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# Guidelines for the management of trigeminal neuralgia

## ABSTRACT

Guidelines for the diagnosis and treatment of patients with trigeminal neuralgia (TN) advocate for a multidisciplinary team approach to improve the care of patients with acute and chronic TN. Evidence-based discussions and decisions are encouraged to establish care pathways for prompt diagnosis and treatment, and long-term outcomes data collection to improve care. The guidelines include summary materials for patients to inform them about their condition and available treatments.

## KEY POINTS

TN is a chronic pain disorder of the trigeminal nerve that causes sudden, intense facial pain.

TN may be caused by vascular contact with the trigeminal nerve (classic TN), an underlying pathology such as multiple sclerosis or tumor (secondary TN), or no known cause (idiopathic TN).

Once dental causes for facial pain are ruled out, prompt diagnosis of TN and initiation of first-line medications for rapid pain control are advised.

Imaging studies to determine the cause of TN and developing a care plan, including surgical options for some patients, should involve a multidisciplinary team.

**T**RIGEMINAL NEURALGIA (TN) IS A condition causing severe, unilateral, episodic facial pain. The diagnosis of TN is clinical, and patients typically report brief, lancinating attacks triggered by eating, drinking, talking, touching the face, or even a puff of wind. There is a distinction between typical TN paroxysms where there is no pain between episodic attacks and TN with concomitant pain where there is background pain between attacks.

Key symptoms and differential diagnosis for TN are summarized in **Table 1**. The lifetime prevalence of TN is estimated to be 0.3% (95% confidence interval [CI] 0.1%–0.5%),<sup>1</sup> but this has not been validated, and it may be more frequent. TN is more common in persons ages 50 to 60, with a slight predominance in women.<sup>2,3</sup> There are 3 etiologic classifications for TN<sup>4</sup>:

- Classic—vascular contact on the trigeminal nerve
- Secondary—possible underlying pathology such as schwannoma or multiple sclerosis
- Idiopathic—no apparent structural cause (**Table 2**).<sup>4</sup>

Secondary TN, due to multiple sclerosis or tumors (mostly benign), can present in a very similar way to classic TN, and these patients can also have periods of remission. It is important to evaluate if there are any auditory symptoms or signs, as these may indicate a tumor, which will require a different management approach. TN can be the primary diagnostic factor in 7% of patients with multiple sclerosis.<sup>5</sup>

Although symptoms of TN may stop spontaneously, the pain is severe and distressing. It was reported that patients with TN experienced a 3-fold higher risk of anxiety and

TABLE 1

## Key symptoms of trigeminal neuralgia and differential diagnosis

Key symptoms	Other possible symptoms	Differential diagnosis
Paroxysmal pain <ul style="list-style-type: none"> <li>• Sharp and shooting</li> <li>• Lasts seconds to minutes</li> <li>• Provoked by light touch</li> </ul>	Burning, prickling, dull tender constant background pain	Trigeminal neuralgia with concomitant, continuous pain
Trigeminal nerve innervation area	Interparoxysmal pain	Temporomandibular disorder
Pain cannot be evoked between attacks (refractory period)	Autonomic symptoms <sup>a</sup>	SUNCT and SUNA
Periods of remission or relapse	Sensory change <sup>b</sup>	Painful trigeminal neuropathy
Abrupt onset	After eating	Dental, cracked tooth

<sup>a</sup>Some facial reddening and tearing, sometimes on both sides, may be seen during acute pain paroxysms. If more pronounced with strictly unilateral conjunctival reddening, eyelid droop, nasal blockage, then consider SUNCT and SUNA.

<sup>b</sup>During a relapse of trigeminal neuralgia and especially just after paroxysms of pain, there may be subtle transient unilateral sensory change in the area innervated by the trigeminal nerve. The presence of permanent sensory alterations and atypical features such as absent refractory period and no pain remission raise the possibility of trigeminal nerve damage and painful trigeminal neuropathy.

SUNA = short-lasting unilateral neuralgiform headache attacks with autonomic features; SUNCT = short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

depression compared with a control group.<sup>6</sup> Another study estimated that 45% (89 of 198) of patients with TN reported more than 15 days of interference in daily activity in the last 6 months, 35.7% (75 of 210) had mild to severe depression, and half had anxiety symptoms.<sup>7</sup> The fear of an attack was reported to lead 30% (30 of 103) of patients with TN to experience symptoms consistent with posttraumatic stress disorder.<sup>8</sup>

### GUIDELINES INCLUDING ALL STAKEHOLDERS

The care pathways for patients with TN are extremely variable, partly due to the wide range of specialists consulted. There is therefore a need to establish evidence-based care plans for the management of both acute and chronic TN, using a multidisciplinary approach endorsed by all stakeholders. It is with this in mind that the Royal College of Surgeons of England issued TN national guidelines for the United Kingdom (UK).<sup>9</sup> These were based on the recently published European Academy of Neurology guidelines.<sup>10</sup> The discussion of guidelines here refers to the UK guidelines unless otherwise noted.

### CLINICAL SETTING: OUTPATIENT AND INPATIENT

These guidelines apply to all patients with TN as outpatients or inpatients in both primary care and secondary care settings.

### INTENDED AUDIENCE: SPECIALIST, GENERAL PRACTICE

The intended audience is primary care, medical, and dental practitioners as well as all specialists who manage patients with TN. Appendix A of the guidelines provides a plain-language summary for patients with TN to inform them of the current care recommendations and help them make informed choices.

### WHO WROTE THE GUIDELINES

The guidelines were written by a multidisciplinary team representing the following organizations:

- Association of British Academic Oral and Maxillofacial Surgeons
- British & Irish Society for Oral Medicine
- British Association for the Study of Headache
- British Association of Oral and Maxillofacial Surgeons
- Faculty of Pain Medicine of the Royal College of Anaesthetists
- Royal College of General Practitioners
- Society of British Neurological Surgeons
- The Faculty of General Dental Practice UK
- The Trigeminal Neuralgia Association UK, a patient support group.

The guidelines were prepared under the auspices of the Faculty of Dental Surgery of the Royal College of

**TABLE 2**  
**Classification of trigeminal neuralgia**

Type	Subtypes
Classic trigeminal neuralgia (neurovascular compression present)	<ul style="list-style-type: none"> <li>• Purely paroxysmal</li> <li>• Concomitant continuous pain</li> </ul>
Secondary trigeminal neuralgia (underlying pathology present)	<ul style="list-style-type: none"> <li>• Attributed to multiple sclerosis</li> <li>• Attributed to space-occupying lesion</li> <li>• Attributed to other causes</li> </ul>
Idiopathic trigeminal neuralgia (no underlying cause found)	<ul style="list-style-type: none"> <li>• Purely paroxysmal</li> <li>• Concomitant continuous pain</li> </ul>

Based on data from reference 4.

Surgeons England using their guideline-development process encompassing literature search, peer review, public engagement, and approval by the Faculty. The guidelines are available on the Royal College of Surgeons of England website (<https://www.rcseng.ac.uk/dental-faculties/fds/publications-guidelines/clinical-guidelines>), with the expectation that there will be timely review and updates.<sup>9</sup>

## ■ WHAT ARE THE MAIN RECOMMENDATIONS?

The guidelines recommend the diagnosis and phenotyping of TN by multidisciplinary teams, especially the early contribution from a qualified dental specialist to exclude local intraoral causes of pain.

### Approach to diagnosis

The diagnosis of TN is noted to be complex and should also include the measurement of patient-related outcomes such as the Brief Pain Inventory, Penn Facial Pain Scale-Revised, and the Hospital Anxiety and Depression Scale. In primary care, documenting the intensity and frequency of symptoms and the impact on quality of life using a rating of mild, moderate, or severe could provide useful data on treatment outcomes after the use of medications. Patients should be provided with written information such as the Brain and Spine Foundation Facial Pain Booklet (<https://www.brainandspine.org.uk/our-publications/booklets/face-pain>).

Use of magnetic resonance imaging (MRI) to investigate the underlying cause of TN is advocated and, if MRI is contraindicated, use brain computed tomography and angiography and neurophysiologic tests such as brainstem auditory evoked potentials. Our standard request is for thin-slice MRI of the brain and internal auditory meatus, and enhancement is not usually required. The images should be reported by experienced

neuroradiologists and reviewed with the treating clinicians. High-quality thin-slice MRI provides high sensitivity (88%; 95% confidence interval 80%–93%) and specificity (94%; 95% confidence interval 91%–96%) of potential nerve compression or distortion.<sup>10</sup>

### Drug therapy

The guidelines summarize the data for recommending pharmacotherapy with the best evidence for carbamazepine, but also includes the use of oxcarbazepine, lamotrigine, baclofen, gabapentin, and botulinum toxin. The recommendation for primary care physicians to start patients with TN on first-line medication before referral to a specialist is pragmatic and avoids treatment delays. First-line and second-line medications, dosage, and side effects are outlined in Table 3. Individuals of Han Chinese or Thai origin are at risk of Stevens-Johnson syndrome when using carbamazepine or oxcarbazepine.<sup>10</sup>

In practice, individualized pharmacotherapy plans are needed, balancing the benefits and side effects experienced by each patient. Because TN is a paroxysmal disorder, it is difficult to judge when to reduce and withdraw treatment. Many patients choose to continue medications even when in remission. Careful guidance and counseling may be needed to help patients de-escalate and withdraw from treatment. These drugs are generally safe, and some primary care physicians may have previously prescribed them for treating epilepsy or other neuropathic pain conditions. Rapid pain control should be the main aim, and there is no reason why primary care physicians cannot initiate second-line therapy depending on their knowledge and experience. Some patients with TN may be adequately managed outside specialist centers, though these guidelines provide a framework for multidisciplinary care.

**TABLE 3**  
**Evidence-based pharmacotherapy for trigeminal neuralgia**

Drug	Dosage regimen	Usual dose range	Common side effects
First-line therapy Carbamazepine <sup>a</sup>	100 mg twice daily; double after 3 days to 200 mg twice daily; increase by 100–200 mg twice daily every 3 days, then 200 mg 4 times daily	800–1,200 mg daily	Sedation, dizziness, blurred vision, nausea, unsteady lethargy, double vision, headache May cause hyponatremia, skin rashes, pancytopenia Risk of osteoporosis with long-term use May reduce oral contraception efficacy
Oxcarbazepine <sup>a</sup>	150 mg twice daily, double to 300 mg twice daily after 3 days; increase by 150–300 mg twice daily every 3 days, then 300 mg 4 times daily	1,200–1,800 mg daily	Drowsiness, dizziness, diplopia, confusion, nausea, abdominal pain, headache, depression, diarrhea High risk of hyponatremia Chronic use risks osteoporosis May reduce oral contraception efficacy
Second-line therapy Lamotrigine	Start 25 mg a day for 7 days, then 25 mg twice daily for 7 days, then 50 mg twice daily for another week; subsequent dose increments of 50 mg every 7 days, up to 10 weeks	200 mg twice daily	Blurred vision, agitation, aggression, unsteadiness, dizziness, nausea, dry mouth, insomnia, joint pains Risk of skin rashes and Stevens-Johnson syndrome with rapid dose escalation Probably safe for pregnant women at a dose of 100 mg twice daily
Baclofen	5 mg 3 times daily for 3 days, then increase to 10 mg 3 times daily for 3 days; increase by 10 mg 3 times daily every 3 days until maximum dose	40–80 mg daily	Anxiety, depression, agitation, unsteadiness, headache, sedation, tremor, skin rash, blurred vision, dry mouth, abdominal pain, withdrawal symptoms if stopped too rapidly
Gabapentin	100 mg 3 times daily day 1, 200 mg 3 times daily day 2 and 300 mg 3 times daily day 3. Increase by 1–300 mg 3 times daily every 3 days to maximum dose; start 100 mg 3 times daily or 300 mg at bedtime; can increase dose up to 300 to 600 mg 3 daily	900–3,600 mg daily	Amnesia, confusion, dizziness, vertigo, drowsiness, depression, nausea, blurred vision, peripheral edema, constipation, abdominal bloating, weight gain
Pregabalin	25 mg twice daily; increase by 25–50 mg twice daily every 3 days	600 mg daily	Confusion, drowsiness, constipation, blurred vision, dizziness, nausea, peripheral edema, increased appetite, weight gain

<sup>a</sup>Carbamazepine and oxcarbazepine are available in liquid form. Dosage ranges vary due to lack of high-quality trials.

### Management of acute relapses

Although few papers in the medical literature address managing acute TN relapses, the guidelines summarize the current literature. The experts advised that lidocaine can be administered in 3 different ways to manage TN, ie, nasal spray, local nerve block, and intravenous infusion. There is some evidence for the use of botulinum toxin, and also a recommendation

for a trial of subcutaneous sumatriptan to alleviate an acute TN attack. Intravenous lidocaine, phenytoin, and fosphenytoin are also suggested for inpatient treatment (Table 4).<sup>9,11</sup>

### Neurosurgical management

The guidelines recommend involvement of neurosurgeons who are experienced in managing TN

**TABLE 4**  
**Treatments for acute episodes of trigeminal neuralgia based on a systematic review**

Provider	Treatment
All clinicians (dentist, general practitioner, specialist)	Lidocaine <ul style="list-style-type: none"> <li>• 10-mg nasal spray, 2 sprays into nostril on affected side; can be used intraorally, but spit out after 1 minute</li> <li>• 5% ointment to trigger area</li> <li>• 2% 1:80,000 adrenaline local infiltration to nerve block trigger area</li> </ul>
General practitioner, specialist	Sumatriptan 6 mg subcutaneous injection, followed by oral sumatriptan 50 mg twice daily for 1 week
Specialist only	Botulinum toxin type A injection, 3 mg in 1 mL
Specialist, inpatient basis	Intravenous Infusions <ul style="list-style-type: none"> <li>• Lidocaine 1.5 mg/kg over 1 hour, up to 5 mg/kg in a randomized clinical trial</li> <li>• Phenytoin 10 mg/kg</li> <li>• Fosphenytoin 15 mg/kg</li> </ul>

Based on data from references 9 and 11.

when pharmacotherapy is ineffective or causes intrusive side effects. To better support informed decision-making, a neurosurgical consult is best done when a patient's pain is in remission. Patients should be aware that invasive procedures are only expected to reduce brief lancinating pain but have unpredictable effects on the interparoxysmal pain, or can even make it worse. The guidelines state that 25% to 40% of patients with TN choose surgery within 2 years of symptom onset.<sup>9</sup>

Surgical treatments for TN include posterior fossa microvascular decompression (MVD) and neuroablative therapies such as stereotactic radiosurgery, radiofrequency thermocoagulation, balloon compression, glycerol rhizolysis, and internal neurolysis. For patients with classic TN (ie, arterial contact on the trigeminal nerve), MVD has the best surgical results for medication-free, long-term pain relief, with 62% to 89% of 5,149 patients reportedly pain-free at follow-up of 3 to 10.9 years.<sup>9,10</sup>

In posterior fossa MVD, any vessels or arachnoid tissue compressing the trigeminal nerve in the root entry zone is moved away. If no compressions are found, internal neurolysis may be performed to separate (or "comb") the fascicles of the trigeminal nerve. Patients need to be medically fit to undergo MVD, and there is a 0.3% mortality rate and a risk of complications such as cerebrospinal fluid leak, infection, and stroke, but a lower risk of sensory changes.<sup>10</sup>

Neuroablative therapies (ie, stereotactic radiosurgery, radiofrequency rhizotomy, balloon compression, glycerol rhizolysis) involve controlled damage to the

trigeminal nerve and have a lower mortality risk but are more likely than MVD to increase the chance of altered sensation including the loss of corneal reflex.<sup>10</sup> Neuroablative treatments have varying levels of success, with an average of 2 to 4 years.<sup>10</sup>

Stereotactic radiosurgery, compared with all other procedures, may have the lowest risk of short-term complications, but it has an increased probability of causing facial numbness and dysesthesia,<sup>10</sup> as well as a long postprocedure duration before expected pain relief or complications. Glycerol rhizolysis (denervation using a chemical) offers the lowest chance for both,<sup>10</sup> while radiofrequency thermocoagulation (denervation using heat) is reported to have a higher chance of success but also a greater risk of sensory loss than with all other procedures.<sup>10</sup>

### Efficacy of surgical procedures

The guidelines include the efficacy of surgical procedures for TN as reported by Bendtsen et al<sup>10</sup> but it is important to emphasize that the results are from single-intervention, nonrandomized studies among select patients in specialized centers.<sup>10</sup> Individual patients may not achieve the same level or duration of pain relief. Patients with interparoxysmal pain need to be cautioned before choosing neuroablative treatments such as glycerol rhizolysis, balloon compression, and radiofrequency rhizotomy. Pain between lancinating exacerbations may indicate existing nerve damage, and further iatrogenic destruction may lead to anesthesia dolorosa (a feeling of pain in an area that is completely numb to the touch).



### Timing and selection of surgical treatment

The guidelines are not prescriptive about when or which surgical operation should be offered, and any such decision must be made jointly between well-informed patients and their clinicians from multiple disciplines. Neuroablative procedures for TN may require an overnight hospital stay and can be performed in patients who have other comorbidities. Surgical complications should be balanced against the side effects of long-term pharmacotherapy.

### Referral for pain management

The guidelines recommend patient referral to pain management programs with access to clinical psychologists and physiotherapists because the pain severity, disruption of daily life, and associated psychological impact of TN can adversely affect a patient's mental health. The fear of a relapse cannot be underestimated. Pain psychologists and pain management nurse specialists can help patients alleviate some of these fears. Patients should be encouraged to join a trigeminal neuralgia support group such as Trigeminal Neuralgia Association UK ([www.tna.org.uk](http://www.tna.org.uk)), which has a multidisciplinary clinician panel offering advice.

### Need for long-term follow-up and outcomes evaluation

A key recommendation of the guidelines is to urge clinicians managing patients with TN to follow up and gather long-term patient outcomes data to evaluate treatment efficacy and results. TN is a relapsing-remitting condition, and initial pain improvement may not always be due to treatment. This is true especially for invasive procedures, where initial good response may be followed by treatment complications and relapses.

### ■ WHAT IS DIFFERENT FROM PREVIOUS GUIDELINES?

Previous guidelines have been developed solely by experts in the field, whereas for the UK guidelines, all potential caregivers were consulted. A patient representative from the Trigeminal Neuralgia Support Group was included, as well as representatives from the Brain and Spine Foundation, a charity specializing in producing booklets for the general public on neurologic conditions. The new guidelines also recommend aids such as the Ottawa Personal Decision Guide (<https://decisionaid.ohri.ca/decguide.html>) to help patients make informed choices.

Pharmacotherapy and surgical treatments are recommended according to the best available evidence, similarly to other published guidelines.<sup>10</sup> The UK guidelines include the use of botulinum toxin injections and emphasize early discussion of neurosurgical

options to inform patients of the full array of possible treatments. There is also strong emphasis on the need for TN care to be delivered by a multidisciplinary team.

### ■ WHAT IS THE EXPECTED CLINICAL IMPACT?

The guidelines encourage primary care physicians to promptly diagnosis TN and initiate pharmacotherapy after ruling out dental causes of facial pain. All patients should be evaluated to rule out secondary causes of facial pain, even if the pain is in remission. If relapses occur, patient referral to a multidisciplinary specialist team is advised to inform patients about the most appropriate treatment for their condition.

The coalescence of interested clinicians can prompt the collection and evaluation of long-term outcomes data to improve TN care. One example of this was an audit of 129 patients with TN evaluating treatment efficacy by choosing outcome measures meaningful to patients.<sup>12</sup> Using the Patient Global Impression of Change score, 79% (102 of 129) of patients reported their condition was better since starting treatment in a specialist center. Notably, even in this study in a multidisciplinary specialist center, 20% of patients did not experience improvement in their condition,<sup>12</sup> a finding that should prompt further research to bridge this management gap.

The data also revealed that the long period of inadequate pain control between symptom onset and specialist referral contributes to patients' perception of treatment failure. A review of outcomes over an 11-year period in 285 patients without prior surgery for TN reported that 54% (153 of 285) had a surgical procedure and 46% (132 of 285) were medically managed.<sup>13</sup> Of the 334 patients included in the study, 93 (28%) were pain-free and off medication. The largest group that was pain-free and off medication were those who had undergone first-time surgery (84 patients, or 55%). Of the 49 patients undergoing surgery for a second time, only 11 (22%) were pain-free and off medication, and the 132 who remained on medication alone (18 patients, or 16%) were pain-free and off medication due to remissions.<sup>13</sup>

### ■ DO OTHER SOCIETIES AGREE OR DISAGREE?

These guidelines are based on other documents first published by the American Academy of Neurology and the European Federation of Neurological Sciences in 2008,<sup>14</sup> which was further updated by the European Academy of Neurology in 2019.<sup>10</sup> They are also in line with the care pathways published by a Danish group in 2015<sup>15</sup> and a UK group in 2020.<sup>12,16</sup> All agree on the need for more research.

## ■ HOW WILL THIS CHANGE DAILY PRACTICE?

These guidelines help patients to choose and clinicians to develop the optimal care pathway using available evidence. If the appropriate expertise is available, some patients with TN should be managed in a multidisciplinary primary care setting. When such services are not available or adequate, access to specialist management may be delayed and fragmented.<sup>17</sup> Streamlining this process should allow faster access to the most appropriate services for individual patients. There is also the recommendation for all clinicians managing this condition to collect long-term outcomes data and disseminate best practices to improve the quality of care.

## ■ WHEN WOULD THE GUIDELINES NOT APPLY?

The guidelines depend on accurate phenotyping of TN. As there are no specific diagnostic tests, clinical assessment is crucial and must be undertaken by experienced clinicians. Many conditions can mimic TN, especially painful trigeminal neuropathy. The pathophysiology and management of trigeminal neuropathy is different, though it may coexist with TN, especially after failed surgery.

Another condition that often coexists with TN is temporomandibular disorder. This is a nociceptive pain condition but may have elements of sharp, shooting pain triggered by eating, talking, or brushing teeth.<sup>18</sup> It

is important to correctly identify the causes triggering pain even in patients known to have TN.

TN may be on the same spectrum of trigeminal autonomic cephalalgias, a group of disorders in which autonomic features such as conjunctival redness, tearing, meiosis, eyelid-dropping, and nasal congestion are noted. These include short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with autonomic features (SUNA).<sup>19</sup> In some patients, one condition may evolve into another over time. The drug treatment of these conditions may overlap, although the role for surgery is less well defined for trigeminal autonomic cephalalgias, and occipital nerve blocks that may alleviate SUNCT or SUNA do not work for TN.<sup>20</sup>

In the UK, many patients do not reach specialist centers for 4 to 10 years after symptom onset, and this increases the risk of developing anxiety, depression, and sleep disorder.<sup>5</sup> These psychologically traumatized patients with TN have increased suicide risk, and it is important to recognize this so that they are offered additional support not previously mentioned in these guidelines.<sup>21,22</sup>

## ■ DISCLOSURES

Dr. Bahra has disclosed consulting for Pfizer. Dr. Zakrzewska has disclosed consulting for Biogen and Noema Pharma. The other authors report no relevant financial relationships, which in the context of their contributions, could be perceived as a potential conflict of interest.

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