Work-Related Neurogenic Thoracic Outlet Syndrome: Diagnosis and Treatment*

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*This guideline does not apply to severe or acute traumatic injury of the upper extremities, nor to vascular categories of TOS.
**I. GUIDELINE SUMMARY**

<table>
<thead>
<tr>
<th>SUBJECTIVE (Symptoms)</th>
<th>OBJECTIVE (Signs)</th>
<th>DIAGNOSTIC</th>
<th>CONSERVATIVE TREATMENT</th>
<th>SURGICAL TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, paresthesias, or weakness affecting the upper extremity (most commonly affecting the ring or small finger)</td>
<td>Tenderness</td>
<td>Electrodiagnostic studies (EDS) are required to objectively confirm the diagnosis of nTOS. EDS criteria are as follows:</td>
<td>Modify job activities that exacerbate symptoms AND/OR</td>
<td>Surgical treatment should only be considered if:</td>
</tr>
<tr>
<td>Weakness</td>
<td>Scalene</td>
<td>1. Absent or reduced amplitude (&lt; 12 uV) of the ulnar SNAP OR Absent or reduced amplitude (&lt; 10 uV) of the medial anterobrachial cutaneous nerve (MABC) SNAP with normal amplitude of the MABC SNAP in the contralateral (unaffected) extremity AND 2. Absent or reduced amplitude (&lt; 5 mV) of the median CMAP OR Absent or prolonged minimum latency (&gt;33 msec) of the ulnar F-wave (with or without abnormalities of the median F-wave), and with normal F-waves in the contralateral (unaffected) upper extremity</td>
<td>Physical therapy with strengthening and stretching, postural exercises AND/OR</td>
<td>1. The patient has met the diagnostic criteria under Section III AND 2. The condition interferes with work or activities of daily living AND 3. The condition does not improve despite conservative treatment</td>
</tr>
<tr>
<td>Loss of finger dexterity</td>
<td>Trapezius</td>
<td>Needle electromyography (EMG) showing denervation (e.g. fibrillation potentials, positive sharp waves) in at least one muscle supplied by each of two different nerves from the lower trunk of the brachial plexus, with normal EMG of the cervical paraspinal muscles and at least one muscle supplied by a nerve from the middle or upper trunk of the brachial plexus</td>
<td>Anti-inflammatory drug therapy</td>
<td>Without confirmation of brachial plexus compression by both objective clinical findings and abnormal EDS, surgery will not be authorized.</td>
</tr>
<tr>
<td>Atrophy</td>
<td>Anterior chest wall</td>
<td>3. Normal amplitude (≥ 15uV) of the median nerve SNAP AND 4. Normal conduction velocity (≥ 50m/s) of the ulnar motor nerve across the elbow</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
II. INTRODUCTION

This guideline is to be used by physicians, claim managers, occupational nurses, and utilization review staff. The emphasis is on accurate diagnosis and treatment that is curative or rehabilitative (see WAC 296-20-01002 for definitions). An electrodiagnostic worksheet and guideline summary are appended to the end of this document.

This guideline was developed in 2010 by the Washington State's Industrial Insurance Medical Advisory Committee (IIMAC) and its subcommittee on Upper Extremity Entrapment Neuropathies. The subcommittee presented its work to the full IIMAC, and the IIMAC voted with full consensus advising the Washington State Department of Labor & Industries to adopt the guideline. This guideline was based on the weight of the best available clinical and scientific evidence from a systematic review of the literature* and a consensus of expert opinion. One of the Committee's primary goals is to provide standards that ensure high quality of care for injured workers in Washington State.

Thoracic Outlet Syndrome (TOS) is characterized by pain, paresthesias, and weakness in the upper extremity, which may be exacerbated by elevation of the arms or by exaggerated movements of the head and neck. There are three categories of thoracic outlet syndrome: arterial, venous and neurogenic. Arterial and venous thoracic outlet syndromes involve obstruction of the subclavian artery or vein, respectively, as they pass through the thoracic outlet. These vascular categories of TOS should include obvious clinical signs of vascular insufficiency: a cold, pale extremity in the case of arterial TOS, or a swollen, cyanotic extremity in the case of venous TOS. There is a separate surgical guideline for vascular TOS. This guideline focuses solely on non-acute, neurogenic TOS (nTOS).

Work-related nTOS occurs due to compression of the brachial plexus, predominantly affecting its lower trunk, at one of three potential sites. Compression can occur between the anterior and middle scalene muscles (or sometimes through the anterior scalene muscle); beneath the clavicle in the costoclavicular space; or beneath the tendon of the pectoralis minor.¹

The medical literature describes two categories of nTOS: “true” nTOS and “disputed” nTOS. A diagnosis of true nTOS requires electrodiagnostic (EDS) abnormalities showing evidence of brachial plexus injury (see Section III.B.). Disputed nTOS describes cases of nTOS for which EDS abnormalities have not been demonstrated. To avoid confusion that has arisen over these categories, this guideline does not use such terms. Rather, it provides guidance regarding treatment for cases of nTOS that have been confirmed by EDS abnormalities compared with those cases for which the provisional diagnosis has not been confirmed by such studies.

In general, work-relatedness and appropriate symptoms and objective signs must be present for Labor and Industries to accept nTOS on a claim. Electrodiagnostic studies (EDS), including nerve conduction velocity studies (NCVs) and needle electromyography (EMG), should be scheduled immediately to confirm the clinical diagnosis. If time loss extends beyond two weeks or if surgery is requested, completion of EDS is required and does not need prior authorization.

¹ Evidence was classified using criteria defined by the American Academy of Neurology (see references)
III. ESTABLISHING WORK-RELATEDNESS

Work-related activities may cause or contribute to the development of nTOS. Because simply identifying an association with workplace activities is not, in itself, adequate evidence of a causal relationship, establishing work-relatedness requires all of the following:

1. Exposure: Workplace activities that contribute to or cause nTOS, and
2. Outcome: A diagnosis of nTOS that meets the diagnostic criteria under Section III, and
3. Relationship: Generally accepted scientific evidence, which establishes on a more probable than not basis (greater than 50%) that the workplace activities (exposure) in an individual case contributed to the development or worsening of the condition (outcome).

When the Department receives notification of an occupational disease, the Occupational Disease & Employment History form is mailed to the worker, employer or attending provider. The form should be completed and returned to the insurer as soon as possible. If the worker’s attending provider completes the form, provides a detailed history in the chart note, and gives an opinion on causality, he or she may be paid for this (use billing code 1055M). Additional billing information is available in the Attending Doctor’s Handbook.

Symptoms of nTOS may be exacerbated by certain work-related activities, usually involving elevation or sustained use of the arms. Such activities may include but are not limited to the following:

<table>
<thead>
<tr>
<th>Lifting overhead</th>
<th>Holding tools or objects above shoulder level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaching overhead</td>
<td>Carrying heavy weights</td>
</tr>
</tbody>
</table>

Several occupations have been associated with nTOS. This is not an exhaustive list and is meant only as a guide in the consideration of work-relatedness:

<table>
<thead>
<tr>
<th>Dry wall hanger or plasterer</th>
<th>Assembly line inspector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welder</td>
<td>Shelf stocker</td>
</tr>
<tr>
<td>Beautician</td>
<td>Dental hygienist</td>
</tr>
</tbody>
</table>

IV. MAKING THE DIAGNOSIS

A. SYMPTOMS AND SIGNS

A case definition of confirmed nTOS includes appropriate symptoms, objective physical findings ("signs"), and abnormal EDS. A provisional diagnosis of nTOS may be made based upon appropriate symptoms and objective signs, but confirmation of the diagnosis requires abnormal EDS.

Classic symptoms of nTOS include pain, paresthesias, or weakness in the upper extremity. Paresthesias most commonly affect the ring and small fingers. Symptom severity tends to increase after certain activities and worsens at the end of the day or during sleep.

Signs on examination may include tenderness to palpation over the brachial plexus, the scalene muscles, the trapezius muscles, or the anterior chest wall. Although tenderness may be a useful objective finding, it cannot support the diagnosis of nTOS alone. Advanced cases of nTOS are characterized by objective signs of weakness of the hand, loss of dexterity of the fingers, and atrophy of the affected muscles.

Provocative tests have been described that may help corroborate the diagnosis of nTOS. These tests are based on creating maximal tension on the anatomical sites of constriction. Studies have found a high false-positive rate for these tests in healthy subjects as well as carpal tunnel syndrome patients. Although they are described for
completeness, the sensitivity and specificity of these tests for nTOS have not been established, and these tests cannot replace confirmatory EDS testing (see Section III.B).

Provocative tests include:
- The elevated arm stress test (EAST or Roos test)- the patient places the affected arm in full abduction and external rotation and then opens and closes the hands slowly for 3 minutes. This test constricts the costoclavicular space. It is considered abnormal if typical symptoms are elicited and the patient cannot sustain this activity for the full 3 minutes.
- The Adson test- the patient extends the neck and rotates the head toward the involved extremity, which is held extended at the side. This test constricts the interscalene triangle. It is considered abnormal if a change in the radial pulse is detected when the patient inhales deeply and holds their breath
- The Wright test- the patient sits or stands with the arm in full abduction and external rotation. This test constricts the costoclavicular space. It is considered abnormal if typical symptoms are elicited and a change in pulse is detected.
- The costoclavicular test- the examiner depresses the patient’s shoulder. This test constricts the costoclavicular space and creates tension across the pectoralis minor. It is considered abnormal if typical symptoms are elicited.

Every effort should be made to objectively confirm the diagnosis of nTOS before considering surgery. A differential diagnosis for nTOS includes musculoskeletal disease (e.g. arthritis, tendinitis) of the cervical spine, shoulder girdle or arm, cervical radiculopathy or upper extremity nerve entrapment, idiopathic inflammation of the brachial plexus (aka Parsonage-Turner syndrome), and brachial plexus compression due to an infiltrative process or space-occupying mass (e.g. Pancoast tumor of the lung apex).

B. ELECTRODIAGNOSTIC STUDIES (EDS)

EDS abnormalities are required to objectively confirm the diagnosis of nTOS. Given the uncertainties in diagnostic assessment of nTOS, EDS should be obtained as soon as the diagnosis is considered. EDS may help gauge the severity of injury. Importantly, EDS can help exclude conditions that may mimic nTOS, such as ulnar nerve entrapment or cervical radiculopathy. EDS evidence that confirms a diagnosis of nTOS requires:

1. Absent or reduced amplitude (< 12 uV) of the ulnar antidromic sensory nerve action potential (SNAP) OR
   Absent or reduced amplitude (< 10 uV) of the medial antibrachial cutaneous nerve (MABC) antidromic SNAP, with normal amplitude of the MABC SNAP in the contralateral (unaffected) extremity AND
2. Absent or reduced amplitude (<5 mV) of the median nerve compound motor action potential (CMAP) OR
   Absent or prolonged minimum latency (>33 msec) of the ulnar F-wave (with or without abnormalities of the median F-wave), and with normal F-waves in the contralateral (unaffected) upper extremity OR
   Needle electromyography (EMG) showing denervation (e.g. fibrillation potentials, positive sharp waves) in at least one muscle supplied by each of two different nerves from the lower trunk of the brachial plexus, with normal EMG of the cervical paraspinal muscles and at least one muscle supplied by a nerve from the middle or upper trunk of the brachial plexus.

To exclude the presence of other focal neuropathies or polyneuropathy as a cause for the abnormalities described above, the following must also be shown:

3. Normal amplitude (≥ 15 uV) of the median nerve antidromic SNAP.
   AND
4. Normal conduction velocity (≥ 50 m/s) of the ulnar motor nerve across the elbow.
C. OTHER DIAGNOSTIC TESTS

Arterial or venous vascular studies may be helpful in the diagnosis of suspected arterial or venous TOS. However, these tests have poor specificity for nTOS, and there is no substantial evidence that vascular studies can reliably confirm the diagnosis of nTOS. Therefore, vascular studies conducted as a diagnostic tool for nTOS will not be authorized.

Some have suggested that magnetic resonance imaging (MRI) neurography may be helpful in the diagnosis of nTOS. However, these services will not be authorized for this condition because the clinical utility of these tests has not yet been proven. While the Committee recognizes that these tests may be useful in unusual circumstances where EDS results are normal but there are appropriate clinical symptoms, the Committee believes that at this time the use of these tests is investigational and should be used only in a research setting.

Anterior scalene muscle (ASM) blocks have been used in the evaluation of suspected nTOS. However, this test has poor specificity for nTOS, and there is no substantial evidence that ASM can reliably confirm the diagnosis of nTOS. Therefore, ASM blocks conducted as a diagnostic tool for nTOS will not be authorized.

X-rays of the chest may be useful to evaluate the possibility of an infiltrative process or space-occupying mass (e.g. Pancoast tumor of the lung apex) compressing the brachial plexus.

V. TREATMENT

Non-surgical therapy may be considered for cases in which a provisional diagnosis of nTOS has been made. Surgical treatment should be provided only for cases in which the diagnosis of nTOS has been confirmed by abnormal EDS. Under these circumstances, the potential benefits of brachial plexus decompression may outweigh the risks of surgery.

A. CONSERVATIVE TREATMENT

Conservative treatment for nTOS has been described in narrative reviews, case reports, and retrospective case series. No randomized controlled trials have been conducted to measure the efficacy of conservative treatments for nTOS. No specific method of conservative treatment has been proven to be most effective due to a lack of comparative studies. However, an observational study (n=50), showed that strengthening and stretching exercises reduced pain among 80% of patients after 3 months and among 94% of patients after 6 months, and a 2007 systematic review of the available literature concluded that conservative treatment appears to be effective in reducing symptoms, improving function, and facilitating return to work. Examples of conservative treatment include modification of activities that exacerbate symptoms, education, postural exercises, physical therapy, and anti-inflammatory drug therapy.

Because surgical outcomes are poor in many situations, conservative interventions, such as stretching and strengthening exercises, should be considered first. If the initial response to conservative treatment is incomplete, modifying or changing the approach should be considered. If there is no response to conservative treatment within six weeks, or if time loss extends longer than 2 weeks, specialist consultation should be obtained.

Although Botulinum toxin (Botox) injections of the scalene muscles have been reported to relieve nTOS symptoms, preliminary results of a randomized trial showed no clear clinical improvement related to this treatment. In addition, it appears that there are substantial technical challenges and potentially severe adverse effects from this procedure. Therefore, Botox injections conducted as a diagnostic tool or for treatment of nTOS will not be authorized.

When feasible, job modifications that reduce the intensity of manual tasks may prevent progression and promote recovery from nTOS. If symptoms persist despite appropriate treatment, permanent job modifications may still
allow the patient to remain at work. Patients do not usually need time off from work activities prior to surgery, unless they present with objective weakness or sensory loss in the upper extremity that limits work activities or poses a substantial safety risk.

B. SURGICAL TREATMENT

Surgical treatment for nTOS has been described in narrative reviews, case reports, and retrospective case series. Surgery should include exploration of the brachial plexus throughout its course in the thoracic outlet in order to decompress it by resecting any compressive and/or constrictive structures. These may include any of the three sites of compression mentioned earlier. No specific method of surgical treatment has been proven to be most effective.

Surgical treatment should only be considered if:
1. The patient has met the diagnostic criteria under Section III, and
2. The condition interferes with work or activities of daily living, and
3. The condition does not improve despite conservative treatment.

Without confirmation of nTOS by both objective clinical findings and abnormal EDS, surgery will not be authorized.

VI. RETURN TO WORK (RTW)

A. EARLY ASSESSMENT

Timeliness of the diagnosis can be a critical factor influencing RTW. Among workers with upper extremity disorders, 7% of workers account for 75% of the long-term disability. A large prospective study in the Washington State workers’ compensation system identified several important predictors of long-term disability: low expectations of return to work (RTW), no offer of a job accommodation, and high physical demands on the job. Identifying and attending to these risk factors when patients have not returned to work within 2-3 weeks of the initial clinical presentation may improve their chances of RTW.

Washington State workers diagnosed accurately and early were far more likely to RTW than workers whose conditions were diagnosed weeks or months later. Early coordination of care with improved timeliness and effective communication with the workplace is also likely to help prevent long-term disability.

A recent quality improvement project in Washington State has demonstrated that delivering medical care according to occupational health best practices similar to those listed in Table 1 can substantially prevent long-term disability. Findings can be viewed at: Centers of Occupational Health & Education.
Table 2. Occupational Health Quality Indicators for Neurogenic Thoracic Outlet Syndrome (nTOS)

<table>
<thead>
<tr>
<th>Clinical care action</th>
<th>Time-frame*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Identify physical stressors from both work and non-work activities;</td>
<td>1st health care visit</td>
</tr>
<tr>
<td>2. Screen for presence of nTOS</td>
<td></td>
</tr>
<tr>
<td>3. Determine work-relatedness</td>
<td></td>
</tr>
<tr>
<td>4. Recommend ergonomic improvements or other appropriate job modifications</td>
<td></td>
</tr>
<tr>
<td>Communicate with employer regarding return to work (RTW) using</td>
<td>Each visit while work restrictions exist</td>
</tr>
<tr>
<td>1. Activity Prescription Form (or comparable RTW form) and/or</td>
<td></td>
</tr>
<tr>
<td>2. Phone call to employer</td>
<td></td>
</tr>
<tr>
<td>1. Assess impediments for RTW</td>
<td>If &gt; 2 weeks of time-loss occurs or if there is no clinical improvement within 6 weeks of conservative treatment</td>
</tr>
<tr>
<td>2. Request specialist consultation</td>
<td></td>
</tr>
<tr>
<td>Specialist consultation</td>
<td>Performed ASAP, within 3 weeks of request</td>
</tr>
<tr>
<td>Electrodiagnostic studies</td>
<td>If the diagnosis of nTOS is being considered, schedule studies immediately.</td>
</tr>
<tr>
<td></td>
<td>These tests are required if time-loss extends beyond 2 weeks, or if surgery is requested.</td>
</tr>
<tr>
<td>Surgical decompression</td>
<td>Performed ASAP, within 4-6 weeks of determining need for surgery</td>
</tr>
</tbody>
</table>

*"Time-frame" is anchored in time from 1st provider visit related to nTOS symptoms.

B. RETURNING TO WORK FOLLOWING SURGERY

How soon a patient can return to work depends on the type of surgery performed and when rehabilitation begins. Most patients can return to light duty work within 4-6 weeks and regular duty within 10-12 weeks of surgery.
VII. ELECTRODIAGNOSTIC WORKSHEET

Claim Number: __________________________

Claimant Name: __________________________

PURPOSE AND INSTRUCTIONS
The purpose of this worksheet is to help interpret electrodiagnostic studies (EDS) done for an injured worker. The worksheet should be used only when the main purpose of the study is to evaluate neurogenic thoracic outlet syndrome (nTOS). It should accompany but not replace the detailed report normally submitted to the insurer.

Electrodiagnostic Worksheet for Work-Related Neurogenic Thoracic Outlet Syndrome (nTOS)

<table>
<thead>
<tr>
<th>Electrodiagnostic criteria for Work-Related nTOS are met if all four boxes are “Yes”.</th>
<th>Check the correct box</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ulnar SNAP* &lt; 12 uV or absent?</td>
<td>Yes</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Medial antebrachial cutaneous nerve (MABC) SNAP* amplitude &lt; 10 uV or absent, with normal amplitude of the MABC SNAP* in the contralateral (unaffected) extremity?</td>
<td></td>
</tr>
<tr>
<td>AND</td>
<td></td>
</tr>
<tr>
<td>2. Median nerve CMAP amplitude &lt; 5 mV or absent?</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Ulnar F-wave (with or without abnormalities of the median F-wave) minimum latency &gt; 33 msec or absent, with normal F-waves in the contralateral (unaffected) upper extremity?</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Needle electromyography (EMG) showing denervation (e.g. fibrillation potentials, positive sharp waves) in at least one muscle supplied by each of two different nerves from the lower trunk of the brachial plexus, with normal EMG of the cervical paraspinal muscles and at least one muscle supplied by a nerve from the middle or upper trunk of the brachial plexus?</td>
<td></td>
</tr>
<tr>
<td>AND</td>
<td></td>
</tr>
<tr>
<td>3. Normal amplitude (≥ 15uV) of the median nerve SNAP*?</td>
<td></td>
</tr>
<tr>
<td>AND</td>
<td></td>
</tr>
<tr>
<td>4. Normal conduction velocity (≥ 50 m/s) of the ulnar motor nerve across the elbow?</td>
<td></td>
</tr>
</tbody>
</table>

*Antidromic

Additional Comments:

________________________________________________________

________________________________________________________

Signed_________________________Date________________________

Effective Date October 1, 2010; hyperlink and formatting update September 2016

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References
Evidence was classified using criteria defined by the American Academy of Neurology†


### Definitions for Classification of Evidence

<table>
<thead>
<tr>
<th>Rating of Therapeutic Article</th>
<th>Rating of Diagnostic Article</th>
<th>Rating of Prognostic Article</th>
<th>Rating of Screening Article</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I:</strong> Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: a) primary outcome(s) clearly defined b) exclusion/inclusion criteria clearly defined c) adequate accounting for drop-outs and cross-overs with numbers sufficiently low to have minimal potential for bias d) relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.</td>
<td><strong>Class I:</strong> Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a reference (gold) standard for case definition, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. All patients undergoing the diagnostic test have the presence or absence of the disease determined.</td>
<td><strong>Class I:</strong> Evidence provided by a prospective study of a broad spectrum of persons who may be at risk for developing the outcome (e.g. target disease, work status). The study measures the predictive ability using an independent gold standard for case definition. The predictor is measured in an evaluation that is masked to clinical presentation and, the outcome is measured in an evaluation that is masked to the presence of the predictor. All patients have the predictor and outcome variables measured.</td>
<td><strong>Class I:</strong> A statistical, population based sample of patients studied at a uniform point in time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients’ clinical presentations.</td>
</tr>
<tr>
<td><strong>Class II:</strong> Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a RCT in a representative population that lacks one criteria a-d.</td>
<td><strong>Class II:</strong> Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well designed retrospective study of a broad spectrum of persons with an established condition (by &quot;gold standard&quot;) compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.</td>
<td><strong>Class II:</strong> Evidence provided by a retrospective study of a narrow spectrum of persons at risk for having the condition, or by a retrospective study of a broad spectrum of persons with the condition compared to a broad spectrum of controls. The study measures the prognostic accuracy of the risk factor using an acceptable independent gold standard for case definition. The risk factor is measured in an evaluation that is masked to the outcome.</td>
<td><strong>Class II:</strong> A statistical, non-referral clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients’ clinical presentation.</td>
</tr>
<tr>
<td><strong>Class III:</strong> All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement,**</td>
<td><strong>Class III:</strong> Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where the reference standard, if not objective, is applied by someone other than the person that performed the test.</td>
<td><strong>Class III:</strong> Evidence provided by a retrospective study where either the persons with the condition or the controls are of a narrow spectrum. The study measures the predictive ability using an acceptable independent gold standard for case definition. The outcome, if not objective, is determined by someone other than the person who measured the predictor.</td>
<td><strong>Class III:</strong> A sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation by someone other than the treating physician.</td>
</tr>
<tr>
<td><strong>Class IV:</strong> Evidence from uncontrolled studies, case series, case reports, or expert opinion.</td>
<td><strong>Class IV:</strong> Any design where test is not applied in an independent evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).</td>
<td><strong>Class IV:</strong> Any design where the predictor is not applied in an independent evaluation OR evidence provided by expert opinion or case series without controls.</td>
<td><strong>Class IV:</strong> Expert opinion, case reports or any study not meeting criteria for class I to III.</td>
</tr>
</tbody>
</table>
# Acknowledgements

Acknowledgement and gratitude go to all subcommittee members, clinical experts, and consultants who contributed to this important guideline:

<table>
<thead>
<tr>
<th>IIMAC Committee Members</th>
<th>Subcommittee Clinical Experts</th>
<th>Consultants:</th>
</tr>
</thead>
<tbody>
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<td>Robert G.R. Lang MD</td>
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</tr>
</tbody>
</table>

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