**The number of studies and patients included in etable 4 and etable 5 have been revised following publication. The total number of studies included in qualitative analysis and the number of studies included in quantitative analysis of the outcomes in these etables can differ because not every study has reported all outcomes analysed. We have reported in the first version of the etables the number of patients included in quantitative analysis. We report in this revision the number of patients randomized at study entry for RCTs and patients included in open label extension studies.*

**E-Table 1: Composition of the guideline group**

**Guideline steering committee**

Prof. Dr. med. Winfried Häuser. Deutsche Schmerzgesellschaft. Deutsche Gesellschaft für Innere Medizin (Chair)

Prof. Dr. med. Frank Petzke: Deutsche Schmerzgesellschaft; Deutsche Gesellschaft für Anästhesie und Intensivmedizin (Chair)

Dr. med. Fritjof Bock: Interdisziplinäre Gesellschaft für orthopädische/unfallchirurgische und allgemeine Schmerztherapie

Prof. Dr. phil. Michael Hüppe. Deutsche Gesellschaft für Psychologische Schmerztherapie und - forschung

Frau Heike Norda (Schmerzlos)

Dr. med. Monika Nothacker. Arbeitsgemeinschaft wissenschaftlicher medizinischer Fachgesellschaften Standing Guideline Commission of the Association of Scientific Medical Societies in Germany)

Prof. Dr. med. Lukas Radbruch: Deutsche Gesellschaft für Palliativmedizin

Prof. Dr. med. Marcus Schiltenwolf, Deutsche Gesellschaft für Orthopädie und Unfallchirurgie

PD Dr. med. Matthias Schuler: Deutsche Gesellschaft für Geriatrie

Prof. Dr. med. Dr. rer. nat. Thomas Tölle: Deutsche Gesellschaft für Neurologie

Dr. med. Anika Viniol: Deutsche Gesellschaft für Allgemein- und Familienmedizin

**Guideline consensus group**

Prof. Dr. med. Dan Ziegler. Deutsche Diabetes Gesellschaft **(DDG)**

Dr. med. Anika Viniol. Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin **(DEGAM)**

Prof. Dr. Michael Schäfer. Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin **(DGAI)**

Dr. med. Kristin Hupfer. Deutsche Gesellschaft für Arbeitsmedizin und Umweltmedizin **(DGAUM)**

Prof. Dr. med. Stephan Freys. Deutsche Gesellschaft für Chirurgie **(DGCH)**

PD Dr. med. Matthias Schuler. Deutsche Gesellschaft für Geriatrie (**DGG)**

Dr. med. Dirk Wolter. Deutsche Gesellschaft für Gerontopsychiatrie und –psychotherapie **(DGGPP)**

Prof. Dr. med. Achim Rody. Deutsche Gesellschaft für Gynäkologie und Geburtshilfe **(DGGG)**

Professor Dr. Jens Büntzel. Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie **(DGHNOKHC)**

Prof. Dr. med. Gerhard Müller. Deutsche Gesellschaft für Innere Medizin **(DGIM)**

Dr. Dr. med. habil. Volker Thieme. Deutsche Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie **(DGMKG)**

Prof. Dr. med. Volker Tronnier. Deutsche Gesellschaft für Neurochirurgie **(DGNC)**

Prof. Dr. med. Dr. re. nat. Thomas R. Tölle. Deutsche Gesellschaft für Neurologie **(DGN)**

Prof. Dr. med. Marcus Schiltenwolf. Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie **(DGOOC)**

Dr. med. Dieter Schöffel. Deutsche Gesellschaft für Osteologie **(DGO)**

Prof. Dr. med. Lukas Radbruch. Deutsche Gesellschaft für Palliativmedizin **(DGP)**

Prof.-Dr. med. Claas Lahmann. Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie **(DGPM)**

Prof. Dr. med. Karl-Jürgen Bär. Deutsche Gesellschaft für Psychiatrie, Psychotherapie, Psychosomatik und Nervenheilkunde **(DGPPN)**

Prof. Dr. med. Christoph G. O. Baerwald. Deutsche Gesellschaft für Rheumatologie **(DGRh)**

Prof. Dr. med. Ursula Havemann-Reinecke. Deutsche Gesellschaft für Suchtforschung und Suchttherapie **(DG-Sucht)**

Dr. med. Matthias Beintker. Deutsche Gesellschaft für Urologie **(DGU)**

Prof. Dr. med. Martin Marziniak. Deutsche Migräne- und Kopfschmerzgesellschaft **(DMKG)**

Prof. Dr. med. Ulrich Kellner. Deutsche Ophthalmologische Gesellschaft **(DOG)**

Prof. Dr. med. Frank Petzke, Deutsche Schmerzgesellschaft **(DGSS)**

Dr. med. Fritjof Bock. Interdisziplinäre Gesellschaft für orthopädische/unfallchirurgische und allgemeine Schmerztherapie **(IGOST)**

Holger Petri. Bundesverband Deutscher Krankenhausapotheker (AKDA)

Prof. Dr. rer. medic. Irmela Gnass. Deutsche Gesellschaft für Pflegewissenschaften (**DGP**)

Prof. Dr. Dipl. psych. Michael Hüppe. Deutsche Gesellschaft für psychologische Schmerztherapie und -forschung e. V. **(DGPSF)**

Corinna Elling-Audersch. Deutsche Rheuma-Liga Bundesverband e. V.

Heike Norda. SchmerzLos e. V. Lübeck

**Evidence synthesis team:** Prof. Dr. med. Winfried Häuser; Dr.phil. Petra Klose; Prof. Dr. med. Frank Petzke; Professor Dr. med. Claudia Sommer, Dr. med. Patrick Welsch

**Review committee:** Dr. Gabriele Grögl; Prof. Dr. med. Heike Rittner; Prof. Dr. med. Rainer Sabatowski, Prof. Dr. med. Michael Zenz

**E-Table 2: Special situations**

Oral versus transdermal opioids

Short-acting versus long-acting opioids

Opioids as rescue medication

Opioids in hepatic insufficiency

Opioids in renal insufficiency

Opioid rotation

Drug interactions

Opioids and tranquilizer

Treatment of nausea

Treatment of constipation

Driving

Opioid withdrawal as a therapeutic measure in patients with persistent severe pain and/or impairments during long-term use of opioid-containing analgesics

Children and adolescents

Pregnancy

Seniors

Comorbid mental disorders including substance abuse and dependence

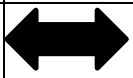
Diagnosis and treatment of abuse and dependence of prescribed opioids for chronic CNCP

**E-Table 3: Meaning of strengths of recommendations**

All recommendations are to be based on balancing the potential benefits and harms of a therapy against the potential benefits and harms of alternative therapies, while taking into account the comorbidities and preferences of the patient within shared decision making. As a basic principle, guidelines‘ recommendations can be deviated from based on patient‘s wishes. If applicable, guidelines‘ recommendations have to be deviated from  if there are individual contraindications for the recommended treatment.

**Evidence-based recommendation**

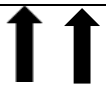
| **Mark of strength** | **Description** | **Wording** | **Meaning** | **Symbol** |
|---|---|---|---|---|
| A | Strong positive Recommend-dation | Should | From the point of view of the guideline group this therapy is to be recommended to great majority of patients. If well grounded, the treatment may not be recommended to a few patients. | ⇑⇑ |
| B | Positive recommen-dation | Ought | From the point of view of the guideline group this therapy should be recommended to the majority of patients. The treatment may not be | ⇑ |

| | | | | |
|---|---|---|---|---|
| | | | recommended to some patients. | |
| 0 | Discretio-nary (open) recommend ation | Can be consi-dered | From the point of view of the guideline group this therapy can be considered in some patients. |  |
| B | Negative recommen-dation | Ought not | From the point of view of the guideline group this therapy should not be recommended to the majority of patients. The treatment may still be considered in some patients. |  |
| A | Strong negative recommen-dation | Should not | From the point of view of the guideline group this therapy is not to be recommended to the great majority of patients. If well grounded, the treatment may be recommended to a few patients. |  |

*From the point of view of the guideline group (=Systematic appraisal of the literature and clinical experience)

**Consensus-based recommendations**

Recommended based on good clinical practice and on the clinical experience of the guideline group. No sufficient data on benefits and harms available.

| **Mark of strength** | **Description** | **Wording** | **Meaning** | **Symbol** |
|---|---|---|---|---|
| No mark | Strong positive recommen-dation | Should | Based on the clinical experience the guideline group considers that this therapy is to be recommended to a great majority of patients. Well grounded, the treatment cannot be recommended to a few patients. |  |
| No mark | Positive recommen-dation | Ought | Based on the clinical experience the guideline group considers that this therapy should be recommended to many patients. The treatment cannot be recommended to some patients. |  |

| | | | | |
|---|---|---|---|---|
| No mark | Discretio-nary (open) recommend ation | Can be consi-dered | Based on the clinical experience the guideline group considers that this therapy can be considered in some patients. |  |
| No mark | Negative recommen-dation | Ought not | Based on the clinical experience the guideline group considers that this therapy should not be recommended to many patients. The treatment can be recommended to some patients. |  |
| No mark | Strong negative recommen-dation | Should not | Based on the clinical experience the guideline group considers that this therapy is not be recommended to a great majority of patients. Well grounded, the treatment can be recommended to a few patients. |  |

***UPDATED May 19, 2021**

**E-Table 4: Evidence table for chronic low back pain (modified from Bialas et al., 2020; Petzke et al., 2020)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of studies / number of patients | 5 studies with parallel or cross over design /839 patients randomized at study entry | 4 studies with parallel or cross over design /2804 randomized at study entry | 5 open label extension studies / 1080 patients included in open label extension phase |
| Level of evidence | 1a | 1a | 2a (SR von open label Studien) |
| Pain relief of 50% or greater* | RD 0.07<br>(0.01, 0.13)<br>($I^2$=0%, p=0.01)<br>NNTB 16 (7,100) | RD 0.08<br>(0.03, 0.13)<br>($I^2$=0%, p=0.007)<br>NNTB 11 (7,33) | No statistically significant change in pain intensity<br>SMD 0.34<br>(-0.17, 0.86) |
| Patient Impression to be much or very much improved* | RD 0.12<br>[-0.03, 0.27]<br>($I^2$=84, p=.11) | RD 0.19<br>(0.12,0.26)<br>($I^2$=0, p<0.0001)<br>NNTB 5(4,6) | Not assessed |

| | | | |
|---|---|---|---|
| Disability* | SMD -0.21<br>(-0.33;– 0.09)<br>$I^2$=0%; p<0.0009 | SMD -0.23 (-0.34,-0.11);<br>$I^2$=0; p<0.0001 | Not assessed |
| Drop out due to adverse events* | RD 0.04<br>( -0.01; 0.10)<br>($I^2$=62%; p=0.13)<br>NNTH 25 (10,100) | RD 0.21<br>(0.14 to 0.27)<br>($I^2$=78%; p<0.001)<br>NNTH 5 (4,7) | 3.8% |
| Serious adverse events* | No statistically significant difference | No statistically significant difference | 4.8% |

NNTB= Number Needed to treat for an additional Benefit; NNTH= Number Needed to treat for an additional Harm; RD= Risk Difference; SMD= Standardized mean difference; SR= Systematic Review.

*The total number of studies included into qualitative analysis and the number of studies included into quantitative analysis of the outcomes can differ because not every study has reported all outcomes analysed.

***UPDATED May 19, 2021**

**E-Table 5: Evidence table for osteoarthritis pain (modifizied from Bialas et al., and from Welsch et al., 2020)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of / Number of patients | 12 studies with parallel or cross over design /5748 patients randomized at study entry | 7 studies with parallel or cross over design /3374 patients randomized at study entry | 3 open label extension studies /797 patients included in open label extension phase |
| Level of evidence | 1a | 1a | 2a (SR of open label Studien |
| Pain relief of 50% or greater* | RD 0.04 (0.01;0.07); $I^2$=46; p=0.006; NNTB 25 (16,100) | RD -0.01 (-0.05;0.03) $I^3$=46;p=0.66 | Not assessed |
| Patient Impression to be much or very much improved* | No data | RD 0.07 (0.00,0.14) ($I^2$=61%, p=0.04) NNTB 16 (7,100) | Not assessed |
| Disability* | SMD -0.23 (-0.30; -0.16); $I^2$=88%; p<0.0001 | SMD -0.23 (-0.30;0.03); $I^2$=69; p=0.11 | Not assessed |
| Drop out due to adverse events* | RD 0.17 (0.13;0.21); $I^2$=72; p<0.001 | RD 0.24 (0.17,0.31) $I^2$=88; p<0.0001 NNTH 4(3,6) | 29.9% |

| | | | |
|---|---|---|---|
| | NNTH 6(5,7) | | |
| Serious adverse events* | RD -0.00 (-0.01; 0.01) $I^2$=0; p=0.55 | RD 0.01 (0.00;0.02); $I^2$=0; p=0.003<br>NNTH 100 (50, infinite) | 5.1% |

*The total number of studies included into qualitative analysis and the number of studies included into quantitative analysis of the outcomes can differ because not every study has reported all outcomes analysed.

**E-Table 6: Evidence table for diabetic polyneuropathy (modifiziert nach Sommer et al., 2019 und Bialas et al., 2019)**

| Duration double-blind period | 4-12 Weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of studies with EERW design / Number of patients | 2/706 | No RCT available | 1/117 |
| Level of evidence | 1a | 5 | 2b Open label extension; |
| Pain relief of 50% or greater | RD 0.11 [0.04, 0.18]<br>NNTB 9 (6,25) | | No statistically significant change of pain intensity |
| Patient Impression to be much or very much improved | RD 0.24 [0.16, 0.31]<br>NNTB 4 (3,6) | | Not assessed |
| Disability | SMD -0.36<br>[-0.60, -0.12] | | Not assessed |
| Drop out due to adverse events | RD 0.06 [0.02, 0.11]<br>NNTH 16 (9,50) | | 11% |
| Serious adverse events | RD 0.02[-0.03, 0.06] | | 8.5% |

**E-Table 7: Evidence table for postherpetic neuropathy (modifiziert nach Sommer et al., 2019)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of studies with parallel or cross over design / Number of patients | 3/323 | No RCT available | No RCT or open label extension study available |
| Level of evidence | 1a | 5 | 5 |
| Pain relief of 50% or greater | SMD -0.49<br>(-0.75,-0.28) | | |
| Patient Impression to be much or very much improved | Data not suited for meta-analysis | | |
| Disability | Data not suited for meta-analysis | | |
| Drop out due to adverse events | RD 0.08 (0.04;0.13)<br>NNTH 12 (8,25) | | |
| Serious adverse events | RD 0.10 (-0.10, 0.12) | | |

**E-Table 8: Evidence table for phantom limb pain (modifiziert nach Sommer et al., 2019)**

| | | | |
|---|---|---|---|
| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
| Number of studies with parallel or cross over design/ Number of patients | 1/60 | No RCT available | No RCT or open label extension study available |
| Level of evidence | 1b | 5 | 5 |
| Pain relief of 50% or greater | RD 0.16 [-0.04, 0.35] | | |
| Patient Impression to be much or very much improved | SMD -0.95 [-1.01, -0.17] | | |
| Disability | Not assessed | | |
| Drop out due to adverse events | RD 0.31[0.02,0.61) NNTH 3 (2,50) | | |
| Serious adverse events | Not reported | | |

**E-Table 9: Evidence table for chronic pain after spinal cord injury (modifiziert nach Sommer et al., 2019)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of studies with parallel or cross over design/ Number of patients | 1/35 | No RCT available | No RCT or open label extension study available |
| Level of evidence | 1b | 5 | 5 |
| Pain relief of 50% or greater | RD 0.17 [-0.01, 0.36] | | |
| Patient Impression to be much or very much improved | RD 0.17 [-0.01, 0.36] | | |
| Disability | SMD -0.68 [-1.40, 0.03] | | |
| Drop out due to adverse events | RD 0.31 [0.02, 0.61]<br>NNTH 3(2,50) | | |
| Serious adverse events | Not reported | | |

**E-Table 10: Evidence table for painful radiculopathy (modifiziert nach Sommer et al., 2019)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| One RCT with parallel and one RCT with EERW design | 2/149 | No RCT available | No RCT or open label extension study available |
| Level of evidence | 1b | 5 | 5 |
| Pain relief of 50% or greater | Inconsistent;<br>Parallel Design: statistically significant difference to placebo<br>EERW- Design: Statistically significant superior over placebo | | |
| Patient Impression to be much or very much improved | Not assessed | | |
| Disability | Both studies: No statistically significant difference to placebo | | |
| Drop out due to adverse events | Both studies: No statistically significant | | |

| | | | |
|---|---|---|---|
| | difference to placebo | | |
| Serious adverse events | Both studies: No statistically significant difference to placebo | | |

**E-Table 11: Evidence table for non-diabetic polyneuropathy (modifiziert nach Sommer et al., 2019)**

| Duration double-blind period | 4-12 weeks | 13-26 weeks | 27-52 weeks |
|---|---|---|---|
| Number of studies with parallel or cross over design/ Number of patients | 2/111 | No RCT available | No RCT or open label extension study available |
| Level of evidence | 1a | 5 | 5 |
| Pain relief of 50% or greater | RD 0.26 [0.09, 0.42]<br>NNTB 4 (2,11) | | |
| Patient Impression to be much or very much improved | Not assessed | | |
| Disability | Not assessed | | |
| Drop out due to adverse events | RD 0.05 [-0.02, 0.13] | | |
| Serious adverse events | RD 0.02 [-0.03, 0.07] | | |