 1++ Helfer et al. 2016 (40). Because negative symptoms were often secondary endpoints in the main studies, consensus was reached for a strength of recommendation 'B' rather than 'A'.	**B**

5.11 Pharmacological treatment resistance – definition, clozapine, high-dose treatment

Various definitions exist for pharmacological treatment resistance. In 2017, an international consensus group proposed a standardised definition for pharmacological treatment resistance that includes a lack of symptomatic improvement and provides specifications for treatment duration, dosage and adherence and the dimensions symptom severity and level of functioning (41). This definition includes the following aspects:

- Drug treatment resistance is defined in a standardised, operationalised way (moderate severity and less than 20% symptom improvement on the PANSS, BPRS, SANS or SAPS during 6-week treatment phases [see below]) and only after pseudo-resistance has been excluded.
- The overall treatment duration with a compound is at least 12 weeks, including ≥ 2 past adequate treatment attempts with different antipsychotics drugs (each usually ≥ 6 weeks).
- The mean dose is 600 mg chlorpromazine equivalents, and at least 80% of the recommended dose (adherence) was taken.
- Early-onset treatment resistance is defined as treatment resistance in the first year, medium-onset resistance as resistance in years 1 to 5 and late-onset treatment as resistance 5 years or more after starting treatment.
- Situations in which patients do not achieve serum levels in the therapeutic range after at least three months' treatment with clozapine are referred to as 'ultra treatment resistance'.
- The clinical endpoints are both symptom severity (positive, negative or cognitive symptoms) and the level of functioning (e.g. measured with SOFAS).

Recommendation 42	Strength of recommendation
Before diagnosing drug treatment resistance, we recommend excluding pseudo-resistance. We recommend considering the following characteristics: adherence, illegal substance use, the presence of debilitating side effects, comorbidities (e.g. trauma), effective dosing (incl. measuring serum levels and checking for interactions) and environmental factors (e.g. stress, high expressed emotions).	**GCP**

Recommendation 43	Strength of recommendation
In cases of proven antipsychotic treatment resistance and after evaluating the risk-benefit profile and providing information, and in accordance with the necessary accompanying tests, we recommend offering an attempt to treat the existing psychotic symptoms with clozapine. Adapted and revised from the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and SIGN guideline 'Management of schizophrenia' (1). Meta-analysis LoE 1++ Samara et al. 2016 (42), meta-analysis LoE 1+ Siskind et al. 2016 (43). Because the NICE and SIGN source guidelines recommend clozapine for this indication with a high strength of recommendation, no additional systematic literature search was performed. Nevertheless, we included the two most recent meta-analyses (both of which appeared after SIGN/NICE were printed) because they contain some contradictory findings (see background text of the German full version).	**A**

Recommendation 44	Strength of recommendation
If clozapine is not tolerated, treatment with olanzapine or risperidone* may be suggested. This recommendation is not based on a systematic search, but on a clinical consensus. *Important literature can be found in the background text (in German). The findings on risperidone were not as consistent as those for olanzapine.	**GCP**

Recommendation 45	Strength of recommendation
If there is no treatment response, we suggest <u>not</u> to increase antipsychotic doses above the approved range. Meta-analysis LoE 1+, meta-analysis: Dold et al. 2015 (44) Such a high-dose treatment is an **off-label use**. 'Off-label use' refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment trial. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared.	**B**

5.12 Augmentation and combination treatment

The recommendation regarding the augmentation of antipsychotic treatment with antidepressants to treat negative symptoms can be found in **Recommendation 39** and to treat depressive symptoms, in **Recommendation 102**.

Recommendation 46	Strength of recommendation
In case of drug treatment resistance, we recommend first offering treatment with an antipsychotic in monotherapy (A). A combination of two antipsychotics may be suggested, with monitoring of side effects and interactions, if adequate response is not achieved with monotherapy with three different antipsychotics, including clozapine (GCP). We recommend documenting this approach and, if there is still no treatment response, discontinuing this strategy (GCP). Meta-analysis LoE 1++ Galling et al. 2017 World Psychiatry 16: 77-89 (45). The evidence for the 'A' strength of recommendation was derived from the finding that the cited meta-analysis was unable to show additional value for the combination treatment compared with monotherapy if only methodologically high-quality studies were included. Most of the studies evaluated in this meta-analysis included people with drug treatment resistance, although the definition was not standardised across the studies.	**A/GCP**

Recommendation 47	Strength of recommendation
In case of drug treatment resistance, we recommend <u>not</u> to offer augmentation treatment with carbamazepine, lithium, lamotrigine or valproate as a standard treatment to improve general, positive or negative symptoms or aggression. Meta-analysis LoE 1+ Correll et al. 2017 (46), meta-analysis LoE 1+ Wang et al. 2016 (47), meta-analysis LoE 1+ Leucht et al. 2014 (48).	**A**

5.13 Non-invasive stimulation techniques (ECT, rTMS)

The recommendation regarding the use of electroconvulsive therapy (ECT) in malignant catatonia can be found in **Recommendation 95**.

Recommendation 48	Strength of recommendation
In case of clear antipsychotic treatment resistance after adequate treatment at a high enough dose for a long enough time, we suggest offering ECT as an augmentation treatment with the aim to improve the overall clinical condition. Adaptation of the SIGN guideline 'Management of schizophrenia' (1); meta-analysis LoE 1- Lally et al. 2016 (49); meta-analysis LoE 1- Tharyan et al. 2005 (50). The studies on which the meta-analyses are based are basically all of low methodological quality. For additional literature that was not systematically searched for, see background text (in German).	**B**

Recommendation 49	Strength of recommendation
In case of antipsychotic treatment resistance, we suggest offering treatment with low-frequency rTMS at 1 Hz, applied over the left temporal lobe, as part of an overall treatment plan in people with schizophrenia and persistent acoustic hallucinations. Meta-analysis LoE 1+ Slotema et al. 2014 (51), meta-analysis LoE 1- He et al. 2017 (52) and additional literature in the background text.	**B**

Recommendation 50	Strength of recommendation
In case of drug treatment resistance, people with schizophrenia and persistent negative symptoms may be offered treatment with high-frequency rTMS at 10/20 Hz, applied over the left dorsolateral prefrontal cortex, as part of an overall treatment plan (0). We recommend informing patients about the high rate of possible non-response (GCP). High-quality randomised controlled study LoE 1+Wobrock et al. 2015 (53), meta-analysis LoE 1- Shi et al. 2014 (54) and additional literature in the background text. Although the available meta-analyses showed added value of rTMS in the indication compared with a sham stimulation, it was decided to reduce the strength of the recommendation from 'B' to '0' because of the heterogeneity of the data and the negative result of the largest and only multicentre study.	**0/GCP**

5.14 Other psychotropic drugs

Recommendation 51	Strength of recommendation
In case of severe agitation, anxiety and inner restlessness, add-on treatment with benzodiazepines (e.g. lorazepam) may be considered for a limited period of time and in accordance with the applicable recommendations. We do not recommend using benzodiazepines for a long period of time.	**GCP**

5.15 Diagnosis and treatment of side effects of antipsychotic treatment

Recommendation 52	Strength of recommendation
We recommend not only informing people with schizophrenia, family members and close confidants about possible adverse drug reactions, but also advising them about the associated symptoms and respective treatment options. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 53	Strength of recommendation
We recommend actively enquiring about and documenting antipsychotic-induced adverse drug reactions and, if suspected, offering suitable tests and treatment.	**GCP**

Recommendation 54	Strength of recommendation
Depending on the severity of the antipsychotic-induced adverse drug reactions, after a risk-benefit evaluation we recommend offering a dose reduction, switch to a different drug or discontinuation.	**GCP**

Recommendation 55	Strength of recommendation
At the start of antipsychotic treatment or at the latest after the occurrence of strong, antipsychotic-induced weight gain (>7% of baseline weight), we recommend offering psychotherapeutic and psychosocial interventions (nutrition advice, psychoeducation, exercise programmes) to prevent weight gain or to reduce weight. This figure was defined in the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and is in agreement with the EPA Consensus Guideline (55). For additional literature, see background text (in German). Adapted and expanded from NICE, so that a strength of recommendation was given in recognition of the enormous clinical relevance and the relevance for service users. In the SIGN guideline 'Management of schizophrenia' 2013 (185) lifestyle interventions were recommended with a strength of recommendation 'A'.	**A**

Recommendation 56	Strength of recommendation
If there is strong weight gain and it is necessary to continue the current antipsychotic medication, after performing the specified psychotherapeutic and psychosocial interventions (see Recommendation 55 and background text) we recommend offering treatment with metformin (first choice) or topiramate (second choice) for weight reduction, taking into account the risks of an additional drug treatment. For metformin, recommendations of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and the SIGN guideline 'Management of schizophrenia' 2013 (1) were adapted and a strength of recommendation 'A' was given because of the clinical importance of this complex situation. Further supplementary literature on this topic can be found in the background text (in German). For topiramate (SIGN guideline 'Management of schizophrenia' 2013 (1)) a meta-analysis was added and evaluated after a manual search (meta-analysis LoE 1- Zehng et al. 2016 (56)) and officially a strength of recommendation 'GCP' would have to be given here; however, in the context of the overall recommendation the strength of recommendation 'A' was retained because of the clinical relevance. This use (metformin, topiramate) is an off-label use. "Off-label use" refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment attempt. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared. Off-label use is thus only permitted in severe illnesses when there is no alternative treatment. According to current scientific knowledge, there must be a reasonable prospect that the treatment will be successful.	**A**

Recommendation 57	Strength of recommendation
We recommend informing service users, family members and close confidants, as well as carers, about the necessary monitoring tests* (see Table 9), and we recommend implementing the monitoring tests as part of the overall treatment plan. *The legal regulations regarding confidentiality must hereby be observed.	**GCP**

Test	Before	Months						Monthly	Quarterly	Biannually	Annually
		1	2	3	4	5	6				
Blood count											
Other APs	X	X	-	-	-	-	-	-	-	-	X
Clozapine	X	XXXX	XXXX	XXXX	XXXX	XX	X	X	-	-	-
Tricyclic APs[a]	X	X	-	X	-	-	-	-	-	X[c]	-
Blood glucose/HbA1c[b,m], blood lipids											
Clozapine, olanzapine	X	X	-	X	-	-	X	-	-	X	
Quetiapine, risperidone	X	X	-	X	-	-	X	-	-	-	X
Other APs	X	-	-	-	-	-	X	-	-	-	X
Renal parameters											
Creatinine/GFR	X	X	-	X	-	-	X	-	-	-	X
Liver enzymes											
Tricyclic APs[a]	X	X	-	X	-	-	X	-	-	X[c]	-
Other APs	X	X	-	X	-	-	X	-	-	X[c]	-
ECG (QTc)[d], electrolytes											
Clozapine[e,f]	X	X	-	X	-	-	X	-	-	X[c]	
Other APs[g,h]	X	X	-	-	-	-	X	-	-	-	X
Sertindole[i]	X	X	-	X	-	-	X	-	X	-	-
Thioridazine, pimozide	X	X	X	X	X	X	X	X	-	-	-
EEG[j]											
Clozapine	X	-	-	-	-	-	-	-	-	-	-
Other APs	(X)	-	-	-	-	-	-	-	-	-	-
RR/Pulse	X	X	-	X	-	-	X	-	X	-	-
Motor side effects	X	X		X			X		-	X[c]	-
Sedation	X	X		X			X		-	X[c]	-
Sexual side effects	X	X		X			X		-	X[c]	-
Body weight (BMI)[k]	X	X	X	X	-	-	X	-	X	-	-
Echocardiography[n]	-	-	-	-	-	-	-	-	-	-	-
Prolactin	X	-	-	-	-	-	-	-	-	-	-
Pregnancy test	X	-	-	-	-	-	-	-	-	-	-

Table 9: This table was prepared on the basis of (23, 57) and revised in expert consensus. It should be noted that these are general recommendations. The scope of the evaluation can be adapted on the basis of the risks described in the respective prescribing information and personalised, broadened or narrowed for the individual patient. Important factors for a risk-based adaptation are comorbidities, cumulation of risk factors, combination treatment, dose increase, age and occurrence of organ-specific symptoms. Particularly in a steady-state condition and if the risk and drug profiles are unchanged, the evaluation intervals can be increased, taking into account the respective prescribing information. The recommended diagnostic procedures in first-episode schizophrenia are presented in Module 2.

APs: antipsychotics
X: number of necessary routine monitoring tests; if measurement is recommended once in the first month, it can take place between the 3rd and 6th week – the follow-up evaluation in the first month refers to the usual uptitration of an antipsychotic.

a Note: Because of their chemical structure, the SGAs olanzapine, quetiapine and zotepine are also tricyclics.
b Possibly also blood glucose profile or glucose tolerance test, in particular with clozapine and olanzapine.
c In case of normal constellations in steady state, once yearly or even longer intervals may be sufficient.
d Absolute values of > 440 ms (men) or > 450 ms (women) and medication-induced increases > 60 ms are abnormal. If the QTc interval > 480 – 520 ms or QTc interval increases by > 60 ms, the patient should be switched to a different antipsychotic.
e Toxic-allergic myocarditis has been described during treatment with clozapine; therefore, additional ECG monitoring is recommended during clozapine treatment and perhaps cardiac echocardiography, in case of cardiac symptoms and fever or after 14 days' treatment.
f In case of initiation of clozapine treatment: ECG, CRP and troponin I or T, RR, pulse, temperature are recommended beforehand; then every week for 4 weeks CRP, troponin I/T, every 2 days RR, pulse, temperature.
g If cardiac symptoms are present or appear or there is a significant prolongation of the QTc interval, cardiological clarification is necessary; this clarification determines the subsequent frequency of ECG monitoring.
h More frequent monitoring is recommended in patients > 60 years old and perhaps also in case of cardiac risks; more frequent ECG monitoring is recommended during treatment with ziprasidone, perazine, fluspirilene and highly potent butyrophenones, if QTc interval prolongations occur and during combination treatments with other substances that can potentially prolong the QTc interval.
i During treatment with sertindole, ECG monitoring is recommended (preferably in the morning) before starting treatment, after reaching steady state (3 weeks) or a dose of 16 mg, after 3 months and thereafter at 3-month intervals, before and after every dose increase during maintenance treatment and after every additional administration or dose increase of a concomitant medication that could result in an increase in the concentration of sertindole.
j EEG before uptitration of clozapine. If there are indications of an organic cause, EEG should be part of the initial diagnostic tests (see Module 2). Further EEG monitoring if indications of seizure activity. More frequent EEG monitoring also in case of preexisting cerebral damage, increased tendency for seizures and possibly if very high doses are given (combinations) before and during AP treatment and in case of unclear changes in consciousness (DD: non-convulsive status).
k In addition to calculating BMI, we recommend measuring waist circumference and additional monthly weight monitoring by patients themselves.
m Only blood glucose and HbA1C, in case of abnormalities and (b) possibly treatment and monthly monitoring; if the patient has a metabolic syndrome, monthly blood glucose monitoring and (b).
n Dyspnoea or unclear fatigue during antipsychotic treatment should be investigated with cardiac ultrasound. This is true in particular during treatment with dibenzodiazepines, dibenzothiazepines and thienobenzodiazepines.
o Before starting antipsychotic treatment, the NICE guideline (58) recommends determining the prolactin level. During the course of treatment, prolactin should only be measured if there are corresponding symptoms.

Stage of MNS	Clinical symptoms	Measures	Additional interventions
Stage I **Medication-induced Parkinsonism**	Rigidity, tremor	Reduce dose, change antipsychotic	Anticholinergics
Stage II **Medication-induced catatonia**	Rigidity, mutism, stupor	Discontinue antipsychotic, reduce dose, change antipsychotic	Lorazepam (up to 8 mg/day)
Stage III **Early (mild) MNS**	Mild rigidity, catatonia or confusion, temperature ≤ 38°C, heart rate ≤ 100	Discontinue antipsychotic, closely monitor progress, mitigate risk factors	Lorazepam (up to 8 mg/day)
Stage IV **Moderate MNS**	Moderate rigidity, catatonia or confusion, temperature 38 - 40°C, heart rate 100 bis 120	Discontinue antipsychotic, optimise fluid balance, optimise risk factors, lower temperature, intensive care	Lorazepam (up to 8 mg/day), bromocriptine (up to 15 mg/day) or amantadine (up to 300 mg/day) ECT (second line)
Stage V **Severe MNS**	Severe rigidity, catatonia confusion, temperature ≥ 40°C, heart rate ≥ 120	Discontinue antipsychotic, optimise fluid balance, optimise risk factors, lower temperature, intensive care	Dantrolene (up to 10 mg/day), bromocriptine (up to 15 mg/day) or amantadine (up to 30 mg/day) ECT (second line)

Table 10: Step-wise treatment of malignant neuroleptic syndrome (MNS) (59). The stages of MNS are based on the suggestions of Woodbury and Woodbury (60).

Side effect	Prevention	Treatment
QTc prolongation	• Choose a suitable antipsychotic for people at risk • Pay attention to comedication • ECG monitoring	• If QTc interval > 480 – 520 ms or QTc interval increases > 60 ms, patient should be switched to a different antipsychotic
Tachycardia	Choose a suitable antipsychotic for people at risk	• Change antipsychotic • Administer a selective beta blocker
Orthostatic dysregulation	• Slow uptitration • Lowest possible dose	• Use an antipsychotic with few antiadrenergic effects • Spread administration of medication over several points in time
Changes in blood count	• Regular blood count monitoring • Inform patient about clinical signs of agranulocytosis	• In case of agranulocytosis (< 500 granulocytes), discontinue immediately and treat; perhaps administer GM-CSF/G-CSF • In case of leukopaenia or granulocytopaenia (< 1500 granulocytes), the blood count must be monitored and, irrespective of the results, additional monitoring must be considered or clozapine discontinued (see prescribing information for clozapine and the corresponding directions for use)

Table 11: Treatment of side effects, Part 1.

Side effect	Prevention	Treatment
Prolactin elevation	• Suitable antipsychotic • Measure prolactin level • Exclude other causes	• Change antipsychotic • Low-dose aripiprazole (2.5-5 mg), higher doses may be necessary in some cases (61) • Cabergoline (250-500 µg) • Bromocriptine 1-5 mg/d
Disorder of sexual function	• Suitable antipsychotic • Exclude other causes • Measure prolactin level	• Advise and observe • Change antipsychotic • Therapeutic treatment of elevated prolactin (see above) • Appropriate pharmacological treatment of disorder of sexual function (e.g. PDE-6 inhibitors after strict risk-benefit evaluation)
Dry mouth	• Lowest dose possible • Suitable antipsychotic	• Advise patient to regularly drink small amounts • Lozenges, chewing gum • Reduce dose
Increased salivation	• Lowest dose possible • Suitable antipsychotic	• Oral administration of pirenzepine 25-50 mg/d • Administration of botulinum toxin in salivary glands
Constipation	• Fibre-rich food • Physical activity • Suitable antipsychotic	• Lactulose 5-10 mg/d • Macrogol 13-40 mg/d • Possibly sodium picosulphate 5-10 mg/d
Micturition disorder	• Suitable antipsychotic with few anticholinergic effects • Lowest dose possible	• Oral carbachol 1-4 mg/d, in case of acute urine retention possibly 0.25 mg i.m. or s.c • Oral distigmine 2.5-5 g/d • Change antipsychotic
Sedation	• Suitable antipsychotic • Pay attention to comedication	• Reduce dose

Table 12: Treatment of side effects, Part 2.

6. Psychotherapeutic and Psychosocial Interventions (Module 4b)

6.1 General aspects of psychotherapy in people with schizophrenia

Recommendation 58	Strength of recommendation
High-quality psychotherapeutic treatment must include opportunities for reflecting on difficult interaction situations, the systematic planning of the treatment team's approach and periods for overcoming stressful experiences. We recommend that everyone involved in treatment therefore has sufficient time and opportunity to participate in regular supervision, intervision and team-based case discussions. We recommend that treatment facilities support these activities by making sufficient resources available.	**GCP**

The chapter is organised according to the psychotherapeutic interventions and **not** according to treatment phases or other characteristics and is arranged primarily according to the way procedures, methods and techniques were conceptualised, described and evaluated in the scientific literature. All the recommendations in this module, unless otherwise noted, refer to the use of psychotherapeutic and psychosocial procedures as add-ons to antipsychotic treatment.

6.2 Psychoeducation for people with schizophrenia, family members and close confidants

Recommendation 59	Strength of recommendation
To improve treatment outcome and illness course, as part of an overall treatment plan we recommend offering structured psychoeducation for a sufficient time and, if possible, in groups to people with schizophrenia. We recommend involving family members and close confidants in the psychoeducational intervention. Adapted and revised from the AWMF guideline 'Psychosocial therapies for severe mental illnesses' 2013 and 2018 (in German) (18) and meta-analysis LoE 1+ Xia et al. 2011 (62).	**A**

6.3 Cognitive behavioural therapy (CBT) – first-episode schizophrenia, relapse, frequency and setting

Recommendation 60	Strength of recommendation
We recommend offering people with a first psychotic episode a specific cognitive behavioural therapy to improve positive and negative symptoms. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and meta-analysis LoE 1- meta-analysis Bird et al. 2010 (63).	**A**

Recommendation 61	Strength of recommendation
We recommend offering people with schizophrenia cognitive behavioural therapy. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10), meta-analysis LoE 1++ Jauhar et al. 2016 (64), meta-analysis LoE 1++ Wykes et al. 2011 (65), meta-analysis LoE 1++ Turner et al. 2014 (66).	**A**

Recommendation 62	Strength of recommendation
We suggest offering cognitive behavioural therapy consisting of ≥ 16 sessions. To optimise the effects of therapy and in case of more complex therapy goals, we suggest offering a course of ≥ 25 sessions. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10), meta-analysis LoE 1- Sarin et al. 2011 (67), LoE 2+ Lincoln et al. 2016 (68).	**B**

Recommendation 63	Strength of recommendation
Cognitive behavioural therapy can be performed in an in- or outpatient setting. If started during inpatient treatment, we suggest continuing the treatment in an outpatient setting. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10), meta-analysis LoE 1- Sarin et al. 2011 (67), LoE 2+ Lincoln et al. 2016 (68), indirect evidence.	**GCP**

Recommendation 64	Strength of recommendation
We suggest that therapists follow the principles of individualised cognitive behavioural therapy (CBT) with individuals and of disorder-specific manuals. Particular characteristics of CBT for psychoses include non-confrontative, supportive relationships, 'normalisation' of complaints, assumption of continuity with regard to symptoms and orientation towards the participants' life goals. Evidence derived from the efficacy studies: adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10). meta-analysis LoE 1++ Jauhar et al. 2016 (64), meta-analysis LoE 1++ Wykes et al. 2011 (65), meta-analysis LoE 1++ Turner et al. 2014 (66).	**B**

6.4 Cognitive behavioural therapy (CBT) for people with schizophrenia who refuse to take antipsychotic medication

Recommendation 65	Strength of recommendation
We suggest also offering cognitive behavioural therapy to reduce psychotic symptoms in patients who refuse treatment with antipsychotics. High quality randomised study LoE 1+ Morrison et al. 2014 (69).	**B**

6.5 CBT/metacognitive training-based interventions

Recommendation 66	Strength of recommendation
We suggest offering metacognitive training to reduce positive symptoms. Meta-analysis LoE 1+ Eichner et al. 2016 (70), meta-analysis LoE 1+van Oosterhout et al. 2016 (71).	**B**

6.6 Collaboration with family members and close confidants

Recommendation 67	Strength of recommendation
Family members and other close confidants of people with schizophrenia are exposed to significant emotional stress. At the same time, family members and close confidants are the most important sources of social support for service users in the long term. Therefore, family members and close confidants should be viewed as also being affected by the illness. We recommend offering them information about schizophrenia, while maintaining confidentiality. We recommend regularly asking family members and close confidants about their need for support. Depending on individual needs, we recommend offering individual support in dealing with the emotional stress.	**GCP**

Recommendation 68	Strength of recommendation
If the service user refuses to involve family members and close confidants in the treatment process, we recommend respecting this decision. Nevertheless, we suggest giving the family members and close confidants the opportunity to provide third party information on the medical history and to indicate their need for support. Even without the patient's agreement, we suggest offering family members and close confidants general, non–person-related information, while maintaining confidentiality, e.g. from therapists who are not involved in treating the patient; in groups for family members or groups involving service users, family members and professionals; or from family members of other service users.	**GCP**

6.7 Systemic therapy

Recommendation 69	Strength of recommendation
Systemic therapy may be considered to improve general symptoms. Meta-analysis LoE 1- Pinquart et al. 2016 (72) with high risk of bias because of the source studies, and positive usefulness assessment by IQWIG, but which stresses the high risk of bias of the included studies. For this reason, consensus was reached for a strength of recommendation of '0' rather than 'B'.	**0**

6.8 Family interventions

Recommendation 70	Strength of recommendation
To reduce the rate of recurrence and hospitalisation, we recommend offering families of people with a first psychotic episode a psychotherapeutic family intervention specifically targeted at first episodes. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and meta-analysis LoE 1- meta-analysis Bird et al. 2010 (63).	**A**

Recommendation 71	Strength of recommendation
In an acute exacerbation or after a relapse, we recommend offering family interventions to families of people with schizophrenia who live with a service user or are in close contact with them. These family interventions can be started in the acute phase or later on and also during the hospital stay. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and meta-analysis LoE 1+ Pharoah et al. 2010 (73)	**GCP**

Recommendation 72	Strength of recommendation
In an acute exacerbation or after a relapse, we recommend that psychotherapeutic treatment involves the family or close confidants/caregivers if the service user and family members live together or are in close contact. This psychotherapeutic treatment can be started in the acute phase or later on and also during the hospital stay. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and meta-analysis LoE 1+ Pharoah et al. 2010 (73).	**A**

Recommendation 73	Strength of recommendation
We suggest performing psychotherapy and involving the family, as follows: • Both the service user and the family members ought to be involved. • The psychotherapeutic treatment ought to last three months to one year. • It ought to include at least 10 planned sessions. • The family's preference for single-family treatment or group psychotherapy with several families ought to be taken into consideration. • The relationship between the family members and service user ought to be taken into consideration. • The psychotherapy ought to have a specific, supportive, psychoeducational and therapeutic orientation and include problem-solving training and the development of a crisis plan. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and meta-analysis LoE 1+ Pharoah et al. 2010 (73). Because only indirect evidence is available, consensus was reached for a strength of recommendation 'B' rather than 'A'.	**B**

6.9 Social skills training

Recommendation 74	Strength of recommendation
We recommend offering social skills training if there are relevant deficits in social skills and in case of persistent negative symptoms. Social skills training should last for several months and be supplemented with tasks for transferring skills to everyday life. Meta-analysis LoE 1+ Turner et al. 2017 (74), meta-analysis LoE 1- Almerie et al. 2015 (75).	**A**

6.10 Cognitive remediation

Recommendation 75	Strength of recommendation
We recommend offering cognitive remediation to people with schizophrenia who have impairments in cognitive processes (attention, learning and memory, executive functions, social cognition or metacognition) to improve cognitive performance and psychosocial functioning. Meta-analysis LoE 1+ Wykes et al. 2011 (76), meta-analysis LoE 1- Kurtz et al. 2016 (77), for additional literature, see background text.	**A**

Recommendation 76	Strength of recommendation
We suggest offering cognitive remediation in combination with other psychosocial and rehabilitative treatment methods. Indirect evidence from meta-analysis LoE 1+ Wykes et al. 2011 (76).	**GCP**

6.11 Psychodynamic or psychoanalytic therapy

Recommendation 77	Strength of recommendation
Psychodynamically oriented psychotherapy may be considered to improve global functioning. Cohort study LoE 2+ Rosenbaum et al. 2012 (78).	**0**

6.12 Client-centred therapy and supportive psychotherapy

Recommendation 78	Strength of recommendation
There is insufficient support for client-centred therapy as a systematic form of psychotherapy for schizophrenia. Because there are similarities between client-centred therapy and supportive therapy, client-centred therapy may be considered if better studied approaches are not available or do not concur with the patient's preferences. Adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**0**

6.13 Occupational therapy (ergotherapy)

Recommendation 79	Strength of recommendation
Occupational therapy (ergotherapy) interventions may be considered as part of an overall treatment plan and in accordance with the patient's individual needs and preferences. Adaptation of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' 2013/2018 (in German) (18). A strength of recommendation 'B' is given there, but this is extrapolated evidence because many of the studies did not include people with schizophrenia. The steering group of the cited guideline was consulted. The new version of the cited guideline still gives the same recommendation and source literature, so that in this S3 Guideline for Schizophrenia a strength of recommendation '0' has been assigned instead of 'B'.	**0**

6.14 Creative therapies

Recommendation 80	Strength of recommendation
To improve psychopathological symptoms, we suggest offering music therapy, art therapy and drama therapy to people with schizophrenia as part of an overall treatment plan and in accordance with the patient's individual needs and preferences. Adaptation of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' 2013/2018 (in German) (18).	**B**

6.15 Body and movement therapy

Recommendation 81	Strength of recommendation
We suggest offering movement interventions to people with schizophrenia as part of a multimodal overall therapy concept, depending on people's symptoms and preferences and taking into account their physical abilities. Adaptation of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' 2013/2018 (in German) (18). The strength of recommendation was decreased on the basis of the LoE because the study results were not uniform enough to justify a higher strength of recommendation. This also applies to the three new meta-analyses that were not included in the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German).	**B**

Recommendation 82	Strength of recommendation
We suggest offering exercise interventions (in particular aerobic endurance training, yoga), taking into account the patient's physical abilities.	**GCP**

7. Treatment in special circumstances (Module 4c)

7.1 Active enquiries about common comorbid mental illnesses

Recommendation 83	Strength of recommendation
We recommend that practitioners actively enquire about the symptoms of comorbid mental disorders that are common in people with schizophrenia. If diagnostic criteria for such a comorbidity are fulfilled and other required tests are positive, we recommend offering a corresponding guideline-based treatment.	**GCP**

7.2 Treatment in case of restlessness, states of agitation and in emergency situations, debriefing after incidents and compulsory measures

Recommendation 84	Strength of recommendation
We recommend implementing procedures to prevent aggressive behaviour and the subsequent compulsory measures by the treating institutions (e.g. by providing a quiet and hospitable environment with opportunities for being alone, needs-oriented design of the treatment setting (see Module 5), de-escalation procedures, open door/access to the outdoors) and treatment team (e.g. through relaxed behaviour, empathetic conversation techniques, individual risk assessment, staff training, de-escalation procedures). Adapted and expanded from the NICE guideline 'Violence and aggression: short-term management in mental health, health and community settings' (79).	**GCP**

Recommendation 85	Strength of recommendation
To avoid compulsory admissions, we recommend giving people with schizophrenia the opportunity to create crisis plans and treatment agreements (A). We recommend taking into account crisis plans, information about the previous course of the illness and treatment and other preventative planning measures, such as treatment agreements, in acute situations (GCP). Adapted and expanded from the NICE guideline 'Violence and aggression: short-term management in mental health, health and community settings' (79). Meta-analysis LoE 1+ de Jong et al. 2016 (80). This meta-analysis was added and evaluated after a manual search – the strength of recommendation 'A' was given for the first part of the recommendation because of the special importance for service users.	**A/GCP**

Recommendation 86	Strength of recommendation
We recommend that the aim of treatment is to calm the patient so that they can participate in the further treatment process. We recommend that measures to avert danger, such as isolation, fixation or medicinal sedation against the patient's will, are only used, in accordance with all statutory provisions and under close monitoring, if de-escalation measures are unsuccessful. Adapted and expanded from the NICE guideline 'Violence and aggression: short-term management in mental health, health and community settings' (79).	**GCP**

Recommendation 87	Strength of recommendation
After aggressive incidents and compulsory measures, we recommend offering a debriefing as soon as possible, depending on the patient's condition, together with the nurses responsible for care, other involved people and the responsible therapists. We suggest that the content of the discussion and the agreements made are documented in the patient's medical record and taken into account when planning treatment, also in case of readmission. In case of serious incidents, we suggest arranging a meeting with patients and offering one-on-one consultations to co-patients who are severely impacted by the incident. As soon as possible after the incident, we suggest offering supervision to the treatment team, preferably through external supervisors, as an opportunity for reflection and learning processes. Adapted from the DGPPN S2 guideline 'Therapeutic approaches for aggressive behaviour in psychiatry and psychotherapy' 2009 (81).	**GCP**

Recommendation 88	Strength of recommendation
If non-pharmacological treatment options are unsuccessful in states of agitation, we suggest first offering oral drug administration. We suggest that the drug is administered parenterally only if oral administration is not possible. An alternative is use of an antipsychotic that can be inhaled. We recommend that the lowest possible effective dose is offered and, if necessary, that the dose is gradually increased. Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17), with the addition of current literature, which can be found in the background text.	**B**

Recommendation 89	Strength of recommendation
In case of comparable efficacy of lorazepam and antipsychotics in the acute treatment of aggression and psychomotor arousal, we suggest offering lorazepam* because of its more favourable side-effect profile. Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17), based on four original studies *The combination of intravenous or sublingual lorazepam and clozapine should be avoided.	**B**

Stage	Intervention
1	Oral lorazepam monotherapy, starting with 1-2.5 mg, possible repeat treatment, or secondary treatment: suitable oral antipsychotic. In case of a psychotic state of arousal, combination of both substances. Perhaps repeat treatment, taking into account daily maximum doses.
2	Intravenous (i.v.) or intramuscular (i.m.) lorazepam (1 to 2 mg), or secondary treatment: antipsychotic i.m., perhaps combination (a combination of olanzapine/clozapine and parenteral benzodiazepines should be avoided). Intravenous administration only with appropriate monitoring, every parenteral administration should be closely monitored (continuous monitoring by doctors and nurses).
3	Repeat Step 2, taking into account daily maximum doses.

Table 13: Stepwise pharmacological treatment of acute agitation in schizophrenia. Fixation should be used in case of acute danger to self or others than cannot be dealt with by alternative means.

Drug	i.v. i.v.i.	i.m. acute	inh./ i.n.	Lozenge	Solution/ drops	Oral solid form
Antipsychotics						
Haloperidol	(+)[a]	+	-/(+)	-	+	+
Benperidol	+[a]	+	-/-	-	+	+
Zuclopenthixol/-acetate[b]	-	+[b]	-/-	-	+	+
Olanzapine	-	+	-/-	+	+	+
Aripiprazole	-	+	-/-	-	+	+[c]
Ziprasidone	-	+	-/-	-	+	+[c]
Risperidone	-	-	-/-	+	+	+
Quetiapine	-	-	-/-	-	-	+
Loxapine	-	-	+/-	-	-	(+)[d]
Melperone	-	-	-/-	-	+	+
Pipamperone	-	-	-/-	-	+	+
Levomepromazine[e]	-	+	-/-	-	+	+
Anxiolytics/Sedatives						
Lorazepam	+	+	-/(+)	+	-	+
Diazepam[f]	+	-[g]	-/(+)	-	+	+
Midazolam[f,h]	(+)	(+)	-/(+)	-	(+)	-
Promethazine	+[a]	+	-/-	-	+	+

Table 14: Routes of administration of various substances used in psychiatric emergency situations. Prepared and adapted from (82). i.v. intravenous, i.v.i. intravenous infusion, i.m. intramuscular, s.c. subcutaneous, inh. inhalation, i.n. intranasal.
+ Suitable and approved; – not available/not suitable/not approved in Germany; (+) suitable/not approved (off label) in Germany. These assessments were based on the approval situation and expert consensus.

[a] Because of the risk of QTc-interval prolongation, haloperidol should only be given i.v. if the patient is continuously monitored. A similar effect on the QTc interval was assumed for benperidol because it is also a butyrophenone; however, a recent study suggested that the QTc prolongation with benperidol is less pronounced than with haloperidol (83). QTc prolongations can also be expected with promethazine.

[b] Zuclopenthixol, an acetate ester, is available as a short-acting depot that is effective for 2-3 days. The legal framework must be considered when administering the drug against a patient's will.

[c] The oral form is not usually suitable for psychiatric emergencies.

[d] In Germany, only approved as a powder for inhalation in limited indications.

[e] Because of the side-effect profile, we recommend using it only in exceptional cases and if suitable alternatives fail.

[f] Diazepam and midazolam are also available in forms for rectal administration (rectal solution, suppository).

[g] Diazepam is approved for i.m. injection. This route of administration is not useful, however, because absorption from muscle tissue of this very lipophilic substance is unreliable and slow.

[h] Not approved in Germany for primarily psychiatric indications (indication: analgosedation).

7.3 Sleep disorders

Recommendation 90	Strength of recommendation
If sleep disorders occur in people with schizophrenia, we recommend clarifying and, if possible, treating the cause (e.g. adverse events, obstructive sleep apnea).	**GCP**

Recommendation 91	Strength of recommendation
Because of their addiction potential, we recommend that benzodiazepines and Z substances are only used for a limited period of time to treat sleep disorders.	**GCP**

Recommendation 92	Strength of recommendation
After a risk-benefit evaluation, antipsychotics with sedative effects may be considered as a treatment for sleep disorders in people with schizophrenia, in compliance with the general directions for combination treatment. Systematic review LoE 2- Kaskie et al. 2017 (84).	**0**

Recommendation 93	Strength of recommendation
After a risk-benefit evaluation, antidepressants with sedative effects may be considered as a treatment for sleep disorders in people with schizophrenia, in compliance with the general directions for combination treatment.	**GCP**

7.4 Catatonia (predominant catatonic symptoms)

Recommendation 94	Strength of recommendation
In case of catatonic symptoms or catatonic schizophrenia, pharmacological treatment with lorazepam (in combination with antipsychotics that have a low risk for malignant neuroleptic syndrome [MNS]) may be considered for a limited period of time. Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**0**

Recommendation 95	Strength of recommendation
Electroconvulsive therapy (ECT) is one of the first-choice treatment options for malignant catatonia and may be considered in this indication (0). If treatment of malignant catatonia with an antipsychotic and lorazepam is unsuccessful, we recommend performing ECT soon thereafter (A). Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17). Meta-analysis LoE 1- Leroy et al. 2017 (85). Even though no high quality randomised controlled studies are available, this is an emergency situation, so that a strength of recommendation 'A' was decided upon for the special case of malignant catatonia and failure of pharmacological therapy because this is a life-threatening situation.	**0/A**

7.5 Suicidality – risk factors, assessment, treatment options

Recommendation 96	Strength of recommendation
We recommend continuously evaluating suicidal thoughts, plans and behaviour. In particular command hallucinations, persecutory delusions, feelings of alien influence, depressive symptoms and anxiety states should be evaluated as to whether they are having an impact on the incidence of suicidal thoughts or self-harming behaviour. We recommend that practitioners strive to avoid akathisia and other debilitating drug side effects and to reduce comorbid substance use. Adaptation of the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 97	Strength of recommendation
In case of suicidality, we recommend discussing it openly and empathetically and assessing the suicide risk during this discussion. We recommend that the decision about the frequency of contacts is based on the reliability of the suicidal person's commitment to attend appointments and the assessment of suicide risk. If the person is unable to commit to attending appointments, even if appointments are offered at short intervals, a 1:1 supervision should be offered.	**GCP**

Recommendation 98	Strength of recommendation
In case of severe and continuously increased suicidality, we suggest offering treatment with clozapine after a risk-benefit evaluation. Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17). Because the evidence base refers to one randomised controlled study (86), there is a relevant risk of bias, so that the strength of recommendation was adjusted from 'A' to 'B'. This is an off-label use. "Off-label use" refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment attempt. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared. Off-label use is thus only permitted in severe illnesses when there is no alternative treatment. According to current scientific knowledge, there must be a reasonable prospect that the treatment will be successful.	**B**

7.6 Depression – assessment, psychotherapy, pharmacotherapy

Recommendation 99	Strength of recommendation
We suggest that people with schizophrenia are regularly evaluated for the presence of depressive symptoms. If an instrument is used for evaluation, we suggest the CDSS as the rating instrument of choice. Adapted from the AWMF guideline 'Schizophrenia' 2006 (in German) (17), with a strength of recommendation given on the basis of the clinical relevance. In addition, after a manual search a LoE 1- publication was added: Lako et al. 2012 (87). This should be understood in the sense of an operationalised diagnostic testing. The CDSS is also an important scale in the largest available meta-analysis on this topic (40), so that the designation of an LoE can also be justified indirectly.	**B**

Recommendation 100	Strength of recommendation
In case of existing depressive symptoms that cannot be explained by other causes, such as current living conditions, adverse drug reactions, sedation or negative symptoms, we recommend first offering to optimise the antipsychotic medication, which may involve switching to a substance with a greater antidepressant effect. Meta-analysis LoE 1++ Leucht et al. 2009 (39) and meta-analysis LoE 1++ Leucht et al. 2009 (88).	**A**

Recommendation 101	Strength of recommendation
We suggest that people with schizophrenia who have comorbid depressive symptoms (with partially remitted psychotic symptoms) are offered psychosis-specific cognitive behavioural therapy (CBT) that takes into account the depressive symptoms. Meta-analysis LoE 1++ Wykes et al. 2008 (65). Strength of recommendation lowered to 'B' because of secondary parameters in the meta-analysis and because the effect is no longer significant in the methodologically high-quality studies.	**B**

Recommendation 102	Strength of recommendation
If depressive symptoms persist even after antipsychotic treatment has been optimised, we recommend offering additional antidepressant drug treatment, as long as the criteria for a depressive episode are fulfilled. When choosing the antidepressant, we recommend taking drug interactions into account and informing the patient about the possibility that more adverse drug reactions may occur. Meta-analysis LoE 1++ Helfer et al. 2016 (40).	**A**

Recommendation 103	Strength of recommendation
We suggest not to offer that lithium, carbamazepine or valproic acid to people with schizophrenia to treat depressive symptoms. Meta-analysis LoE 1+ Wang et al. 2016 (47), meta-analysis LoE 1+ Leucht et al. 2014 (48), meta-analysis LoE 1- Leucht et al. 2015 (48).	**B**

7.7 Posttraumatic stress disorder

No research was performed to identify studies on this topic and no recommendations were adopted. Information and studies on this topic can be found in the background text of the long version of this guideline (in German).

7.8 Anxiety disorders

Recommendation 104	Strength of recommendation
If people with schizophrenia have comorbid anxiety disorder, the established and evidence-based treatment options for anxiety disorders may be suggested, taking into account the primary illness.	**GCP**

7.9 Obsessive-compulsive disorder

Recommendation 105	Strength of recommendation
If people with schizophrenia have obsessive-compulsive symptoms or obsessive-compulsive disorder that is suspected to be related to the antipsychotic treatment, a dose reduction or switch to a medication with a low risk of obsessive-compulsive symptoms (e.g. aripriprazole, risperidone) may be suggested, but the patient must be informed about the risk of an increase in psychotic experiences. Alternatively, and in situations in which an adjustment of the primary antipsychotic is not an option, we recommend providing treatment in accordance with the AWMF guideline ‘Obsessive-compulsive disorders’ (in German).	**GCP**

7.10 General aspects of substance use and substance dependence (substance use disorder)

In clinical practice, practitioners must remember that a change in substance use can result in a change in drug levels, so that monitoring of the level and dose adjustment may be required.

Recommendation 106	Strength of recommendation
We recommend specifically asking people with schizophrenia about substance and drug use and exploring this issue in detail. If substance use is suspected, we suggest performing a toxicological evaluation, if possible. In people with schizophrenia and a comorbid substance use disorder, we suggest choosing an integrative treatment approach in which appropriate interventions for both disorders are offered in the same setting and with the same team of therapists. It is important that the person providing care is available also for long-term outpatient treatment and that there is low threshold access to the health care system. Adaptation of the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 107	Strength of recommendation
We recommend offering antipsychotic treatment to people with a dual diagnosis of schizophrenia and comorbid substance, after they have been given personalised information on the risks and benefits of such treatment. We suggest preferential use of drugs with as few anticholinergic and extrapyramidal motor side effects as possible in this population. Equally, we suggest offering substance-specific psychotherapeutic and psychosocial interventions.	**GCP**

7.10.1 Treatment of comorbid nicotine dependence

Recommendation 108	Strength of recommendation
Taking into account the acuteness and characteristic features of schizophrenia, for people with comorbid nicotine dependence we recommend in principle the same guideline-based psychotherapeutic and drug approaches for the reduction or cessation of tobacco use as for smokers with no additional psychotic disorder. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of harmful and addictive nicotine use' 2015 (in German) (89).	**GCP**

Recommendation 109	Strength of recommendation
We suggest offering bupropion or varenicline to people with stable schizophrenia who smoke, after taking into account possible risks and providing information on these risks. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of harmful and addictive nicotine use' 2015 (in German) (89); for additional literature, see background text.	**B**

7.10.2 Treatment of comorbid alcohol dependence

Recommendation 110	Strength of recommendation
We suggest that in people with schizophrenia and alcohol dependence/abuse, treatment for both disorders is integrated into one treatment approach. If that is not possible, we recommend guaranteeing a structured coordination of treatment, e.g. via case management. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of alcohol-related disorders' 2016 (in German) (90).	**GCP**

Recommendation 111	Strength of recommendation
We recommend offering guideline-based psychotherapeutic/psychosocial treatment for schizophrenia and alcohol use to people with both disorders. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of alcohol-related disorders' 2016 (in German) (90). Evidence upgraded after consensus building and because of the efficacy of this approach in general in schizophrenia (see Module 4b)	**A**

Recommendation 112	Strength of recommendation
We suggest offering motivational interventions alone or in combination with cognitive behavioural therapy (CBT) to people with schizophrenia and alcohol-related disorders. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of alcohol-related disorders' 2016 (in German) (90).	**GCP**

Recommendation 113	Strength of recommendation
We recommend combining psychotherapy or psychosocial treatment with guideline-based pharmacotherapy for schizophrenia and alcohol dependence/abuse in people with both disorders. Adapted from the AWMF guideline 'Screening, diagnosis and treatment of alcohol-related disorders' 2016 (in German) (90).	**GCP**

7.10.3 Treatment of comorbid cannabis dependence

Recommendation 114	Strength of recommendation
In people with schizophrenia and cannabis abuse/dependence, we recommend that the goal is reduced use or abstinence to decrease the risk of relapse and psychotic experiences and to improve the level of functioning, as well as to improve compliance. No systematic literature search, therefore GCP. Additional literature can be found in the background text (in German).	**GCP**

7.11 Pregnancy and breastfeeding

Recommendation 115	Strength of recommendation
We recommend offering women of reproductive age who have schizophrenia advice on family planning, aspects specific to pregnancy (in particular medication) and supportive measures.	**GCP**

Recommendation 116	Strength of recommendation
During pregnancy and in the weeks afterwards, we recommend offering multidisciplinary care by professionals from the fields of psychiatry, psychotherapy, gynaecology, paediatrics and perhaps endocrinology.	**GCP**

Recommendation 117	Strength of recommendation
We suggest offering pregnant women with schizophrenia the non-pharmacological and pharmacological treatments (preferentially olanzapine, risperidone, haloperidol, quetiapine)* described in this guideline. We suggest offering treatment with psychotropic drugs during pregnancy only in situations where the consequences of not providing drug treatment outweigh the possible risks of exposing the child to the medicine. Adapted and expanded from the AWMF guideline 'Schizophrenia' (in German) (17), extrapolated from the cited systematic review papers. *The drugs named here are the most comprehensively studied. In routine clinical care, each case must be considered individually with the assistance of applicable databases, e.g. Embryotox (http://www.embryotox.de/einfuehrung.html).	**GCP**

7.12 Sex-specific aspects

Recommendation 118	Strength of recommendation
The menstrual cycle, pregnancy, the postpartum period and menopause result in hormonal changes that can change the clinical symptoms of women with schizophrenia and may require a change in medication or dose. We suggest that during these periods, the development of clinical symptoms is carefully monitored. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Effects	Side effects
Women require lower doses	Early dyskinesia (men > women)
Women are more responsive to antipsychotics	Tardive dyskinesia (women > men)
Women are more responsive to family interventions	Clozapine agranulocytosis (women > men)
Men are more responsive to social skills training	Sexual side effects (women > men)
	Prolactin elevation (women > men)
	Metabolic side effects (women > men)

Table 15: Sex differences in the effects and side effects of antipsychotic medication. This qualitative summary is not proven by evidence from controlled clinical studies.

7.13 Ethical and cultural aspects

No research was performed to identify studies on this topic and no recommendations were adopted. Information and studies on this topic can be found in the background text of the long version of this guideline (in German).

7.14 Childhood and adolescence

7.14.1 Antipsychotic treatment in childhood and adolescence – general treatment principles, drugs and treatment monitoring

Recommendation 119	Strength of recommendation
We recommend that children and adolescents (< 18 years old) with schizophrenia are offered the same approaches as adults as regards general pharmacotherapy, dose finding, treatment frequency and duration, therapeutic drug monitoring, switching antipsychotics, determining drug treatment resistance and monitoring and treating side effects (see Module 4a). However, we recommend that because of the greater sensitivity of children and adolescents to side effects, attention is paid to the special characteristics presented in the text regarding dosing, switching and the frequency of side-effect monitoring.	**GCP**

Recommendation 120	Strength of recommendation
We recommend that after a risk-benefit evaluation has been performed and information has been provided to their parents, children and adolescents (< 18 years old) with schizophrenia are offered oral antipsychotic monotherapy to treat positive symptoms (A). Positive proof of efficacy in children and adolescents (< 18 years old) with schizophrenia is available for aripiprazole, (haloperidol)*, (olanzapine)#, quetiapine, paliperidone and risperidone (A). Although not all drugs with proven efficacy are approved for use in children and adolescents, if they are indicated, we suggest that they are perhaps used off-label, taking into account the respective side-effect spectrum (GCP). Meta-analysis LoE 1+ Pagsberg et al. 2017 (91) and meta-analysis LoE 1+ Harvey et al. 2016 (92), extrapolated to strength of recommendation 'A' because findings are comparable to adults, where LoE 1++ meta-analyses are available. Positive proof of efficacy is available for lurasidone and molindone, but these drugs are not available in Germany. * Haloperidol was not evaluated in the highest quality meta-analysis, and the high risk for EPS means that it should not be used as a first-choice treatment in this population. # Because of the high risk for weight gain and changes in glucose and lipid metabolism, olanzapine is not recommended as a first-choice treatment in this population. [1]'Off-label use' refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment attempt. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared. Off-label use is thus only permitted in severe illnesses when there is no alternative treatment. According to current scientific knowledge, there must be a reasonable prospect that the treatment will be successful.	**A/GCP**

Recommendation 121	Strength of recommendation
We recommend that in addition to the principles applied in adult patients, side-effect monitoring in children and adolescents (< 18 years old) receiving antipsychotics takes into account the specific characteristics of this age group. These include: • Sex- and age-dependent assessment of side effects (in particular motor side effects) • Consideration of the high sensitivity for motor side effects • Consideration of the differences in the objective and subjective perception of side effects • Effect of elevated prolactin levels on sexual development • Effect of treatment on height and weight development, with regular follow-up monitoring of these two important physical parameters • Recognition of early onset medical comorbidities • Compared with adults, more frequent monitoring of possible metabolic side effects	**GCP**

Recommendation 122	Strength of recommendation
In case of confirmed drug treatment resistance, after risk-benefit evaluation and provision of information to the parents, and in accordance with the necessary concomitant evaluations, we suggest offering treatment with clozapine[1] to treat existing psychotic symptoms. This recommendation was extrapolated on the basis of the data from adults and therefore the strength of the recommendation was decreased. The NICE guideline 'Psychosis and schizophrenia in children and young people: recognition and management' 2013 (93) recommends such an approach. The systematic literature search identified three double-blind studies in small samples, which are presented in the background text (in German). [1]Clozapine is not approved for patients < 16 years old (off label), but because of the extrapolation of the data from adults, the cited data in children and adolescents and the special treatment situation a strength of recommendation 'B' was assigned. 'Off-label use' refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment attempt. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared. Off-label use is thus only permitted in severe illnesses when there is no alternative treatment. According to current scientific knowledge, there must be a reasonable prospect that the treatment will be successful.	**B**

7.14.2 Psychotherapy in childhood and adolescence

Recommendation 123	Strength of recommendation
We recommend offering cognitive behavioural therapy (CBT) to children and adolescents with a first psychotic episode or schizophrenia. Adapted from the NICE guideline 'Psychosis and schizophrenia in children and young people: recognition and management' 2013 (93). Additional available literature is discussed in the background text (in German). In principle, LoE 2+ is applicable because of the lack of controlled studies; however, because of the respective studies in adults (see Module 4b) and the proof of efficacy in the transition period the strength of recommendation was extrapolated from 'B' to 'A'.	**A**

Recommendation 124	Strength of recommendation
We recommend offering families with children or adolescents with a first or multiple psychotic episodes of schizophrenia and/or their relatives or close confidants family interventions in the various phases of the illness in in- or outpatient settings to ease the burden on the family system and reduce the risk of relapse. Adapted from the NICE guideline 'Psychosis and schizophrenia in children and young people: recognition and management' 2013 (93). Although no studies are available specifically for the age group < 18 years, a strength of recommendation 'A' was assigned because corresponding studies are available in adult patients and also specifically in young patients with a first episode (see Module 4b) that have a proof of efficacy of LoE 1+.	**A**

7.14.3 Education and vocational training

Recommendation 125	Strength of recommendation
After the acute phase, we recommend that doctors and child and adolescent psychotherapists and other people involved in the treatment of children and adolescents with schizophrenia offer to mediate between the service user and the responsible person at the place of education or training. We recommend thereby ensuring that, whenever possible, the school/vocational education can be continued and that, if necessary, appropriate complementary support is made available. We recommend offering service users programmes that support reintegration or provide help with finding an apprenticeship/job. In case of severe negative symptoms and/or persistent positive symptoms that cause severe impairment, professionals may consider that the service user needs to attend a specialised institution because of the existing empowerment issues. Appropriate integration support (according to Section 35a of the German social code VIII) should perhaps be suggested, if applicable. We recommend regularly observing the social and educational/vocational activities and integrating them into the overall treatment plan. Adapted from the NICE guideline 'Psychosis and schizophrenia in children and young people: recognition and management' 2013 (93).	**GCP**

7.14.3 Electroconvulsive therapy in malignant catatonia in childhood and adolescence

Recommendation 126	Strength of recommendation
In case of malignant catatonia and unsuccessful treatment with an antipsychotic and lorazepam or confirmed drug treatment resistance after adequate treatment at a high enough dose for long enough, and after all pharmacological and non-pharmacological treatment options have been exhausted, we recommend determining the indication for ECT only in a multidisciplinary team that includes a psychiatrist who treats adults.	**GCP**

7.15 Treatment of higher age groups – general aspects, antipsychotics, psychotherapy, monitoring

Recommendation 127	Strength of recommendation
In first manifestations of paranoid-hallucinatory symptoms in higher age groups (> 65 years old), we recommend offering the tests recommended in Module 2 to exclude an organic cause. In higher age groups, we thereby recommend paying special attention to delirium, comorbid medical conditions and drug treatments that were newly started or stopped shortly before the symptoms appeared.	**GCP**

Recommendation 128	Strength of recommendation
We suggest offering antipsychotic monotherapy for positive symptoms at lower doses in people with schizophrenia in higher age groups (> 65 years old) than in younger patients because older patients have a higher sensitivity for side effects. Adaptation of the AWMF guideline 'Schizophrenia' 2006 (in German) (17) and increase of the strength of recommendation from 'C' to 'B'. Additional literature can be found in the background text (in German).	**B**

Recommendation 129	Strength of recommendation
We recommend offering the same psychotherapeutic and psychosocial therapies to people with schizophrenia in higher age groups (> 65 years old) as to younger patients, taking into account the specific characteristics of older age. Extrapolated because the respective studies that resulted in a strength of recommendation 'A' in younger populations rarely included people aged > 65 years. After discussion in the guideline group, the strength of recommendation 'A' was nevertheless maintained because the principles of treatment in higher age groups are comparable to those in the age range 18 to 65 years (comprehensive studies are available for this age group, see Modules 4a and 4b).	**A**

Recommendation 130	Strength of recommendation
Before uptitrating an antipsychotic in people in higher age groups (> 65 years old) with schizophrenia, we recommend assessing the age-specific increased risks for side effects and possible interactions with other drugs. In case of polypharmacy before starting treatment, the number of drugs should be decreased as far as possible to reduce the risk for drug interactions.	**GCP**

Recommendation 131	Strength of recommendation
We suggest that older people (> 65 years old) who receive long-term antipsychotic treatment are specifically evaluated for the presence of tardive dyskinesia. Besides an exact diagnostic classification of the dyskinesia, the functional effects and extent of the impairments in quality of life should be assessed. We recommend that treatment of tardive dyskinesia follows the recommendations described in Module 4a.	**GCP**

7.16 Special features of the treatment of first-episode schizophrenia

Recommendation 132	Strength of recommendation
We recommend that first episodes of schizophrenia are recognised as early as possible and the duration of untreated psychosis (DUP) is kept as short as possible. We recommend offering the following interventions as part of the multiprofessional treatment of people with a first episode: • Pharmacotherapy according to the recommendations in Module 4a for first-episode schizophrenia • Specialised cognitive behavioural therapy and family interventions for people with first-episode schizophrenia in accordance with Module 4b • Psychosocial interventions to enable integration into the primary labour market[1] • Possibility of low-threshold treatment options or outreach treatment • Closer collaboration on the level of general practioners, specialists and company doctors (Modul 5) Adapted from the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10). Corresponding meta-analyses that were supplementary to the NICE guideline 2014 were found in other systematic or manual searches and are presented in the background text (in German). Because the NICE adaptation is sufficient to justify the A recommendation, the most recent meta-analysis LoE 1+ Correll et al. 2018 (94) was evaluated to make the most current data available. [1]Proof of efficacy is available for supported employment and education according to the individual placement and support (IPS) model.	**A**

7.17 Diagnosis and treatment in people at increased risk for psychosis

7.17.1 Diagnosis

It must be noted that the stage of increased risk for psychosis is not a diagnostic category in ICD-10 or DSM-5. An ‘attenuated psychosis syndrome‘, which is based on the American definition of the ultra–high-risk criterion of attenuated positive symptoms (APS), was incorporated into the ‘Conditions for further study’ in DSM-5 (95, 96). The stage of increased risk for psychosis will also not be a diagnostic category in Chapter 6 (Mental, behavioural or neurodevelopmental disorders) of ICD-11 (96, 97).

Recommendation 133	Strength of recommendation
We suggest offering an evaluation of an increased risk for psychosis (with the established instruments; see tables in the Appendix) to the following people: a) People seeking professional help of their own accord because they have symptoms that are compatible with today’s established concepts of early diagnosis and an associated subjective level of suffering. b) People with an established risk (e.g. positive family history) for a psychotic illness who desire further diagnostic evaluation. We suggest that the established criteria, scales and interviews are used, in accordance with current scientific knowledge. We recommend that the evaluation is performed by professionals (doctors, psychologists, psychotherapists or other experienced psychiatric professionals) trained in the use of the diagnostic instruments[1]. We recommend not to perform a general screening of people who do not fulfil the above-mentioned criteria. Adapted from the NICE guideline ‘Psychosis and schizophrenia in children and young people’ 2013 (93) and the NICE guideline ‘Psychosis and schizophrenia in adults’ 2014 (10). [1]The final diagnosis according to ICD-10 must be made by people (specialists, psychological psychotherapists or child and adolescent psychotherapists) authorised according to the law regulating health care professionals.	**GCP**

Recommendation 134	Strength of recommendation
We suggest that people with an increased risk for psychosis are: • Informed about their current condition with reasonable therapeutic optimism and be given psychotherapeutic and psychosocial support in the processing of this information. • Not stressed and stigmatised through a premature diagnosis of schizophrenia. We recommend talking about an increased ‘risk for further worsening of the person’s mental health’ or the risk of ‘developing a psychotic crisis’, for example. Adapted from the AWMF guideline ‘Schizophrenia’ 2006 (in German) (17).	**GCP**

Recommendation 135	Strength of recommendation
We recommend offering screening for depressive disorders and psychoactive substance use (in particular drugs with noradrenergic and dopaminergic actions, such as amphetamines, cannabis, cocaine) to people with an increased risk for psychosis. Attention should be paid to possible comorbidity with medical illnesses.	**GCP**

In principle, **none** of the instruments specified in the long version of this guideline (SIPS/SOPS and CAARMS) for identifying risk criteria is suitable for diagnosing manifest psychotic illness (here: schizophrenia). Manifest illness should always be diagnosed with the diagnostic instruments specified in ICD-10 or, when available, ICD-11.

7.17.1 Treatment

Recommendation 136	Strength of recommendation
We recommend offering cognitive behavioural therapy (CBT; see Module 4b) to reduce the risk of or to delay transition to psychosis in people with an increased risk for psychosis (A). We recommend not to offer antipsychotics as the primary approach to prevent transition to full-blown psychosis (GCP). In cases in which CBT is insufficient and in which attenuated psychotic symptoms are occurring with increasing severity or brief psychotic episodes with increasing frequency, we suggest offering additional low-dose second-generation antipsychotics temporarily to reduce symptoms after a comprehensive risk-benefit evaluation * (GCP). Adapted from a systematic review/meta-analysis LoE 1+ Schmidt et al. 2015 (98). Adapted from the NICE guideline 'Psychosis and schizophrenia in children and young people: recognition and management' 2013 (93) and the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10). *Aripiprazole (one open study), risperidone (two controlled studies), amisulpride (one controlled study) and olanzapine (one controlled study) were evaluated in clinical studies (see Table 28). The choice of antipsychotic should be guided by the findings and this guideline's recommendations for the use of antipsychotics. If ICD-10 criteria for schizophrenia are not fulfilled, the use is off label. 'Off-label use' refers to the use of a medicine outside the approved use, in particular the use of an approved medicine outside the uses approved by the national or European licensing authorities (definition of the Federal Joint Committee). The following criteria must be fulfilled if substances are to be used off label in clinical practice: • Proven efficacy; • Favourable risk/benefit profile; • Lack of alternatives – treatment attempt. In addition, the treating doctor has a special duty to inform the patient about possible consequences (no manufacturer liability, etc). Decision-making must be shared. Off-label use is thus only permitted in severe illnesses when there is no alternative treatment. According to current scientific knowledge, there must be a reasonable prospect that the treatment will be successful.	**A/GCP**

8. Rehabilitation (Module 4d)

8.1 General aspects of rehabilitation

Recommendation 137	Strength of recommendation
We suggest offering rehabilitation services to people with schizophrenia if they are interested in them and if such procedures appear to be necessary for their rehabilitation.	**GCP**

Recommendation 138	Strength of recommendation
We recommend that people with schizophrenia who are receiving rehabilitation treatment are offered pharmacotherapeutic, psychotherapeutic and psychosocial treatment as basic therapies to reduce symptoms and prevent relapse.	**GCP**

8.2 Medical rehabilitation

Recommendation 139	Strength of recommendation
The efficacy of approaches that follow the principles of supported employment can be increased by cognitive remediation. We suggest that such remediation is therefore performed, depending on the individual need. Meta-analysis LoE 1- Suijkerbuijk et al. 2017 (99) and meta-analysis LoE 1+ Chan et al. 2015 (100).	**B**

8.3 Social rehabilitation

Recommendation 140	Strength of recommendation
We suggest that people with schizophrenia live autonomously in the community and are supported at home in accordance with their individual needs and preferences. Meta-analysis LoE 1+ Stergiopoulos al. 2015 (101) and meta-analysis LoE 1+ Aubry T et al. 2016 (102).	**B**

8.4 Occupational rehabilitation

Recommendation 141	Strength of recommendation
As part of occupational rehabilitation, we recommend offering programmes to people with schizophrenia who want to work in the general labour market that aim to quickly place them directly in a job in the general labour market and provide the necessary support (supported employment). Meta-analysis LoE 1+ Kinoshita et al. 2013 (103), meta-analysis LoE 1+ Modini et al. 2016 (104) and meta-analysis LoE 1+ Suijkerbuijk et al. 2017 (99); for additional literature, see background text.	**A**

Recommendation 142	Strength of recommendation
We suggest making options also available to people with schizophrenia that take the approach 'train first – then place'. Such options are especially important in the subgroup of patients who do not want to be immediately employed in the general labour market. The aim is supported employment in the general labour market. Non-randomised, open, controlled study LoE 2+ Watzke et al. 2009 (105), LoE 2+ open, controlled cross-sectional study Holzner et al. 1998 (106) and LoE 2+ open, controlled cross-sectional study Rüesch et al. 2004 (107).	**B**

Recommendation 143	Strength of recommendation
We suggest that the occupational rehabilitation of people with schizophrenia aims to avoid job loss. To this aim, early involvement of appropriate services or aids* is required in case of mental illness. *The services and aids are presented in the new version of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German) (18).	**GCP**

Recommendation 144	Strength of recommendation
A completed education as the basis for participation in working life is of enormous importance for people with schizophrenia. We therefore suggest that schools and academic, occupational and special training facilities with appropriate accompanying support services are available near where people live (supported education).	**GCP**

9. Care coordination (Module 5)

9.1 General aspects of care coordination

Recommendation 145	Strength of recommendation
We recommend that low-threshold access to the care system is made available to everyone with schizophrenia. An important component of the care system is thereby the coordination of psychiatric and psychotherapeutic, psychosocial and general medical and rehabilitative measures. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 146	Strength of recommendation
We recommend that a collaboration between all those involved in the care system and the service user is a feature of the treatment of schizophrenia. We suggest that all support approaches have the goal to promote the service user's social connections. We suggest that self-help by the service user, as well as family members and close confidants, is encouraged, service users' self-confidence is strengthened and their wish for information and involvement in treatment decisions is strongly supported. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

9.2 Primary care

No research was performed to identify studies on this topic and no recommendations were adopted. Information and studies on this topic can be found in the background text of the long version of this guideline (in German).

9.3 Specialist-centred outpatient treatment and criteria for referral to a specialist (people aged ≥ 18 years)

Recommendation 147	Strength of recommendation
We suggest that outpatient treatment by a specialist is considered to confirm the diagnosis in people with suspected schizophrenia and to treat and coordinate outpatient and accompanying treatment options in people with a diagnosis of schizophrenia, in consultation with the service user.	**GCP**

9.4 Outpatient psychotherapeutic care

No research was performed to identify studies on this topic and no recommendations were adopted. Information and studies on this topic can be found in the background text of the long version of this guideline (in German).

9.5 Multiprofessional community psychiatric teams; case management; team-based community psychiatric treatment

Recommendation 148	Strength of recommendation
We suggest establishing team-based community psychiatric multiprofessional outpatient treatment in defined regions to care for people with schizophrenia. Adapted from the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German) (the target group was changed) (18). A limitation is that the studies evaluated heterogeneous samples, i.e. not only people with schizophrenia (therefore strength of recommendation adjusted from 'A' to 'B').	**B**

Recommendation 149	Strength of recommendation
Case management may not be unconditionally recommended for the routine care of all patients, but it should be considered in a targeted way after reviewing the respective requirements (e.g. low availability of community psychiatric approaches in a region and/or high utilisation of inpatient treatments). Adapted from the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German) the target group was changed) (18). A limitation is that the studies evaluated heterogeneous samples, i.e. not only people with schizophrenia. LoE was decreased because there are no studies in Germany.	**B**

Recommendation 150	Strength of recommendation
The availability of an outreach approach is especially important in case of impending treatment discontinuation. We recommend that the opportunity to receive outreach treatment is available in particular for treating homeless people with schizophrenia. Adaptation of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German) (18). A limitation is that the studies evaluated heterogeneous samples, i.e. not only people with schizophrenia. However, people with schizophrenia represent a risk group for treatment discontinuation and homelessness, so that a greater relevance for patient care is assumed.	**A**

Recommendation 151	Strength of recommendation
We recommend that people with chronic and severe mental illnesses (e.g. schizophrenia) have the opportunity to be treated through outreach treatment in their familiar environment over a longer period of time and after recovery from acute illness phases. Adaptation of the AWMF guideline 'Psychosocial therapies for severe mental illnesses' (in German) (18). A limitation is that the studies evaluated heterogeneous samples, i.e. not only people with schizophrenia. However, this issue is highly relevant for patient care and a definite patient preference.	**A**

9.6 Psychiatric home health care (outpatient psychiatric nursing)

No recommendations. For details, see background text of the long version (in German).

9.7 Outpatient sociotherapy

No recommendations. For details, see background text of the long version (in German).

9.8 Day hospitals, night hospitals and psychiatric hospital outpatient clinics

Recommendation 152	Strength of recommendation
We suggest offering acute treatment in a day hospital as an alternative to inpatient treatment, if the associated requirements are fulfilled (see background text; in German). Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17). Strength of recommendation was assigned on the basis of the available meta-analysis (see background text; in German) and the relevance for patients. The strength of recommendation was decreased to 'B' because evidence had to be extrapolated for people with schizophrenia. Additional literature, including a recent meta-analysis, can be found in the background text.	**B**

Recommendation 153	Strength of recommendation
For patients who cannot or do not want to sleep at home because they are anxious or do not have an acceptable environment, or who are not yet able to receive only outpatient treatment, treatment in a night hospital or other transitional institution or in a crisis house may be suggested. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 154	Strength of recommendation
If patients require treatment by a multiprofessional team or need intensive psychopharmacological, psychotherapeutic or psychosocial measures, we recommend that practitioners consider referring patients to the outpatient clinic of a psychiatric hospital or an outpatient treatment network in which, depending on the staffing, complex treatment programmes can also be provided.	**GCP**

9.9 Inpatient psychiatric-psychotherapeutic treatment

Recommendation 155	Strength of recommendation
Inpatient treatment can have a significantly adverse impact on patients' lives, so we suggest that alternatives to inpatient admission are always considered. If inpatient treatment is required, we suggest that hospitalisations are short and planned, if possible. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17).	**GCP**

Recommendation 156	Strength of recommendation
We recommend that inpatient psychiatric-psychotherapeutic treatment is offered if patients require particular diagnostic and therapeutic measures or need the special protection of the hospital because they pose an acute risk to themselves or others. This may be the case in the following situations, for example: • Treatment resistance, • Acute suicidality, • Severe delirium or anxiety, • Nutrition or care cannot be guaranteed, • Severe inhibition of drive or adynamia, • Domestic situations that interfere with remission and healing, • Treatment of complicating concomitant illnesses, • Complex treatment situations, • Unclear medical comorbidities, • Severe adverse drug reactions, • Other problems that cannot be treated as an outpatient. Adapted and expanded from the AWMF guideline 'Schizophrenia' 2006 (in German) (17). The above are examples only. In clinical practice, there are additional indications for inpatient admission. This recommendation was developed for people aged ≥ 18 years. Other factors can play a role in children and adolescents.	**GCP**

Recommendation 157	Strength of recommendation
As part of inpatient treatment, we recommend that multiprofessional treatment with various interventions is offered consisting of consensus-based, relationship-building and needs-oriented interventions, as well as evidence-based, disorder-oriented ones.	**GCP**

	Minutes/week	No. of patients
Admission (see Module 2)	**180**	
Psychiatric-psychotherapeutic and physical diagnostic tests, incl. introduction of organic diagnostic tests (perhaps at various points in time)	180 (once)	1
General treatment (see Modules 2, 3, 4a, 4c)	**65**	
25-50 minutes during ward round (e.g. 5 x 10 or 2 x 15 minutes), incl. side effect management, advice regarding pharmacotherapy and treatment for medical illnesses, etc.	50	1
15 minutes with consultant	15	1
Psychiatric-psychotherapeutic treatment (see Modules 3, 4b)	**150 - 300**	
2 x 25-50 minutes medical and/or psychological psychotherapy[1] in a one-on-one setting (perhaps at various points in time)	50 - 100	1
1 - 2 x 50 minutes group therapy	50 - 100	6 - 8
and/or		
1 - 2 x 50 minutes group therapy psychoeducation	50 - 100	6 - 8
2 - 3 x 25-50 minutes cognitive training/remediation[2]	50 - 150	6 - 8
Psychosocial treatment (see Modules 3, 4b)	**400 - 1035**	
1 - 5 x 50-100 minutes group therapy: occupational therapy and/or creative therapies	50 - 500	6 - 8
2 - 3 x 30-50 minutes group therapy: body or movement therapy (physiotherapy, endurance training, yoga)	60 - 150	6 - 8
Socio-educational consultation	25	1
Training for everyday life and/or lifestyle interventions	50	6 - 8
Individual therapies led by nursing staff (primary nursing)	25 - 50	1
Brief contacts with nursing staff (several times)	140 - 210	1
Other treatment (see Modules 3, 4b)	**75 - 200**	
One-on-one consultation with family members/close confidants	25 - 50[3]	1
Group consultation with family members/close confidants	50 - 150[3]	6 - 8
Discharge and preparation of aftercare (see e.g. 4c and Section 39 of the German Social Code V (1a))	**75 - 150**	
Drug training by nursing staff (individual/group)	25	1/ 6 - 8
Discharge management (planning of further treatment, prescriptions, discussion of the discharge letter, certificates of incapacity to work, involvement of family members, etc.)	25 - 75	1[4]
Development of crisis plans/treatment agreements	25 - 75	1[4]

Table 16: Suggestion for a complex inpatient treatment plan to implement the new key recommendations of this guideline. This table presents an example week. All of the suggested interventions are included in key evidence-based recommendations (see Modules 2, 3, 4a, 4b, 4c) – this treatment plan itself was not evaluated in any study. [1]This includes both disorder-specific, manualised psychotherapy and psychotherapeutic interventions by medical and psychological practitioners, e.g. to build relationships, clarify treatment goals or create a therapeutic work alliance.[2]This also covers trainings, including specialised therapeutic interventions. [3]These times refer to the full duration of the inpatient treatment and are not included in the total time per patient and week. [4]Once at the end of the inpatient stay.

9.10 Treatment in an early recognition and treatment centre

Recommendation 158	Strength of recommendation
To identify adults with an increased risk for psychosis, ***early recognition and early intervention networks*** may be considered in cooperation with other professional groups and institutions, e.g. general practioners, practising specialists, psychological psychotherapists, other psychiatric hospitals, administrative bodies and educational and training institutions. We suggest that these networks include outreach services. In young people, the networks can be formed by child and adolescent psychiatry in collaboration with adult psychiatry. Adapted and revised from the AWMF guideline 'Schizophrenia' 2006 (in German) (17), adaptation of the NICE guideline 'Psychosis and schizophrenia in adults' 2014 (10) and the NICE guideline 'Psychosis and schizophrenia in children and young people' 2013 (93). For further details, see Recommendations 133 to 136.	**GCP**

9.11 Milieu therapy-oriented treatment structures and soteria

Recommendation 159	Strength of recommendation
For people with schizophrenia, treatment in a standard care institution that follows the principles of soteria and uses elements of soteria may be considered, depending on the availability of this care model. Meta-analysis LoE 1+ Calton et al. 2008 (108) and meta-analysis LoE 1- MacPherson et al. 2009 (109).	**0**

9.12 Peer-to-peer approaches

Recommendation 160	Strength of recommendation
Peer-to-peer concepts may be considered for people with schizophrenia with the aim to achieve greater optimism and recovery (0). Psychoeducational approaches based on the peer-to-peer model may be considered for patients, family members and close confidants to enable alternative paths, have a positive effect on the growth of knowledge and concept of the illness and reduce subjective distress (GCP). Meta-analysis LoE 1- Lloyd-Evans et al. 2014 (110); there are few findings specifically for schizophrenia; AWMF guideline 'Psychosocial therapies for severe mental illnesses' 2013/2018 (in German) (not specifically for schizophrenia) (18).	**0/GCP**

9.13 Psychosis seminar/trialogues

No research was performed to identify studies on this topic and no recommendations were adopted. Information and studies on this topic can be found in the background text of the long version of this guideline (in German).

9.14 Care networks associated with the workplace

Recommendation 161	Strength of recommendation
We suggest that people with schizophrenia are supported and treated by multiprofessional care networks associated with their places of work to enable early recognition and treatment of possible illness-related deficits and avoid interruptions in the ability to participate in education and work in the primary labour market. Adapted from the NICE guideline 'Psychosis and schizophrenia in adults: prevention and management' 2014 (10).	**GCP**

10. Cost Effectiveness of Treatment (Module 6)

10.1 General aspects of cost effectiveness and socioeconomic costs

Statement 4	Strength of recommendation
According to empirical cost studies, in 2001 to 2008 the average direct annual per capita costs of caring for people with schizophrenia in Germany were approx. €10,454 to €25,144. These costs included all psychiatric measures in the inpatient, outpatient and rehabilitative (so-called complementary) areas of care. One must assume, however, that the sample characteristics (severity, duration of illness, etc.) and the regional differences in the structure of psychiatric care networks influenced costs. For literature, see Table 30 and background text (in German): LoE 2+ (Karow et al. 2012 (998), König et al. 2010 (997); LoE 2- (Salize et al. 2007 (996), Salize et al. 2009 (995)).	

10.2 Cost effectiveness of antipsychotic therapy

Statement 5	Strength of recommendation
The vast majority of systematic reviews and overviews of health economics studies on antipsychotic treatment identified methodological shortcomings and found that the results on the cost effectiveness of antipsychotics were ambiguous and not generalisable. In particular, there is no clear indication of superior cost effectiveness of SGAs versus FGAs. Clinical decisions on antipsychotics cannot currently be justified or substantiated by evidence on their cost effectiveness. LoE 2-: Hamann et al. 2003 (1004), Hudson et al. 2003 (1005), Basu (2004) (1007), Barbui et al. 2005 (1002), Hargreaves & Gibson 2005 (1003), Haycox 2005 (1009), Hanrahan et al. 2006 (1008), Achilla & McCrone 2013 (1000).	

Statement 6	Strength of recommendation
Compared with non-treatment, treatment with antipsychotics reduces the readmission rate. For literature, see background text; also, indirect evidence through the reduction in the number of hospitalisations (see evidence in Module 4a) LoE 3: Kilian & Angermeyer 2004 (1010).	

10.3 Cost effectiveness of psychotherapeutic or psychosocial therapies

Statement 7	
There is no robust evidence for the cost effectiveness of psychotherapeutic treatment of people with schizophrenia in the German health care system. In view of the high direct total costs of care, the additional costs for psychotherapeutic treatment of people with schizophrenia appear justifiable if there is proven need and efficacy (see Module 4b). No LoE.	

11. Quality Management (Module 7)

11.1 Quality indicators

Statement 8	
Quality indicators for the treatment of people with schizophrenia are feasible instruments of quality management. No LoE, expert consensus on the basis of AQUA 2016 (1015), Großimlinghaus et al. 2013 (1016), Weinmann & Becker 2009 (1017), GBA 2016 (1018), Großimlinghaus et al. 2015 (1019), Kösters et al. 2017 (1020), Großimlinghaus et al. 2017 (1021).	

See also Table 31 in the long version (in German) for a presentation of the DGPPN Quality Indicators for Schizophrenia (111-113).

11.2 Quality assurance

Recommendation 162	Strength of recommendation
We suggest implementing the guideline in a structured way because it can improve treatment outcome in people with schizophrenia. For literature, see background text of the long version (in German).	**GCP**

12. Literature

1. SIGN SIGN. SIGN 131 • Management of schizophrenia • A national clinical guideline. 2013.

2. Zielasek J, Gaebel W. Diagnose und Differenzialdiagnose, Verlauf und Prognose. In: Falkai P, editor. Praxishandbuch Schizophrenie. 1. München: Urban & Fischer Verlag/Elsevier GmbH; 2016. p. 41 - 54.

3. Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, Cellucci T, et al. A clinical approach to diagnosis of autoimmune encephalitis. The Lancet Neurology. 2016;15(4):391-404.

4. Prüß H. Neuroimmunologie: Neues zur limbischen Enzephalitis. Akt Neurologie. 2013;40:127 - 36.

5. Schmitt SE, Pargeon K, Frechette ES, Hirsch LJ, Dalmau J, Friedman D. Extreme delta brush: a unique EEG pattern in adults with anti-NMDA receptor encephalitis. Neurology. 2012;79(11):1094-100.

6. Herken J, Pruss H. Red Flags: Clinical Signs for Identifying Autoimmune Encephalitis in Psychiatric Patients. Frontiers in psychiatry. 2017;8:25.

7. Oldham M. Autoimmune Encephalopathy for Psychiatrists: When to Suspect Autoimmunity and What to Do Next. Psychosomatics. 2017;58(3):228-44.

8. Steiner J, Pruss H, Kohler S, Hasan A, Falkai P. [Autoimmune encephalitis with psychotic symptoms : Diagnostics, warning signs and practical approach]. Der Nervenarzt. 2018.

9. Prüss H. Autoantikörper als Ursache neuropsychiatrischer Störungsbilder. Neurotransmitter. 2017;28:34 - 41.

10. NICE. NICE clinical guideline 178 - Psychosis and schizophrenia in adults: treatment and management - Issued: February 2014 last modified: March 2014 2014 [Available from: guidance.nice.org.uk/cg178

11. Petermann F. Wechsler Adult Intelligence Scale–Fourth Edition (WAIS-IV), Deutsche Bearbeitung. Frankfurt: Pearson Assessment; 2012.

12. Zimmermann P, Fimm B. Testbatterie zur Aufmerksamkeitsprüfung, Version 2.3.1 (TAP). Herzogenrath: Psytest; 2017.

13. Petermann F, Lepach AC. Wechsler Memory Scale–Fourth Edition (WMS-IV), Deutsche Version. Frankfurt: Pearson Assessment; 2012.

14. Niemann H, Sturm W, Thöne-Otto AIT, Willmes-von-Hinckeldey K. CVLT - California Verbal Learning Test -Deutsche Adaption. Frankfurt: Pearson; 2008.

15. Helmstaedter C, Lendt M, Lux S. Verbaler Lern- und Merkfähigkeitstest (VLMT). Göttingen: Hogrefe; 2001.

16. Steinmayr R, Schütz A, Hertel J, Schröder-Abé M. Mayer-Salovey-Caruso Test zur Emotionalen Intelligenz. Deutschsprachige Adaptation des Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) von John D. Mayer, Peter Salovay, David R. Caruso. Bern: Verlag Hans Huber; 2011.

17. DGPPN. S3 Praxisleitlinien in Psychiatrie und Psychotherapie. Band 1 - Behandlungsleitlinie Schizophrenie. Gaebel Wf, Falkai, P., Weinmann, S., Wobrock T., editor. Darmstadt: Steinkopff-Verlag; 2006.

18. DGPPN. S3 Leitlinie Psychosoziale Therapien bei schweren psychischen Erkrankung - 2013er Version und Teile der revidierten 2018er Version lagen der Leitliniengruppe vor: Springer; 2013/18.

19. DGPPN. S3-Leitlinie/Nationale Versorgungsleitlinie Unipolare Depressionen - Langfassung. 2015;2. Auflage 2015 Version 3.

20. Hiemke C, Bergemann N, Clement HW, Conca A, Deckert J, Domschke K, et al. Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology: Update 2017. Pharmacopsychiatry. 2017; 51(1-02):9-62.

21. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, et al. The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophrenia bulletin. 2010;36(1):71-93.

22. Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthoj B, Gattaz WF, et al. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, part 1: update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry. 2012;13(5):318-78.

23. Müller MJ, Benkert O. Antipsychotika. In: Benkert O, Hippius H, editors. Kompendium der Psychiatrischen Pharmakotherapie,. 11. Berlin, Heidelberg: Springer Verlag; 2017. p. 269 - 488.

24. Leucht S, Samara M, Heres S, Patel MX, Woods SW, Davis JM. Dose equivalents for second-generation antipsychotics: the minimum effective dose method. Schizophrenia bulletin. 2014;40(2):314-26.

25. Schimmelmann BG, Schmidt SJ, Carbon M, Correll CU. Treatment of adolescents with early-onset schizophrenia spectrum disorders: in search of a rational, evidence-informed approach. Current opinion in psychiatry. 2013;26(2):219-30.

26. Leucht S, Leucht C, Huhn M, Chaimani A, Mavridis D, Helfer B, et al. Sixty Years of Placebo-Controlled Antipsychotic Drug Trials in Acute Schizophrenia: Systematic Review, Bayesian Meta-Analysis, and Meta-Regression of Efficacy Predictors. The American journal of psychiatry. 2017;174(10):927-42.

27. Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet. 2013;382(9896):951-62.

28. Kuo CJ, Yang SY, Liao YT, Chen WJ, Lee WC, Shau WY, et al. Second-generation antipsychotic medications and risk of pneumonia in schizophrenia. Schizophrenia bulletin. 2013;39(3):648-57.

29. Uchida H, Suzuki T, Takeuchi H, Arenovich T, Mamo DC. Low dose vs standard dose of antipsychotics for relapse prevention in schizophrenia: Meta-analysis. Schizophr Bull. 2011;37(4):788-99.

30. De Hert M, Sermon J, Geerts P, Vansteelandt K, Peuskens J, Detraux J. The Use of Continuous Treatment Versus Placebo or Intermittent Treatment Strategies in Stabilized Patients with Schizophrenia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials with First- and Second-Generation Antipsychotics. CNS drugs. 2015;29(8):637-58.

31. Sampson S, Mansour M, Maayan N, Soares-Weiser K, Adams CE. Intermittent drug techniques for schizophrenia. The Cochrane database of systematic reviews. 2013(7):CD006196.

32. Samara MT, Leucht C, Leeflang MM, Anghelescu IG, Chung YC, Crespo-Facorro B, et al. Early Improvement As a Predictor of Later Response to Antipsychotics in Schizophrenia: A Diagnostic Test Review. The American journal of psychiatry. 2015;172(7):617-29.

33. Zhu Y, Krause M, Huhn M, Rothe P, Schneider-Thoma J, Chaimani A, et al. Antipsychotic drugs for the acute treatment of patients with a first episode of schizophrenia: a systematic review with pairwise and network meta-analyses. The lancet Psychiatry. 2017;4(9):694-705.

34. Zhu Y, Li C, Huhn M, Rothe P, Krause M, Bighelli I, et al. How well do patients with a first episode of schizophrenia respond to antipsychotics: A systematic review and meta-analysis. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2017;27(9):835-44.

35. Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2013;16(6):1205-18.

36. Alvarez-Jimenez M, Parker AG, Hetrick SE, McGorry PD, Gleeson JF. Preventing the second episode: a systematic review and meta-analysis of psychosocial and pharmacological trials in first-episode psychosis. Schizophrenia bulletin. 2011;37(3):619-30.

37. Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Salanti G, et al. Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. Lancet. 2012;379(9831):2063-71.

38. Kishimoto T, Agarwal V, Kishi T, Leucht S, Kane JM, CorrellI CU. Relapse prevention in schizophrenia: A systematic review and meta-analysis of second-generation antipsychotics versus first-generation antipsychotics [Schizophrenia & Psychotic States 3213]. United Kingdom: Nature Publishing Group

United Kingdom; 2013 [1:[53-66]. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=psyc10&NEWS=N&AN=2013-00409-012.

39. Leucht S, Arbter D, Engel RR, Kissling W, Davis JM. How effective are second-generation antipsychotic drugs? A meta-analysis of placebo-controlled trials. Molecular psychiatry. 2009;14(4):429-47.

40. Helfer B, Samara MT, Huhn M, Klupp E, Leucht C, Zhu Y, et al. Efficacy and Safety of Antidepressants Added to Antipsychotics for Schizophrenia: A Systematic Review and Meta-Analysis. The American journal of psychiatry. 2016;173(9):876-86.

41. Howes OD, McCutcheon R, Agid O, de Bartolomeis A, van Beveren NJ, Birnbaum ML, et al. Treatment-Resistant Schizophrenia: Treatment Response and Resistance in Psychosis (TRRIP) Working Group Consensus Guidelines on Diagnosis and Terminology. The American journal of psychiatry. 2017;174(3):216-29.

42. Samara MT, Dold M, Gianatsi M, Nikolakopoulou A, Helfer B, Salanti G, et al. Efficacy, Acceptability, and Tolerability of Antipsychotics in Treatment-Resistant Schizophrenia: A Network Meta-analysis. JAMA psychiatry. 2016;73(3):199-210.

43. Siskind D, McCartney L, Goldschlager R, Kisely S. Clozapine v. first- and second-generation antipsychotics in treatment-refractory schizophrenia: systematic review and meta-analysis. The British journal of psychiatry : the journal of mental science. 2016;209(5):385-92.

44. Dold M, Fugger G, Aigner M, Lanzenberger R, Kasper S. Dose escalation of antipsychotic drugs in schizophrenia: a meta-analysis of randomized controlled trials. Schizophrenia research. 2015;166(1-3):187-93.

45. Galling B, Roldan A, Hagi K, Rietschel L, Walyzada F, Zheng W, et al. Antipsychotic augmentation vs. monotherapy in schizophrenia: systematic review, meta-analysis and meta-regression analysis. World psychiatry : official journal of the World Psychiatric Association. 2017;16(1):77-89.

46. Correll CU, Rubio JM, Inczedy-Farkas G, Birnbaum ML, Kane JM, Leucht S. Efficacy of 42 Pharmacologic Cotreatment Strategies Added to Antipsychotic Monotherapy in Schizophrenia: Systematic Overview and Quality Appraisal of the Meta-analytic Evidence. JAMA psychiatry. 2017;74(7):675-84.

47. Wang Y, Xia J, Helfer B, Li C, Leucht S. Valproate for schizophrenia. The Cochrane database of systematic reviews. 2016;11:CD004028.

48. Leucht S, Helfer B, Dold M, Kissling W, McGrath JJ. Lithium for schizophrenia. The Cochrane database of systematic reviews. 2015(10):CD003834.

49. Lally J, Tully J, Robertson D, Stubbs B, Gaughran F, MacCabe JH. Augmentation of clozapine with electroconvulsive therapy in treatment resistant schizophrenia: A systematic review and meta-analysis. Schizophrenia research. 2016;171(1-3):215-24.

50. Tharyan P, Adams CE. Electroconvulsive therapy for schizophrenia. The Cochrane database of systematic reviews. 2005(2):CD000076.

51. Slotema CW, Blom JD, van Lutterveld R, Hoek HW, Sommer IE. Review of the efficacy of transcranial magnetic stimulation for auditory verbal hallucinations. Biological psychiatry. 2014;76(2):101-10.

52. He H, Lu J, Yang L, Zheng J, Gao F, Zhai Y, et al. Repetitive transcranial magnetic stimulation for treating the symptoms of schizophrenia: A PRISMA compliant meta-analysis. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. 2017;128(5):716-24.

53. Wobrock T, Guse B, Cordes J, Wölwer W, Winterer G, Gaebel W, et al. Left prefrontal high-frequency repetitive transcranial magnetic stimulation for the treatment of schizophrenia with predominant negative symptoms: a sham-controlled, randomized multicenter trial. Biological psychiatry. 2015;77(11):979-88.

54. Shi C, Yu X, Cheung EF, Shum DH, Chan RC. Revisiting the therapeutic effect of rTMS on negative symptoms in schizophrenia: a meta-analysis. Psychiatry research. 2014;215(3):505-13.

55. De Hert M, Dekker JM, Wood D, Kahl KG, Holt RI, Moller HJ. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC). European psychiatry : the journal of the Association of European Psychiatrists. 2009;24(6):412-24.

56. Zheng W, Xiang YT, Xiang YQ, Li XB, Ungvari GS, Chiu HF, et al. Efficacy and safety of adjunctive topiramate for schizophrenia: a meta-analysis of randomized controlled trials. Acta psychiatrica Scandinavica. 2016;134(5):385-98.

57. Correll CU. Antipsychotic use in children and adolescents: minimizing adverse effects to maximize outcomes. Journal of the American Academy of Child and Adolescent Psychiatry. 2008;47(1):9-20.

58. NICE TNIfHaCE. Psychosis and schizophrenia in adults: prevention and management. 2014.

59. Strawn JR, Keck PE, Jr., Caroff SN. Neuroleptic malignant syndrome. The American journal of psychiatry. 2007;164(6):870-6.

60. Woodbury MM, Woodbury MA. Neuroleptic-induced catatonia as a stage in the progression toward neuroleptic malignant syndrome. Journal of the American Academy of Child and Adolescent Psychiatry. 1992;31(6):1161-4.

61. Chen JX, Su YA, Bian QT, Wei LH, Zhang RZ, Liu YH, et al. Adjunctive aripiprazole in the treatment of risperidone-induced hyperprolactinemia: A randomized, double-blind, placebo-controlled, dose-response study. Psychoneuroendocrinology. 2015;58:130-40.

62. Xia J, Merinder LB, Belgamwar MR. Psychoeducation for schizophrenia. The Cochrane database of systematic reviews. 2011(6):CD002831.

63. Bird V, Premkumar P, Kendall T, Whittington C, Mitchell J, Kuipers E. Early intervention services, cognitive-behavioural therapy and family intervention in early psychosis: systematic review. The British journal of psychiatry : the journal of mental science. 2010;197(5):350-6.

64. Jauhar S, McKenna P, Radua J, Fung E, Salvador R, Laws K. Cognitive-behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias. Brit J Psychiat. 2014;204(1):20 - 9.

65. Wykes T, Steel C, Everitt B, Tarrier N. Cognitive behavior therapy for schizophrenia: effect sizes, clinical models, and methodological rigor. Schizophrenia bulletin. 2008;34(3):523-37.

66. Turner DT, van der Gaag M, Karyotaki E, Cuijpers P. Psychological Interventions for Psychosis: A Meta-Analysis of Comparative Outcome Studies. The American journal of psychiatry. 2014;171(5):523-38.

67. Sarin F, Wallin L, Widerlov B. Cognitive behavior therapy for schizophrenia: A meta-analytical review of randomized controlled trials. Nord J Psychiat. 2011;65(3):162-74.

68. Lincoln TM, Jung E, Wiesjahn M, Schlier B. What is the minimal dose of cognitive behavior therapy for psychosis? An approximation using repeated assessments over 45 sessions. European psychiatry : the journal of the Association of European Psychiatrists. 2016;38:31-9.

69. Morrison AP, Turkington D, Pyle M, Spencer H, Brabban A, Dunn G, et al. Cognitive therapy for people with schizophrenia spectrum disorders not taking antipsychotic drugs: a single-blind randomised controlled trial. Lancet. 2014;383(9926):1395-403.

70. Eichner C, Berna F. Acceptance and Efficacy of Metacognitive Training (MCT) on Positive Symptoms and Delusions in Patients With Schizophrenia: A Meta-analysis Taking Into Account Important Moderators. Schizophrenia bulletin. 2016;42(4):952-62.

71. van Oosterhout B, Smit F, Krabbendam L, Castelein S, Staring AB, van der Gaag M. Metacognitive training for schizophrenia spectrum patients: a meta-analysis on outcome studies. Psychological medicine. 2016;46(1):47-57.

72. Pinquart M, Oslejsek B, Teubert D. Efficacy of systemic therapy on adults with mental disorders: A meta-analysis. Psychother Res. 2016;26(2):241-57.

73. Pharoah F, Mari J, Rathbone J, Wong W. Family intervention for schizophrenia. Cochrane database of systematic reviews (Online). 2010(12):CD000088-CD.

74. Turner DT, McGlanaghy E, Cuijpers P, van der Gaag M, Karyotaki E, MacBeth A. A Meta-Analysis of Social Skills Training and Related Interventions for Psychosis. Schizophrenia bulletin. 2017.

75. Almerie MQ, Okba Al Marhi M, Jawoosh M, Alsabbagh M, Matar HE, Maayan N, et al. Social skills programmes for schizophrenia. The Cochrane database of systematic reviews. 2015(6):CD009006.

76. Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. Am J Psychiat. 2011;168(5):472-85.

77. Kurtz MM, Gagen E, Rocha NB, Machado S, Penn DL. Comprehensive treatments for social cognitive deficits in schizophrenia: A critical review and effect-size analysis of controlled studies. Clin Psychol Rev. 2016;43:80-9.

78. Rosenbaum B, Harder S, Knudsen P, Koster A, Lajer M, Lindhardt A, et al. Supportive Psychodynamic Psychotherapy versus Treatment as Usual for First-Episode Psychosis: Two-Year Outcome. Psychiatry-Interpers Biol Process. 2012;75(4):331-41.

79. NICE TNIfHaCE. Violence and aggression: short-term management in mental health, health and community settings. 2015.

80. de Jong MH, Kamperman AM, Oorschot M, Priebe S, Bramer W, van de Sande R, et al. Interventions to Reduce Compulsory Psychiatric Admissions: A Systematic Review and Meta-analysis. JAMA psychiatry. 2016;73(7):657-64.

81. DGPPN. Therapeutische Maßnahmen bei aggressivem Verhalten in der Psychiatrie und Psychotherapie 2009 [Available from: https://www.dgppn.de/_Resources/Persistent/fa128e27b086d7a72813034b7532cee62c025848/S2-LL_Aggres.Verhalten_Kurzversion_21.10.2009.pdf.

82. Müller MJ, Benkert O. Pharmakotherapie psychiatrischer Notfallsituationen. In: Benkert O, Hippius H, editors. Kompendium der Psychiatrischen Pharmakotherapie,. 11. Berlin, Heidelberg: Springer; 2017. p. 839 - 87.

83. Schmidt A, Fischer P, Wally B, Scharfetter J. Influence of intravenous administration of the antipsychotic drug benperidol on the QT interval. Neuropsychiatrie : Klinik, Diagnostik, Therapie und Rehabilitation : Organ der Gesellschaft Osterreichischer Nervenarzte und Psychiater. 2017;31(4):172-5.

84. Kaskie RE, Graziano B, Ferrarelli F. Schizophrenia and sleep disorders: links, risks, and management challenges. Nature and science of sleep. 2017;9:227-39.

85. Leroy A, Naudet F, Vaiva G, Francis A, Thomas P, Amad A. Is electroconvulsive therapy an evidence-based treatment for catatonia? A systematic review and meta-analysis. European archives of psychiatry and clinical neuroscience. 2017;268(7):675-87.

86. Meltzer HY, Alphs L, Green AI, Altamura AC, Anand R, Bertoldi A, et al. Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). Archives of general psychiatry. 2003;60(1):82-91.

87. Lako IM, Bruggeman R, Knegtering H, Wiersma D, Schoevers RA, Slooff CJ, et al. A systematic review of instruments to measure depressive symptoms in patients with schizophrenia. Journal of affective disorders. 2012;140(1):38-47.

88. Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. Lancet. 2009;373(9657):31-41.

89. DGPPN. Screening, Diagnostik und Behandlung des schädlichen und abhängigen Tabakkonsums. AWMF, DGPPN, editors2015.

90. DGPPN. Screening, Diagnose und Behandlung alkoholbezogener Störungen. AWMF, DGPPN, editors: Springer; 2016.

91. Pagsberg AK, Tarp S, Glintborg D, Stenstrom AD, Fink-Jensen A, Correll CU, et al. Acute Antipsychotic Treatment of Children and Adolescents With Schizophrenia-Spectrum Disorders: A Systematic Review and Network Meta-Analysis. Journal of the American Academy of Child and Adolescent Psychiatry. 2017;56(3):191-202.

92. Harvey RC, James AC, Shields GE. A Systematic Review and Network Meta-Analysis to Assess the Relative Efficacy of Antipsychotics for the Treatment of Positive and Negative Symptoms in Early-Onset Schizophrenia. CNS drugs. 2016;30(1):27-39.

93. NICE. Psychosis and Schizophrenia in Children and Young People: Recognition and Managemen 2013 [Available from: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0078141/pdf/PubMedHealth_PMH0078141.pdf.

94. Correll CU, Galling B, Pawar A, Krivko A, Bonetto C, Ruggeri M, et al. Effectiveness of Coordinated Specialty Care for Early Psychosis: Systematic Review, Meta-analysis, and Metaregression-Analysis Submitted to journal (Persönliche Kommunikation). 2018

95. Carpenter WT, van Os J. Should attenuated psychosis syndrome be a DSM-5 diagnosis? The American journal of psychiatry. 2011;168(5):460-3.

96. Gaebel W. Status of psychotic disorders in ICD-11. Schizophrenia bulletin. 2012;38(5):895-8.

97. Gaebel W, Zielasek J, Cleveland HR. Psychotic disorders in ICD-11. Asian journal of psychiatry. 2013;6(3):263-5.

98. Schmidt SJ, Schultze-Lutter F, Schimmelmann BG, Maric NP, Salokangas RK, Riecher-Rossler A, et al. EPA guidance on the early intervention in clinical high risk states of psychoses. European psychiatry : the journal of the Association of European Psychiatrists. 2015;30(3):388-404.

99. Suijkerbuijk YB, Schaafsma FG, van Mechelen JC, Ojajarvi A, Corbiere M, Anema JR. Interventions for obtaining and maintaining employment in adults with severe mental illness, a network meta-analysis. The Cochrane database of systematic reviews. 2017;9:CD011867.

100. Chan JY, Hirai HW, Tsoi KK. Can computer-assisted cognitive remediation improve employment and productivity outcomes of patients with severe mental illness? A meta-analysis of prospective controlled trials. Journal of psychiatric research. 2015;68:293-300.

101. Stergiopoulos V, Hwang SW, Gozdzik A, Nisenbaum R, Latimer E, Rabouin D, et al. Effect of scattered-site housing using rent supplements and intensive case management on housing stability among homeless adults with mental illness: a randomized trial. Jama. 2015;313(9):905-15.

102. Aubry T, Goering P, Veldhuizen S, Adair CE, Bourque J, Distasio J, et al. A Multiple-City RCT of Housing First With Assertive Community Treatment for Homeless Canadians With Serious Mental Illness. Psychiatric services. 2016;67(3):275-81.

103. Kinoshita Y, Furukawa TA, Kinoshita K, Honyashiki M, Omori IM, Marshall M, et al. Supported employment for adults with severe mental illness. The Cochrane database of systematic reviews. 2013(9):CD008297.

104. Modini M, Tan L, Brinchmann B, Wang MJ, Killackey E, Glozier N, et al. Supported employment for people with severe mental illness: systematic review and meta-analysis of the international evidence. The British journal of psychiatry : the journal of mental science. 2016;209(1):14-22.

105. Watzke S, Galvao A, Brieger P. Vocational rehabilitation for subjects with severe mental illnesses in Germany. A controlled study. Social psychiatry and psychiatric epidemiology. 2009;44(7):523-31.

106. Holzner B, Kemmler G, Meise U. The impact of work-related rehabilitation on the quality of life of patients with schizophrenia. Social psychiatry and psychiatric epidemiology. 1998;33(12):624-31.

107. Ruesch P, Graf J, Meyer PC, Rossler W, Hell D. Occupation, social support and quality of life in persons with schizophrenic or affective disorders. Social psychiatry and psychiatric epidemiology. 2004;39(9):686-94.

108. Calton T, Ferriter M, Huband N, Spandler H. A systematic review of the Soteria paradigm for the treatment of people diagnosed with schizophrenia. Schizophrenia bulletin. 2008;34(1):181-92.

109. Macpherson R, Edwards TR, Chilvers R, David C, Elliott HJ. Twenty-four hour care for schizophrenia. The Cochrane database of systematic reviews. 2009(2):CD004409.

110. Lloyd-Evans B, Mayo-Wilson E, Harrison B, Istead H, Brown E, Pilling S, et al. A systematic review and meta-analysis of randomised controlled trials of peer support for people with severe mental illness. BMC psychiatry. 2014;14:39.

111. Grossimlinghaus I, Hauth I, Falkai P, Janssen B, Deister A, Meyer-Lindenberg A, et al. [DGPPN recommendations on quality indicators for schizophrenia]. Der Nervenarzt. 2017;88(7):779-86.

112. Grossimlinghaus I, Falkai P, Gaebel W, Hasan A, Janner M, Janssen B, et al. [Assessment of quality indicators with routine data: Presentation of a feasibility test in ten specialist clinics for psychiatry and psychotherapy]. Der Nervenarzt. 2015;86(11):1393-9.

113. Grossimlinghaus I, Falkai P, Gaebel W, Janssen B, Reich-Erkelenz D, Wobrock T, et al. [Developmental process of DGPPN quality indicators]. Der Nervenarzt. 2013;84(3):350-65.

Initial release:	1998-10
Revision of:	2019-03
Review planned:	2023-03